JUHA KIISKI

Surgical, Oncological and Reconstructive Outcomes After Complex Oncological Pelvic Resections

The Development of an Algorithm Based on a Multidisciplinary Approach

JUHA KIISKI

Surgical, Oncological and Reconstructive Outcomes After Complex Oncological Pelvic Resections

The Development of an Algorithm Based on a Multidisciplinary Approach

ACADEMIC DISSERTATION
To be presented, with the permission of
the Faculty of Medicine and Health Technology
of Tampere University,
for public discussion in the auditorium F115
of the Arvo building, Arvo Ylpön katu 34, Tampere,
on 18 September 2020, at 12 o'clock.

ACADEMIC DISSERTATION
Tampere University, Faculty of Medicine and Health Technology
Finland

The originality of this thesis has been checked using the Turnitin OriginalityCheck service.

Cover design: Roihu Inc.

To my Family

ABSTRACT

Pelvic tumours can originate from the musculoskeletal system (sarcoma) or from epithelial tissue (carcinoma) of the visceral organs or skin. Large and advanced pelvic tumours are extremely rare and they pose a significant surgical and oncological challenge due to their complex anatomical location. The majority of the malignant pelvic tumours can be treated with limb salvage pelvic resection or pelvic exenteration (PE), but most advanced or recurrent tumours will still require pelvic amputation (hindquarter amputation or hip disarticulation). The aim of this thesis was to evaluate the surgical, oncological and reconstructive results after surgical treatment of malignant pelvic tumours resulting in complex pelvic defects. The secondary aim was to create algorithms for the management of these rare tumours.

Study I comprised the retrospective evaluation of patients (n=21) undergoing sacrectomy for primary bone malignancy. The patients were treated with the following algorithm: Patients (n=5) with sacrectomy distal to the S3/4 level with a small soft-tissue defect did not require any soft-tissue reconstruction. The majority of the patients (n=11) with a moderate to large soft-tissue defect after tumour resection were immediately reconstructed with local gluteal flaps. The largest and most complex defects (n=5) were reconstructed in two stages: Tumour resection and spinopelvic fixation were performed in the first operation and the wound temporarily closed with a negative-pressure wound therapy device. Reconstruction was carried out at 7 days after a short recovery and rehabilitation period. There were no differences in complications between the immediate reconstruction or delayed reconstruction groups.

Study II was a retrospective chart review comprising 38 patients who underwent PE, with 26 total pelvic exenterations (TPE), 11 posterior pelvic exenterations (PPE) and 2 anterior pelvic exenterations (APE). One patient first underwent APE and later required a PPE for local recurrence. The 5-year overall survival (OS) was 48%. Lymph node metastasis (HR 3.1, p=0.027) and positive surgical margins (HR 3.9, p=0.009) were poor prognostic factors for OS. 71% of the patients experienced at least one

complication during the follow-up. 69% of the patients had a flap reconstruction and all but one flaps were transverse myocutaneous gracilis (TMG) flaps. The following algorithm for pelvic floor and vaginal reconstruction was used: Bilateral TMG was indicated for patients who underwent TPE and requested vaginal reconstruction and for PPE patients whose vaginal resection was not only limited to the posterior wall of the vagina but extended to the lateral sidewall(s) as well. Unilateral TMG was sufficient for the remainder of the cases.

Study III consisted of the evaluation of a retrospective cohort of patients (n=12) who underwent pelvic amputation in three tertiary sarcoma units and required free flap reconstruction. All patients were reconstructed with a free fillet flap harvested from the amputated extremity. Three patients required reoperation due to vascular compromise. The flap survival rate was 92% as one flap was lost due to extensive arterial thrombosis. All the remaining flaps survived completely and provided stable coverage without hernias or other flap-related complications during follow-up. The 3-year OS was 58% (95%CI 26–92). 58% (n=7) of the patients were able to ambulate with crutches after the initial rehabilitation period and none of the patients remained confined to bed.

Study IV was a retrospective study of 136 patients who underwent hindquarter amputation (HQA) for sarcoma between 1996 and 2018 in a single tertiary referral hospital. Bone sarcoma was the indication for the majority of the patients (67%), whilst the remaining patients (33%) were operated on for a soft-tissue sarcoma (STS). 61% of the operations were primary surgeries and the remainder were salvage operations for tumour recurrence. The mean OS for bone sarcoma was 91 months (95%CI 64–117) and 90 months (95%CI 58–123) for primary and salvage surgery patients, respectively (p=0.727). The mean OS for soft-tissue sarcoma was 59 months (95%CI 31–89) and 13 months (95%CI 9.4–16) for patients undergoing primary and salvage surgery, respectively (p=0.038). The 30-day mortality for patients undergoing surgery with a curative intent was 0.8%. Six patients underwent palliative surgery and their outcome was poor, as two patients died within two weeks after surgery. 54% of the patients had at least one complication with 24% requiring re-operation.

In conclusion, malignant pelvic tumours are challenging to treat and are associated with a high morbidity. With careful patient selection and a meticulous multidisciplinary team approach low perioperative mortality can be achieved. Three different treatment algorithms were introduced for sacrectomy, PE and HQA. Pedicled TMG and free flaps provide feasible and reliable methods of reconstruction for complex pelvic defects after oncological resection. Palliative surgery should be considered with extreme caution.

TIIVISTELMÄ

Lantion syöpäkasvain voi olla lähtöisin tukikudoksesta (sarkoomat) tai epiteelikudoksesta (karsinoomat). Kookkaat kasvaimet ovat erittäin harvinaisia ja ne ovat haasteellisia hoitaa lantion anatomian vuoksi. Suurin osa lantion syöpäkasvaimista voidaan hoitaa alaraajan säästävällä lantion resektiolla tai lantion tyhjennysleikkauksella (pelvic exenteration, PE), mutta osa pitkälle edenneistä syöpäkasvaimista vaatii edelleen lantion alueen amputaation. Tämän väitöskirjatutkimuksen tavoitteena oli arvioida lantion alueen syöpäleikkauksien jälkeisiä tuloksia etenkin kirurgisen hoidon, potilaiden selviytymisen ja käytettyjen korjausmenetelmien osalta. Toisena tavoitteena oli luoda algoritmi näiden potilaiden hoidon avuksi.

Potilaiden (n=21), joille tehtiin ristiluun poistoleikkaus (sakrektomia) primaarin luusyövän vuoksi, leikkaustulokset arvioitiin takautuvasti osatyössä I. Potilaita hoidettiin seuraavan algoritmin mukaisesti: 1) Potilaat (n=5), joille tehtiin ainoastaan S3/4-tasoa distaalisempi sakrektomia, pehmytkudospuutos oli pieni eivätkä he siten tarvinneet pehmytkudosrekonstruktioita. 2) Potilaat (n=11), joilla oli kohtalainen tai suuri pehmytkudospuutos, kudospuutos voitiin korjata samassa leikkauksessa, jossa syöpäkasvain poistettiin. Yleisimmin käytettyjä kielekkeitä olivat paikalliset pakaran alueen kielekkeet. 3) Kaikkein suurimmat ja vaikeimmat kudospuutokset (n=5) korjattiin kaksivaiheisesti. Ensimmäisessä leikkauksessa poistettiin ristiluu, jonka jälkeen lantio ja selkäranka kiinnitettiin toisiinsa. Haava peitettiin väliaikaisesti aliapaineimusidoksella. Pehmytkudoksien korjaus toteutettiin seitsemän vuorokauden kuluttua. Välittömän ja viivästetyn rekonstruktion ryhmien välillä ei ollut eroja komplikaatioiden esiintyvyydessä.

II osatyö koostui 38 potilaasta, joille tehtiin lantion alueen tyhjennysleikkaus. 26 potilaalle tehtiin koko lantion tyhjennysleikkaus (total pelvic exenteration, TPE), 11 potilaalle tehtiin lantion takaosan tyhjennysleikkaus (posterior pelvic exenteration, PPE) ja kahdelle etuosan tyhjennysleikkaus (anterior pelvic exenerartion, APE). Yhdelle potilaalle tehtiin ensin APE ja myöhemmin paikallisuusiutuman vuoksi PPE.

48 % potilaista oli elossa 5 vuoden kuluttua leikkauksesta. Imusolmukemetastaasi (HR 3.1, p=0.027) ja syöpäkasvaimen ulottuminen leikkausmarginaaliin (HR 3.9, p=0.009) olivat huonoja ennustetekijöitä selviytymisen suhteen. 71 % potilaista sai vähintään yhden komplikaation seurannan aikana. 69 %:lla potilaista käytettiin kielekettä lantion kudospuutoksen korjaukseksi. Yhtä kielekettä lukuun ottamatta käytettiin reisikielekettä (transverse myocutaneus gracilis, TMG). TMG-kieleke oli luotettava lantionpohjan korjauksessa. Lantion pohjan ja emättimen korjauksessa käytettiin seuraavaa algoritmiä: TPE potilaat, joille tehtiin myös uusi emätin sekä PPE potilaat, joilla emättimen resektio ei rajoittunut vain takaseinään tarvitsivat molemminpuolisen TMG-kielekkeen. Muilla potilailla käytettiin yhtä kielekettä.

Potilaat (n=12), joille tehtiin lantion alueen amputaatio sarkooman vuoksi ja jotka tarvitsivat mikrokirurgisen kielekkeen kudospuutoksen korjaukseksi, tutkittiin osatyössä III. Leikkaukset tehtiin kolmessa eri sarkoomakeskuksessa ja kaikissa tapauksissa käytettiin amputoidusta alaraajasta otettua mikrovaskulaarista kielekettä. Kielekkeistä 92 % (n=11) parani täysin. Yksi kieleke menetettiin verenkierto-ongelman vuoksi. Kaikki parantuneet kielekkeet peittivät kudospuutoksen luotettavasti eikä myöhäisongelmia tai tyriä seuranta-aikana todettu. 58 % potilaista oli elossa 3 vuoden kuluttua leikkauksesta.

IV osatyö oli takautuva tutkimus, joka koostui 136 potilaasta, joille oli tehty lantion amputaatio (hindquarter amputation, HQA) sarkooman vuoksi. Potilaat oli leikattu vuosina 1996–2018. Suurimmalla osalla (67 %) oli luusarkooma. 61 %:lle potilaista amputaatio oli ensimmäinen kirurginen toimenpide sarkooman vuoksi ja lopuille amputaatio tehtiin taudin paikallisen uusiutuman vuoksi. Keskimääräinen elossaoloaika amputaation jälkeen luusarkoomapotilailla oli 91 kuukautta (95%CI 64–117) primaarin amputaation jälkeen ja 90 kuukautta (95%CI 58–123) paikallisuusiutuman jälkeen (p=0.727). Pehmytkudossarkoomapotilaiden keskimääräinen elossaoloaika oli 59 kuukautta (95%CI 31–89) primaariamputaation jälkeen ja 13 kuukautta (95%CI 9.4–16) paikallisuusiutuman jälkeen (p=0.038). 30-päivän kuolleisuus leikkauksen jälkeen oli 0,8 % potilailla joiden hoidon tavoitteena oli pysyvä parantuminen. Kuusi potilasta leikattiin palliatiivisella indikaatiolla. Kaksi näistä potilaista kuoli kahden viikon sisällä leikkauksesta. 54% potilaista sai vähintään yhden komplikaation ja 24 % tarvitsi uusintaleikkauksen komplikaation vuoksi.

Yhteenvetona voidaan todeta, että lantion alueen syöpäkasvaimet ovat haastavia hoitaa ja niistä aiheutuu potilaille huomattavaa sairastavuutta, mutta huolellisella suunnittelulla ja erikoisalojen välisellä yhteistyöllä leikkauskuolleisuus on matala. Kolme erilaista algoritmiä kehitettiin ristiluun poiston, lantion tyhjennysleikkauksen ja lantion amputaation hoidon avuksi. TMG-kieleke ja mikrokirurgiset kielekkeet ovat luotettavia lantion alueen kookkaiden ja monimutkaisten kudospuutosten korjauksessa. Pelkkää palliatiivista lantion alueen leikkausta pitää harkita erityisen tarkasti.

LIST OF ABBREVIATIONS

3D	Three-dimensional
ALT	Anterolateral thigh
BMI	Body-mass index
CFA	Common femoral artery
CI	Confidence interval
CIA	Common iliac artery
CT	Computed tomography
DR	Delayed reconstruction
DFS	Disease-free survival
DSS	Disease-specific survival
DIEP	Deep inferior epigastric perforator
DFS	Disease free survival
DSS	Disease specific survival
EIA	External iliac artery
ERAS	Enhanced recovery after surgery
FACTBr	Functional Assessment of Cancer Therapy - Brain
FIGO	Féderation Internationale de Gynécologie et d'Obstétrique
FNCLCC	Fédération Nationale des Centres de Lutte Contre le Cancer
HQA	Hindquarter amputation
HR	Hazard radio
HRQoL	Health-related quality of life
IIA	Internal iliac artery

IGA	Inferior gluteal artery
IR	Immediate reconstruction
LRFS	Local recurrence-free survival
LR	Local recurrence
LRFS	Local recurrence-free survival
MDT	Multidisciplinary team
MFS	Metastatic free survival
MRI	Magnetic resonance imaging
MSTS	Musculoskeletal Tumour Society
NR	No reconstruction
NPWT	Negative-pressure wound therapy
OS	Overall survival
PE	Pelvic exenteration
PROM	Patient reported outcome measures
PROMIS	National institute of Health's Patient Reported Measurement Information System
QOL-CS	Quality of Life for Cancer Survivors
SGA	Superior gluteal artery
STS	Soft-tissue sarcoma
TESS	Toronto Extremity Salvage Score
TME	Total mesorectal excision
TRAM	Transverse rectus abdominis myocutaneous
UPS	Undifferentiated pleomorphic sarcoma

LIST OF ORGINAL PUBLICATIONS

The present study is based on the following original publications. The publications are referred to in the text by their Roman numbers (I–IV).

I Kiiski J, Kuokkanen HO, Kääriäinen M, Kaartinen IS, Pakarinen TK, Laitinen MK. Clinical results and quality of life after reconstruction following sacrectomy for primary bone malignancy. J Plast Reconstr Aesthet Surg. 2018 Dec;71(12):1730-1739.

II Kiiski J, Räikkönen K, Vuento MH, Hyöty MK, Kallio J, Kuokkanen HO, Kaartinen IS. Transverse myocutaneous gracilis flap reconstruction is feasible after pelvic exenteration: 12-year surgical and oncological results. Eur J Surg Oncol. 2019 Sep;45(9):1632-1637.

III Kiiski J, Laitinen MK, Le Nail LR, Kuokkanen HO, Peart F, Rossert P, Bourdais-Sallot A, Jeys LM, Parry MC. Soft tissue reconstruction after pelvic amputation: The efficacy and reliability of free fillet flap reconstruction. Submitted.

IV Kiiski J, Parry MC, Le Nail LR, Sumathi VP, Stevenson J, Kaartinen IS, Jeys LM, Laitinen MK Surgical and oncological outcomes after hindquarter amputation for sarcoma – who will benefit from the procedure? Bone Joint J. 2020 Jun;102-B(6):788-794.

The original articles have been reproduced with kind permission from the original publishers.

TABLE OF CONTENTS

List of Tables

1   INTRODUCTION

Malignant pelvic tumours continue to pose a significant challenge to the surgical/ orthopaedic and gynaecological oncologist as well as to the reconstructive surgeon. Complete *en bloc* surgical resection with adequate margins are paramount for survival in pelvic sarcomas as well as recurrent and advanced pelvic carcinomas (Bergh et al. 2001, Zoucas et al. 2010, Mayerson, Wooldridge, and Scharschmidt 2014). The incidence of malignant pelvic tumours is low and they often initially present with non-specific and mild symptoms and can progress to imperceptibly large tumours (Toro et al. 2006, Ottaviani and Jaffe 2009, Varga, Szoverfi, and Lazary 2014). The closely located vital neurovascular, reproductive and visceral organs as well as the absence of strong natural anatomical barriers often lead to multiorgan resections when aiming for adequate surgical margins (Sole et al. 2014, Mayerson, Wooldridge, and Scharschmidt 2014, Chao et al. 2015, Puchner et al. 2017). The potential need to resect some of the vital neurovascular structures as well as the high mechanical loading to the pelvic bone are challenging issues when restoring limb function after tumour resection (Shao et al. 2015, Morris et al. 2017).

Malignant pelvic sarcomas were treated mainly with hindquarter amputation (HQA) until the late 1970's (Enneking and Dunham 1978, Eilber et al. 1979). The evolution of oncological adjuvant treatment in the 1970's lead to paradigm shift towards limb salvage surgery (Rosen et al. 1981, Bleyer et al. 1982). Further advances in medical imaging and the development of computed tomography (CT) and magnetic resonance imaging (MRI) have allowed more precise pre-operative planning and examination of the extent of the disease (Ambrose and Hounsfield 1973, Mansfield and Maudsley 1977). Therefore, the majority of pelvic sarcomas can nowadays be managed with limb-sparing pelvic resection (Kawai et al. 1998, Nakamura et al. 2013, Mayerson, Wooldridge, and Scharschmidt 2014, Puchner et al. 2017).

In properly selected patients, limb-salvaging pelvic resection (sometimes referred to as internal HQA) can result in good oncological outcome in terms of overall survival

(OS) (Shin, Rougraff, and Simon 1994, Wirbel, Schulte, and Mutschler 2001, Puchner et al. 2017). Functional outcome after pelvic resection is reported to be superior to HQA (Wirbel et al. 2000). However, some studies have found functional outcome and health-related quality of life to be similar between patients following pelvic resection and HQA (Beck et al. 2008, Griesser et al. 2012). The contemporary indications for amputation in pelvic sarcoma are the inability to achieve adequate surgical margins with limb salvage pelvic resection or a non-functional extremity after tumour resection. However, there is no absolute or objective definition of a non-functional limb. The most critical structures for preservation of reasonable function in the remaining extremity are the femoral neurovascular bundle, sciatic nerve and hip joint. If two of these structures need to sacrificed during the tumour resection HQA should be considered (Mayerson, Wooldridge, and Scharschmidt 2014).

Pelvic exenteration (PE) is a complex multiorgan resection to remove all or part of the pelvic organs for treatment of advanced or recurrent gynaecological or other malignancies. Though it was first described as a palliative procedure (Brunschwig 1948), it is nowadays most commonly indicated in cases of recurrent or advanced tumours of pelvic organs with a curative intent (Marnitz et al. 2006, Ferenschild et al. 2009, Knight et al. 2018).

Reconstruction of complex pelvic defects presents several challenges. The principle to reconstruct 'like-with-like' is not often possible in cases of urogenital resection and these defects needs to be reconstructed with alternative methods. Prior radiation therapy and ablative surgery might have had a detrimental effect on the blood circulation of the local tissues (Kim et al. 1997, Senchenkov et al. 2008). A patient's overall health status is very important; in particular, nutritional status can be compromised and there may be limited possibilities to optimize the patient prior to major surgery with an oncological indication (Lyell et al. 2019). In general, the objectives for complex pelvic defect reconstruction are 1) maintain a structural integrity to allow full weight transfer from the axial skeleton to the lower extremity; 2) stable wound cover; 3) securing the abdominal wall and pelvic floor to prevent visceral herniation; 4) fill any dead space and cover the spinopelvic fixation or other osteosynthesis/prosthetic devices and 5) restoration of external genitalia and vagina to allow sexual function.

The primary aim of this thesis was to evaluate the oncological, surgical and reconstructive outcomes of patients with a malignant pelvic tumour who require complex *en bloc* resection of the tumour. The secondary aim was to develop algorithms for reconstructing complex pelvic defects after oncological resections.

2   REVIEW OF THE LITERATURE

2.1   Overview of pelvic anatomy

The pelvis is the lower part of the trunk formed by the basin-shaped ring of the sacrum and two innominate bones that are tightly connected with ligamentous structures. The pelvis can be divided into the greater (false) pelvis (*pelvis major*) and the lesser (true) pelvis (*pelvis minor*). The greater pelvis is located above the pelvic inlet and is part of the abdominopelvic cavity containing some of the abdominal viscera. The lesser pelvis is located between the pelvic inlet and outlet and it contains pelvic viscera including the urinary bladder, rectum and reproductive organs. (Standring, Borley, and Gray 2008, Moore 2018.)

2.1.1   Bony pelvis

The main functions of the bony pelvis are 1) transfer the forces from the upper body to the lower extremities during standing and locomotion 2) provide attachments and withstand the forces of the muscles needed for locomotion 3) protect the abdominal and pelvic viscera (Verbruggen and Nowlan 2017).

The bony pelvis composes of four bones, a sacrum, two hip bones (*os coxae*) and a coccyx (Figure 1). A mature hip bone is formed by the fusion of three separate bones – ilium, ischium and pubis. The hip bones are connected anteriorly at the midline at the pubic symphysis and articulate bilaterally with the sacrum by sacroiliac joints. Four fused rudimental coccygeal vertebrae form the coccyx inferior to the sacrum. (Vleeming et al. 2012, Verbruggen and Nowlan 2017, Moore 2018.)
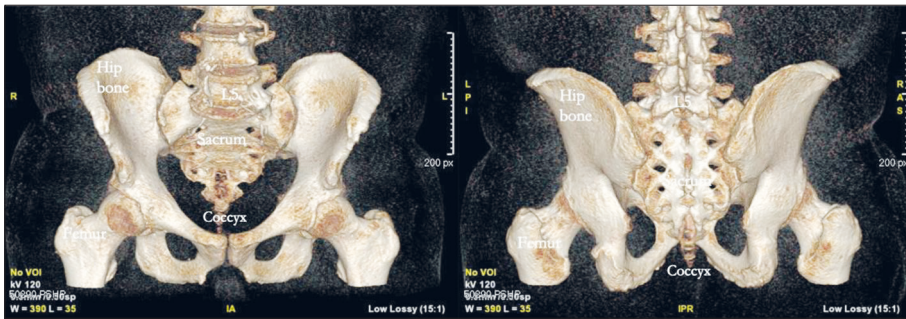
Figure 1. 3D CT-scan of the pelvic bones. Anterior (left) and posterior (right) view of the pelvic bones.

The pelvis is connected to the axial skeleton via strong iliolumbar ligaments and prevertebral disc (Vleeming et al. 2012). The load of the upper body is transferred through the sacral plateau to the pelvis and via the femoral joints to the lower extremities (Le Huec et al. 2011).

2.1.2 Vascular and neural structures

The pelvic blood supply is complex with multiple anastomotic connections. Variations in the course of specific vessels is possible. Malignant pelvic tumours can cause rich neovascularization and displace or distend the vascular structures. (Lang et al. 1995, Dietrich, Gehrich, and Bakaya 2008, Bilhim et al. 2014.)

The aorta divides into two common iliac arteries (CIA) in the cranial part of the greater pelvis. The common iliac artery divides into the external (EIA) and internal iliac arteries (IIA). The external iliac artery continues to the lower extremity as the common femoral artery via the femoral canal (Moore 2018). The EIA is the only artery in the pelvis that does not have a rich collateral system and therefore it cannot be ligated without sequelae (Dietrich, Gehrich, and Bakaya 2008). The inferior epigastric and deep circumflex iliac arteries are clinically the most important branches of the EIA for the reconstructive plastic surgeon (Ireton, Lakhiani, and Saint-Cyr 2014, Shin et al. 2018) (Figure 2).

The lesser pelvis is supplied by the IIA, ovarian artery (originating from the aorta), unpaired media sacral artery (originating from aorta) and unpaired superior rectal artery (continuous with the inferior mesenteric artery). The IIA branches into anterior and posterior divisions (Dietrich, Gehrich, and Bakaya 2008, Moore 2018). Numerous branches of the IIA supply the pelvic viscera, pelvic and abdominal wall, gluteal region and the upper medial thigh. The clinical importance of this is demonstrated if the common iliac vessel is ligated in HQA. This will result in nearly a 3-fold increase in the posterior flap necrosis rate (Senchenkov et al. 2008). The most commonly used end

branches of the IIA for reconstructive purposes are the superior and inferior gluteal as well as internal pudendal arteries (Unal et al. 2011, Hashimoto, Abe, and Nakanishi 2014, Georgantopoulou et al. 2014). All of these branches can be used as recipient vessels in cases of microvascular surgery.
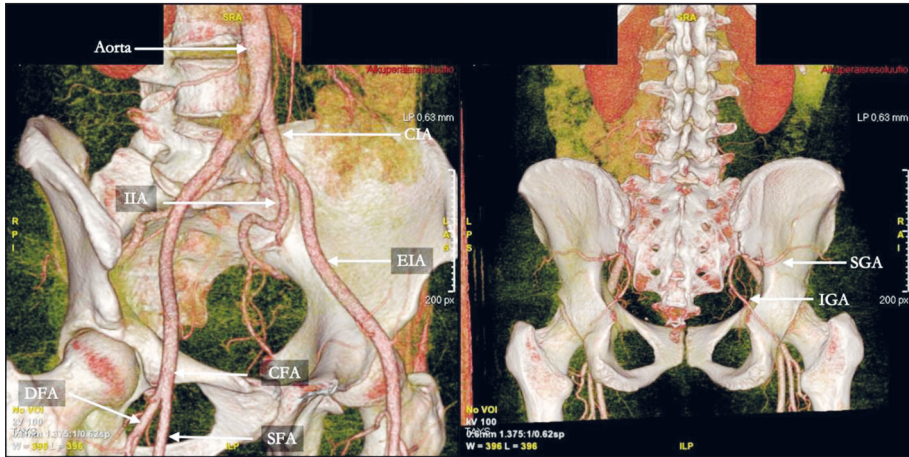
Figure 2. Oblique (left) and posterior (right) view of the major pelvic arteries on 3D-reconstruction of an angio-CT.

CIA = common iliac artery, IIA = internal iliac artery, EIA = external iliac artery, CFA = common femoral artery, DFA = deep femoral artery, SFA = superficial femoral artery, SGA = superior gluteal artery, IGA = inferior gluteal artery.

The pelvic veins lie in close proximity to the aforementioned arteries, except for the ovarian/testicular veins. An intercommunicating network of pelvic veins form the pelvic venous plexus. During pelvic surgery, venous plexus haemorrhage can be challenging to control (Hata, Kawahara, and Tomita 1998, Casal Nunez et al. 2017).

The lymph nodes of the pelvis are located adjacent to the main pelvic vessels. The superficial inguinal pathway drains to the superficial inguinal nodes located next to the femoral vessels. Lymph from the pelvic organs drain to the lymph nodes via four different routes. The anterior pelvic pathway drains to the internal iliac nodes. The lateral route drains to the external iliac nodes. The hypogastric route carries lymph to junctional nodes located at the iliac bifurcation. The presacral route drains to the lymphatic plexus anterior to the coccyx and sacrum and up to the common iliac nodes. (McMahon, Rofsky, and Pedrosa 2010, Pano et al. 2011, Pano et al. 2015)

The lumbosacral plexus is formed from lumbar, sacral and coccygeal nerves originating from the 12th thoracic to coccygeal nerve roots (Sforsini 2006, Standring, Borley, and Gray 2008, Moore 2018). The lumbar plexus is formed by the first four lumbar nerve roots and the lower branch of the 12th thoracic nerve root. The femoral

nerve, formed from the anterior rami of L2–4 nerve roots, is the largest branch of the lumbar plexus. It descends in the groove between the psoas major and iliacus muscles and continues into the pelvis posterolaterally and passes the inguinal ligaments to enter the femoral triangle to continue into the thigh. The main motor function of the femoral nerve is to innervate the hip flexors and quadriceps muscles. The sacral plexus is formed by anterior rami of the S1–4 spinal nerves and receives branches from the L4–5 lumbar nerve roots and runs down in the posterior pelvic wall. The sciatic nerve is the largest nerve of the sacral plexus and the main motor nerve of the lower extremity. Its tibial portion innervates the hamstring muscles of the thigh and the muscles of the posterior compartment of the leg. The fibular portion innervates the muscles of the anterior and lateral compartment of the leg. The pudendal nerve is formed from the S2–4 roots and it innervates the levator ani muscles, coccygeus muscle, external urethral and external anal sphincter muscles. It is the sensory nerve of the external genitalia, perineal region and distal portion of the anal canal.

2.1.3   Pelvic floor and perineum

The pelvic floor is a funnel shaped structure and it separates the pelvic cavity from perineum. The function of the pelvic floor is to support the abdominopelvic viscera, maintain urinary and faecal continence and it forms part of the birth canal in women. The pelvic floor is formed from four layers (from deep to superficial): endopelvic fascia, muscular pelvic diaphragm, perineal membrane and superficial transverse perineii (Stoker 2009). The pelvic floor is traversed by the urethral and rectal hiatuses and the vaginal hiatus in women.

The endopelvic fascia serves as a passive support for the visceral organs. The muscular pelvic diaphragm is formed by the levator ani muscles (iliococcygeus, puborectalis and pubococcygeus) and the coccygeus muscle. The perineal membrane is located below the muscular pelvic diaphragm. It is triangular shaped and in women it is connected to the vaginal sidewalls. The muscles of the urogenital triangle are the superficial transverse perineal muscle, bulbospongiosus muscle and the ischiocarvernosus muscle. These muscles have both a sexual function and supportive role. (Sforsini 2006, Stoker 2009.)

The vagina is an elastic musculomembranous tube between the cervix and vestibule of the vagina. The vagina forms an excretory tract for menstrual fluid, is part of the birth canal and it receives the penis during sexual intercourse (Moore 2018). There is considerable variation of the length and dimensions of the vagina (Barnhart et al. 2006).

The perineum is a diamond-shaped area lying superficial to the pelvic floor. The anatomical borders are the pubic symphysis (anteriorly), tip of coccyx (posteriorly) and inferior pubic rami (anterolaterally) and sacrotuberous ligaments (posterolaterally). It can be divided into two theoretical triangles, the anterior urogenital triangle and

the posterior anal triangle, by drawing a line between the anterior ends of the ischial tuberosities. The central point of the perineum, the perineal body, is located at the midpoint of this line. (Moore 2018.)

2.2 Tumours requiring complex pelvic surgery

2.2.1 Bone sarcoma

Primary malignant bone tumours are very rare and they account for less than 0.2% of all malignancies registered in the EUROCARE (European Cancer Registry based study on survival and care of cancer patients) database (Stiller et al. 2013). Of all the malignant bone tumours, only approximately 15% are located in pelvis (Damron, Ward, and Stewart 2007, Ottaviani and Jaffe 2009). Survival after pelvic bone sarcoma is inferior to extremity bone sarcoma (Mirabello, Troisi, and Savage 2009, Serlo et al. 2013, Nie, Lu, and Peng 2018). Malignant bone tumours include over 25 different subtypes (Fletcher et al. 2013).

Osteosarcoma is the most common histology of bone sarcoma, with an overall incidence of approximately 0.3/100 000 per year. Incidence is higher in adolescence and it is most commonly located around the knee, in the proximal tibia or distal femur. The proportion of tumours located in the axial skeleton increases with age. Age over 40 years and non-extremity location are poor prognostic factors for survival in osteosarcoma (Bielack et al. 2002, Whelan et al. 2012). Conventional osteosarcoma is always a high-grade sarcoma and it is treated with neoadjuvant chemotherapy followed by surgical resection of the tumour. Adjuvant chemotherapy is continued after surgical treatment (Casali, Bielack, et al. 2018). Poor response from chemotherapy and inadequate surgical margin are independent prognostic factors for lower survival (Bielack et al. 2002). Low-grade parosteal osteosarcoma is most commonly treated with surgical resection (Laitinen et al. 2015). Radiotherapy is not generally used in the treatment of osteosarcoma (Casali, Bielack, et al. 2018). The 5-year disease-specific survival (DSS) after pelvic osteosarcoma is approximately 27% (Parry et al. 2016).

Chondrosarcoma is the second most common subtype of bone sarcomas, with an incidence around 0.2 / 100 000 per year. The median age at diagnosis is between 30 and 60 years. Chondrosarcoma often develops in the metaphyseal areas of long bones, but it can also arise from flat bones including pelvic bones. The pelvis is the most common location for chondrosarcoma (Fletcher et al. 2013, Stevenson et al. 2018). Chondrosarcoma is radiotherapy and chemotherapy-resistant rendering *en bloc* surgery the only curative treatment option (Casali, Bielack, et al. 2018). The 5-year OS after pelvic chondrosarcoma is approximately 50% (Fromm et al. 2018). Tumour grade and surgical margins are the most important prognostic factors for survival in chondrosarcoma (Bus et al. 2018, Tsuda et al. 2019). After local recurrence (LR),

curative treatment of recurrent pelvic chondrosarcoma requires resection of the tumour with wide surgical margins (Laitinen et al. 2019).

Ewing sarcoma is the third most common bone sarcoma. It is most commonly diagnosed in children and adolescence with a median age of 15 years at the time of diagnosis, but more rarely, it can also occur in adults (Whelan et al. 2012, Stiller et al. 2013, Serlo et al. 2013). Non-extremity location, positive surgical margins, age over 15 years and metastasis at diagnosis, all have a poor effect on survival (Cotterill et al. 2000, Serlo et al. 2015). OS without any systemic therapy is inferior to multimodal treatment. Treatment is started with neoadjuvant chemotherapy. In the extremities, local treatment of the tumour is surgical *en bloc* resection with wide margins when feasible. In pelvic cases, surgery is quite often accompanied by radiotherapy and in axial tumours like in the vertebrae, radiotherapy alone is quite often the only local treatment. Intralesional surgery should always be avoided as it has a worse prognosis compared to radiotherapy alone (Schuck et al. 2003). Adjuvant chemotherapy is administered following the local treatment. In cases of a poor chemotherapy response, post-operative radiotherapy or adjuvant high-dose chemotherapy can be considered to improve the survival (Casali, Bielack, et al. 2018). In the literature, the 5-year OS after pelvic Ewing sarcoma varies between 37%–73% (Ahmed et al. 2017, Laitinen et al. 2018).

Chordoma is a slow-growing malignant neoplasm arising from persistent notochordal elements of the spine and has an incidence of only approximately 0.5 / million per year. Chordoma presents most commonly after the age of 50 (van Wulfften Palthe et al. 2019). Approximately 50% of chordomas are located in the sacrum and although extremely rare it is the most common primary malignant tumour of the sacrum (Whelan and Davis 2018, Pillai and Govender 2018). The 5-year OS after surgical treatment for primary sacral chordoma is around 80% (Yu et al. 2016, van Wulfften Palthe et al. 2019). LR is a negative prognostic factor for DSS in sacral chordoma. 10-year OS is 84% and 44% without and with LR (Houdek et al. 2019). *En bloc* resection with R0 margins is the aim of treatment. Post-operative radiotherapy can be included in cases of R1 resection. High-dose proton or carbon ion therapy can be considered in cases of unresectable disease. Chordoma is not chemotherapy sensitive and it is therefore not indicated. (Casali, Bielack, et al. 2018)

2.2.2   Soft tissue sarcoma

STS are rare tumours originating from mesenchymal cells with an incidence of 4–5/100 000 per year (Stiller et al. 2013). However, it is not a uniform disease. STS includes over 80 different histological entities and even more molecular subsets (Fletcher et al. 2013). STS occurs predominantly in older adults as the incidence for people over 65 years , between 25–65 years and under 25 years are 13.1/100 000, 4.4/100 000 and 1.3/100 000, respectively (Stiller et al. 2013).

Less than 5% of all the STSs are located in pelvic region (Toro et al. 2006, Mastrangelo et al. 2012). The most common location of STS is the lower extremity, accounting for nearly 30% of tumours. Of the lower extremity, 44% of the tumours are located in the thigh (Brennan et al. 2014). In addition to pelvic sarcomas, some proximal thigh STS will require pelvic amputation for primary or salvage therapy for local control of the disease.

Liposarcoma and leiomyosarcoma are the most common histologies of STS, with an incidence of less than 1/100 000 per year. The remainder of STS has an incidence of less than 0.2/100 000 per year (Stiller et al. 2013). Undifferentiated pleomorphic sarcoma (UPS) is relatively commonly found in a deep pelvic location, following liposarcoma (Nakamura et al. 2013). UPS is a heterogenous group of STSs and it does not show any evidence of a specific line of differentiation. (Fletcher et al. 2013). Favourable prognostic factors for DSS in STS are metastasis-free at presentation, superficial location, size under 5 cm, wide surgical margin and low grade (Brennan et al. 2014, Maretty-Nielsen et al. 2014).

Surgical treatment with *en bloc* resection with negative margins (R0 resection, no tumour on ink/margin) is the standard treatment for STS. The minimal acceptable margin depends on multiple factors (Casali, Abecassis, et al. 2018). Marginal resection, with planned close margin, is often considered adequate in low grade liposarcoma (atypical lipomatous tumours). Even active surveillance has been proposed for these tumours (Vos et al. 2019). A wide surgical margin is most commonly considered an adequate margin for both low grade and high-grade STS. Neoadjuvant or adjuvant radiotherapy is considered especially for deep tumours measuring over 5 cm or with close contact to critical anatomical structures (Casali, Abecassis, et al. 2018). Neoadjuvant and adjuvant radiotherapy have a similar effect on OS and local control. Wound complications are more common with neoadjuvant radiotherapy, but tissue fibrosis and late complications are more common with adjuvant radiotherapy (O'Sullivan et al. 2002, Casali, Abecassis, et al. 2018). Adjuvant chemotherapy is not routinely used for STS (Woll et al. 2012).

2.2.3   Carcinomas

Carcinoma is a malignant neoplasm originating from epithelial cells (Kemp, Burns, and Brown 2008). Multiple carcinomas can occur in the pelvic area, but the majority of gynaecological, gastrointestinal and urothelial carcinomas can be treated with resection of the tumour and/or radiotherapy or chemoradiotherapy (Benson et al. 2012, Di Donato et al. 2012, Marth et al. 2017, Glynne-Jones et al. 2017). Only a minority of carcinomas require complex resections of multiple tissues that require resection and reconstruction of the pelvic floor or bony pelvis. Complete *en bloc* surgical resection

with clear margins is also paramount for patient survival in advanced and recurrent pelvic carcinoma malignancies (Zoucas et al. 2010).

Gynaecological indication for PE is a locally advanced or recurrent central gynaecological tumour including cervical, vaginal, vulvar and ovarian carcinomas (Diver, Rauh-Hain, and Del Carmen 2012, Kaur et al. 2014). Local cervical carcinomas are treated with either surgery or chemoradiotherapy depending on the Féderation Internationale de Gynécologie et d'Obstétrique (FIGO) stage (Marth et al. 2017). Up to 28% of patients with FIGO stage IB-IIA will have a recurrence (Landoni et al. 2017). Advanced (FIGO IVa) stage or recurrence is an indication for PE after chemotherapy (Marth et al. 2017). The 5-year OS after PE for cervical cancer is 37% (Marnitz et al. 2006). PE is indicated in selected cases of advanced uterine tumours, including carcinomas, carcinosarcomas and sarcomas. The 5-year OS of patients undergoing PE for uterine tumours is 40%. Patients with endometroid and sarcoma histology had a tendency for better survival, with 50% and 66% 5-year OS, respectively (Khoury-Collado et al. 2012). Chemoradiation is often preferred for advanced stage III/IV vulvar cancer. PE is often considered as a salvage therapy after possible recurrence. The 5-year OS after PE for advanced vulvar carcinoma was 67% for primary disease and 59% for recurrent disease (Forner and Lampe 2012).

Up to 33% of rectal carcinoma patients present initially with locally advanced disease. Neoadjuvant radiotherapy or chemotherapy and total mesorectal excision (TME) will achieve clear surgical margins in 90% of patients and a low recurrence rate (MacFarlane, Ryall, and Heald 1993, Law and Chu 2004). *En bloc* resection is paramount for survival in cases of locally advanced colorectal carcinoma (McGlone, Bernie, and Elliott 1982, Hunter, Ryan, and Schultz 1987). PE is therefore indicated in advanced colorectal carcinoma after MDT evaluation. R0 resection and node-negative status are the most important prognostic factors for survival. Contraindications for PE in advanced colorectal carcinoma are major comorbidities, technically impossible R0 resection, metastatic disease or patient not consenting to the surgery (Davies et al. 2011). Survival after PE for primary advanced or recurrent rectal carcinoma is 78% and 65%, respectively. Positive lymph node status and positive surgical margins are the only factors affecting survival in the multivariate model (Bhangu et al. 2014).

2.3   Treatments options

2.3.1   Principles of tumour resection

Pelvic tumours can be surgically treated with pelvic resection (sometimes referred to as internal hemipelvectomy or internal hindquarter amputation) or with HQA (sometimes referred as hemipelvectomy or external hemipelvectomy). The type of pelvic

resection can be defined according to the Enneking and Dunham classification (Figure 3) (Enneking and Dunham 1978).
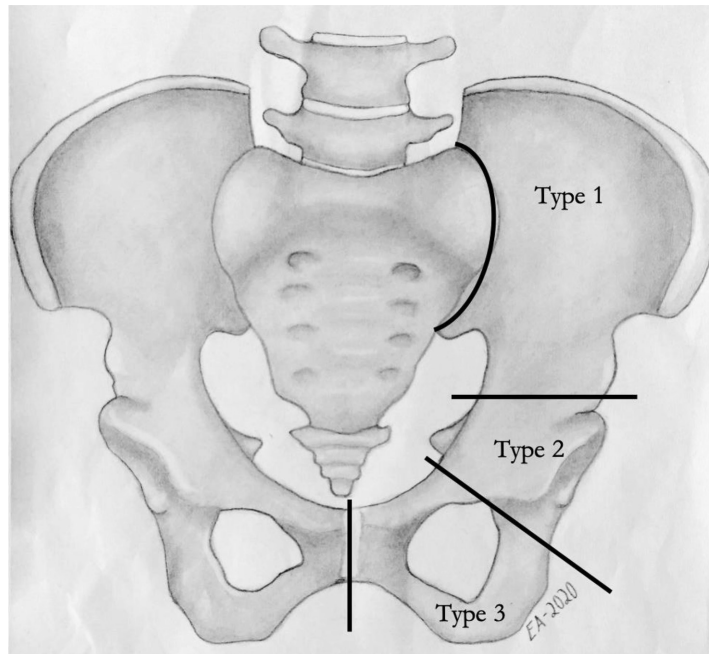
Figure 3. Classification of pelvic resections.

The definition of surgical margins in surgical oncology is not uniform. The most commonly used methods for reporting surgical margins are the Musculoskeletal Tumour Society (MSTS) system (Enneking, Spanier, and Goodman 1980), the American Joint Committee on Cancer (AJCC) R system (Amin et al. 2017) or measuring the margins in millimetres as recommended by the College of American Pathologists and the Association of Directors of Anatomic and Surgical Pathology (Table 1). The tumour grade is determined in this thesis according to the Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading system (Table 2) (Trojani et al. 1984, Guillou et al. 1997).

Table 1. MSTS and AJCC surgical margin classification systems.

MSTS		
Intralesional	Macroscopic or microscopic tumour on margin	
Marginal	Resection on the pseudocapsule or through the reactive zone around the tumour	
Wide	The presence of normal tissue between the tumour and margin	
Radical	Entire anatomical compartment resected	
AJCC		
R0	No residual disease	No tumour on margin/ink
R1	Microscopic residual tumour	Tumour on margin/ink
R2	Macroscopic residual tumour	Macroscopically incomplete resection

Table 2. Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) grading system. The grade is determined by the sum of the three criteria. Grade 1 = ≤3 points, grade 2 = 4–5 points, grade 3 ≥6 points.

Tumour differentiation	Necrosis	Mitotic count / 10 high power fields
1: Well	0: No	1: <10
2: Moderate	1: <50%	2: 10–19
3: Poor	2: ≥50%	3: ≥20

The adequacy of the surgical margins not only depends on millimetres, but also on the histological subtype and grade of the tumour, preoperative or postoperative radiotherapy, and possible presence of resistant anatomical barriers (fascia, periosteum, perineurium, etc) on the surgical margin (Casali, Abecassis, et al. 2018). Planned close or positive margins when combined with radiotherapy yields similar local control to wide excision for STS. Unplanned positive surgical margins in contrast, is associated with a high LR (Gerrand et al. 2001). For STS, myxofibrosarcoma and dermatofibrosarcoma protuberans have an infiltrative pattern rather than the more common pushing type pattern and they have a higher rate of LR when compared to other STSs (Hersant et al. 2013, Crago and Brennan 2015, Scoccianti et al. 2016).

In chondrosarcoma, a surgical margin of >4mm yields a reduction in LR compared to a lesser margin (Stevenson et al. 2018). In a recent meta-analysis, osteosarcoma patients who had a marginal vs. wide margin had a higher risk for LR (OR 3.66, 95% CI 1.41–9.52). The meta-analysis did not however define the criteria for a wide margin (He et al. 2016). On the other hand, in high-grade osteosarcoma, the response to chemotherapy in addition to margin is a significant factor in both local control as well as overall survival (Jeys et al. 2017). Surgical margins of ≥2mm reduces the risk of LR in osteosarcoma (Cates 2017, Jeys et al. 2017).

2.3.2 Sacrectomy

2.3.2.1 Oncological resection

Sacrectomy is a rare procedure due to the very low incidence of sacral tumours. It was first performed by Bowers in 1945 for giant cell tumour of the sacrum (Bowers 1948). Depending on the extent of the tumour extension, they can be treated with partial (distal) sacrectomy, total sacrectomy, (sagittal) hemisacrectomy or extended sacrectomy (Li et al. 2011, Fourney et al. 2005). Extended sacrectomy includes resection of the lumbar vertebrae (Figure 4). In extensive pelvic tumours, sacrectomy can be combined with *en bloc* PE (Sasikumar et al. 2017).
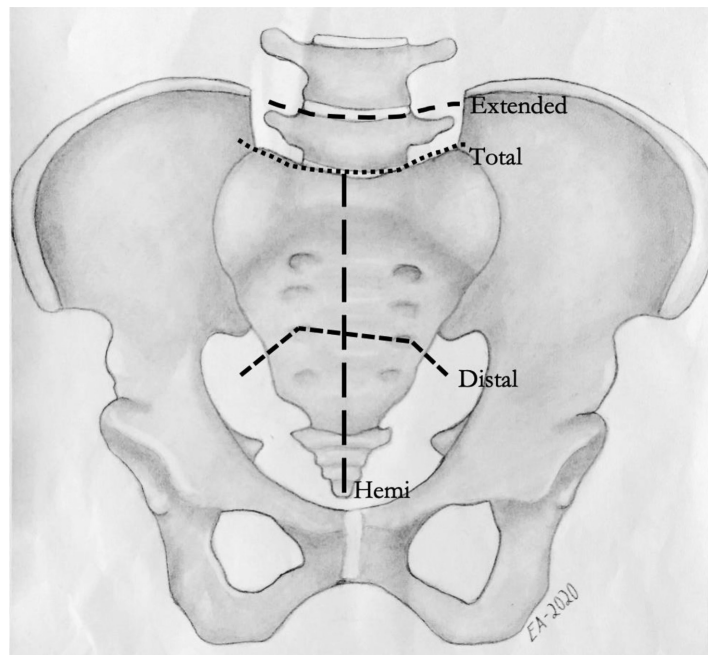
Figure 4. Classification of different sacrectomies.

Sacrectomy can be performed through the posterior or combined anterior-posterior approach. Total sacrectomy is most commonly performed with a combined approach. The anterior procedure begins with the patient in the supine position. An abdominal incision is performed and care is taken to preserve the inferior epigastric vessels and their perforators especially if a transabdominal pedicled vertical rectus abdominal myocutaneus (VRAM) flap is planned for reconstruction (Garvey et al. 2013). Depending on tumour extension, the distal part of the sigmoid colon and rectum are either mobilised from the sacrum or resected along with the tumour. The internal iliac,

middle sacral and tumour vessels are all ligated. The sacral nerves are transected. After completing the anterior resection of the tumour, the abdominal incision is closed, and a possible colostomy is performed. The patient is then turned to the prone position. The posterior incision and possible gluteal flaps are developed. The sacrum is exposed, taking care to preserve an adequate soft tissue margin considering the prior biopsy track and/or surgery. A L5 laminectomy is performed and the dural sac is ligated and cut. Finally, bilateral osteotomies are performed, and the sacrum is removed. (Zhang et al. 2003, Li et al. 2011, Garvey et al. 2013.) The posterior-only approach has also been described for total sacrectomy. (Zang et al. 2015.)

Partial sacrectomy is most commonly performed with a similar surgical technique as for total sacrectomy if the resection is at the S2-level. Surgery is usually carried out with a posterior approach for more distal sacrectomies when no bowel surgery is necessary (Fourney et al. 2005).

Function after sacrectomy depends on the level of sacral resection. All patients who undergo bilateral nerve root resection above the S1 level have major disabilities with motor, bowel, urinary and sexual functions. Approximately half of the patients who have sparing of both S1-roots will regain a near normal gait, but over 95% will have major problems with urinary and bowel function. 94% of the patients will regain normal gait after sparing of bilateral S2-roots, but less than half will retain normal bowel and bladder function. Sparing of bilateral S2- and unilateral S3-roots will result in normal gait in all patients and only a 10% risk of a major problem in bowel and bladder function. More distal resections result in a near normal gait and normal urinary and bowel function. (Zoccali et al. 2016.)

Post-operative patient-reported outcome measures (PROM) after sacrectomy correlate with the level of nerve root resection. Resection of bilateral S3-nerve roots results in an inferior PROM on mental health and physical health scores compared to patients that had a more caudal resection. Resection of S2-nerve roots yielded a lower orgasm score compared to that measured on the National institute of Health's Patient Reported Measurement Information System (PROMIS) (van Wulfften Palthe, Houdek, et al. 2017). In a qualitative interview study, patients expressed that they are satisfied with the immediate care after sacrectomy but would need more information on the long-term recovery and functional outcome. All patients experienced chronic pain and especially an inability to sit for a prolonged time. This impacted on the patients' quality of life in many aspects. The majority of patients in the study had sacrectomy at the S1-2 or S2-3 level (Davidge et al. 2010).

Survival after sacrectomy for chordoma is associated with local control of the disease. The 5-, 10- and 15-year OS after sacrectomy are 88%, 69% and 61% without LR and only 76%, 37% and 16% with LR . Female gender, age under 65 years, wide surgical margins and adjuvant therapy are associated with a better survival in a systematic review (Kerekes et al. 2019, Fujiwara et al. 2020). The 5-year OS after sacrectomy for

osteosarcoma is less than 40% (Wang et al. 2017). The mean OS after *en bloc* sacrectomy with PE for recurrent rectal carcinoma is 123 months for a R0 resection and 8 months for a R1 resection (Sasikumar et al. 2017).

2.3.2.2 Reconstruction after sacrectomy

The aims of reconstruction after sacretomy are (Reynolds et al. 2016):

1) The restoration of spinopelvic continuity if it has been disrupted
2) Securing the posterior pelvic wall to prevent internal organ prolapse
3) Filling of the dead space
4) Closure of the wound with minimal tension

In addition to a large soft tissue and bone defect, total sacrectomy will result in a spinopelvic discontinuity. A recent systematic review with expert recommendations concluded that all total sacrectomy patients should undergo spinopelvic reconstruction when ilio-lumbar stability is lost (Reynolds et al. 2016). Anterior spinal column support in spinopelvic reconstruction might improve surgical outcomes (Bederman et al. 2014). Bone reconstruction after sacrectomy is carried out with allogenous or autogenous bone grafts, extracorporeal radiation therapy and reimplantation or with a custom-made prosthesis. Autogenous bone reconstruction options are vascularized bone graft transfer or the more commonly used non-vascularized bone grafts (Choudry, Moran, and Karacor 2006, Arkader, Yang, and Tolo 2012). More recently 3D printed customized sacrum prostheses have been introduced, but long-term results are lacking (Goodwin et al. 2019, Wei et al. 2019). In extracorporeal radiation and reimplantation, *en bloc* sacrectomy is carried out, the sacrum is irradiated at 200 grays during the operation and reimplanted (Nishizawa et al. 2014, Goodwin et al. 2019). Reconstruction is usually accompanied with fixation using a rod-screw spinopelvic system (Zhang et al. 2003).

For a total sacrectomy defect, the most commonly used flap for soft tissue reconstruction is the pedicled VRAM flap. The VRAM flap was first described by Mathes and Bostwick (1977) and was used for pelvic floor reconstruction by Shukla and Hughes (1984). It has a constant vascular pedicle of the inferior epigastric artery and vein, and it provides adequate bulk of soft tissue to reconstruct the defect. The flap is harvested in the supine position prior to the anterior approach for sacral resection. (Miles et al. 2000, Garvey et al. 2011, Kim et al. 2015). The VRAM flap is versatile and can be used in cases of planned staged resection and reconstruction. A flow-through VRAM flap can provide donor vessels for microvascular bone transfer if needed (Garvey et al. 2013). Previous abdominal surgery can be a contraindication for the use of the VRAM flap (Miles et al. 2000).

Pedicled gluteal muscle flaps are Mathes and Nahai type III muscle flaps. Bilaterally they have been used especially when the posterior only approach is used. The posterior pelvic floor is usually reconstructed with a biological or synthetic mesh. The latissimus

dorsi (LD) muscle provides a Mathes and Nahai type V muscle flap. It is most commonly used with its dominant pedicle, the thoracodorsal vessel, but it can also be utilized as a turn-over flap with its minor pedicles in limited cases (Kim et al. 2015). The VRAM flap donor site complication rate is about 25% with a 2–12% abdominal wall hernia rate. (Maricevich et al. 2014, Houdek et al. 2018). A recent meta-analysis demonstrated a pooled complication rate of 37% and 50% for gluteal flap and VRAM reconstructions, respectively (Asaad et al. 2020). Free flap reconstruction is indicated if the VRAM flap is not available due to previous surgery or radiotherapy or when the gluteus muscle or turn-over LD flap does not provide adequate tissue bulk (Miles et al. 2000, Garvey et al. 2011, Kim et al. 2015).

Partial sacrectomy results in more heterogenous defects than total sacrectomy. Garvey et al (2011) have published an algorithm for partial sacrectomy reconstruction. The algorithm factors are the volume of the defect, presence of radiation-induced fibrosis and patency of the local vessels. Small ($<400cm^3$) and medium ($400–2000cm^3$) volume defects are most commonly reconstructed with gluteal flaps when their pedicles are patent. A free flap is indicated if local tissues (due to radiation fibrosis or compromised gluteal vessels) are unavailable. The VRAM flap is not feasible, because of the bulkiness of the flap, for small defects but is useful in large ($>2000cm^3$) volume defect reconstruction. In the case of a frozen abdomen, gluteal, thigh or free flaps are appropriate.

Only a few publications have addressed the timing of the reconstruction. The MD Anderson group have described three-stage total sacrectomy procedures, where the stages are performed in two or three separate surgeries depending on the duration of the operation and homeostasis of the patient. In their protocol, the first stage is the abdominal approach to sacrectomy, harvesting of a VRAM flap and free fibula flap (leaving the fibula flap perfused on the peroneal vessels) and saphenous vein graft harvest. The second stage is performed in the prone position. The sacrectomy and spinopelvic fixation are completed and the VRAM flap is retrieved. The third stage includes completing the harvest of the fibula, osteotomy and anastomosing of the peroneal vessels to the deep inferior epigastric vessels run-off of the VRAM flap. Finally, the VRAM flap is used to close the defect. (Garvey et al. 2013.). Staged sacrectomy has been shown to reduce blood transfusion, length of stay and wund complications (Ramamurthy et al. 2009).

2.3.3 Pelvic exenteration

2.3.3.1 Oncological resection

Pelvic exenteration (PE) is a complex surgical procedure involving partial or total removal of the pelvic organs. PE was first described by Brunschwig in 1948 as a palliative

procedure, but PE is now mainly performed in selected patients with a curative intent (Brunschwig 1948, Brown, Solomon, and Koh 2017).

Total pelvic exenteration (TPE) includes removal of the rectum, genital organs, and bladder. Anterior pelvic exenteration (APE) includes partial or total removal of the vagina, removal of the uterus and bladder. Posterior pelvic exenteration (PPE) includes partial or total removal of the vagina, removal of the uterus and rectum. Types of PE are summarised in Figure 5. Based on the extent of surgical resection, pelvic exenterations are classified as type I (supralevator), type II (infralevator), or type III (infralevator with vulvectomy) (Magrina, Stanhope, and Weaver 1997).
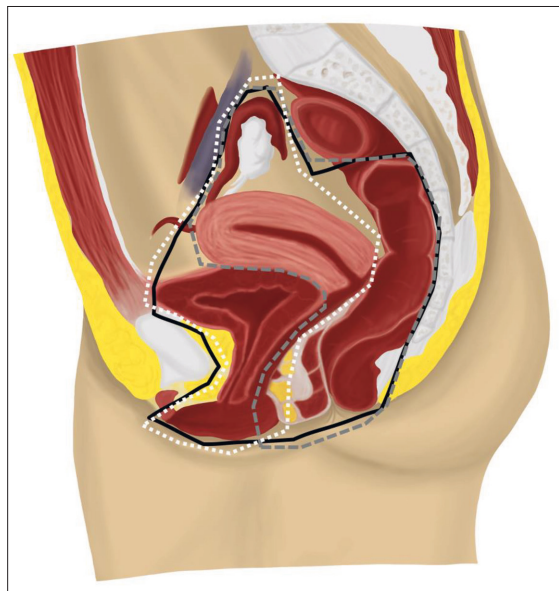
Figure 5. Types of pelvic exenterations.

TPE = total pelvic exenteration (black solid line), PPE = posterior pelvic exenteration (grey dashed line), APE = anterior pelvic exenteration (white dotted line).

PE is generally performed after failed primary therapy (for locally recurrent disease) or in locally advanced stages. Fibrosis following previous radiotherapy or surgery or a locally advanced tumour will result in obliteration of normal anatomical tissue planes. The pelvis can be divided into five arbitrary compartments: central, anterior, posterior and two lateral compartments. Achieving a R0 resection in these conditions requires an extensive and extra-anatomical compartmental surgical approach analogous to sarcoma surgery rather than the conventional colorectal approach whereby natural tissue planes are used within compartments. (Koh et al. 2017.)

PE originally included the resection of the central compartment as it was mainly used for treatment of cervical cancer (Brown, Solomon, and Koh 2017). The first *en bloc* resections that included bony resection were carried out in the late 1960's by Brunschwig (Brunschwig and Barber 1969). Posterior compartment resection including partial or total sacrectomy are currently performed in many units with a 5-year OS being between 24–46% and with a perioperative mortality of <5%. The complication rate remains high, at approximately 75% (Milne et al. 2014, Bosman et al. 2014, Colibaseanu et al. 2014). The anterior margin is usually feasible with normal dissection along the Retzius retropubic space. If the tumour extends anteriorly, pubic bone can be resected along with the genitourinal structures (Solomon, Austin, et al. 2015). A R0 resection can be achieved in up to 76% of patients with this technique (Austin et al. 2016). Lateral sidewall involvement has long been considered a contraindication for PE due to the inability to achieve clear surgical margins (Pawlik, Skibber, and Rodriguez-Bigas 2006). Lateral compartment resection during PE is however nowadays considered feasible. A R0 resection can be obtained in 67% of these patients (Solomon, Brown, et al. 2015). With a radical and compartmental approach together with vascular resection, clear surgical margins can be achieved in approximately 50% of the cases involving the iliac vessels (Austin and Solomon 2009).

Oncological outcome after PE has improved during the last 70 years. For gynaecological malignancies 5-year OS survival is approximately 40% (Westin et al. 2014, Baiocchi et al. 2012). The 5-year OS for rectal cancer is around 30%. Patients who undergo PE for advanced primary cancer have a significantly better 5-year OS, when compared to patients operated on for recurrent cancer. (Platt, Dovell, and Smolarek 2018) Although perioperative mortality has declined over time, morbidity related to PE has remained high, as up to 86% of the patients experience at least one complication. (Matsuo et al. 2019, Platt, Dovell, and Smolarek 2018).

2.3.3.2 Reconstruction after pelvic exenteration

The reconstructive phase after TPE consist four parts:

1) Construction of urinary diversion
2) Performing the colostomy or low rectal anastomosis
3) Securing the pelvic floor to prevent internal organ prolapse
4) Reconstruction of the vagina to allow sexual intercourse

Patients undergoing TPE or APE will need urinary diversion because the bladder is resected *en bloc* with the tumour. In Brunschwig's (1948) original publication, ureters were neo-implanted to the proximal colon as a wet colostomy. For over 70 years, the Bricker's ileal conduit, has been the main method of urinary diversion after PE surgery (Bricker 1950). Continent urinary diversions are associated with similar post-operative morbidity when compared to non-continent diversions, except for a higher incidence of

urinary stone formation (Urh et al. 2013). The majority of PE patients are reconstructed with the lower morbidity non-continent ileal conduit.

Patients undergoing TPE or PPE require either a low rectal anastomosis or a permanent colostomy. Low rectal anastomosis can only be considered in the case of supralevator PE (Ungar and Palfalvi 2006). The risk of anastomotic leakage or fistulas is about 8% and 35% for nonirradiated and irradiated patients, respectively (Angioli et al. 2003). The incidence of colostomy has increased in recent years. Approximately 70% of patients had a colostomy in a population-based study (Matsuo et al. 2019).

Pelvic floor reconstruction is important to prevent fistula formation after PE (Miller et al. 1995). The omental flap was the first flap used to address the empty pelvic syndrome (Valle and Ferraris 1969). The omental flap fills the pelvic cavity and reduces the pelvic infection rate. However, it is not always available and does not necessarily have sufficient volume to fill the defects. Furthermore, it does not offer any structural support either (Miyamoto et al. 2016). Absorbable and non-absorbable mesh as well as other avascular materials have a high incidence of urinary and/or bowel fistulas. Some centers have even abandoned their use because of the high morbidity related to them (Goldberg et al. 2006). An absorbable synthetic mesh together with an omental flap have been used in pelvic floor reconstruction after PE with a low number of post-operative fistulas (Lee et al. 2019). Even breast implants have been used as an obturator in pelvic cavities to prevent herniation and for filling of the dead space (Valle et al. 2011, Carboni et al. 2019).

Primary closure, when compared to the use of myocutaneous flaps, results in twice as much perineal wound complications according to a systematic review and meta-analysis (Devulapalli et al. 2016). The VRAM flap has been used in many units as a workhorse for pelvic floor reconstruction following oncological resections (Goldberg et al. 2006, Nelson and Butler 2009, Horch et al. 2014). Donor site complications or delayed donor site healing after VRAM flap reconstruction ranges from 6% to 15% (Nelson and Butler 2009, Horch et al. 2014). Contralateral component separation has been proposed to facilitate a tension-free fascial closure of the VRAM flap donor site to reduce donor site herniation and other complication rates (Espinosa-de-Los-Monteros et al. 2016). One study demonstrated how the VRAM flap was associated with a lower incidence of major complications, both at the recipient and donor site, than thigh-based flaps. This study included myocutaneous gracilis flaps, anterolateral thigh (ALT) flaps and posterior thigh flaps in the thigh cohort of the study (Nelson and Butler 2009). In a retrospective study from Stein et al, VRAM and gracilis flaps were used to reconstruct the PE defects and the outcomes and complication rates were similar across both groups. When the gracilis flap was used as a muscle only flap, total wound healing time was faster in comparison to the myocutaneous flap (Stein et al. 2019). The myocutaneous gracilis flap is a Mathes and Nahai type II muscle flap. It was originally designed with vertical skin paddle (McCraw et al. 1976, Wheeless et al. 1979, Berek, Hacker, and

Lagasse 1984). Schoeller et al. (2008) first published the transverse myocutaneous gracilis (TMG) flap for microvascular breast reconstruction. They demonstrated that the transverse skin island over the gracilis muscle is reliable and offers up to 30cm of well vascularized skin. The TMG flap has also been shown to be reliable for pelvic floor and vaginal reconstruction following PE (Kaartinen et al. 2015). Other flaps that have been described for pelvic floor reconstruction are the ALT and vastus lateralis flaps (di Summa et al. 2016). The LD free flap has also been described for reconstructing large PE defects (Abdou et al. 2016).

Vaginal reconstruction is indicated after partial vaginal resections or after TPE for patients who request it. The neovagina can be reconstructed concurrently with pelvic floor reconstruction. For total vaginal reconstruction after PE, numerous techniques have been used. The first flap to reconstruct the neovagina was performed with myocutaneous gracilis flaps with a vertical skin island (McCraw et al. 1976). However, the vertical skin island over the gracilis muscle has an unreliable perfusion and a high rate of skin necrosis, up to 38%, was observed in early published series (Copeland et al. 1989, Cain et al. 1989). The TMG flap, in which the skin island is orientated transversely over the gracilis muscle, has overcome these skin perfusion complications and has been successfully used for pelvic floor and vaginal reconstruction after PE (Kaartinen et al. 2015). The omental flap, with skin grafting, has been mostly used in the late 20th century (Berek, Hacker, and Lagasse 1984, Wheeless 1989, Kusiak and Rosenblum 1996). Transposition of a right colon segment to create a neovagina is possible after supralevator PE when the pelvic floor remains intact (Bridoux et al. 2010). The VRAM flap was shown to have a lower complication rate (vaginal stenosis, necrosis, and colon anastomosis leakage) compared to the Singapore flap (Jurado et al. 2009). The Singapore flap is a pudendal thigh fasciocutaneus flap mainly supplied by the posterior labial (scrotal) vessels (Wee and Joseph 1989, Tham et al. 2010). In one study, the deep inferior epigastric perforator (DIEP) flap had a better total flap survival compared to the transverse rectus abdominis myocutaneous (TRAM) flap (100% vs. 62%). The DIEP cohort also had a significantly lower donor site morbidity (0% vs 19%) (Qiu, Jurado, and Hontanilla 2013). In McArdle's (2012) systematic review, about 50% of the patients who underwent vaginal reconstruction were sexually active after surgery.

Cordeiro et al. (2002) proposed a classification system for vaginal defects. Type I defects are partial and are further divided into IA (anterior or lateral wall) and IB (posterior wall). Type II defects are circumferential. Type IIA defects affect the upper two-thirds of the vagina and IIB defects include total vaginal resection. Type IA defects were reconstructed with the Singapore flap and IB defects with the VRAM flap. Type IIA defects were mostly reconstructed with the VRAM flap and in one case with a colon flap. Type IIB defects were reconstructed with bilateral myocutaneous gracilis flaps with vertical skin islands. (Cordeiro, Pusic, and Disa 2002, Pusic and Mehrara 2006.)

2.3.4 Pelvic amputation

2.3.4.1 Indication for amputation in oncological patients

Limb salvage has been the primary aim of management of pelvic sarcomas since the end of the 1970's (Enneking and Dunham 1978, Eilber et al. 1979). The oncological outcome of patients who are treated with pelvic resection instead of pelvic amputation is similar when adequate surgical margins are achieved (Shin, Rougraff, and Simon 1994, Wirbel et al. 2000, Wirbel, Schulte, and Mutschler 2001, Puchner et al. 2017).

The current indication for pelvic amputation is inability to achieve adequate surgical margins or an unusable limb after tumour resection. However, there is no objective definition of an unusable limb. The resection of either the femoral or sciatic nerve alone is not an indication for amputation. The femoral vessels can be reconstructed if resected. (Mavrogenis et al. 2012). The three most vital structures for a well-functioning limb are the sciatic nerve, femoral neurovascular bundle and the hip joint. If two of these are resected, HQA should be considered over limb salvage (O'Connor and Sim 1989). These factors should be evaluated in the preoperative MDT meeting when a surgical approach is planned.

The World Health Organization (WHO) defines palliative care as an approach that neither postpones nor hastens death but instead provides relief from pain and amelioration of other distressing symptoms (WHO 2020). The term palliative surgery is not unequivocally defined in the literature. It can be defined, as in this thesis, as the sole intent to relieve or prevent symptoms. It can also be defined postoperatively in which the primary aim of surgery was curative but failed to do so (McCahill et al. 2002). This definition by outcome and not as intention is problematic as it makes informed consent and patient counselling difficult (Hofmann, Håheim, and Søreide 2005). For carefully selected patients with pathological fractures, a fungating tumour or other severe symptoms, major palliative surgery with amputation has increased their quality of life and decreased pain with a low perioperative mortality (Merimsky et al. 1997, Daigeler et al. 2009).

2.3.4.2 Hip disarticulation

Hip disarticulation was first performed in 1774 by Perault, before the modern anaesthesia era (Kaufman and Wakelin 2004). In elective surgery, the most common indication for hip disarticulation is a malignant tumour (Endean et al. 1991, Wakelin, Oliver, and Kaufman 2004, Yari, Dijkstra, and Geertzen 2008).

In the hip disarticulation procedure, the patient is most commonly placed in the lateral decubital position. A racket type or inguinal skin incision is made and the neurovascular bundle in the femoral triangle is exposed. The femoral vessels are ligated and the femoral nerve divided. The adductor, psoas and gracilis muscles are all

divided at their insertion. The hamstring and gluteal muscles are divided and the joint is opened, the round ligament divided and the extremity is removed (Wakelin, Oliver, and Kaufman 2004). The wound is closed most commonly with a posterior flap to fill the acetabulum. For posterior tumours, the gluteal muscles can be resected along with the leg. In cases of a large resection of the buttock region either an anterior/medial flap or free flap can be used to cover the wound (Jain et al. 2005, Roulet et al. 2019).

The outcome after hip disarticulation for sarcoma remains poor. The 5-year OS is less than 30% and none of the patients with synchronous metastasis survived over 12 months (Jain et al. 2005).

2.3.4.3   Hindquarter amputation

In spite of advanced oncological treatments, limb salvage for patients with pelvic tumours is not always possible. However, hindquarter amputation (HQA) still has a role in orthopaedic oncology. HQA (or hemipelvectomy) implies the removal of one side of hemipelvis along with the lower extremity.

HQA was first attempted by Billroth in 1889, but the patient died within a few hours after operation. The procedure was first successfully performed by Girard in 1895 (Werne 1953). The most common indication for hindquarter amputation was originally, as well as recently, a malignant tumour around the pelvis and proximal thigh (Yari, Dijkstra, and Geertzen 2008).

Surgical resection is determined by the histology of the tumour and location of the lesion. Reconstruction is dictated by the resection and the remaining structures. The procedure requires a multidisciplinary team approach and the patient and family should undergo thorough preoperative counselling to discuss morbidity and mortality, as well as the extensive rehabilitation process and life expectancy.

Hindquarter amputation causes a high degree of disability. The functional outcome after lower extremity amputation is generally inversely proportional to the level of amputation. Functional outcome after hindquarter amputation is obviously limited. Approximately 40% of the amputees prefer to use an external prosthesis, but the most common reason for not using a prosthesis is that they haven't been offered one (Houdek, Kralovec, and Andrews 2014). Hindquarter amputees perform better in a 400 metre walk, 5 metre walk and a timed up-and-go test with crutches when compared to patients walking with only a prosthesis. There is no difference for stair climb speed between the groups (Houdek et al. 2016). The majority of the amputees use their prosthesis for less than 8 hours a day (Yari, Dijkstra, and Geertzen 2008).

The 5 year OS for all sarcomas, after HQA with a curative intent, is approximately 40% (Grimer et al. 2013, Guder et al. 2015, van Houdt et al. 2018). Large tumour size (>15cm) and age over 65 years have been associated with an inferior OS (van Houdt et al. 2018), but this finding is not consistent (Grimer et al. 2013). Mean OS after amputation for a palliative intent is less than six months (van Houdt et al. 2018).

2.3.4.4 Reconstruction after pelvic amputation

Reconstruction after pelvic amputation requires (Knox et al. 2006):

1) Securing the abdominopelvic wall to prevent organ prolapse
2) Filling the dead space
3) Tension-free wound closure with well-vascularized tissue

The hemipelvectomy musculocutaneous flap is most commonly sufficient to provide adequate tissue to secure the abdominopelvic wall. Less than 2% of the patients required either a biologic or synthetic mesh reconstruction in a large 160 patient retrospective cohort study (Senchenkov et al. 2009).

Tumour extension and resection of the tumour determines the available locoregional tissues available for wound reconstruction. The posterior flap closure is most commonly used for reconstructing the hindquarter amputation defect, accounting for approximately 2/3 of the flaps commonly used (Figure 6). The second most common type of closure is the anterior flap based on the femoral vascular system (Figure 7). Up to 90% of hindquarter defects can be reconstructed with these two standard flaps. (Senchenkov et al. 2008.)

A minority of hindquarter amputation patients require more complex reconstructive surgical procedures. When standard wound closure is not sufficient, the composite pelvic defect can be reconstructed with regional pedicled flaps, pedicled fillet flaps
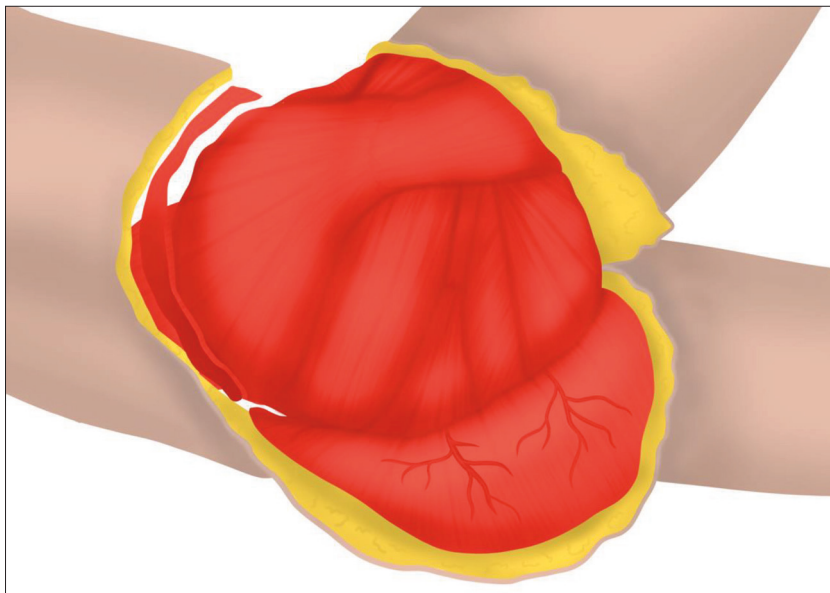
Figure 6. Diagram of the posterior hemipelvectomy flap.
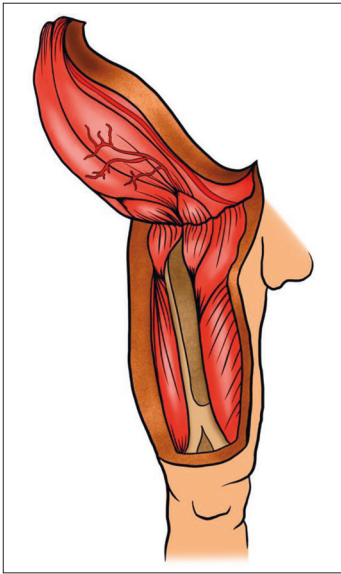
Figure 7. Diagram of the anterior hemipelvectomy flap.

or microvascular free flaps (Ross et al. 1998, Knox et al. 2006, Mat Saad et al. 2012, Kreutz-Rodrigues et al. 2019).

Regional flaps. Several locoregional flaps are available for reconstruction. The VRAM flap based on the inferior epigastric vessels, can be harvested on the ipsilateral or contralateral side. The ipsilateral VRAM flap has an increased risk of vascular compromise as the resection or retraction of the tissues can compromise flap perfusion (Ross et al. 1998). The majority of VRAM flaps are currently used in salvage situations after failed primary closure (Senchenkov et al. 2009). The latissimus dorsi turnover flap can be used for smaller defects on the posterior pelvis (Ross et al. 1998). Limitations of regional flaps include insufficient arc of rotation and insufficient amount of tissue. Potential donor site morbidity has to be considered, as these patients will already suffer from impaired gait and mobility.

Pedicled fillet flaps. Fillet flaps are harvested from the amputated or otherwise sacrificed extremity. The major advantage of the fillet flap is that it can often provide a large amount of well-vascularized tissue, without any donor site morbidity (Kuntscher et al. 2001). The thigh fillet flap includes all or selected femoral muscles and is available when external iliac and femoral vessels can be spared. The total thigh flap is a modification of the anterior flap where both the superficial and deep femoral vessels are utilized to harvest all the thigh muscles and skin (Senchenkov et al. 2009). A fillet flap from the lower extremity can be used for a hindquarter amputation defect reconstruction either as a pedicled or free flap (Kreutz-Rodrigues et al. 2019). Fillet osteocutaneous flaps have also been used to reconstruct the pelvic ring in selected cases. These constitute only single cases or small case series and the effect on mobility, sitting balance or other functional outcomes has not been well documented. The femur, tibia

and fibula bones have all been used for pelvic ring reconstruction (McKnight et al. 2013, Talarczyk et al. 2013, Kreutz-Rodrigues et al. 2019).

Free flaps. Microvascular free flaps offer a means to reconstruct large defects after hindquarter amputation. The flap size and reach are not limited by the availability of locoregional tissue, but the flap can be tailored to cover the defect. Free flaps have been successfully used to cover hindquarter amputation defects. The most commonly used free flaps are the latissimus dorsi, anterolateral thigh and tensor fascia lata flaps (Ross et al. 1998, Samant et al. 2012, Tashiro et al. 2019). Large flaps needed for reconstructing large hindquarter amputation defects will inevitably result in some donor site morbidity (Lakhiani et al. 2016, Lee and Mun 2014). Therefore, the free fillet flap harvested from the amputated extremity, provides a large robust and well-vascularized flap, without any donor site morbidity. Workman (1992) and Yamamoto (1997) were the first authors to describe the free fillet flap to reconstruct the hindquarter amputation defect. Only very limited numbers of these cases have been previously reported. The outcomes of free fillet flap reconstructions are summarized in Table 3.

Table 3. Summary of the studies on free fillet flap to reconstruct hindquarter amputation defect. N/A = not available, FU = follow-up.

Author (year)	Number of patients	Flap survival	Complications	Oncological outcome
Workman (1992)	1	1/1	None	N/A
Yamamoto (1997)	1	1/1	None	Less than 12 months
Ross (1998)	2	2/2	None	N/A
Templeton (2001)	1	1/1	None	N/A
Yamamoto (2003)	2	2/2	None	Less than 12 months
Senchenkov (2009)	1	N/A for free flap patient	N/A for free flap patient	N/A for free flap patient
Boehmler (2010)	1	1/1	Wound dehiscence 1/1	Expired, time N/A
McKnight (2013)	1	1	None	Alive, 12months FU.
Bibbo (2015)	3	3/3	None	3/3, minimum of 2.75 years FU
Roulet (2019)	7	6/7	Reoperation for vascular compromise: 2/7 Infection: 2/7 Wound deschience:0/7 Other: 2/7 None: 1/7	2/7 alive, mean survival 14 months
Kreutz-Rodrigues (2019)	7	7/7	N/A for free flap cohort	N/A for free flap cohort

2.4 Health-Related Quality of Life

Health-related quality of life (HRQoL) has several definitions in the literature (Karimi and Brazier 2016). It is a multidimensional domain that includes physical, mental, emotional and social aspects of a person's life. HRQoL can be measured with several different questionnaires that measure previous aspects of a person's life. Commonly used questionnaires to measure HRQoL are the EuroQol (EQ-5D) (Brooks 1996), Short Form 36 (SF-36) (Ware and Sherbourne 1992) and 15D (Sintonen 2001). Quality of Life for Cancer Survivors (QOL-CS) is a HRQoL tool developed and validated for cancer survivors (Ferrell, Dow, and Grant 1995).

EQ-5D comprises of five different domains: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each of the domains are rated on three levels giving (35) 243 different possible health states (Devlin and Brooks 2017). These dimensions are used to calculate the EQ-5D index, that ranges from 0 to 1 and a higher value meaning better HRQoL. EQ-5D has been validated and is a widely-used instrument for assessing HRQoL in ICU patients (Angus and Carlet 2003, Linko et al. 2010, Nisula et al. 2013). The EQ-5D instrument has been used for evaluating HRQoL in sarcoma patients as well (Davidson et al. 2016, Reichardt et al. 2012). The minimally important difference in EQ-5D index based on performance status ranges between 0.089 and 0.10 in cancer (Pickard, Neary, and Cella 2007, Tsiplova et al. 2016).

After treatment of bone sarcoma, HRQoL measured by SF-36 is reduced when compared to the general population. The physical health domain of the sarcoma survivors was significantly lower than the general population (Holzer et al. 2020). HRQoL measured by QOL-CS showed that patients surviving pelvic osteosarcoma reported similar HRQoL compared to those after lower extremity bone sarcoma (Nagarajan et al. 2004). A prospective study of children and adolescents with bone sarcoma demonstrated that HRQoL as measured by the SF-36 increased until 18 months post operatively. (Bekkering et al. 2012.) A recent systematic review and meta-analysis attempted to evaluate HRQoL after sarcoma surgery, but heterogeneity of the histology, location and treatment strategies made it difficult to detect the trends of HRQoL (Stokke et al. 2015).

Measuring HRQoL of sacrectomy patients is complex and an optimal method is lacking (van Wulfften Palthe, Janssen, et al. 2017). Prospective assessment of HRQoL following treatment for sacral or spinal chordoma and skull base chondrosarcoma showed no significant deterioration within two years of treatment as measured by the Functional Assessment of Cancer Therapy – Brain (FACTBr) questionnaire. However only five of the 17 patients in the latter cohort had sacral chordoma (Baumann et al. 2019). The level of sacrectomy has an effect on HRQoL as measured by the SF-36. Patients who underwent PE and low sacrectomy scored significantly higher scores on both the physical and mental components of the SF-36 compared to patients with PE and high sacrectomy (McCarthy et al. 2019).

In addition to HRQoL assessment, several different functional outcome measures are used to evaluate the functional outcome after sarcoma surgery. The functional outcome measures can be PROM or clinician reported outcome measure (Kask et al. 2019). The most commonly used clinician reported outcome measure is the MSTS score (Enneking et al. 1993) and the most commonly used PROM is the Toronto Extremity Salvage Score (TESS) (Davis et al. 1999).

3   AIMS OF THE STUDY

The aim of this thesis was to evaluate surgical, reconstructive, oncological and PROM outcomes after complex oncological pelvic resections. The secondary aim of the thesis was to develop reconstructive algorithms for patients undergoing sacrectomy, PE and pelvic amputation. The detailed aims of this study were:

1. To evaluate the oncological outcome of pelvic tumours requiring complex pelvic resection and reconstruction (studies I–IV)

2. To examine the surgical outcome and complications after major pelvic resection of malignant tumours (studies I–IV)

3. To study the reconstructive methods after major pelvic resection for malignancy (studies I–IV)

4. To investigate the quality of life after sacrectomy (study I)

4   SUBJECTS AND METHODS

This study was conducted in Tampere University Hospital, Finland (studies I–III) in collaboration with the Royal Orthopaedic Hospital, Birmingham, UK (studies III–IV) and Tours University Hospital, France (study III). The studies were approved by the institutional review boards.

4.1   Patient identification and data collection

4.1.1   Study I

Patients who underwent sacrectomy for primary bone malignancy between January 1st, 2008 and June 30th, 2017 in Tampere University Hospital were identified from the oncological database. All tumours originated in the sacrum. Patients who had sacral resection for tumours originating from another pelvic location (for example extended P1-resection of the pelvis with concomitant sacral resection) were excluded from the study.

Electronic and paper medical records were used to collect the following data: patient demographics, surgical details, tumour histopathology, imaging studies, possible pre- or postoperative chemotherapy, possible pre- or postoperative radiotherapy and complications. EQ-5D scores were obtained from the prospectively maintained intensive care database.

Sacrectomy was classified into total sacrectomy, hemisacrectomy, partial (distal) sacrectomy or extended sacrectomy (Li et al. 2011). Reconstruction was classified into three categories depending on the need and timing of the reconstruction. The no reconstruction (NR) group did not require any soft tissue or bone reconstruction and the wound was closed directly with suction drains. The immediate reconstruction (IR) group underwent immediate soft tissue and/or bone reconstruction after tumour

resection. The delayed reconstruction (DR) group underwent tumour resection, temporary wound closure with a negative-pressure wound therapy (NPWT) system and was followed by a recovery period and planned second stage soft tissue and/or bone reconstruction after seven days. The decision to reconstruct immediately or in delayed manner was made according to the following algorithm: patients undergoing total sacrectomy or partial sacrectomy requiring a free flap were reconstructed in a delayed manner and all others were reconstructed immediately.

4.1.2   Study II

Patients who underwent PE for a gynaecological indication between January 1st, 2005 and December 31st, 2016 in Tampere University Hospital were identified from medical records and an electronic surgical database.

The following data were collected retrospectively from the electronic and paper medical records: patient demographics, comorbidities, surgical details, histopathological results, possible pre- or postoperative radiotherapy, possible pre- or postoperative chemotherapy and complications. Complications were classified according to the Clavien-Dindo classification (Dindo, Demartines, and Clavien 2004) and recorded from the date of the PE until the end of the follow-up period. Complications were divided into mild or severe (Clavien-Dindo 3b or higher) for the statistical analysis. Details on complications, local recurrence or metastasis were collected from the medical records. The date of death was identified from the national registry (The Finnish Population Information System).

4.1.3   Study III

Patients undergoing pelvic amputation for an oncological indication and requiring a concomitant free flap reconstruction were identified from the oncological database and electronic surgical database in Tampere University Hospital and the Royal Orthopaedic Hospital, Birmingham, UK between January 1st, 2012 and December 31st, 2018. Patients operated between May 1st, 2018 and December 31st, 2018 in Tours University Hospital, Tours, France were also included in the study.

Data was collected in each institution from electronic medical records and included patient demographics, tumour histology, imaging studies, surgical details and postoperative complications. The complications were collected until the date of last contact.

4.1.4   Study IV

Patients who required hindquarter amputation to treat pelvic sarcoma in the Royal Orthopaedic Hospital, Birmingham, UK, between January 1st, 1996 and August 31st, 2018 were identified from the oncological database. Six patients, who were reconstructed with a free fillet flap in Birmingham, were included into both studies III and IV.

The following data was collected from a prospectively maintained institution's oncological database and pathology database: Patient demographics, surgical details, postoperative complications, radiotherapy, chemotherapy and histology of the tumour, including grade and closest margin, date and the status of the last follow-up visit.

4.2   Multidisciplinary planning and pre-operative examinations

All sarcoma patients (studies I, III, IV) were reviewed in a sarcoma MDT meeting in a tertiary sarcoma unit. All patients underwent pelvic MRI and whole-body CT for staging prior to the meeting. The MDT included at least the following specialists: orthopaedic oncologist, radiologist, medical oncologist, pathologist and plastic surgeon. The decision and the extent of the surgical procedure was based on the histology and staging of the disease and it was further discussed with the patient. After discussion and patient consent, the final plan of the surgical resection and reconstruction was made.

All PE patients (study II) were staged with pelvic MRI and whole-body PET-CT before the operative planning. PE patients were clinically evaluated together with a gynaecologic oncologist, gastroenterological surgeon, urologist and plastic surgeon prior to the operation. All patients planned for TPE were offered vaginal reconstruction and were further counselled by a specialized nurse.

4.3   Surgical technique

4.3.1   Sacrectomy

Resection for partial sacrectomy is performed solely through a posterior approach, when unilateral or bilateral S3 nerve roots are preserved. The anterior aspect of the sacrum is mobilised with blunt dissection after posterior exposure of the sacrum. Resection of bilateral S3 nerve roots results in sphincter incontinence and this causes post-operative faecal contamination of the wound. Therefore, either temporary or permanent colostomy is favoured. In this case, a combined anterior-posterior approach was used for tumour resection and colostomy. This approach commenced with a laparotomy in a supine position to mobilise the sigmoid colon anteriorly, whilst leaving the posterior part of the colon untouched and lying on the sacrum. Temporal colostomy is performed

by leaving the dissected distal sigmoid colon and rectum in place. After anterior tumour dissection, vascular mobilisation and creation of a colostomy, the patient is turned to the prone or Mecca position. The procedure then continued from the posterior approach. Dissecting down to the deep musculature, an osteotomy was performed through the sacrum and the tumour removed *en bloc* with the sigmoid colon and anal canal.

When sacrectomy results in spinopelvic discontinuity, a spinopelvic fixation is performed by a spine surgeon in collaboration with an orthopaedic oncologist. A plastic surgeon is responsible for soft tissue coverage and possible vascularised bone reconstruction. The soft tissue reconstruction is planned depending on the defect size, available local tissue, and local vessel patency. A medium-sized defect is planned to be reconstructed usually with regional gluteal muscle or fasciocutaneous flaps. The pelvic floor and posterior abdominal wall are reconstructed using either autologous tissue or a synthetic mesh. For planned delayed reconstruction, the skin is closed directly when possible, accepting a dead space that is temporarily drained with large suction drains. In case of skin defect that cannot be directly closed, a negative-pressure wound therapy (NPWT) sponge is applied to cover the wound and possible fixation material.

4.3.2   Pelvic exenteration

Colostomy and possible uretero-ileo-cutaneostomy locations, as well as TMG flap landmarks, are marked preoperatively by a specialised nurse and plastic surgeon, respectively. The PE is performed in the dorsal lithotomy position. The pelvis is approached by a midline laparotomy incision. At the beginning of the laparotomy, the entire abdomen and pelvis are carefully examined for any evidence of metastatic or intraperitoneal cancer, and the lower para-aortic lymph nodes are sampled for frozen section analysis. If these are negative, a bilateral pelvic lymphadenectomy is performed, and an immediate frozen section analysis is performed to determine whether the operation should continue. Distant metastasis and peritoneal masses are contraindications, but para-aortic nodal involvement as a contraindication is more controversial (Kaur et al. 2014). The size and the extent of the tumour determine the type of the PE (APE, PPE, TPE) as well as the extent of the pelvic floor resection (type I, II, or III). The aim is always for clear surgical margins (R0 resection).

After tumour resection, the reconstructive team starts with the flap harvest, whilst the oncology team performs the urinary diversion. Our TMG flap harvest technique for pelvic floor and vagina reconstruction has been described in detail previously (Kaartinen et al. 2015). For unilateral reconstruction, a skin paddle width measuring 8cm to 10cm lying transverse to the gracilis muscle belly is harvested. The gracilis muscle is divided distally near the knee joint. Bilateral TMG flaps are used when the vagina is to be reconstructed as well as in cases with an extended perineal skin resection. In these cases, a skin island measuring 8–7cm by 20cm is most commonly sufficient. Flap

harvesting begins with the distal skin incision that is continued down to the muscular fascia. The fascia is opened over the gracilis muscle and the muscle is dissected distally to near the knee joint. The vascular pedicle and motor nerve are identified under the adductor muscle. The motor nerve is divided. The vascular pedicle is dissected all the way to the deep medial circumflex vessels and all side branches are divided. The rest of the skin paddle and distal muscle insertion are incised to finalize the flap harvest. The flap is tunnelled subcutaneously under the labia, and then the flap(s) is pulled through. The posterior and anterior parts of the skin island are de-epithelialized, and a neovagina is formed by suturing the skin paddles together, starting from the ventral portion of the neovagina. The flap is secured by suturing the de-epithelialised skin to Cooper's ligaments and the distal portion of the muscles are sutured posteriorly to the pelvic floor through the laparotomy wound in order to fill the dead space and also secure the pelvic floor to prevent bowel herniation. Donor sites are closed directly with a suction drain.

4.3.3   Pelvic amputation

All procedures were performed by specialist orthopaedic oncologists simultaneously whilst the soft tissue reconstruction in the case of free tissue transfer was performed by a team of plastic surgeons with advanced training in sarcoma surgery. The procedures for pelvic amputation depend on tumour involvement and resectability. Depending on the location of the tumour, an anterior or posterior flap is chosen. Massive pelvic resection may result in such a large defect of soft tissue that closure with a local flap is impossible and a free fillet flap from the amputated extremity is necessary.

Posterior flap HQA begins with an ilioinguinal incision and is continued through the abdominal wall into the retroperitoneal space. The iliac vessels are identified as well as all of the visceral organs. The incision is continued along the inferior pubic ramus and the ischiorectal space is explored. The posterior flap is raised and the dissection is continued up to the sacroiliac joint. The limb is abducted and the pelvic floor musculature is divided. Finally, a medial osteotomy is performed to the iliac wing, sacroiliac joint or to the sacrum depending on the extent of the tumour.

For anterior flap HQA, a posterior incision is made and the iliac crest and sacrum are exposed. The incision is continued down to the perianal region and the gluteus muscles are divided. The anterior flap is raised and the superficial femoral vessels are ligated distally. The profunda branch is ligated and the pubic symphysis is exposed. The limb is then flexed and abducted and the pelvic floor muscles are divided. A medial osteotomy is carried out at the level dictated by the tumour extension and then the hemipelvis and limb are removed.

The HQA and free fillet flap reconstruction were performed with a similar technique in all study institutions. The HQA and free fillet flap procedure involves two phases.

In the first phase, the patient is positioned in a floppy lateral or semisupine position, which allows the limb and torso to be rolled both backward and forward to allow circumferential access to the hemipelvis and lower limb. The patient is draped with the limb exposed down to the ankle, and the abdomen up to the midline. Posteriorly, the drapes are placed to allow exposure of the sacrum across the midline but covering the anal margin. In the majority of cases, the incision for the HQA adopts an extended utilitarian exposure extending posteriorly to the midline sacral structures and extending around the perineum to join the anterior limb of the incision, thereby resecting the hemipelvis with the buttock flap in continuity.

In contrast to the conventional HQA or hip disarticulation, the vessels are mobilised proximal to the tumour but not ligated at this stage to minimise the ischaemic time for the flap. Once circumferentially dissected, the osteotomies can be performed at the predesignated level but maintaining the continuity of the vessels.

The second phase of the procedure comprises the harvest of the fillet flap. In many cases, this can proceed in tandem with the tumour dissection. The two-team approach requires close co-operation between the orthopaedic team and reconstructive team to minimize the ischemia time and to optimize the surgical flow. Banking of the fillet flap is a salvage option in case of need of early ligation of the iliac vessels due to a bleeding problem or complicated resection. For the harvest of the flap, the popliteal vessels are exposed together with 1–2 superficial veins. Popliteal vessels should always be dissected above the sural vessels to ensure adequate circulation to gastrocnemii muscles and posterior calf skin. Anteriorly, an incision is made over the proximal tibial joint line and both the tibia and fibula are dissected subperiosteally free from the surrounding soft tissues. Distally, the flap is then elevated from the distal tibial joint line at the level of the ankle. Having elevated the flap in its entirety, the popliteal vessels can be divided and flushed locally with heparin solution. Simultaneous intravenous 5000IU heparin is administered prior to iliac vessel ligation. At the same time, the HQA is completed by dividing the iliac vessels proximal to the resection margin. The limb can then be removed in its entirety.

The harvested flap is now placed over the HQA defect and orientated to give the best coverage. The popliteal vessels of the flap are anastomosed most commonly end-to-end to the stump of the iliac vessels using 7-0 vascular sutures. There is always a mismatch between the iliac and popliteal vessels, but this can be managed by taking a small side wedge out from the larger vessel. Having restored the arterial and venous circulation, the flap can then be inset and sutured, over large suction or Penrose drains.

All patients recovered in an intensive care unit to allow careful monitoring of blood pressure and fluid balance as well as regular flap observations looking in particular for any evidence of venous congestion or ischaemic failure. The fillet flap is large and heavy, and the positioning of the patient and the flap needs to be closely monitored within the

first few post-operative days. The patient is allowed to be in a supine or lateral position for the first few postoperative days.

4.4   Health-related quality of life measures

The EQ-5D instrument was used in study I to measure pre- and postoperative HRQoL of the sacrectomy patients who were admitted to the intensive care unit (ICU) postoperatively. Pre-operative data was obtained upon ICU admission. For patients admitted between January 1st 2008 and December 31st 2010 a post-operative questionnaire was sent six months after ICU admission and for patients admitted from January 1st 2011 or later, post-operative data was obtained 12 months after admission.

4.5   Statistical methods

Median values and ranges were calculated for continuous variables. The statistical significance of continuous variables between two groups were tested using the Mann-Whitney U-test (studies I, III, IV) or an independent sample t-test (study II), and between three groups using the Kruskal-Wallis tests (study I). Categorial variables were tested by using the chi-squared test (studies I–IV). Pre-operative and post-operative EQ-5D scores were tested using the Wilcoxon signed rank test (study I).

Kaplan-Meier curves were constructed to assess patient survival (studies I–IV). Statistical significance between the groups was determined using a log-rank test (studies II and IV). Cox regression analysis was used to identify independent factors affecting survival in univariate and multivariate models (studies II and IV). OS was measured from the date of surgery to the date of death or date of last follow-up (studies I–IV). The disease-free survival (DFS) was measured from the date of the surgery until local recurrence or death (study II). Local recurrence-free survival (LRFS) was measured from the date of surgery to the date of local recurrence, date of death or date of last follow-up (studies III, IV). Metastasis-free survival (MFS) was measured from the date of surgery to the recorded date of the development of metastases, date of death or date of last follow-up (study III).

All statistical analyses were performed by using the SPSS software package (IBM SPSS Statistics, Version 24.0. Armonk, NY).

5   RESULTS

5.1   Patient demographics and indications

Patient demographics of all the studies are presented in Table 4.

Table 4. Patient demographics of the studies.

	Study I	Study II	Study III	Study IV
Number of patients	21	39	12*	136*
Female : Male	9 : 12	39 : 0	3 : 9	56 : 80
Age; mean(range)	57(22–81)	59(30–78)	54(12–76)	51(12–83)

*Six patients were included to both study III and IV.

5.1.1   Sacrectomy (Study I)

A total of 21 patients with a mean age of 57 years were included in study I. Indications for sacrectomy were chordoma (n=15), chondrosarcoma (n=4) and high-grade dedifferentiated sarcoma (n=2). The mean follow-up was 38 (range 0–108) months.

Two patients (9.5%) had pre-operative radiotherapy and three patients (14%) had post-operative radiotherapy.

All patients were operated on with a curative intent.

5.1.2   Pelvic exenteration (Study II)

In study II, 38 women underwent a total of 39 exenteration operations. One patient underwent first APE and then, two years later, underwent PPE after local recurrence. The mean patient age was 59 years. Adenocarcinoma was the most common histology (51%),

followed by spinocellular carcinoma (31%), melanoma (13%) and cystadenocarcinoma (5.1%). Location of the tumours is presented in Table 5. The mean follow-up was 35 (range 2.5–123) months.

Table 5. Primary location of the tumour in pelvic exenteration patients.

Location	n	%
Cervix	12	31
Vagina	7	18
Vulva	6	15
Uterus	5	13
Rectum	5	13
Ovary	3	7.7
Urethra	1	2.6

The majority of the patients, 24 (62%), had PE as a secondary salvage procedure after previously failed primary therapy. 15 (39%) patients had PE as a primary surgical procedure for locally advanced tumours. 29 (74%) patients had pre-operative radiotherapy, and 1 (2.6%) patient had post-operative radiotherapy.

All patients were operated on with a curative intent.

5.1.3   Pelvic amputation (Studies III & IV)

The pelvic amputation study population comprised of two cohorts. The first cohort (study III) consisted of 12 patients who underwent HQA and required a free fillet flap reconstruction for wound coverage. The mean age of the patients was 54 years and the mean follow-up time was 16 months (range 0–51). The second cohort (study IV) was composed of 136 patients who underwent HQA amputation during the study period. The mean follow-up time was 38 months (range 0–210), with a minimum of 12 months follow-up for survivors. The histology of the tumours is presented in Table 6.

Table 6. Histology of the tumours in patients who underwent pelvic amputation.
UPS = Undifferentiated pleomorphic sarcoma, MPNST = Malignant peripheral nerve sheet tumour.

	Study III		Study IV	
	n	%	n	%
Chondrosarcoma	4	25	56	41
Osteosarcoma	4	25	28	21
Ewing's sarcoma			2	1.5
Parosteal osteosarcoma			1	0.7
Periosteal osteosarcoma			1	0.7
UPS			23	17
Leiomyosarcoma	1	8.3	6	4.4
Myxoid liposarcoma			4	2.9
Synovial sarcoma			4	2.9
MPNST			3	2.2
Angiosarcoma	1	8.3	2	1.5
Triton tumour			2	1.5
Fibrosarcoma			2	1.5
Extraskeletal chondrosarcoma			1	0.7
Liposarcoma	1	8.3	1	0.7
Spindle cell sarcoma	1	8.3		

In study III, 8 patients underwent amputation as the primary surgical procedure and 4 were salvage surgeries for the treatment of recurrent disease following a previous pelvic resection or following an intralesional resection at another institution. In study IV, 83 patients (61%) underwent HQA as a primary surgical procedure, whilst 53 patients (39%) underwent HQA as a secondary salvage surgery following tumour recurrence or intralesional surgery.

All 12 patients were operated on with a curative intent in study III. In study IV, 128 patients (94%) were operated on with a curative intent and 6 patients (4.4%) were operated on with a palliative intent. The initial treatment intent was not documented in two patients.

5.2 Oncological outcome

The 1-, 3- and 5-year OS for the studies are presented in Table 7.

Table 7. Overall survival at 1-, 3- and 5 years (95%CI).
STS = soft tissue sarcoma. OS = overall survival. N/A = not available.

	1-year OS (95%CI) %	3-year OS (95%CI) %	5-year OS (95%CI) %
Study I	83 (66–100)%	83 (66-100)%	83 (66-100)%
Study II	72 (58–86)%	51 (35-68)%	48 (31-65)%
Study III	58 (26–92)%	58 (26-92)%	N/A
Study IV – bone – STS	 72 (62–81)% 62 (32–63)%	 53 (42–64)% 28 (12–43)%	 47 (36–59)% 24(9–39)%

5.2.1 Sacrectomy (Study I)

Seventeen patients (81%) had a R0 resection and four (19%) had a R1 resection. Patients who had a R0 resection consisted of two with a S3/4 resection, one with a hemisacrectomy, and one with an extended sacrectomy.

The OS was 83% at 1-year and remained the same at 5-years (Figure 8). Three patients died due to disease progression and one patient had a fatal post-operative intracranial haemorrhage on the first post-operative day.
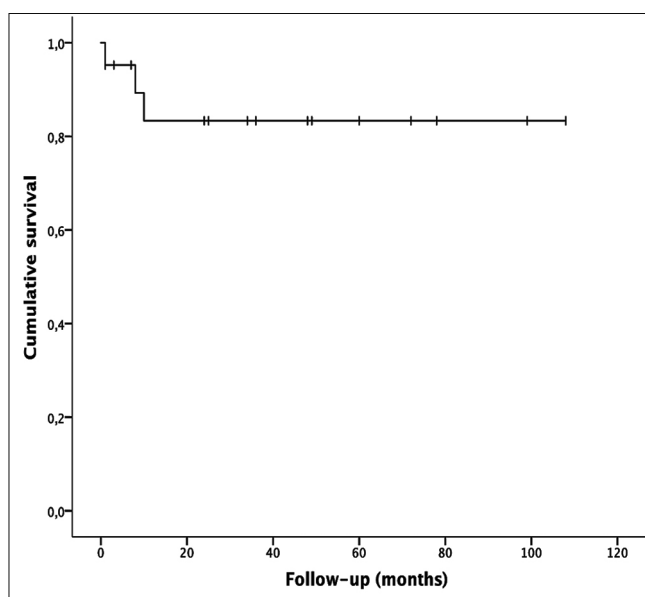
Figure 8. Overall survival of the sacrectomy patients.

Four patients (19%) had a LR; two patients with a primary R0 resection and two patients with a R1 resection. The mean time to LR was 23 (range 5–48) months. Three of the LRs occurred in chordoma and one in high grade dedifferentiated sarcoma. All of the LRs occurred in soft tissue and no bony recurrences were noted.

5.2.2   Pelvic exenteration (Study II)

The 1- and 5-year OS of all PE patients was 72% (95%CI 58–86) and 48% (95%CI 31–65), respectively (Figure 4). The 1- and 5-year DFS for all patients was 58% (95%CI 43–74) and 45% (95%CI 28–68), respectively (Figure 9). The 1-year OS of patients with a R2 resection (n=3) was 33% (range, 10–15 months).
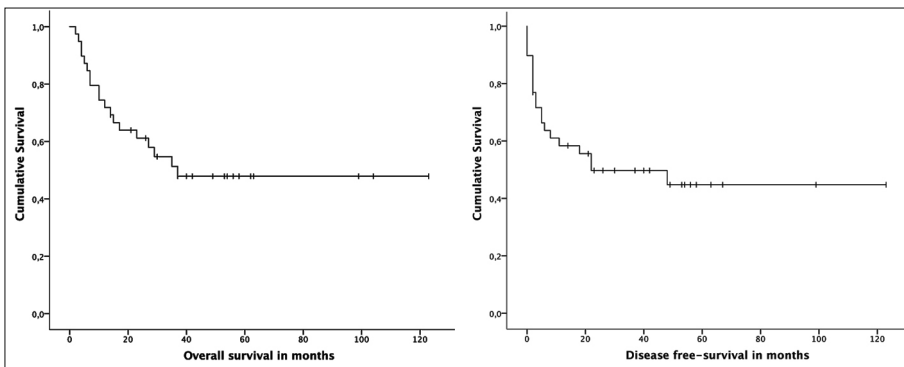
Figure 9. Overall survival and disease-free survival after pelvic exenteration.

OS was affected in univariate analysis by a BMI of over 30 (p=0.028), lymph node metastasis (p=0.048), and positive surgical margins (p=0.001) (Table 8). In multivariate analysis, only positive surgical margins (p=0.009) and lymph node metastasis (p=0.027) influenced OS (Table 9). The mean OS for patients with negative surgical margins was 84 months (95%CI 64–105 months) and 17 months (95%CI 7.8–27 months) for patients with positive surgical margins (p<0.001) (Figure x). The mean OS was 20 months (95%CI 12–29 months) for patients with lymph node metastasis and 77 months (95%CI 58–97 months) for patients without lymph node metastasis (p=0.039) (Figure 10).

Table 8. Factors affecting overall survival in univariate model using Cox proportional hazards model.

Factor	HR	95% CI	p-value
Lymph node metastasis	2.6	1.007–6.900	0.048
BMI over 30	2.9	1.120–7.363	0.028
Positive surgical margin	4.6	1.806–1.480	0.001

Table 9. Factors affecting overall survival in multivariate model.

Factor	HR	95% CI	p-value
Lymph node metastasis	3.1	1.133–8.318	0.027
Positive surgical margin	3.9	1.402–11.006	0.009
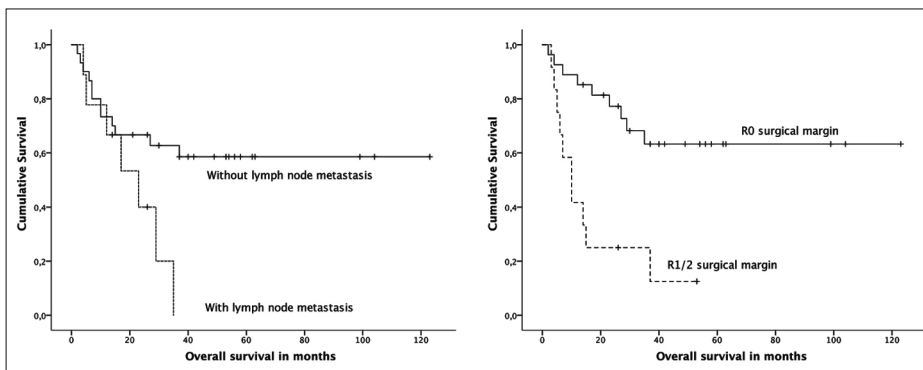
Figure 10. Overall survival with or without lymph node metastasis at time of the pelvic exenteration surgery and with R0 or R1/2 resection margin.

5.2.3   Pelvic amputation (Studies III & IV)

The OS for patients who were reconstructed with a free fillet flap in study III was 58% (95% CI 26–92) both at 1-year and 3-years. The median tumour volume in the free flap cohort was 6442 cm^3.

In study IV, the mean OS was 91 months (95%CI 64–117) for patients undergoing HQA for a primary sarcoma of bone with primary curative surgery, in comparison to 90 months (95%CI 58–123) in patients undergoing secondary salvage surgery (p=0.727). The tumour volume for the primary and salvage groups was 3748 cm^3 and 1519 cm^3, respectively (p<0.001). The mean OS was 59 months (95%CI 31–89) for patients undergoing HQA as treatment for STS with a primary curative intent, which compared to 13 months (95%CI 9.4–16) for patients undergoing secondary salvage surgery (p=0.038). The tumour volume for primary and salvage groups was 3 318 cm^3 and 2 227 cm^3, respectively (p=0.162). The 1-, 3- and 5-year OS is presented in Tables

7 and 10. In the multivariate analysis, the factors associated with a poor prognosis for overall survival included HQA as a treatment for STS (HR 1.7; 95%CI 1.027–2.660, p=0.039) and high grade histological subtypes, including both bone and soft tissue (HR 2.0; 95%CI 1.127–3.676, p=0.018). The 30-day mortality for patients undergoing surgery with a curative intent was 0.8%.

The OS of the patients in studies III and IV are presented in Figure 11.

Table 10. 1-, 3- and 5-year overall survival in study IV.
Log-rank test was used for mean survival time (p-value). CS = Chondrosarcoma, UPS = undifferentiated pleomorphic sarcoma, STS = soft-tissue sarcoma, gr = grade.

	1-year OS (95%CI) %	3-year OS (95%CI) %	5-year OS (95%CI) %	p-value
Tumour location				
– bone	72 (62–81)%	53 (42–64)%	47 (36–59)%	
– STS	62 (32–63)%	28 (12–43)%	24 (9.1–39)%	0.008
Histology				
– CS	78 (67–90)%	64 (50–78)%	58 (43–73)%	
– Osteosarcoma	64 (46–83)%	37 (18–55)%	32 (14–51)%	0.017 vs CS
– UPS	67 (46–87)%	42 (16–67)%	31 (4.9–58)%	0.100 vs CS
– Other	56 (37–76)%	20 (4.5–36)%	20 (4.5–36)%	<0.001 vs CS
Grade				
– 1	100%	100%	100%	0.010 vs gr. 3
– 2	95 (85–100)%	66 (44–88)%	52 (27–77)%	0.018 vs. gr 3
– 3	60 (51–70)%	38 (27–49)%	35 (24–45)%	
Closest margin				
– >1mm	79 (70–89)%	49 (36–62)%	46 (33–59)%	
– ≤1mm	56 (43–69)%	41 (28–55)%	34 (21–47)%	0.017
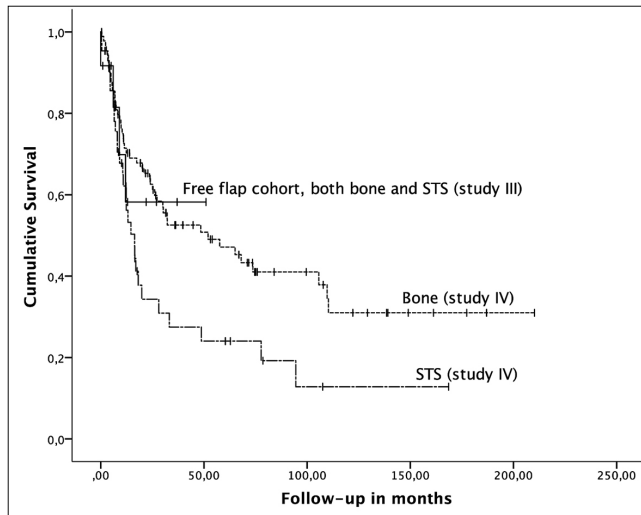
Figure 11. Overall survival after hindquarter amputation in studies III–IV. STS = soft tissue sarcoma.

The incidence of LR in patients undergoing HQA as treatment for bone sarcomas was 13% (95%CI 5.6–20) and in those undergoing HQA as treatment for STS it was 16% (95%CI 3.9–27). LRFS was 97% (95% CI 93–100) at 1-year and 62% (48–75) at 5-years for bone sarcoma patients, and 88% (77–98) at 1-year and 43% (19–67) at 5-years for STS patients (p=0.216). LRFS was not affected by any of the variables investigated, including tumour grade, margin or tumour volume. LRFS for patients reconstructed with a free fillet flap in study III was 86% (95%CI 60–100) at 1-year and 3-years. MFS was 73% (95% CI 46–99) at 1-year and 3-years. All recurrences and metastases occurred within 12 months from the amputation.

Six patients were operated on with purely a palliative intent. Three patients underwent HQA for treatment of a bone sarcoma and three patients for treatment of a STS. The median tumour volume was 5600 cm^3, which was significantly larger when compared to patients undergoing HQA with a curative intent (2830 cm^3) (p=0.019). The margins achieved at HQA were significantly smaller (p=0.020) and four patients had intralesional resections. The median OS was 2.4 months (95%CI 0.0–6.1) and two out of six patients died whilst still in hospital, within two weeks of surgery.

5.3   Surgical outcome

Surgical outcomes of studies I-IV are summarised in Table 11.

Table 11. Mean (range) tumour size, length of stay and time in intensive care unit, surgical time and blood loss of the studies.
ICU = intensive care unit. N/A = not available. *In study I the size is measured as the resection specimen and in studies III-IV the maximum size the tumour.

	Study I	Study II	Study III	Study IV
Mean of the maximum diameter of the tumour, cm*	17 (11–28)	N/A	24 (12–49)	16 (5–49)
Length of stay, days	16 (3–60)	20 (7–66)	18 (10–42)	N/A
Time in ICU, days	2.0 (0–15)	N/A	3.0 (1.0–8)	N/A
Surgical time in minutes (range) – **1st operation** – **2nd operation**	451 (95–940) 387 (289–498)	411 (298–514) –	440 (249–650) –	N/A
Blood loss, ml	2450 (100–10 000)	N/A	2400 (950–10000)	N/A

5.3.1   Sacrectomy (Study I)

Five (24%) of the sacrectomy patients did not require any soft tissue or bone reconstruction and were classified as 'no reconstruction' (NR) group. 11 patients (52%) were reconstructed immediately and 5 patients (24%) underwent planned delayed

reconstruction. Resection size, length of hospital stay, surgical time, and peri-operative blood loss differed significantly between the reconstruction groups (Table 12).

Table 12. Surgical outcomes in different reconstruction groups of sacrectomy patients.
Data are presented as mean (SD) unless otherwise noted. * Kruskal-Wallis and chi-squared tests as appropriate. ** Four values were missing from the analysis.

	No reconstruction (n=5)	Immediate reconstruction (n=11)	Delayed reconstruction (n=5)	p-value*
Tumour volume, cm^3**	347 (88)	1 252 (688)	2 274 (2321)	0.007
Hospital stay, days	16 (13)	16 (11)	36 (19)	0.055
– ICU stay, days	0 (0)	1.6 (1.9)	5.0 (6.1)	0.006
Surgical time (minutes) – Resection (and reconstruction) – Delayed reconstruction	149 (48) -	488 (181) -	671 (107) 387 (82)	0.001
Blood loss (ml)	450 (320)	3 400 (2600)	4 600 (1600)	0.004
Number of unplanned re-operations	3	7	6	0.397

5.3.2 Pelvic exenteration (Study II)

Of the PE patients, 26 patients (67%) underwent TPE, 11 patients (28%) underwent PPE, and 2 patients (5.1%) underwent APE. The mean surgical time was 428±56 minutes for TPE and 374±49 minutes for combined APE and PPE (p=0.032). The mean length of stay was 23 days for the TPE group and 16 days for the combined PPE and APE groups (p=0.024). The length of stay was 16±5.9 days for patients without severe complications and 29±15 days for patients with severe complications (p=0.001).

5.3.3 Pelvic amputation (Studies III & IV)

The mean surgical time, blood loss and lengths of ICU and hospital stay are summarised in Table 12 for the free flap cohort of study III. This data was not available for study IV patients.

In study III, the level of proximal resection was through the sacrum in 6 patients, through the SI-joint in 5 patients and through the hip joint in 1 patient. Comparing those who underwent an extended hindquarter amputation (amputation through the sacrum) to those who underwent either a standard hindquarter amputation or hip disarticulation, no significant differences in resection margin, surgical time, length of hospital / ICU stay or blood loss were noted . The mean tumour size and volume were 24 cm (range 12–49cm) and 9 413 cm^3 (range 1 071–39 690cm^3).

For study IV, 92 patients (68%) and 40 patients (29%) underwent standard and extended HQA amputation, respectively. The data regarding extent of the HQA was missing for 4 of the patients. The mean maximum tumour diameter and volume were 16cm (range 5–49cm) and 2 944cm^3 (range 100–39 700cm^3), respectively.

5.4 Reconstruction after pelvic resections

5.4.1 Sacrectomy (Study I)

All of the patients in the NR group had a partial sacrectomy distal to the S3/4 level. Patients whose sacrectomies were distal to the S1/2 level or who underwent less extensive hemisacrectomies, were reconstructed immediately. Nine of the 11 patients in the IR group had only a soft tissue reconstruction and two had a spinopelvic fixation and soft tissue reconstruction (Figure 12). All extended, total sacrectomies, and hemisacrectomies demanding microvascular tissue transfer were reconstructed in two stages (Figures 13 and 14). For all patients in the DR group, secondary reconstruction was planned for within a week of the resection. This occurred in four patients, but one patient had a postponed reconstruction 14 days after the primary surgery due to a complicated ICU period. The reconstructive algorithm is shown in Figure 15.
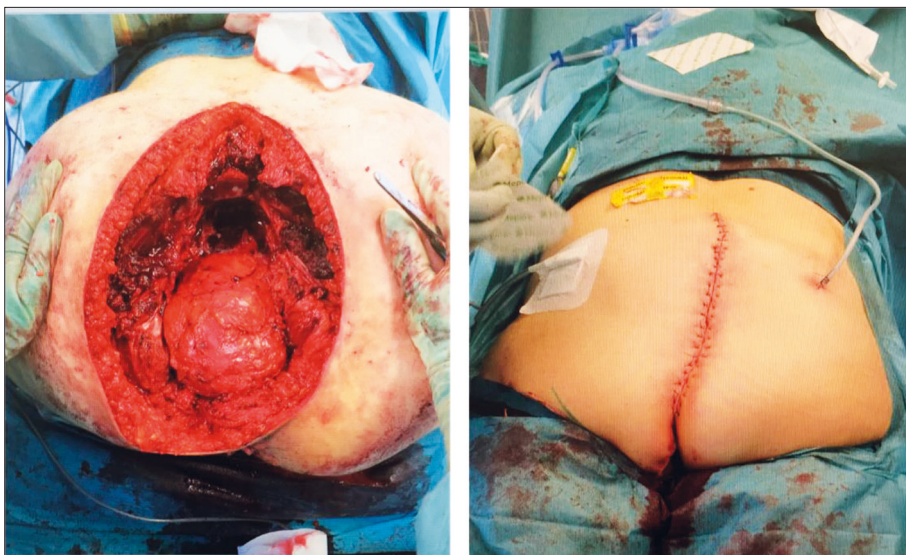
Figure 12. Sacrectomy defect (on left) before mesh and bilateral gluteal muscle reconstruction. The skin was closed directly over muscle flaps (on right).
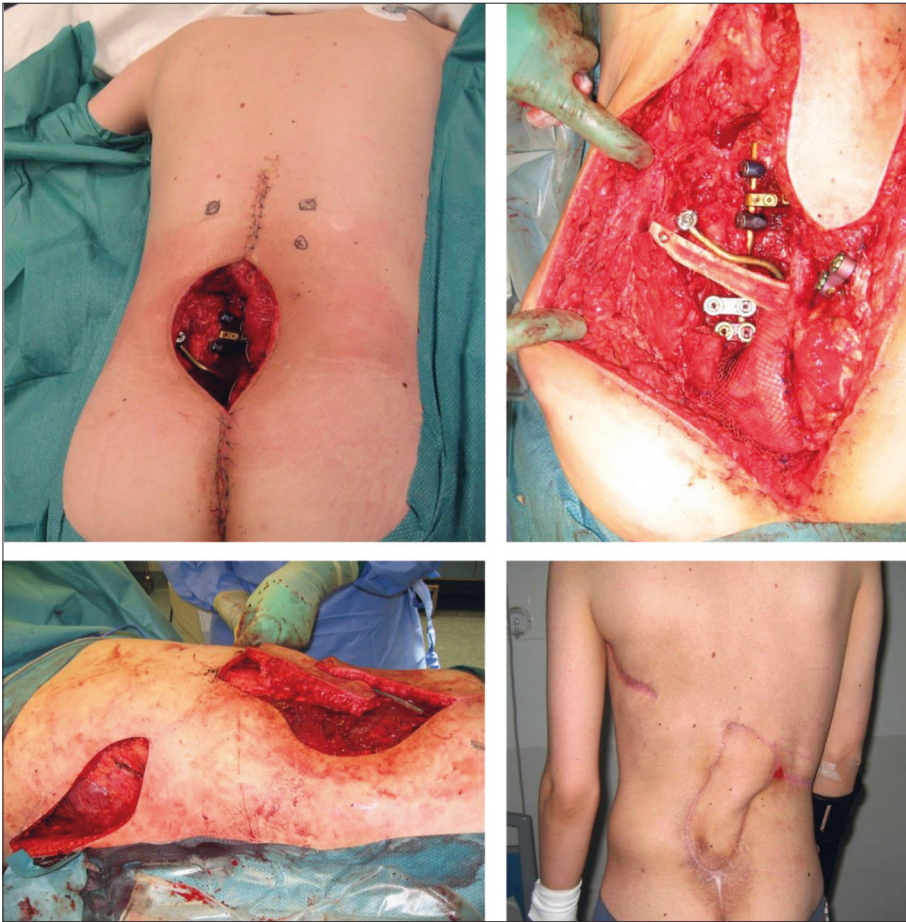
Figure 13. Planned delayed reconstruction after hemisacrectomy with concomitant partial L5 resection and spinopelvic fixation (top left). Allograft bone was used to reconstruct the posterior pelvic ring (top right). Turn-over latissimus dorsi muscle flap was used to cover the allograft and osteosynthesis material and right lumbar artery perforator flap was used to reconstruct the skin defect (bottom left). Post-operative result (bottom right)
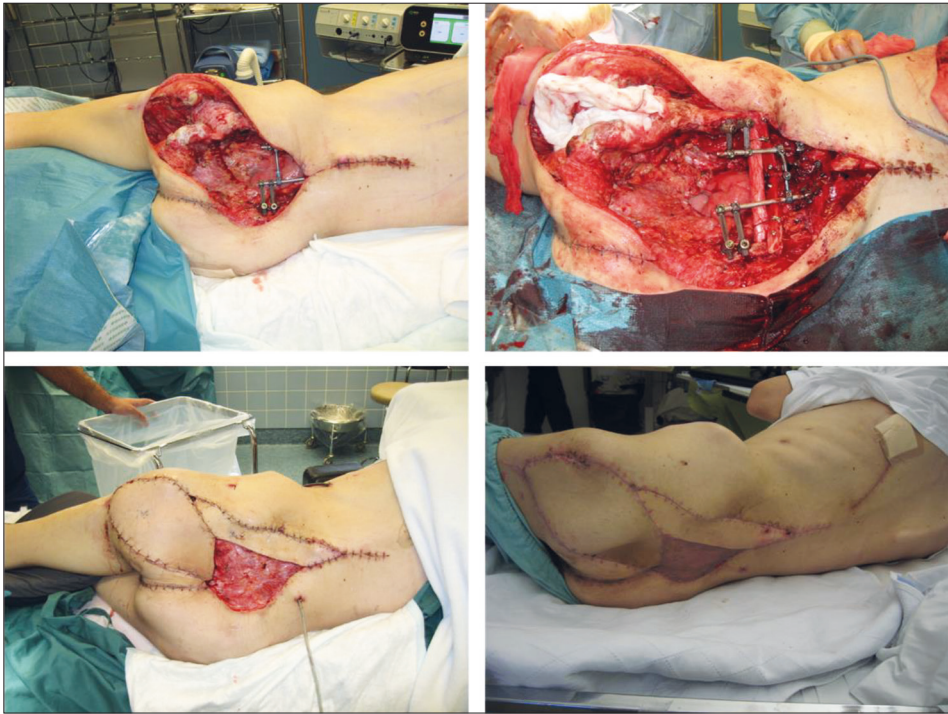
Figure 14. Planned delayed reconstruction after extended total sacrectomy. Defect one week after tumour resection and spinopelvic fixation (top left). Posterior pelvic ring and spinopelvic reconstructed with autologous fibula graft (top right). The soft tissue defect reconstructed with pedicled vastus lateralis and anterolateral thigh flaps and with latissimus dorsi free flap (bottom left). Two weeks post operatively (bottom right).
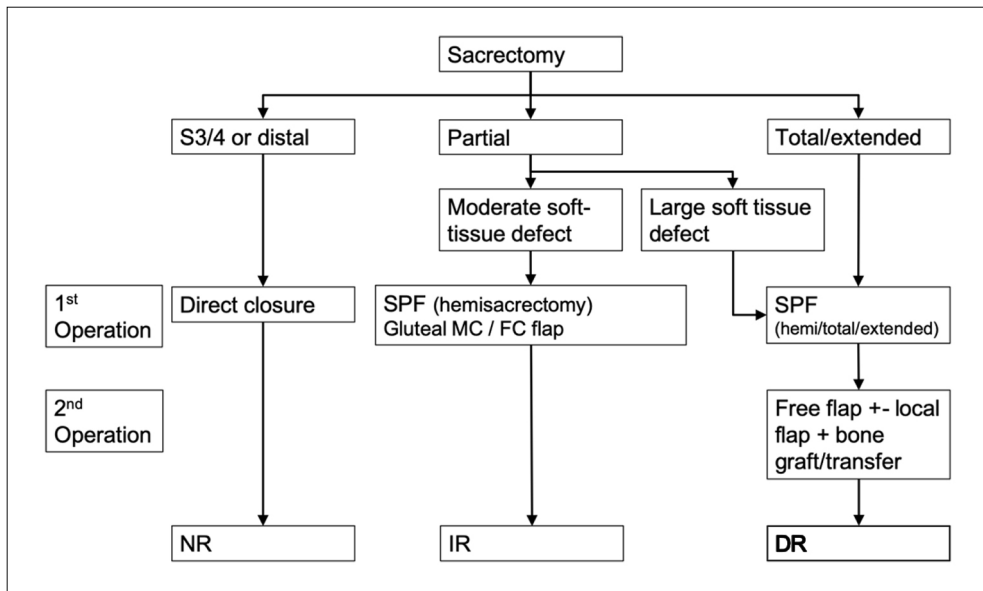
Figure 15. Algorithm for reconstructing the sacrectomy defect in study I.
SPF = spinopelvic fixation, MC = musculocutaneous flap, FC = fasciocutaneus flap, NR = No reconstruction, IR = immediate reconstruction, DR = delayed reconstruction.

A total of 20 soft-tissue flap reconstructions were performed in 16 patients. Bilateral gluteal muscle flaps were counted as one flap. The most commonly used flaps were pedicled gluteal muscle flaps, followed by gluteal fasciocutaneous flaps. The fasciocutaneous flaps were based on the superior gluteal artery perforator or simple random rotational flaps. In three cases, a latissimus dorsi (LD) free flap was used when free tissue transfer was required (Table 13). Recipient vessels for microvascular transfer were end-to-end to a branch of the internal iliac vessel (n=1), end to side to the internal iliac vessel (n=1), gluteal perforator vessel (n=1), and a long saphenous vein arteriovenous loop from the groin (n=1).

Mesh was used to secure the abdominopelvic cavity in 16 patients. There was no protocol for mesh use, and it was used according to the surgeons' preference.

Table 13. Flaps and microvascular bone transfer used to reconstruct the sacrectomy defects in study I.
ALT = anterolateral thigh flap, FC = fasciocutaneous, LAP = lumbar artery perforator flap, LD = latissimus dorsi flap, VRAM = vertical rectus abdominis muscle flap

Flap	Immediate reconstruction	Delayed reconstruction
Gluteal muscle		
– unilateral	2	
– bilateral	6	1
Gluteal FC flap	4	
LD free flap		3
VRAM	1	
LAP		1
Distally based LD		1
Vastus lateralis and ALT		1
Vascularised fibula bone		1
Total	13	8

A spinopelvic instrument reconstruction was performed using double iliac screw fixation combined with a posterior lumbar segmental fixation. Bone reconstruction was performed using a non-vascularised autologous fibula in four patients, vascularised fibula in one patient, and a tibia allograft in one patient. The bone graft was fixed to the host bone with additional cortical screws.

5.4.2   Pelvic exenteration (Study II)

A total of 27 (69%) patients underwent flap reconstruction for pelvic floor and/ or vaginal reconstruction (Figure 16). Of these, 17 (44%) had a bilateral TMG flap reconstruction, 9 (23%) had a unilateral TMG flap reconstruction, and 1 (2.6%) had a TRAM flap reconstruction. 12 (31%) patients had no flap reconstruction for the pelvic floor defect. All of these patients were operated on before 2010. Out of 26 patients who underwent TPE, 12 (46%) had a vaginal reconstruction. Bilateral TMG flaps was used for all vaginal reconstructions in the TPE group. Reconstructive outcomes are demonstrated in Figures 17 and 18.
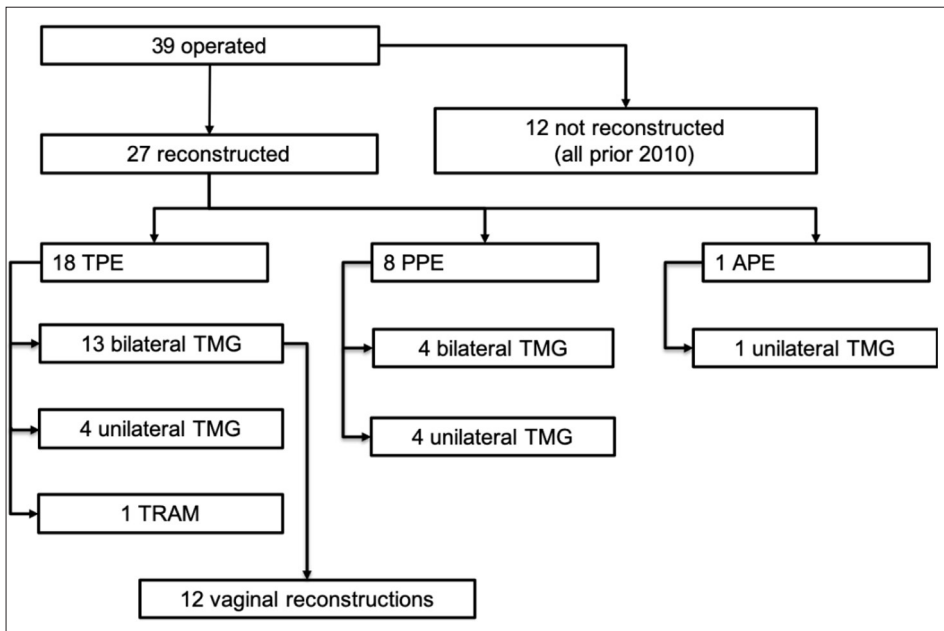
Figure 16. Algorithm for reconstructing pelvic exenteration defects in study II.
TPE = total pelvic exenteration, PPE = posterior pelvic exenteration, APE = anterior pelvic exenteration, TMG = transverse musculus gracilis flap, TRAM = transverse rectus abdominis flap.
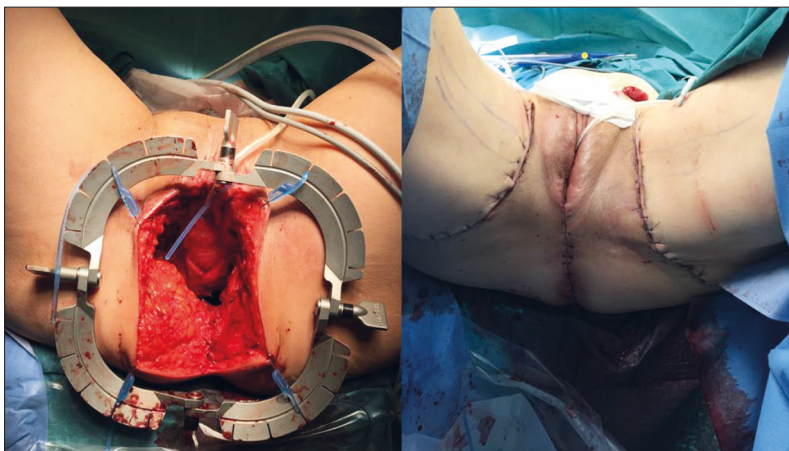
Figure 17. Reconstruction of the posterior pelvic exenteration defect extending to lateral sidewalls of the vagina (left) and immediate reconstruction outcome (right).
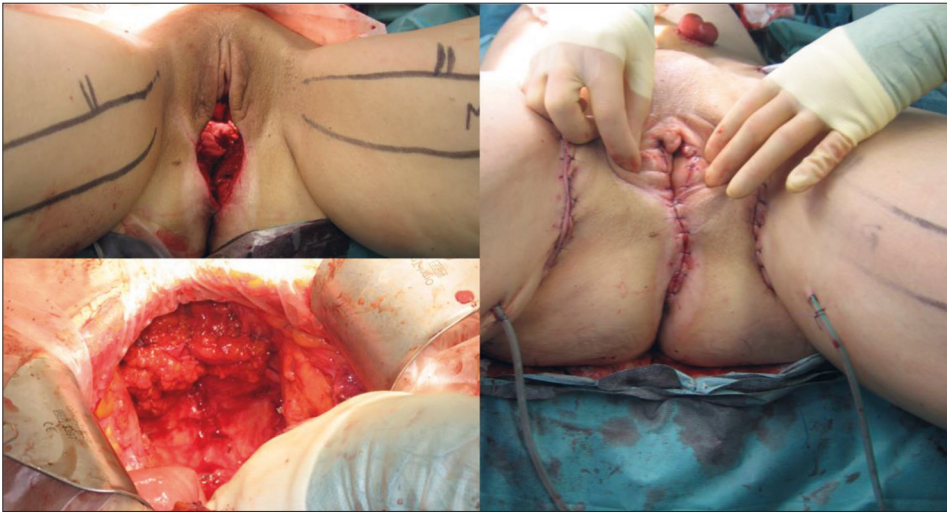
Figure 18. Reconstruction of the total pelvic exenteration defect with vaginal reconstruction. Pelvic floor after tumour resection (top left corner), view from the abdominal cavity after pelvic floor reconstruction with bilateral TMG-flaps (bottom left corner) and immediate outcome after reconstructing pelvic floor and neovagina (right).

5.4.3   Pelvic amputation (Studies III & IV)

The resultant HQA wound was reconstructed most commonly with a posterior gluteal flap (PTF) (n=50, 37%) or anterior thigh flap (ATF) (n=42, 31%) (Figure 19). The contralateral vertical rectus abdominis musculocutaneous (VRAM) flap was used in two patients. Six patients had a massive soft-tissue defect following HQA necessitating a free flap reconstruction. All free flaps were microvascular fillet flaps from amputated extremities. Flap description was insufficient in 23% (n=31) of the cases. Direct wound closure was used in five patients. Flap loss required a secondary flap reconstruction in two cases. There were no significant differences between the method of local or free flap used for reconstruction in terms of flap-related complications, flap survival, re-operation or primary healing rate.
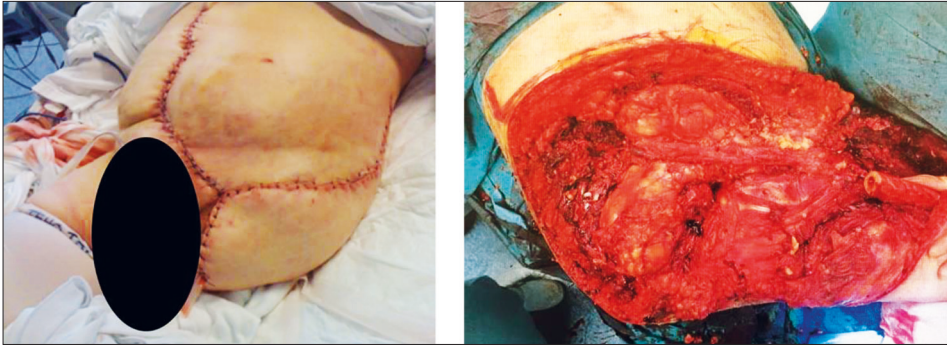
Figure 19. Hindquarter amputation reconstructed with posterior gluteal flap (left). Perioperative view of the anterior thigh flap (right).

All patients requiring a free flap were reconstructed with a free fillet flap from the amputated lower extremity (Figure 20). In one patient, a vascularised fibula was also included to the fillet flap and used to bridge the defect between the resected hemisacrum and the anterior resection margin, in an attempt to give a better sitting balance. The remaining patients were reconstructed with a musculocutaneous flap alone. The popliteal artery was anastomosed to the iliac or femoral artery end-to-end for all patients. The popliteal vein was anastomosed to the iliac or femoral vein for 11 patients. The anastomosis was end-to-end in 10 patients and end-to-side due to size discrepancy between vessels, in 1 patient. In 1 patient, due to the development of a deep vein thrombosis whilst receiving chemotherapy for an osteosarcoma, the long saphenous vein was anastomosed to the femoral vein by an end to end anastomosis. No double vein anastomoses were used.
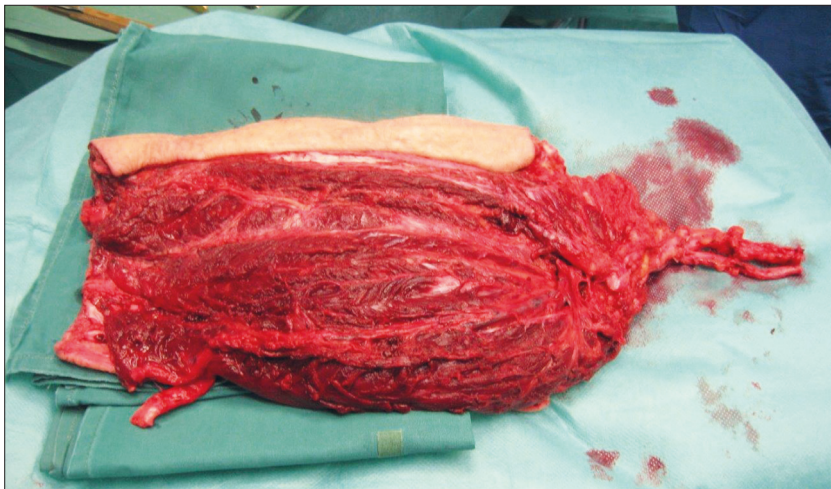
Figure 20. Harvested fillet flap before flap inset and vascular anastomosis.

5.5   Complications

Complications of all the studies are summarised in Table 14.

Table 14. Rate of complications of the studies.
Complications with over 5% rate in any of the studies are listed. PE = pulmonary embolism. * = Defined as need for secondary flap reconstruction.

	Study I	Study II	Study III	Study IV
Infection	38%	44%	4.7%	22%
Wound dehiscence	9.5%	33%	0%	28%
Systemic venous thromboembolism / PE	9.5%	2.6%	0%	2.2%
Flap loss – partial – total	 4.8% 4.8%	 2.6% 0%	 0% 8.3%	 19% 1.5%*
Enteral fistula	0%	7.7%	0%	0%
Decubital ulcer	0%	7.7%	0%	0%
Acute kidney injury	4.7%	5.1%	0%	0%
In-hospital death	4.7%	0%	8.3%	2.2%
Any Complication	62%	72%	50%	54%

5.5.1   Sacrectomy (Study I)

Thirteen of the 21 patients (62%) had a total of 25 complications. The most common complication was post-operative infection (n=8). Five patients required surgical interventions to control the infection. Three patients suffered wound complications, two had venous thromboembolism, and two required lower extremity fasciotomies due to compartment syndrome or rhabdomyolysis. Only one pedicled VRAM flap was lost. No other total or partial flap losses were noted in this study. All microvascular flaps survived completely.

5.5.2   Pelvic exenteration (Study II)

There was a total of 49 complications in 28 (72%) patients. The complication rate for patients with versus without flap reconstruction was 65% and 85%, respectively (p=0.191). Prior radiotherapy, BMI, diabetes, and age did not affect the complication rate. A total of 12 patients (31%) had at least one severe complication, and the most common complications were infection (44%) and local wound dehiscence (33%). There was a minor edge necrosis of a TMG flap that was considered a partial flap loss. This was treated with excision and direct closure.

5.5.3   Pelvic amputation (Studies III & IV)

The majority of the HQA patients (54%) in study IV had at least one complication. 24% of the patients required re-operation(s) for complication management. Tumour histology (bone or soft-tissue), pre-operative radiotherapy, chemotherapy, the chosen reconstructive flap and the treatment intent did not affect the rate of complications. The incidence of complete wound healing was lower in those who underwent direct wound closure when compared to those in whom the defect was reconstructed using either a local or free flap (60% vs. 81%, p=0.023).

Half of the patients in study III suffered at least one complication. Four patients required a return to theatre to manage the complication. In 3 patients, this was due to vascular compromise which comprised of 1 venous anastomosis thrombosis, 1 venous kink and 1 extensive arterial thrombosis. The fourth patient required a return to theatre to trim the transplanted vascularised fibula as it had resulted in pressure necrosis to the overlying skin. All patients who required a return to theatre to address a vascular compromise required multiple further theatre visits, 2 for secondary wound closure and one for drainage of an infected seroma. 11 fillet flaps (92%) survived completely whilst 1 patient (8%) suffered a total flap loss due to extensive arterial thrombosis that could not be resolved. This patient underwent flap debridement, negative-pressure therapy and eventual wound closure with a local flap and secondary healing. There was one unexpected post-operative death on the tenth post-operative day due to a massive cardiac event.

5.6   Quality of life before and after pelvic surgery

5.6.1   Sacrectomy (Study I)

EQ-5D baseline data at ICU admission was available for 10 of the 14 patients treated in the ICU. Follow-up data was available for eight patients. Two of the patients with follow-up data were lacking the baseline EQ-5D data and therefore six of the 14 patients (43%) treated in the ICU were included in the analysis. Patients with follow-up data had a higher pre-operative EQ-5D index than patients without follow-up data (0.819 vs. 0.603, p=0.01). No significant difference was found between the pre- and post-operative EQ-5D index or any of its dimensions in the 6 patients with complete data (Table 15).

Table 15. EQ-5D index and its dimensions on patients treated in ICU with full pre- and post-operative data.

	Pre-operative	Post-operative	p-value
EQ-5D index	0.81933	0.78933	0.600
Mobility	1.33	1.83	0.180
Self-care	1.00	1.33	0.157
Usual activities	1.17	1.50	0.317
Pain/discomfort	2.17	1.67	0.180
Anxiety/depression	1.17	1.00	0.317

6 DISCUSSION

6.1 General considerations

Advanced and recurrent pelvic tumours continue to pose a surgical challenge to both the orthopaedic/surgical/gynaecological oncologist and reconstructive surgeon. The results of this thesis demonstrate that multidisciplinary collaboration and meticulous planning is needed for resection and reconstruction of complex pelvic defects. However, in spite of the use of imaging technology, careful planning and multidisciplinary execution of the operation, pelvic surgery is still associated with a high peri- and post-operative morbidity. Pertinently, low perioperative mortality was demonstrated in this thesis. Free flap reconstruction is feasible for reconstructing the largest defects after ablative pelvic surgery and the TMG flap(s) can be used for pelvic floor and vaginal reconstruction after PE. It was possible to develop three different treatment and reconstructive algorithms for these heterogenous and rare tumours.

6.2 Oncological outcome

The 5 year OS after complex pelvic resection and reconstruction varied from 24% in STS patients undergoing HQA to 83% in bone sarcoma patients undergoing sacrectomy. The 5-year OS after PE and bone sarcoma HQA patients was 48% and 47%, respectively.

The 5 year OS of 83% in sacrectomy patients in this cohort was similar or slightly higher to the rates published in previous literature on sacral chordoma or sacral osteosarcoma (York et al. 1999, Kayani et al. 2015, Ji et al. 2017, Wang et al. 2017). The LR rate in study I was 19%. Half of the patients who experienced LR had a microsculous positive marginal R1 resection in the primary operation. In accordance to the literature, our results demonstrate that clear surgical margins are paramount for improved LRFS

in sacral chordoma (Kayani et al. 2014). It is noteworthy that all LRs occurred in the soft tissues, not in the bone. This highlights the need for adequate surgical resection, not only of bone, but also the surrounding soft tissues. The oncological orthopaedic surgeon should therefore never need to limit the planned resection of local soft tissues as large soft tissue defects can be reconstructed with local and/or free flaps as required.

The oncological outcome of PE patients in study II, with a 48% 5-year OS, is similar to that reported in previous publications with larger patient cohorts (Brown, Solomon, and Koh 2017, Knight et al. 2018). The finding in this thesis was that negative surgical margin and negative lymph node status at the time of the surgery were predictive for OS in multivariate model. The predictive value of a negative surgical margin (Berek et al. 2005, Park et al. 2007, Maggioni et al. 2009, Zoucas et al. 2010) and lymph node status (Park et al. 2007, Maggioni et al. 2009) has been demonstrated earlier. Obesity has been shown to not diminish survival after PE (Iglesias et al. 2012). However, this was not replicated in study II. A high BMI of over 30 was a negative predictive factor for OS in the univariate model, but not in the multivariate model.

The 3-year OS after HQA and free flap surgery was 58%. The literature on fillet flap reconstruction after hindquarter amputation is scarce and there are no prior publications regarding oncological outcome after HQA in patients with large pelvic defects that require free flap reconstruction. Although large tumour size has been shown to predict inferior survival in pelvic sarcoma (Puchner et al. 2017, van Houdt et al. 2018) there are no studies comparing oncological outcome between HQA standard HQA flap closures to HQA with fillet flap reconstruction. Patients requiring free flap reconstruction are highly selected with large tumours often involving common or external iliac vessels. The outcome of these patients is not necessarily similar to patients who can be reconstructed with standard HQA flaps. However, when the fillet flap reconstructions in study III were compared with standard HQA flaps in study IV, the short term OS of these cohorts were similar. The fillet flap patients' OS in study III was also similar to earlier published cohorts with conventional HQA flaps, with a 5-year OS between 27-45% (Grimer et al. 2013, Nakamura et al. 2013, Couto et al. 2016, Puchner et al. 2017, van Houdt et al. 2018).

There was a significant difference in 5-year OS depending on the tumour location in study IV. The 5-year OS for bone sarcoma was significantly better than that for STS (47% vs. 24%, p=0.008). STS patients have been shown to have an inferior survival compared to bone sarcoma patients (Couto et al. 2016). For bone sarcoma, the results of this thesis supports previous observations that HQA can offer long term cure especially in the case of bone sarcoma (Sherman, O'Connor, and Sim 2012). The number of patients allowed us to calculate the OS for chondrosarcoma, osteosarcoma and UPS. Chondrosarcoma has a better OS compared to osteosarcoma, as shown earlier (Parry et al. 2016, Tsagozis et al. 2019), which might be due to the difference in grades between osteo- and chondrosarcomas. For bone sarcoma, OS following a salvage procedure was

similar to that following HQA as a primary surgical procedure. This demonstrates the need for close follow-up after pelvic resection as the disease can still be controlled with good results if LR presents without distant metastasis. The mean survival after bone LR requiring HQA was 90 months, whereas STS LR requiring HQA has a poor prognosis with a mean OS of only 13 months. Our results are in accordance with the literature, as outcome after STS LR in the pelvic location is worse than LR in the extremities (Daigeler et al. 2014).

Indications for palliative HQA needs to be seriously considered in light of study IV. There are some anecdotal reports of favourable outcomes after palliative HQA (Grimer et al. 2013). We found that the outcome of these patients was extremely poor as 2 of the 6 patients died within two weeks from surgery and were never able to leave the hospital. The median survival time after palliative HQA in study IV was only 2.4 months. In the absence of PROM data from these palliative patients, it cannot be concluded from this data whether or not these patients experienced any meaningful palliation. Whilst there is evidence that proximal amputations can improve a patient's quality of life (Daigeler et al. 2009), there are no studies however, comparing pelvic or other proximal amputations vs. other non-surgical palliative methods. Based on these results, palliative HQA should only be considered with extreme caution when all other palliative means have failed and patients as well as their family members have been counselled properly about the realistic outcome of palliative HQA.

6.3   Reconstructive outcome

Reconstruction after complex pelvic resection continues to pose a challenge to the reconstructive plastic surgeon. The usual reconstructive challenges such as the amount and vascularity of local tissues, possible donor site morbidity from the local and free flaps and availability of recipient vessels must all be considered. In addition to these challenges, there are two additional factors that need to be contemplated. Firstly, all these procedures require a two-team approach. The team responsible for the resection may sometimes include several different specialists. Meticulous planning and communication between the resection and reconstructive team is paramount. When possible, the reconstructive team should harvest the flap simultaneously with the resection in order to minimize the surgical time. Secondly, patients undergoing complex pelvic resection can become hypovolemic, hypothermic and/or develop a hypercoagulable state during the resection. (Garvey et al. 2013). The communication between the two surgical teams and anaesthetic team is vital for optimal outcome.

Our algorithm for sacrectomy and reconstruction based on the results of this thesis is as follows:

1) Partial sacrectomy distal to S3/4 level: The majority of these patients don't need any soft tissue reconstruction. Patients with more extensive soft tissue resections are reconstructed with gluteal muscle or fasciocutaneous flaps.

2) Partial sacrectomy proximal to S3/4 level: This results in usually moderate size defects and they can be reconstructed with gluteal muscle or fasciocutaneous flaps. A mesh is used if the posterior pelvic wall cannot be secured with a flap.

3) Sagittal hemisacrectomy with a moderate size (<2 000cm³) soft tissue defect: Spinopelvic fixation is combined with a non-vascularized fibula autograft. The soft tissue defect is reconstructed with gluteal muscle or fasciocutaneous flaps.

4) Sagittal hemisacrectomy with large volume (>2 000cm³) tissue defect: Spinopelvic fixation is performed, and the wound is closed temporarily, either directly or with NPWT. After 1 week, the soft tissues are reconstructed with a free flap and non-vascularized fibula autograft is used for the pelvic ring reconstruction.

5) Total sacrectomy or partial sacrectomy with a large soft tissue defect: Resection is carried out in a combined anterior-posterior approach. In cases of disruption of the spinopelvic continuity, spinopelvic fixation is carried out and the wound is temporarily closed with NPWT. 1 week later a free flap is used for soft tissue reconstruction in addition to bone graft or transfer.

6) Any major disturbances in a patient's homeostasis during the resection: If there is an unexpected major event during the tumour resection the wound is temporarily closed, and reconstruction is delayed until after an ICU period and patient rehabilitation.

The use of muscle, musculocutaneous or fasciocutaneous flaps based on gluteal vessels in study I is in line with other authors (Miles et al. 2000, Garvey et al. 2011, Maricevich et al. 2014, Kim et al. 2015, Asaad et al. 2020). The major difference in our reconstructive algorithm compared to that previously described is the use of the VRAM flap, which is a workhorse for sacral and pelvic floor reconstruction in many units (Miles et al. 2000, Garvey et al. 2011, Maricevich et al. 2014, Kim et al. 2015). The abandonment of VRAM flap in our practice is due to two main reasons. Firstly, a patient undergoing sacrectomy above the S2 nerve root will lose the sphincter function and in our practice will inevitably have an end-colostomy. Leaving the abdominal wall untouched allows the colorectal surgeon to place the stoma in their desired position without a need to take into account an abdominal wall defect. Secondly, when we began the planned delayed reconstruction approach we considered the VRAM flap to be unfeasible as the anterior approach is done 1 week prior to the reconstruction. Garvey et al (2013) however, proved our reasoning flawed as they demonstrate a very elegant way to use the VRAM in a planned delayed manner without any complications. This approach seems very reasonable, especially in cases of prior radiotherapy and preference for vascularised bone transfer as the flap can be used as a flow-through flap for free fibula transfer. We

were able to use local vessels as recipients for free tissue transfer in all except one case. A long great saphenous venous loop can also be used in these cases as they provide good vessel calibre and high flow recipient vessels (Fudem and Marble 1996).

TMG flaps were used to reconstruct the pelvic floor and vagina after PE in study II. TMG seems the optimal reconstruction method for these cases for the following reasons: 1) they provide a sufficient amount of well vascularised tissue to secure the pelvic floor, 2) the amount of bulk provided by either unilateral or bilateral flaps is sufficient to obliterate the dead space (as demonstrated in Figure 18 bottom left corner), 3) a vaginal wall or entire vagina can be reconstructed with the flap(s), 4) flap harvest can be carried out whilst the resection team is working in the abdomen and finally 5) a stoma or stomas can be freely placed in the optimal position on the abdominal wall. The VRAM flap is also used in many units to reconstruct the pelvic floor and vagina (Goldberg et al. 2006, Nelson and Butler 2009, Horch et al. 2014). The VRAM flap has been favoured over thigh-based flaps because of the reported lower incidence of donor and recipient site complications. It is however noteworthy, that the study by Nelson and Butler (2009) had only a small number of thigh-based flaps and the gracilis flap was not used as a TMG. A comparative study between the gracilis and VRAM flap for reconstruction after abdominoperineal resection or PE did not find any difference in donor or recipient site complications (Stein et al. 2019). In study II, the mean surgical time of 428 minutes compares well to 335-725 minutes reported in previous abdominal flap reconstructions (Qiu, Jurado, and Hontanilla 2013, Ferron et al. 2015).

Our algorithm for reconstruction after PE based on the results of this thesis is as follows:

1) APE/PPE patients with only anterior/posterior wall vaginal resection are reconstructed with a unilateral TMG flap.

2) APE/PPE patients with vaginal wall resection continued to the lateral wall(s) in addition to the anterior/posterior vaginal wall (wider than 6–8cm resection) are reconstructed with bilateral TMG flaps.

3) TPE patients who don't request a neovagina reconstruction are in most cases reconstructed with a unilateral TMG flap. In cases of a large skin resection, wide pelvis or limited amount of thigh tissue, bilateral TMG flaps can be used.

4) TPE patients who request a neovagina reconstruction are reconstructed with bilateral TMG flaps.

The free fillet flap harvested from the amputated extremity proved to be a reliable method to reconstruct the largest HQA defects in study III, with 11 of the 12 flaps surviving completely. In addition to flap survival, all flaps provided durable and stable wound coverage without any postoperative abdominopelvic hernias or other late complications. The use of free flaps has been shown to be feasible in earlier small patient series (Workman, Bailey, and Cunningham 1992, Yamamoto, Minakawa, and Takeda

1997, Samant et al. 2012, Bibbo et al. 2015, Roulet et al. 2019, Kreutz-Rodrigues et al. 2019, Tashiro et al. 2019). The mean ischemia time in study III was 88 minutes. There were no ischemia time-related complications, even if the flap dissection was performed after the hemipelvis had been removed. Bibbo et al. (2015) have described a surgical method where the flap is dissected before the tumour resection is finished, in order to minimize the ischemia time. In the case of unexpected difficulty in tumour resection or other complications, banking of the harvested flap is one salvage possibility (Boehmler et al. 2010).

In study IV, the HQA defects were reconstructed mainly with the standard posterior (37%) and anterior (31%) HQA flaps. The flap description in the database was insufficient in 23% of the patients. The third most common flap used in this cohort was the free fillet flap from the amputated extremity (4.4%). Direct closure (3.7%) and VRAM flaps (1.5%) were seldom used. The flap choice is most commonly determined by the location of the tumour and the patency of the vessels after tumour resection. In previous large patient size cohorts, the posterior flap has been used in approximately half of the cases and the anterior flap in approximately a quarter of the cases or less. Flap choice slightly favoured the anterior flap in this study when compared to earlier publications (Senchenkov et al. 2009, Grimer et al. 2013).

Based on the results of this thesis and previous literature, our current algorithm for reconstructing HQA defects is summarised in Figure 21. The majority of the defects are reconstructed with the standard posterior or anterior HQA flaps. Our results showed no difference in complications between the flaps. In the case of a large defect that cannot be reconstructed with standard flaps or in cases where local flaps are not available due to compromised circulation; a free flap is needed. The first choice for free tissue transfer is the free fillet flap from the amputated extremity as it does not have any donor site morbidity. If the fillet flap is not available for example due to venous thrombosis, significant atherosclerosis, massive lymphoedema or leg ulcers, another free flap is needed. A novel indication in our algorithm is the ligation of CIA. This prevents the use of the standard anterior flap. CIA ligation also increases the risk of posterior flap necrosis nearly threefold by up to 46% (Senchenkov et al. 2008). This in our opinion justifies the use of a free flap, and we have demonstrated good free flap survival and a low number of wound complications, although requiring the reconstructive microvascular team.
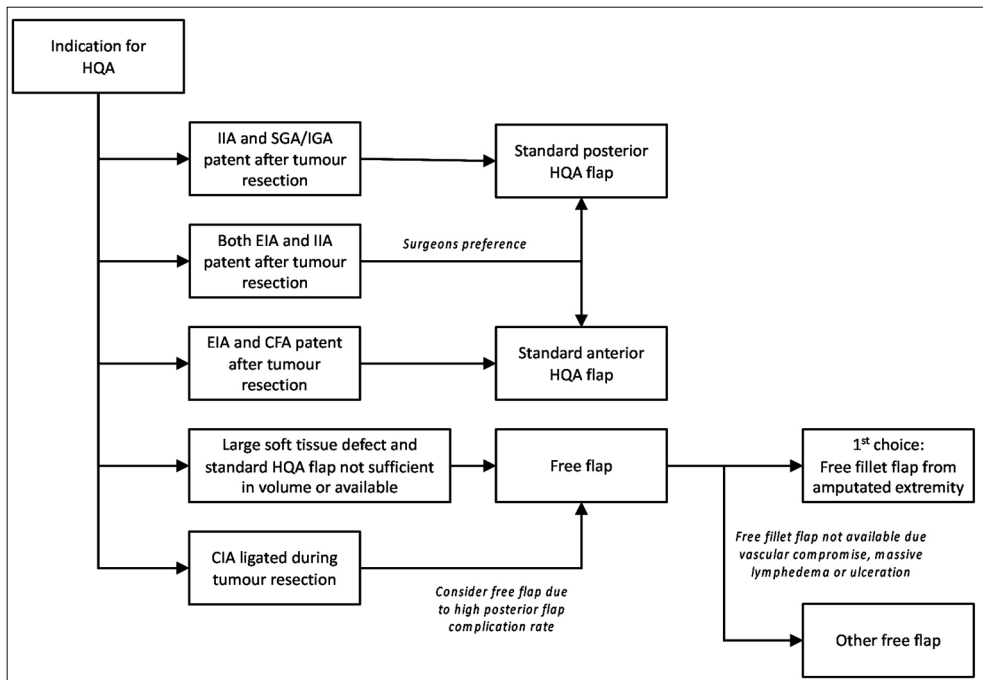
Figure 21. Algorithm for HQA reconstruction.
HQA = hindquarter amputation, IIA = internal iliac artery, SGA = superior gluteal artery, IGA = inferior gluteal artery, EIA = external iliac artery, CFA = common femoral artery, CIA = common iliac artery.

6.4 Complications

Complex pelvic surgery remains a highly morbid surgical procedure even with careful MDT planning and execution. At least 50% of patients in this thesis experienced at least one complication after surgery. In-hospital mortality was low, ranging between 0% and 8.3%. PE was associated with the most complications (72%), but no in-hospital mortality.

The majority (62%) of patients who underwent sacrectomy in study I had at least one complication. The incentive to develop the planned delayed reconstruction algorithm originated from an early experience managing an extremely complicated sacrectomy patient. This patient had multiple complications, a prolonged ICU period, flap loss and prolonged wound healing after sacrectomy with poor intra-operative homeostasis and major blood loss. Even though the number of complications was high, the rate of complications in this study is comparable to those published earlier (Miles et al. 2000, Garvey et al. 2011, Vartanian et al. 2018). For sacrectomy, after implementing the planned delayed reconstruction approach, the number of unplanned reoperations was similar in all the reconstructive cohorts (NR, IR and DR) and was not dependent on the extent of the surgical resection. Some studies have shown an increased risk for

reoperation after a large volume resection (Vartanian et al. 2018). Our original concern was whether the use of NPWT might increase the risk of infection complications in the DR group but our data demonstrated that DR does not increase infectious or other complications in the MDT setting for sacrectomy reconstructions.

Patients undergoing PE experienced the highest rate of complications (72%) in this thesis. However, the rate of complications was comparable to previous studies, highlighting the complexity and morbid nature of the operation (Berek et al. 2005, Maggioni et al. 2009, Zoucas et al. 2010). It is noteworthy, however, that only 31% of the patients experienced severe complication, classified as Clavien-Dindo 3b or higher. This hasn't been clearly defined in previous publications. More importantly, the complications or severe complications did not affect the OS of patients in study II. Moreover, there was only one direct flap-related complication, which consisted of partial flap edge necrosis that was defined as partial flap loss. The flap edge necrosis was debrided and the wound was directly closed and no secondary flap reconstructions were needed. Our TMG flap-related complication rate was lower than those reported with abdominal-based flaps (Berger et al. 2012, Qiu, Jurado, and Hontanilla 2013). There were three totally preventable decubital ulcer complications. Unfortunately, we were not able to trace whether the preventive measures failed or were overlooked during the post-operative period. Patients remained mainly on bedrest for the first three post-operative days and were mobilised thereafter. Air mattresses were also used to help prevent decubital ulcers.

The complication rate after HQA was 50% and 54% in studies III and IV, respectively. There were notable differences in distribution of the complications, however. The free fillet flap patients in study III experienced only one late infection and no wound dehiscences, whereas patients in study IV had a 22% wound infection rate and 28% wound dehiscence rate. The complication rate of approximately 50% is similar to other reports. The wound complications, dehiscence and infection, are the most common complications reported also in the literature (Apffelstaedt et al. 1996, Senchenkov et al. 2008, Grimer et al. 2013).

Although, there was a low incidence of wound complications in the free fillet flap cohort of the study, there were significant take backs to theatre due to vascular compromise in three cases. Two cases with a venous outflow problem (one venous kinking and one venous thrombosis) were successfully repaired, but one flap was lost due to an extensive arterial thrombosis that couldn't be resolved. All flaps were harvested with either the great saphenous vein or another superficial vein as a secondary outflow back-up vein. However, no double venous anastomoses were performed in this study, nor in previously published studies neither.

In study IV, the wound complication and infection rates were similar to earlier studies, but the reconstructive failure rate of 1.5% was lower than that reported earlier (Senchenkov et al. 2009). Complete surgical wound healing was more problematic in

the direct closure group when compared to any flap in the study IV. No other significant differences between the flaps were noted when comparing complete survival, re-operation or primary healing rate. There were no identifiable risk factors contributing to the complication risk. Extended HQA has been previously shown to increase the complication rate (Senchenkov et al. 2008). However, our data did not demonstrate this as a risk factor. The high mortality rate of the palliative group in study IV reflects the fragility of the patients with advanced pelvic sarcoma as well as the extent and burden of the hindquarter amputation. The main intention for palliation (pain/ fracture/ fungating tumour) was not recorded.

6.5   Quality of life

Quality of life assessment was conducted only in Study I. This study did not find any significant decline in the EQ-5D or any of its five dimensions. This is somewhat unexpected taking into consideration the extent of the surgery and associated morbidity. Sacrectomy has a significant impact on the patient's life in several dimensions when evaluated with qualitative methods (Wang et al. 2019). There are several possible factors that need to be addressed. Firstly, there were only 6 patients available with both pre-operative and post-operative data. Patients with follow-up HRQoL data had a higher baseline EQ-5D index than patients that were lost in the follow-up. Previous publications of PROM after sacrectomy have used MSTS or PROMIS instruments, but both of these studies lack the baseline measurement comparison (Kiatisevi et al. 2017, van Wulfften Palthe, Houdek, et al. 2017). The optimal instrument to evaluate HRQoL after sacrectomy has not yet been determined and the EQ-5D might not be optimal instrument for these patients (van Wulfften Palthe, Janssen, et al. 2017).

6.6   Strengths

This thesis summarizes the results and outcomes of complex pelvic tumour resection and reconstruction from four studies. The incidence of pelvic tumours is low and there is limited knowledge of the outcomes and reconstructive methods for these tumours.

There are two major strengths of study I. Firstly, it was possible to study the change in HRQoL before and after the sacrectomy. This comparison between a baseline and 6 or 12 months post-operative follow-up data is a novel finding demonstrating that patients adjust better than expected to the surgical outcome. Secondly, an algorithm was constructed for reconstructing the sacrectomy defects. The algorithm does not only include flap choice or anterior/ posterior approach, but also timing of the reconstruction. Previous publications about sacrectomy reconstruction haven't addressed the timing of the reconstruction in detail (Garvey et al. 2011, Maricevich et al. 2014, Kim et al. 2015).

Study II included outcomes of 39 PE operations. In this study also, an algorithm was developed for reconstruction after PE with TMG flaps. PE defects, both total and partial, including extended PE with concomitant vulvectomy can be reconstructed reliably with unilateral or bilateral TMG flaps. In addition to this algorithmic approach the complications were classified by the Clavien-Dindo classification and discriminate between minor and major complications over the study period.

Free flap surgery was found to be feasible in the reconstruction of large pelvic defects after sacrectomy and HQA in studies I and III. There are usually local perforators or other vessels patent after sacrectomy, even after a one week rehabilitation period. In cases of absent local vessels, a long great saphenous vein loop can be used to provide the free flap with high inflow and outflow in the pelvis.

Knowledge has been limited concerning the oncological outcome of patients after HQA requiring free fillet flap reconstruction to cover the large pelvic defects. Study III demonstrated for the first time that at least in the short term, 3-year OS is similar to patients who undergo HQA with conventional anterior or posterior flap reconstruction.

Study IV included all the patients (n=136) who underwent HQA in a large volume supra-regional sarcoma unit over a 21-year study period. The patient cohort was homogenous as all other indications for HQA were excluded from the study. No patients were lost during follow-up making the survival outcome reliable. Indications for limb salvaging pelvic resection and HQA remained unchanged during the study period and all the patients were reviewed in a MDT meeting.

6.7   Limitations

There are several limitations related to this thesis. Firstly, all studies are retrospective cohort studies. It is noteworthy however, that the oncological databases used in studies I, III and IV are prospectively maintained. In study I, the EQ-5D data is prospectively collected and recorded in the intensive care database, but the number of patients that had full pre- and postoperative data was limited to six patients.

There was a limited number of patients in studies I-III. The incidence of sacral tumours, PE and HQA is indeed low and the number of patients in our studies is in line with previous reports (Miles et al. 2000, Maggioni et al. 2009, Petruzziello et al. 2014). We elected to limit the inclusion criteria in study I to only primary bone malignancies, as inclusion of other malignancies (e.g. metastases) would have made the results more heterogenous. To overcome the low incidence of HQA and free flap surgery, a multicentre study was conducted in three supra-regional sarcoma units. This multicentre study has the largest number of patients with HQA and free flap reconstruction published to date. The number of patients limited the statistical power for detecting risk factors for complications and histology specific survival in studies I-III. Unfortunately, in study IV flap description was insufficient in 23% cases.

Due to the retrospective nature of the studies it was not possible to classify the complications according to the Clavien-Dindo classification except in study II (Dindo, Demartines, and Clavien 2004). However, the comprehensive nature of the databases used in studies I, III and IV enabled the capture of all the secondary surgical procedures after the primary operation. The majority of severe complications were therefore captured.

The major limitations of studies II-IV is the lack of any kind of PROM. Both PE and HQA are extremely extensive and partly even disfiguring procedures. HRQoL has been reported to decline at three months after PE, but the majority of the patients adjust to their post-operative situation with restoration of most of the domains of HRQoL (Rezk et al. 2013). The HRQoL measured with SF-36 shows that the patients' physical component scores are lower than amongst the general population (Griesser et al. 2012). The overall quality of life parameters are similar amongst patients after HQA and internal hemipelvectomy (Beck et al. 2008). There is a lack the knowledge of PROM in the cohorts of studies II-IV.

6.8   Future perspectives

The incidence of pelvic tumours is low in general. Furthermore, the number of patients is low even in large supra regional units. This limits the possibility of meaningful prospective study designs. For future studies it is paramount to conduct multicentre studies involving major sarcoma or other tertiary units. Collaboration and possible international collective databases should aim to increase the number of patients in any future studies.

PROM's, including HRQoL and functional outcome measures, should routinely be collected from all patients. This is the only possibility that would allow surgeons and other treating physicians to evaluate not only survival outcomes, but also assess the impact of the treatment on the patient's life.

In clinical practice, it would be worth considering to increase the use of free flaps to reconstruct the largest HQA defects as they are associated with a low rate of wound complications post-operatively. In particular, in cases where the common iliac vessels require ligation the posterior flap necrosis rate increases 2.7-fold (Senchenkov et al. 2008) and therefore these cases would benefit from reconstruction with free fillet flaps. However, this requires an experienced microvascular reconstructive team and a MDT approach, which on the other hand should always be available when treating complicated malignant pelvic tumours in a tertiary referral hospital.

The incidence of peri- and postoperative complications remains high. Certain approaches to reduce the complication rate could be considered. Firstly, enhanced recovery after surgery (ERAS) pathways have been developed for several surgical and oncological patient groups and it has been shown to reduce the length of stay,

complications and costs (Ljungqvist, Scott, and Fearon 2017). For advanced pelvic cancer the ERAS pathways have been implemented and it has been shown to reduce post-operative ileus (Funder et al. 2017). Further research is needed to validate the benefit of ERAS in PE patients (Nelson et al. 2019). No ERAS pathways have been published for pelvic sarcoma patients thus far. Secondly, the development of cancer and procedure-specific risk models could help the preoperative shared-decision making process and patient education. These models have been developed for example in head and neck surgery, but are lacking in patients with advanced pelvic tumours (Sindhar et al. 2019).

7 CONCLUSIONS

Advanced and recurrent pelvic tumours are rare and constitute a heterogenous entity of tumours that present several challenges for the surgical team. A MDT approach is paramount to treat these patients and the algorithms presented in this thesis can offer a means to standardize the treatment of these rare tumours.

Planned delayed reconstruction after total sacrectomy is feasible and safe. Large sacrectomy defects can be reconstructed with free flaps and in cases of absent local perforators or other vessels, a long saphenous vein loop offers a reliable high flow vascular pedicle to the flap.

Uni- or bilateral TMG flaps are a reliable method of reconstructing the pelvic floor and vagina after PE. Flap reconstruction most likely reduces the total complication rate without significantly prolonging the operation.

The oncological outcome after large HQA requiring free flap reconstruction is similar to those patients in whom their wounds can be closed with standard HQA flaps. The free fillet flap from the amputated extremity is a feasible method of reconstruction without any donor site morbidity.

HQA continues to be a procedure associated with high morbidity, although the 30-day mortality has decreased to 1%. HQA offers a very limited chance of survival in cases of recurrent STS. Palliative HQA has an exceptionally poor outcome and should only be performed in highly selected cases when all other possible palliative measures have failed.

8   ACKNOWLEDGEMENTS

This dissertation forms the culmination of research conducted during the years 2017 and 2020 whilst working in Tampere University Hospital and Helsinki University Central Hospital. I have had the privilege to work with many friendly, enthusiastic, brilliant and talented people during my career and only some of you can be mentioned by name, but many others have influenced me as a surgeon and as a human being.

First and foremost, I want to express my deepest gratitude to my supervisor and mentor Docent Minna Laitinen. You have guided me through this project and without your prompt comments, corrections and support this thesis would not have been possible. Your surgical skills and bedside manners have a set a fine example of what to strive for as a successful sarcoma surgeon. Docent Ilkka Kaartinen, my other supervisor and a good friend, we have worked together for over a decade. You are one of the most skillful surgeons I have ever had the pleasure to operate with. Not a day goes by without you proposing an idea for a new research project and you have shown me, that every day we should aim to do things better.

Professor Hannu Aro from University of Turku and Docent Andrew Lindford reviewed the thesis. Your comments, questions and corrections have improved this final version tremendously. Andrew Lindford also revised the English language of the thesis.

I want to acknowledge three plastic surgeons who have most influenced my career. Docent Minna Kääriäinen, you were my clinical teacher over 15 years ago when I was a medical student and you are now my boss. You were the first person who got me interested in plastic surgery. Professor Hannu Kuokkanen, I met you for the first time during my last year of medical school and later you were my boss during my training. Without you, I would not have become a plastic surgeon and you also provided the original idea for this thesis. MD Terhi Järvinen, you have provided me with all the necessary core skills of a plastic surgeon during my three years in training in Kanta-Häme Central Hospital. I am forever grateful for your patient teaching and friendship.

This thesis is about teamwork and I want to sincerely thank every one of the 17 co-authors of these studies. This would not have been possible without all of your work. Thank you Hannu, both Minnas, Ilkka, Toni-Karri, Kim, Maarit, Marja, Jukka, Luis-Romee, Vaiyapuri, Jonathan, Francis, Philippe, Aurélie, Michael and Lee! Special thanks to DSC, Professor Lee Jeys and BSc, MBChS, MD, FRCS Michael Parry for the fruitful collaboration and making it possible for me to come to Birmingham. I want thank MD, PhD Niko Sillanpää and talented Ella Aho for providing the majority of the illustrations for this thesis.

I want to thank all of my co-workers in the Department of Plastic Surgery. You have supported my research and helped me immensely by relieving me of some of my workload during the busiest times. A special thanks goes also to my colleagues in the Sarcoma Unit. The unit would not work without our nurses Virpi and Nina and secretary Helena. I am truly thankful of your support and friendly reminders. Anne and Thea, I met you in the very first day of the medical school. We have learned how to become surgeons, parents and hopefully better people together. I am grateful of our friendship. Seija and Satu, thank you for all your help during this project and on my way to becoming a researcher.

My parents, father Kai and late mother Aili, you have always given me your unlimited assistance, support and love. Your help with my life has been a blessing. My brother Jyrki, thank you for taking me for bike rides and you have always been there for me.

Finally, this thesis is dedicated to my family. Jasper, you have shown me the true joy of life in all of its dimensions. Heidi, my wonderful wife, you have been a love of my life for over 27 years. Your love and support has made everything possible for me and I am forever grateful that you are in my life.

Hämeenlinna, July 2020

9 REFERENCES

Abdou, A. H., L. Li, K. Khatib-Chahidi, A. Troja, P. Looft, E. M. Gudewer, H. R. Raab, and D. Antolovic. 2016. "Free latissimus dorsi myocutaneous flap for pelvic floor reconstruction following pelvic exenteration." *Int J Colorectal Dis 31* (2):385-91. doi: 10.1007/s00384-015-2402-8.

Ahmed, S. K., S. I. Robinson, C. A. S. Arndt, I. A. Petersen, M. G. Haddock, P. S. Rose, and N. N. Issa Laack. 2017. "Pelvis Ewing sarcoma: Local control and survival in the modern era." *Pediatr Blood Cancer 64* (9). doi: 10.1002/pbc.26504.

Ambrose, J., and G. Hounsfield. 1973. "Computerized transverse axial tomography." *Br J Radiol 46* (542):148-9.

Amin, M.B., S. Edge, F. Greene, D.R. Byrd, R.K. Brookland, M.K. Washington, J.E. Gershenwald, C.C. Compton, K.R. Hess, D.C. Sullivan, J.M. Jessup, J.D. Brierley, L.E. Gaspar, R.L. Schilsky, C.M. Balch, D.P. Winchester, E.A. Asare, M. Madera, D.M. Gress, and L.R. Meyer. 2017. *AJCC Cancer Staging Manual*. 8th ed: Springer.

Angioli, R., P. B. Panici, R. Mirhashemi, L. Mendez, G. Cantuaria, S. Basile, and M. Penalver. 2003. "Continent urinary diversion and low colorectal anastomosis after pelvic exenteration. Quality of life and complication risk." *Crit Rev Oncol Hematol 48* (3):281-5. doi: 10.1016/s1040-8428(03)00126-4.

Angus, D. C., and J. Carlet. 2003. "Surviving intensive care: a report from the 2002 Brussels Roundtable." *Intensive Care Med 29* (3):368-77. doi: 10.1007/s00134-002-1624-8.

Apffelstaedt, J. P., D. L. Driscoll, J. E. Spellman, A. F. Velez, J. F. Gibbs, and C. P. Karakousis. 1996. "Complications and outcome of external hemipelvectomy in the management of pelvic tumors." *Ann Surg Oncol 3* (3):304-9.

Arkader, A., C. H. Yang, and V. T. Tolo. 2012. "High long-term local control with sacrectomy for primary high-grade bone sarcoma in children." *Clin Orthop Relat Res 470* (5):1491-7. doi: 10.1007/s11999-011-2199-x.

Asaad, M., A. Rajesh, W. Wahood, K. S. Vyas, M. T. Houdek, P. S. Rose, and S. L. Moran. 2020. "Flap reconstruction for sacrectomy defects: A systematic review and meta-analysis." *J Plast Reconstr Aesthet Surg 73* (2):255-268. doi: 10.1016/j.bjps.2019.09.049.

Austin, K. K., A. J. Herd, M. J. Solomon, K. Ly, and P. J. Lee. 2016. "Outcomes of Pelvic Exenteration with en Bloc Partial or Complete Pubic Bone Excision for Locally Advanced Primary or Recurrent Pelvic Cancer." *Dis Colon Rectum 59* (9):831-5. doi: 10.1097/dcr.0000000000000656.

Austin, K. K., and M. J. Solomon. 2009. "Pelvic exenteration with en bloc iliac vessel resection for lateral pelvic wall involvement." *Dis Colon Rectum* 52 (7):1223-33. doi: 10.1007/DCR.0b013e3181a73f48.

Baiocchi, G., G. C. Guimaraes, R. A. Rosa Oliveira, L. Y. Kumagai, C. C. Faloppa, S. Aguiar, M. D. Begnami, F. A. Soares, and A. Lopes. 2012. "Prognostic factors in pelvic exenteration for gynecological malignancies." *Eur J Surg Oncol* 38 (10):948-54. doi: 10.1016/j.ejso.2012.07.002.

Barnhart, K. T., A. Izquierdo, E. S. Pretorius, D. M. Shera, M. Shabbout, and A. Shaunik. 2006. "Baseline dimensions of the human vagina." *Hum Reprod* 21 (6):1618-22. doi: 10.1093/humrep/del022.

Baumann, B. C., R. A. Lustig, S. Mazzoni, S. M. Grady, B. W. O'Malley, J. Y. K. Lee, J. G. Newman, J. M. Schuster, S. Both, A. Lin, J. F. Dorsey, and M. Alonso-Basanta. 2019. "A prospective clinical trial of proton therapy for chordoma and chondrosarcoma: Feasibility assessment." *J Surg Oncol* 120 (2):200-205. doi: 10.1002/jso.25502.

Beck, L. A., M. J. Einertson, M. H. Winemiller, R. W. DePompolo, K. M. Hoppe, and F. F. Sim. 2008. "Functional outcomes and quality of life after tumor-related hemipelvectomy." *Phys Ther* 88 (8):916-27. doi: 10.2522/ptj.20070184.

Bederman, S. S., K. N. Shah, J. M. Hassan, B. H. Hoang, P. D. Kiester, and N. N. Bhatia. 2014. "Surgical techniques for spinopelvic reconstruction following total sacrectomy: a systematic review." *Eur Spine J* 23 (2):305-19. doi: 10.1007/s00586-013-3075-z.

Bekkering, W. P., T. P. Vliet Vlieland, H. M. Koopman, G. R. Schaap, A. Beishuizen, J. K. Anninga, R. Wolterbeek, R. G. Nelissen, and A. H. Taminiau. 2012. "A prospective study on quality of life and functional outcome in children and adolescents after malignant bone tumor surgery." *Pediatr Blood Cancer* 58 (6):978-85. doi: 10.1002/pbc.23328.

Benson, A. B., 3rd, J. P. Arnoletti, T. Bekaii-Saab, E. Chan, Y. J. Chen, M. A. Choti, H. S. Cooper, R. A. Dilawari, P. F. Engstrom, P. C. Enzinger, M. G. Fakih, J. W. Fleshman, Jr., C. S. Fuchs, J. L. Grem, L. A. Leong, E. Lin, K. S. May, M. F. Mulcahy, K. Murphy, E. Rohren, D. P. Ryan, L. Saltz, S. Sharma, D. Shibata, J. M. Skibber, W. Small, Jr., C. T. Sofocleous, A. P. Venook, C. Willett, and D. A. Freedman-Cass. 2012. "Anal Carcinoma, Version 2.2012: featured updates to the NCCN guidelines." *J Natl Compr Canc Netw* 10 (4):449-54. doi: 10.6004/jnccn.2012.0046.

Berek, J. S., N. F. Hacker, and L. D. Lagasse. 1984. "Vaginal reconstruction performed simultaneously with pelvic exenteration." *Obstet Gynecol* 63 (3):318-23.

Berek, J. S., C. Howe, L. D. Lagasse, and N. F. Hacker. 2005. "Pelvic exenteration for recurrent gynecologic malignancy: survival and morbidity analysis of the 45-year experience at UCLA." *Gynecol Oncol* 99 (1):153-9. doi: 10.1016/j.ygyno.2005.05.034.

Berger, J. L., S. N. Westin, B. Fellman, V. Rallapali, M. Frumovitz, P. T. Ramirez, A. K. Sood, and P. T. Soliman. 2012. "Modified vertical rectus abdominis myocutaneous flap vaginal reconstruction: an analysis of surgical outcomes." *Gynecol Oncol* 125 (1):252-5. doi: 10.1016/j.ygyno.2011.12.427.

Bergh, P., B. Gunterberg, J. M. Meis-Kindblom, and L. G. Kindblom. 2001. "Prognostic factors and outcome of pelvic, sacral, and spinal chondrosarcomas: a center-based study of 69 cases." *Cancer* 91 (7):1201-12.

Bhangu, A., S. M. Ali, G. Brown, R. J. Nicholls, and P. Tekkis. 2014. "Indications and outcome of pelvic exenteration for locally advanced primary and recurrent rectal cancer." *Ann Surg* 259 (2):315-22. doi: 10.1097/SLA.0b013e31828a0d22.

Bibbo, C., A. S. Newman, R. D. Lackman, L. S. Levin, and S. J. Kovach. 2015. "A simplified approach to reconstruction of hemipelvectomy defects with lower extremity free fillet flaps to minimize ischemia time." *J Plast Reconstr Aesthet Surg* 68 (12):1750-4. doi: 10.1016/j. bjps.2015.07.006.

Bielack, S. S., B. Kempf-Bielack, G. Delling, G. U. Exner, S. Flege, K. Helmke, R. Kotz, M. Salzer-Kuntschik, M. Werner, W. Winkelmann, A. Zoubek, H. Jurgens, and K. Winkler. 2002. "Prognostic factors in high-grade osteosarcoma of the extremities or trunk: an analysis of 1,702 patients treated on neoadjuvant cooperative osteosarcoma study group protocols." *J Clin Oncol* 20 (3):776-90. doi: 10.1200/jco.2002.20.3.776.

Bilhim, T., J. A. Pereira, L. Fernandes, H. Rio Tinto, and J. M. Pisco. 2014. "Angiographic anatomy of the male pelvic arteries." *AJR Am J Roentgenol* 203 (4):W373-82. doi: 10.2214/ajr.13.11687.

Bleyer, W. A., J. E. Haas, P. Feigl, T. K. Greenlee, R. T. Schaller, Jr., A. Morgan, T. W. Pendergrass, F. L. Johnson, I. D. Bernstein, R. L. Chard, Jr., and J. R. Hartmann. 1982. "Improved three-year disease-free survival in osteogenic sarcoma." *J Bone Joint Surg Br* 64 (2):233-8.

Boehmler, J. H., S. H. Francis, R. K. Grawe, and J. L. Mayerson. 2010. "Reconstruction of an external hemipelvectomy defect with a two-stage fillet of leg-free flap." *J Reconstr Microsurg* 26 (4):271-6. doi: 10.1055/s-0030-1248236.

Bosman, S. J., T. A. Vermeer, R. L. Dudink, I. H. de Hingh, G. A. Nieuwenhuijzen, and H. J. Rutten. 2014. "Abdominosacral resection: long-term outcome in 86 patients with locally advanced or locally recurrent rectal cancer." *Eur J Surg Oncol* 40 (6):699-705. doi: 10.1016/j. ejso.2014.02.233.

Bowers, R. F. 1948. "Giant Cell Tumor of the Sacrum: A Case Report." *Ann Surg* 128 (6):1164-72. doi: 10.1097/00000658-194812000-00011.

Brennan, M. F., C. R. Antonescu, N. Moraco, and S. Singer. 2014. "Lessons learned from the study of 10,000 patients with soft tissue sarcoma." *Ann Surg* 260 (3):416-21; discussion 421-2. doi: 10.1097/sla.0000000000000869.

Bricker, E. M. 1950. "Bladder substitution after pelvic evisceration." *Surg Clin North Am* 30 (5):1511-21. doi: 10.1016/s0039-6109(16)33147-4.

Bridoux, V., B. Kianifard, F. Michot, B. Resch, L. Sibert, and J. J. Tuech. 2010. "Transposed right colon segment for vaginal reconstruction after pelvic exenteration." *Eur J Surg Oncol* 36 (11):1080-4. doi: 10.1016/j.ejso.2010.08.136.

Brooks, R. 1996. "EuroQol: the current state of play." *Health Policy* 37 (1):53-72. doi: 10.1016/0168-8510(96)00822-6.

Brown, K. G. M., M. J. Solomon, and C. E. Koh. 2017. "Pelvic Exenteration Surgery: The Evolution of Radical Surgical Techniques for Advanced and Recurrent Pelvic Malignancy." *Dis Colon Rectum* 60 (7):745-754. doi: 10.1097/dcr.0000000000000839.

Brunschwig, A. 1948. "Complete excision of pelvic viscera for advanced carcinoma; a one-stage abdominoperineal operation with end colostomy and bilateral ureteral implantation into the colon above the colostomy." *Cancer* 1 (2):177-83.

Brunschwig, A., and H. R. Barber. 1969. "Pelvic exenteration combined with resection of segments of bony pelvis." *Surgery* 65 (3):417-20.

Bus, M. P. A., D. A. Campanacci, J. I. Albergo, A. Leithner, M. A. J. van de Sande, C. L. Gaston, G. Caff, J. Mettelsiefen, R. Capanna, P. U. Tunn, L. M. Jeys, and P. D. S. Dijkstra. 2018. "Conventional Primary Central Chondrosarcoma of the Pelvis: Prognostic Factors and Outcome of Surgical Treatment in 162 Patients." *J Bone Joint Surg Am* 100 (4):316-325. doi: 10.2106/jbjs.17.00105.

Cain, J. M., A. Diamond, H. K. Tamimi, B. E. Greer, and D. C. Figge. 1989. "The morbidity and benefits of concurrent gracilis myocutaneous graft with pelvic exenteration." *Obstet Gynecol* 74 (2):185-9.

Carboni, F., O. Federici, M. Giofre, S. Zazza, and M. Valle. 2019. "Empty pelvis syndrome: the use of breast prosthesis in the prevention of complications." *Colorectal Dis* 21 (11):1321-1325. doi: 10.1111/codi.14737.

Casal Nunez, J. E., V. Vigorita, A. Ruano Poblador, A. M. Gay Fernandez, M. A. Toscano Novella, N. Caceres Alvarado, and L. Perez Dominguez. 2017. "Presacral venous bleeding during mobilization in rectal cancer." *World J Gastroenterol* 23 (9):1712-1719. doi: 10.3748/wjg. v23.i9.1712.

Casali, P. G., N. Abecassis, H. T. Aro, S. Bauer, R. Biagini, S. Bielack, S. Bonvalot, I. Boukovinas, Jvmg Bovee, T. Brodowicz, J. M. Broto, A. Buonadonna, E. De Alava, A. P. Dei Tos, X. G. Del Muro, P. Dileo, M. Eriksson, A. Fedenko, V. Ferraresi, A. Ferrari, S. Ferrari, A. M. Frezza, S. Gasperoni, H. Gelderblom, T. Gil, G. Grignani, A. Gronchi, R. L. Haas, B. Hassan, P. Hohenberger, R. Issels, H. Joensuu, R. L. Jones, I. Judson, P. Jutte, S. Kaal, B. Kasper, K. Kopeckova, D. A. Krakorova, A. Le Cesne, I. Lugowska, O. Merimsky, M. Montemurro, M. A. Pantaleo, R. Piana, P. Picci, S. Piperno-Neumann, A. L. Pousa, P. Reichardt, M. H. Robinson, P. Rutkowski, A. A. Safwat, P. Schoffski, S. Sleijfer, S. Stacchiotti, K. Sundby Hall, M. Unk, F. Van Coevorden, W. T. A. van der Graaf, J. Whelan, E. Wardelmann, O. Zaikova, and J. Y. Blay. 2018. "Soft tissue and visceral sarcomas: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up." *Ann Oncol* 29 (Suppl 4):iv51-iv67. doi: 10.1093/annonc/mdy096.

Casali, P. G., S. Bielack, N. Abecassis, H. T. Aro, S. Bauer, R. Biagini, S. Bonvalot, I. Boukovinas, Jvmg Bovee, B. Brennan, T. Brodowicz, J. M. Broto, L. Brugieres, A. Buonadonna, E. De Alava, A. P. Dei Tos, X. G. Del Muro, P. Dileo, C. Dhooge, M. Eriksson, F. Fagioli, A. Fedenko, V. Ferraresi, A. Ferrari, S. Ferrari, A. M. Frezza, N. Gaspar, S. Gasperoni, H. Gelderblom, T. Gil, G. Grignani, A. Gronchi, R. L. Haas, B. Hassan, S. Hecker-Nolting, P. Hohenberger, R. Issels, H. Joensuu, R. L. Jones, I. Judson, P. Jutte, S. Kaal, L. Kager, B. Kasper, K. Kopeckova, D. A. Krakorova, R. Ladenstein, A. Le Cesne, I. Lugowska, O. Merimsky, M. Montemurro, B. Morland, M. A. Pantaleo, R. Piana, P. Picci, S. Piperno-Neumann, A. L. Pousa, P. Reichardt, M. H. Robinson, P. Rutkowski, A. A. Safwat, P. Schoffski, S. Sleijfer, S. Stacchiotti, S. J. Strauss, K. Sundby Hall, M. Unk, F. Van Coevorden, W. T. A. van der Graaf, J. Whelan, E. Wardelmann, O. Zaikova, and J. Y. Blay. 2018. "Bone sarcomas: ESMO-PaedCan-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up." *Ann Oncol* 29 (Suppl 4):iv79-iv95. doi: 10.1093/annonc/mdy310.

Cates, J. M. 2017. "Reporting Surgical Resection Margin Status for Osteosarcoma: Comparison of the AJCC, MSTS, and Margin Distance Methods." *Am J Surg Pathol* 41 (5):633-642. doi: 10.1097/pas.0000000000000815.

Chao, A. H., S. A. Neimanis, D. W. Chang, V. O. Lewis, and M. M. Hanasono. 2015. "Reconstruction after internal hemipelvectomy: outcomes and reconstructive algorithm." *Ann Plast Surg* 74 (3):342-9. doi: 10.1097/SAP.0b013e31829778e1.

Choudry, U. H., S. L. Moran, and Z. Karacor. 2006. "Functional reconstruction of the pelvic ring with simultaneous bilateral free fibular flaps following total sacral resection." *Ann Plast Surg* 57 (6):673-6. doi: 10.1097/01.sap.0000237058.57395.1d.

Colibaseanu, D. T., E. J. Dozois, K. L. Mathis, P. S. Rose, M. L. Ugarte, Z. M. Abdelsattar, M. D. Williams, and D. W. Larson. 2014. "Extended sacropelvic resection for locally recurrent rectal cancer: can it be done safely and with good oncologic outcomes?" *Dis Colon Rectum* 57 (1):47-55. doi: 10.1097/dcr.0000000000000015.

Copeland, L. J., K. C. Hancock, D. M. Gershenson, C. A. Stringer, E. N. Atkinson, and C. L. Edwards. 1989. "Gracilis myocutaneous vaginal reconstruction concurrent with total pelvic exenteration." *Am J Obstet Gynecol* 160 (5 Pt 1):1095-101. doi: 10.1016/0002-9378(89)90168-3.

Cordeiro, P. G., A. L. Pusic, and J. J. Disa. 2002. "A classification system and reconstructive algorithm for acquired vaginal defects." *Plast Reconstr Surg* 110 (4):1058-65. doi: 10.1097/01.Prs.0000020988.13244.A0.

Cotterill, S. J., S. Ahrens, M. Paulussen, H. F. Jurgens, P. A. Voute, H. Gadner, and A. W. Craft. 2000. "Prognostic factors in Ewing's tumor of bone: analysis of 975 patients from the European Intergroup Cooperative Ewing's Sarcoma Study Group." *J Clin Oncol* 18 (17):3108-14. doi: 10.1200/jco.2000.18.17.3108.

Couto, A. G., B. Araujo, R. A. Torres de Vasconcelos, M. J. Renni, C. O. Da Fonseca, and I. L. Cavalcanti. 2016. "Survival rate and perioperative data of patients who have undergone hemipelvectomy: a retrospective case series." *World J Surg Oncol* 14 (1):255. doi: 10.1186/s12957-016-1001-7.

Crago, A. M., and M. F. Brennan. 2015. "Principles in Management of Soft Tissue Sarcoma." *Adv Surg* 49:107-22. doi: 10.1016/j.yasu.2015.04.002.

Daigeler, A., M. Lehnhardt, A. Khadra, J. Hauser, L. Steinstraesser, S. Langer, O. Goertz, and H. U. Steinau. 2009. "Proximal major limb amputations--a retrospective analysis of 45 oncological cases." *World J Surg Oncol* 7:15. doi: 10.1186/1477-7819-7-15.

Daigeler, A., I. Zmarsly, T. Hirsch, O. Goertz, H. U. Steinau, M. Lehnhardt, and K. Harati. 2014. "Long-term outcome after local recurrence of soft tissue sarcoma: a retrospective analysis of factors predictive of survival in 135 patients with locally recurrent soft tissue sarcoma." *Br J Cancer* 110 (6):1456-64. doi: 10.1038/bjc.2014.21.

Damron, T. A., W. G. Ward, and A. Stewart. 2007. "Osteosarcoma, chondrosarcoma, and Ewing's sarcoma: National Cancer Data Base Report." *Clin Orthop Relat Res* 459:40-7. doi: 10.1097/BLO.0b013e318059b8c9.

Davidge, K. M., C. Eskicioglu, J. Lipa, P. Ferguson, C. J. Swallow, and F. C. Wright. 2010. "Qualitative assessment of patient experiences following sacrectomy." *J Surg Oncol* 101 (6):447-50. doi: 10.1002/jso.21517.

Davidson, D., R. D. Barr, S. Riad, A. M. Griffin, P. W. Chung, C. N. Catton, B. O'Sullivan, P. C. Ferguson, A. M. Davis, and J. S. Wunder. 2016. "Health-related quality of life following treatment for extremity soft tissue sarcoma." *J Surg Oncol* 114 (7):821-827. doi: 10.1002/jso.24424.

Davies, M. L., D. Harris, M. Davies, M. Lucas, P. Drew, and J. Beynon. 2011. "Selection criteria for the radical treatment of locally advanced rectal cancer." *Int J Surg Oncol* 2011:678506. doi: 10.1155/2011/678506.

Davis, A. M., R. S. Bell, E. M. Badley, K. Yoshida, and J. I. Williams. 1999. "Evaluating functional outcome in patients with lower extremity sarcoma." *Clin Orthop Relat Res* (358):90-100.

Devlin, N. J., and R. Brooks. 2017. "EQ-5D and the EuroQol Group: Past, Present and Future." *Appl Health Econ Health Policy* 15 (2):127-137. doi: 10.1007/s40258-017-0310-5.

Devulapalli, C., A. T. Jia Wei, J. R. DiBiagio, M. L. Baez, P. A. Baltodano, S. M. Seal, J. M. Sacks, C. M. Cooney, and G. D. Rosson. 2016. "Primary versus Flap Closure of Perineal Defects following Oncologic Resection: A Systematic Review and Meta-Analysis." *Plast Reconstr Surg* 137 (5):1602-13. doi: 10.1097/prs.0000000000002107.

Di Donato, V., F. Bellati, M. Fischetti, F. Plotti, G. Perniola, and P. B. Panici. 2012. "Vaginal cancer." *Crit Rev Oncol Hematol* 81 (3):286-95. doi: 10.1016/j.critrevonc.2011.04.004.

di Summa, P. G., M. Matter, D. F. Kalbermatten, O. Bauquis, and W. Raffoul. 2016. "Transabdominal-pelvic-perineal (TAPP) anterolateral thigh flap: A new reconstructive technique for complex defects following extended abdominoperineal resection." *J Plast Reconstr Aesthet Surg* 69 (3):359-67. doi: 10.1016/j.bjps.2015.10.044.

Dietrich, C. S., 3rd, A. Gehrich, and S. Bakaya. 2008. "Surgical exposure and anatomy of the female pelvis." *Surg Clin North Am* 88 (2):223-43, v. doi: 10.1016/j.suc.2008.01.003.

Dindo, D., N. Demartines, and P. A. Clavien. 2004. "Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey." *Ann Surg* 240 (2):205-13.

Diver, E. J., J. A. Rauh-Hain, and M. G. Del Carmen. 2012. "Total pelvic exenteration for gynecologic malignancies." *Int J Surg Oncol* 2012:693535. doi: 10.1155/2012/693535.

Eilber, F. R., T. T. Grant, D. Sakai, and D. L. Morton. 1979. "Internal hemipelvectomy--excision of the hemipelvis with limb preservation. An alternative to hemipelvectomy." *Cancer* 43 (3):806-9. doi: 10.1002/1097-0142(197903)43:3<806::aid-cncr2820430305>3.0.co;2-y.

Endean, E. D., T. H. Schwarcz, D. E. Barker, N. A. Munfakh, R. Wilson-Neely, and G. L. Hyde. 1991. "Hip disarticulation: factors affecting outcome." *J Vasc Surg* 14 (3):398-404.

Enneking, W. F., W. Dunham, M. C. Gebhardt, M. Malawar, and D. J. Pritchard. 1993. "A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system." *Clin Orthop Relat Res* (286):241-6.

Enneking, W. F., and W. K. Dunham. 1978. "Resection and reconstruction for primary neoplasms involving the innominate bone." *J Bone Joint Surg Am* 60 (6):731-46.

Enneking, W. F., S. S. Spanier, and M. A. Goodman. 1980. "A system for the surgical staging of musculoskeletal sarcoma." *Clin Orthop Relat Res* (153):106-20.

Espinosa-de-Los-Monteros, A., L. Arista-de la Torre, O. Vergara-Fernandez, and N. Salgado-Nesme. 2016. "Contralateral Component Separation Technique for Abdominal Wall Closure in Patients Undergoing Vertical Rectus Abdominis Myocutaneous Flap Transposition for Pelvic Exenteration Reconstruction." *Ann Plast Surg* 77 (1):90-2. doi: 10.1097/sap.0000000000000327.

Ferenschild, F. T., M. Vermaas, C. Verhoef, A. C. Ansink, W. J. Kirkels, A. M. Eggermont, and J. H. de Wilt. 2009. "Total pelvic exenteration for primary and recurrent malignancies." *World J Surg* 33 (7):1502-8. doi: 10.1007/s00268-009-0066-7.

Ferrell, B. R., K. H. Dow, and M. Grant. 1995. "Measurement of the quality of life in cancer survivors." *Qual Life Res* 4 (6):523-31. doi: 10.1007/bf00634747.

Ferron, G., D. Gangloff, D. Querleu, M. Frigenza, J. J. Torrent, L. Picaud, L. Gladieff, M. Delannes, E. Mery, B. Boulet, G. Balague, and A. Martinez. 2015. "Vaginal reconstruction with pedicled vertical deep inferior epigastric perforator flap (diep) after pelvic exenteration. A consecutive case series." *Gynecol Oncol* 138 (3):603-8. doi: 10.1016/j.ygyno.2015.06.031.

Fletcher, CDM, JA Bridge, PCW Hogendoorn, and F Mertens. 2013. *Pathology and genetics of tumours of soft tissue and bone*. Vol. 5: WHO Classification of Tumours.

Forner, D. M., and B. Lampe. 2012. "Exenteration in the treatment of Stage III/IV vulvar cancer." *Gynecol Oncol* 124 (1):87-91. doi: 10.1016/j.ygyno.2011.09.014.

Fourney, D. R., L. D. Rhines, S. J. Hentschel, J. M. Skibber, J. P. Wolinsky, K. L. Weber, D. Suki, G. L. Gallia, I. Garonzik, and Z. L. Gokaslan. 2005. "En bloc resection of primary sacral tumors: classification of surgical approaches and outcome." *J Neurosurg Spine* 3 (2):111-22. doi: 10.3171/spi.2005.3.2.0111.

Fromm, J., A. Klein, A. Baur-Melnyk, T. Knosel, L. Lindner, C. Birkenmaier, F. Roeder, V. Jansson, and H. R. Durr. 2018. "Survival and prognostic factors in conventional central chondrosarcoma." *BMC Cancer* 18 (1):849. doi: 10.1186/s12885-018-4741-7.

Fudem, G. M., and K. R. Marble. 1996. "Latissimus dorsi free flap for sacral wound closure: the world's longest vein grafts for free tissue transfer." *Microsurgery* 17 (8):449-51. doi: 10.1002/(sici)1098-2752(1996)17:8<449::aid-micr6>3.0.co;2-9.

Fujiwara, T., Y. Tsuda, J. Stevenson, M. Parry, and L. Jeys. 2020. "Sacral chordoma: do the width of surgical margin and the use of photon/proton radiotherapy affect local disease control?" *Int Orthop* 44 (2):381-389. doi: 10.1007/s00264-019-04460-5.

Funder, J. A., R. Tolstrup, B. N. Jepsen, and L. H. Iversen. 2017. "Postoperative paralytic ileus remains a problem following surgery for advanced pelvic cancers." *J Surg Res* 218:167-173. doi: 10.1016/j.jss.2017.05.044.

Garvey, P. B., M. W. Clemens, L. D. Rhines, and J. M. Sacks. 2013. "Vertical rectus abdominis musculocutaneous flow-through flap to a free fibula flap for total sacrectomy reconstruction." *Microsurgery* 33 (1):32-8. doi: 10.1002/micr.21990.

Garvey, P. B., L. D. Rhines, L. Feng, X. Gu, and C. E. Butler. 2011. "Reconstructive strategies for partial sacrectomy defects based on surgical outcomes." *Plast Reconstr Surg* 127 (1):190-9. doi: 10.1097/PRS.0b013e3181f95a19.

Georgantopoulou, A., S. Papadodima, D. Vlachodimitropoulos, N. Goutas, C. Spiliopoulou, and O. Papadopoulos. 2014. "The microvascular anatomy of superior and inferior gluteal artery perforator (SGAP and IGAP) flaps: a fresh cadaveric study and clinical implications." *Aesthetic Plast Surg* 38 (6):1156-63. doi: 10.1007/s00266-014-0398-z.

Gerrand, C. H., J. S. Wunder, R. A. Kandel, B. O'Sullivan, C. N. Catton, R. S. Bell, A. M. Griffin, and A. M. Davis. 2001. "Classification of positive margins after resection of soft-tissue sarcoma of the limb predicts the risk of local recurrence." *J Bone Joint Surg Br* 83 (8):1149-55. doi: 10.1302/0301-620x.83b8.12028.

Glynne-Jones, R., L. Wyrwicz, E. Tiret, G. Brown, C. Rodel, A. Cervantes, and D. Arnold. 2017. "Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up." *Ann Oncol* 28 (suppl_4):iv22-iv40. doi: 10.1093/annonc/mdx224.

Goldberg, G. L., P. Sukumvanich, M. H. Einstein, H. O. Smith, P. S. Anderson, and A. L. Fields. 2006. "Total pelvic exenteration: the Albert Einstein College of Medicine/Montefiore Medical Center Experience (1987 to 2003)." *Gynecol Oncol* 101 (2):261-8. doi: 10.1016/j.ygyno.2005.10.011.

Goodwin, M. L., M. K. Gundavda, R. Reddy, K. Deogaonkar, M. Lala, A. Baliarsing, D. M. Sciubba, K. B. Jones, and M. Agarwal. 2019. "Extracorporeal radiation and reimplantation: a safe and viable option for reconstruction after sacral tumor resection?" *Ann Transl Med* 7 (10):229. doi: 10.21037/atm.2019.01.79.

Griesser, M. J., B. Gillette, M. Crist, X. Pan, P. Muscarella, T. Scharschmidt, and J. Mayerson. 2012. "Internal and external hemipelvectomy or flail hip in patients with sarcomas: quality-of-life and functional outcomes." *Am J Phys Med Rehabil* 91 (1):24-32. doi: 10.1097/PHM.0b013e318232885a.

Grimer, R. J., C. R. Chandrasekar, S. R. Carter, A. Abudu, R. M. Tillman, and L. Jeys. 2013. "Hindquarter amputation: is it still needed and what are the outcomes?" *Bone Joint J* 95-b (1):127-31. doi: 10.1302/0301-620x.95b1.29131.

Guder, W. K., J. Hardes, G. Gosheger, M. P. Henrichs, M. Nottrott, and A. Streitburger. 2015. "Analysis of surgical and oncological outcome in internal and external hemipelvectomy in 34 patients above the age of 65 years at a mean follow-up of 56 months." *BMC Musculoskelet Disord* 16:33. doi: 10.1186/s12891-015-0494-5.

Guillou, L., J. M. Coindre, F. Bonichon, B. B. Nguyen, P. Terrier, F. Collin, M. O. Vilain, A. M. Mandard, V. Le Doussal, A. Leroux, J. Jacquemier, H. Duplay, X. Sastre-Garau, and J. Costa. 1997. "Comparative study of the National Cancer Institute and French Federation of Cancer Centers Sarcoma Group grading systems in a population of 410 adult patients with soft tissue sarcoma." *J Clin Oncol* 15 (1):350-62. doi: 10.1200/jco.1997.15.1.350.

Hashimoto, I., Y. Abe, and H. Nakanishi. 2014. "The internal pudendal artery perforator flap: free-style pedicle perforator flaps for vulva, vagina, and buttock reconstruction." *Plast Reconstr Surg* 133 (4):924-33. doi: 10.1097/prs.0000000000000008.

Hata, M., N. Kawahara, and K. Tomita. 1998. "Influence of ligation of the internal iliac veins on the venous plexuses around the sacrum." *J Orthop Sci* 3 (5):264-71.

He, F., W. Zhang, Y. Shen, P. Yu, Q. Bao, J. Wen, C. Hu, and S. Qiu. 2016. "Effects of resection margins on local recurrence of osteosarcoma in extremity and pelvis: Systematic review and meta-analysis." *Int J Surg* 36 (Pt A):283-292. doi: 10.1016/j.ijsu.2016.11.016.

Hersant, B., P. May, M. Battistella, C. Pages, C. Lebbe, and M. Revol. 2013. "Reducing surgical margins in dermatofibrosarcoma protuberans using the pathological analysis technique 'vertical modified technique': a 5-year experience." *J Plast Reconstr Aesthet Surg* 66 (5):617-22. doi: 10.1016/j.bjps.2013.01.016.

Hofmann, B., L. L. Håheim, and J. A. Søreide. 2005. "Ethics of palliative surgery in patients with cancer." *Br J Surg* 92 (7):802-9. doi: 10.1002/bjs.5104.

Holzer, L. A., N. Huyer, J. Friesenbichler, and A. Leithner. 2020. "Body image, self-esteem, and quality of life in patients with primary malignant bone tumors." *Arch Orthop Trauma Surg* 140 (1):1-10. doi: 10.1007/s00402-019-03205-8.

Horch, R. E., W. Hohenberger, A. Eweida, U. Kneser, K. Weber, A. Arkudas, S. Merkel, J. Gohl, and J. P. Beier. 2014. "A hundred patients with vertical rectus abdominis myocutaneous (VRAM) flap for pelvic reconstruction after total pelvic exenteration." *Int J Colorectal Dis* 29 (7):813-23. doi: 10.1007/s00384-014-1868-0.

Houdek, M. T., K. Andrews, M. E. Kralovec, B. Kotajarvi, F. C. Smither, T. C. Shives, P. S. Rose, and F. H. Sim. 2016. "Functional outcome measures of patients following hemipelvectomy." *Prosthet Orthot Int* 40 (5):566-72. doi: 10.1177/0309364615574164.

Houdek, M. T., K. Bakri, M. E. Tibbo, E. R. Wagner, P. S. Rose, F. H. Sim, and S. L. Moran. 2018. "Outcome and Complications following Vertical Rectus Abdominis Myocutaneous Flap Surgery to Reconstruct Sacrectomy Defects." *Plast Reconstr Surg* 142 (5):1327-1335. doi: 10.1097/prs.0000000000004890.

Houdek, M. T., M. Hevesi, J. H. Schwab, M. J. Yaszemski, A. M. Griffin, J. H. Healey, P. C. Ferguson, F. J. Hornicek, P. J. Boland, F. H. Sim, P. S. Rose, and J. S. Wunder. 2019. "Association between patient age and the risk of mortality following local recurrence of a sacral chordoma." *J Surg Oncol*. doi: 10.1002/jso.25774.

Houdek, M. T., M. E. Kralovec, and K. L. Andrews. 2014. "Hemipelvectomy: high-level amputation surgery and prosthetic rehabilitation." *Am J Phys Med Rehabil* 93 (7):600-8. doi: 10.1097/phm.0000000000000068.

Hunter, J. A., J. A. Ryan, Jr., and P. Schultz. 1987. "En bloc resection of colon cancer adherent to other organs." *Am J Surg* 154 (1):67-71. doi: 10.1016/0002-9610(87)90292-3.

Iglesias, D. A., S. N. Westin, V. Rallapalli, M. Huang, B. Fellman, D. Urbauer, M. Frumovitz, P. T. Ramirez, and P. T. Soliman. 2012. "The effect of body mass index on surgical outcomes and survival following pelvic exenteration." *Gynecol Oncol* 125 (2):336-42. doi: 10.1016/j.ygyno.2012.01.010.

Ireton, J. E., C. Lakhiani, and M. Saint-Cyr. 2014. "Vascular anatomy of the deep inferior epigastric artery perforator flap: a systematic review." *Plast Reconstr Surg* 134 (5):810e-821e. doi: 10.1097/prs.0000000000000625.

Jain, R., R. J. Grimer, S. R. Carter, R. M. Tillman, and A. A. Abudu. 2005. "Outcome after disarticulation of the hip for sarcomas." *Eur J Surg Oncol* 31 (9):1025-8. doi: 10.1016/j.ejso.2005.07.014.

Jeys, L. M., C. J. Thorne, M. Parry, C. L. Gaston, V. P. Sumathi, and J. R. Grimer. 2017. "A Novel System for the Surgical Staging of Primary High-grade Osteosarcoma: The Birmingham Classification." *Clin Orthop Relat Res* 475 (3):842-850. doi: 10.1007/s11999-016-4851-y.

Ji, T., W. Guo, R. Yang, X. Tang, Y. Wang, and L. Huang. 2017. "What Are the Conditional Survival and Functional Outcomes After Surgical Treatment of 115 Patients With Sacral Chordoma?" *Clin Orthop Relat Res* 475 (3):620-630. doi: 10.1007/s11999-016-4773-8.

Jurado, M., A. Bazan, J. L. Alcazar, and E. Garcia-Tutor. 2009. "Primary vaginal reconstruction at the time of pelvic exenteration for gynecologic cancer: morbidity revisited." *Ann Surg Oncol* 16 (1):121-7. doi: 10.1245/s10434-008-0171-0.

Kaartinen, I. S., M. H. Vuento, M. K. Hyoty, J. Kallio, and H. O. Kuokkanen. 2015. "Reconstruction of the pelvic floor and the vagina after total pelvic exenteration using the transverse musculocutaneous gracilis flap." *J Plast Reconstr Aesthet Surg* 68 (1):93-7. doi: 10.1016/j.bjps.2014.08.059.

Karimi, M., and J. Brazier. 2016. "Health, Health-Related Quality of Life, and Quality of Life: What is the Difference?" *Pharmacoeconomics* 34 (7):645-9. doi: 10.1007/s40273-016-0389-9.

Kask, G., I. Barner-Rasmussen, J. P. Repo, M. Kjäldman, K. Kilk, C. Blomqvist, and E. J. Tukiainen. 2019. "Functional Outcome Measurement in Patients with Lower-Extremity Soft Tissue Sarcoma: A Systematic Literature Review." *Ann Surg Oncol* 26 (13):4707-4722. doi: 10.1245/s10434-019-07698-w.

Kaufman, M. H., and S. J. Wakelin. 2004. "Amputation through the hip joint during the pre-anaesthetic era." *Clin Anat* 17 (1):36-44. doi: 10.1002/ca.10138.

Kaur, M., S. Joniau, A. D'Hoore, and I. Vergote. 2014. "Indications, techniques and outcomes for pelvic exenteration in gynecological malignancy." *Curr Opin Oncol* 26 (5):514-20. doi: 10.1097/cco.0000000000000109.

Kawai, A., J. H. Healey, P. J. Boland, P. P. Lin, A. G. Huvos, and P. A. Meyers. 1998. "Prognostic factors for patients with sarcomas of the pelvic bones." *Cancer* 82 (5):851-9.

Kayani, B., S. A. Hanna, M. D. Sewell, A. Saifuddin, S. Molloy, and T. W. Briggs. 2014. "A review of the surgical management of sacral chordoma." *Eur J Surg Oncol* 40 (11):1412-20. doi: 10.1016/j.ejso.2014.04.008.

Kayani, B., M. D. Sewell, K. A. Tan, S. A. Hanna, R. Williams, R. Pollock, J. Skinner, and T. W. Briggs. 2015. "Prognostic Factors in the Operative Management of Sacral Chordomas." *World Neurosurg* 84 (5):1354-61. doi: 10.1016/j.wneu.2015.06.030.

Kemp, Walter L., Dennis K. Burns, and Travis G. Brown. 2008. *Pathology: The Big Picture*.

Kerekes, D., C. R. Goodwin, A. K. Ahmed, J. J. Verlaan, C. Bettegowda, N. Abu-Bonsrah, and D. M. Sciubba. 2019. "Local and Distant Recurrence in Resected Sacral Chordomas: A Systematic Review and Pooled Cohort Analysis." *Global Spine J* 9 (2):191-201. doi: 10.1177/2192568217741114.

Khoury-Collado, F., M. H. Einstein, B. H. Bochner, K. M. Alektiar, Y. Sonoda, N. R. Abu-Rustum, C. L. Brown, G. J. Gardner, R. R. Barakat, and D. S. Chi. 2012. "Pelvic exenteration with curative intent for recurrent uterine malignancies." *Gynecol Oncol* 124 (1):42-7. doi: 10.1016/j.ygyno.2011.09.031.

Kiatisevi, P., C. Piyaskulkaew, S. Kunakornsawat, and B. Sukunthanak. 2017. "What Are the Functional Outcomes After Total Sacrectomy Without Spinopelvic Reconstruction?" *Clin Orthop Relat Res* 475 (3):643-655. doi: 10.1007/s11999-016-4729-z.

Kim, H. K., J. M. Jessup, C. J. Beard, B. Bornstein, B. Cady, M. D. Stone, R. Bleday, A. Bothe, Jr., G. Steele, Jr., and P. M. Busse. 1997. "Locally advanced rectal carcinoma: pelvic control and morbidity following preoperative radiation therapy, resection, and intraoperative radiation therapy." *Int J Radiat Oncol Biol Phys* 38 (4):777-83. doi: 10.1016/s0360-3016(97)89476-x.

Kim, J. E., J. Pang, J. M. Christensen, D. Coon, P. L. Zadnik, J. P. Wolinsky, Z. L. Gokaslan, A. Bydon, D. M. Sciubba, T. Witham, R. J. Redett, and J. M. Sacks. 2015. "Soft-tissue reconstruction after total en bloc sacrectomy." *J Neurosurg Spine* 22 (6):571-81. doi: 10.3171/2014.10.spine14114.

Knight, S., E. Lambaudie, L. Sabiani, D. Mokart, M. Provansal, A. Tallet, and G. Houvenaeghel. 2018. "Pelvic exenterations for gynecologic cancers: A retrospective analysis of a 30-year experience in a cancer center." *Eur J Surg Oncol*. doi: 10.1016/j.ejso.2018.08.017.

Knox, K., I. Bitzos, M. Granick, R. Datiashvili, J. Benevenia, and F. Patterson. 2006. "Immediate reconstruction of oncologic hemipelvectomy defects." *Ann Plast Surg* 57 (2):184-9. doi: 10.1097/01.sap.0000215288.83924.6c.

Koh, C. E., M. J. Solomon, K. G. Brown, K. Austin, C. M. Byrne, P. Lee, and J. M. Young. 2017. "The Evolution of Pelvic Exenteration Practice at a Single Center: Lessons Learned from over 500 Cases." *Dis Colon Rectum* 60 (6):627-635. doi: 10.1097/dcr.0000000000000825.

Kreutz-Rodrigues, L., J. M. Weissler, S. L. Moran, B. T. Carlsen, S. Mardini, M. T. Houdek, P. S. Rose, and K. Bakri. 2019. "Reconstruction of complex hemipelvectomy defects: A 17-year single-institutional experience with lower extremity free and pedicled fillet flaps." *J Plast Reconstr Aesthet Surg*. doi: 10.1016/j.bjps.2019.09.028.

Kuntscher, M. V., D. Erdmann, H. H. Homann, H. U. Steinau, S. L. Levin, and G. Germann. 2001. "The concept of fillet flaps: classification, indications, and analysis of their clinical value." *Plast Reconstr Surg* 108 (4):885-96.

Kusiak, J. F., and N. G. Rosenblum. 1996. "Neovaginal reconstruction after exenteration using an omental flap and split-thickness skin graft." *Plast Reconstr Surg* 97 (4):775-81; discussion 783-3. doi: 10.1097/00006534-199604000-00013.

Laitinen, M. K., M. C. Parry, L. R. Le Nail, C. H. Wigley, J. D. Stevenson, and L. M. Jeys. 2019. "Locally recurrent chondrosarcoma of the pelvis and limbs can only be controlled by wide local excision." *Bone Joint J* 101-b (3):266-271. doi: 10.1302/0301-620x.101b3.Bjj-2018-0881.R1.

Laitinen, M., M. Parry, J. I. Albergo, L. Jeys, A. Abudu, S. Carter, V. Sumathi, and R. Grimer. 2015. "The prognostic and therapeutic factors which influence the oncological outcome of parosteal osteosarcoma." *Bone Joint J* 97-b (12):1698-703. doi: 10.1302/0301-620x.97b12.35749.

Laitinen, M., M. Parry, J. I. Albergo, L. Jeys, V. Sumathi, and R. Grimer. 2018. "Outcome of Pelvic Bone Sarcomas in Children." *J Pediatr Orthop* 38 (10):537-542. doi: 10.1097/bpo.0000000000000860.

Lakhiani, C., M. V. DeFazio, K. Han, R. Falola, and K. Evans. 2016. "Donor-Site Morbidity Following Free Tissue Harvest from the Thigh: A Systematic Review and Pooled Analysis of Complications." *J Reconstr Microsurg* 32 (5):342-57. doi: 10.1055/s-0036-1583301.

Landoni, F., A. Colombo, R. Milani, F. Placa, V. Zanagnolo, and C. Mangioni. 2017. "Randomized study between radical surgery and radiotherapy for the treatment of stage IB-IIA cervical cancer: 20-year update." *J Gynecol Oncol* 28 (3):e34. doi: 10.3802/jgo.2017.28.e34.

Lang, P., S. Grampp, M. Vahlensieck, J. O. Johnston, G. Honda, W. Rosenau, K. K. Matthay, C. Peterfy, C. B. Higgins, H. K. Genant, and et al. 1995. "Primary bone tumors: value of MR angiography for preoperative planning and monitoring response to chemotherapy." *AJR Am J Roentgenol* 165 (1):135-42. doi: 10.2214/ajr.165.1.7785572.

Law, W. L., and K. W. Chu. 2004. "Anterior resection for rectal cancer with mesorectal excision: a prospective evaluation of 622 patients." *Ann Surg* 240 (2):260-8. doi: 10.1097/01. sla.0000133185.23514.32.

Le Huec, J. C., R. Saddiki, J. Franke, J. Rigal, and S. Aunoble. 2011. "Equilibrium of the human body and the gravity line: the basics." *Eur Spine J* 20 Suppl 5:558-63. doi: 10.1007/s00586-011-1939-7.

Lee, K. T., and G. H. Mun. 2014. "A systematic review of functional donor-site morbidity after latissimus dorsi muscle transfer." *Plast Reconstr Surg* 134 (2):303-14. doi: 10.1097/prs.0000000000000365.

Lee, P., W. J. Tan, K. G. M. Brown, and M. J. Solomon. 2019. "Addressing the empty pelvic syndrome following total pelvic exenteration: does mesh reconstruction help?" *Colorectal Dis* 21 (3):365-369. doi: 10.1111/codi.14523.

Li, D., W. Guo, X. Tang, T. Ji, and Y. Zhang. 2011. "Surgical classification of different types of en bloc resection for primary malignant sacral tumors." *Eur Spine J* 20 (12):2275-81. doi: 10.1007/s00586-011-1883-6.

Linko, R., R. Suojaranta-Ylinen, S. Karlsson, E. Ruokonen, T. Varpula, and V. Pettila. 2010. "One-year mortality, quality of life and predicted life-time cost-utility in critically ill patients with acute respiratory failure." *Crit Care* 14 (2):R60. doi: 10.1186/cc8957.

Ljungqvist, O., M. Scott, and K. C. Fearon. 2017. "Enhanced Recovery After Surgery: A Review." *JAMA Surg* 152 (3):292-298. doi: 10.1001/jamasurg.2016.4952.

Lyell, N. J., M. Kitano, B. Smith, A. L. Gleisner, F. J. Backes, G. Cheng, M. D. McCarter, S. Abdel-Misih, and E. L. Jones. 2019. "The effect of preoperative nutritional status on postoperative complications and overall survival in patients undergoing pelvic exenteration: A multi-disciplinary, multi-institutional cohort study." *Am J Surg* 218 (2):275-280. doi: 10.1016/j.amjsurg.2019.03.021.

MacFarlane, J. K., R. D. Ryall, and R. J. Heald. 1993. "Mesorectal excision for rectal cancer." *Lancet* 341 (8843):457-60. doi: 10.1016/0140-6736(93)90207-w.

Maggioni, A., G. Roviglione, F. Landoni, V. Zanagnolo, M. Peiretti, N. Colombo, L. Bocciolone, R. Biffi, L. Minig, and C. P. Morrow. 2009. "Pelvic exenteration: ten-year experience at the European Institute of Oncology in Milan." *Gynecol Oncol* 114 (1):64-8. doi: 10.1016/j.ygyno.2009.03.029.

Magrina, J. F., C. R. Stanhope, and A. L. Weaver. 1997. "Pelvic exenterations: supralevator, infralevator, and with vulvectomy." *Gynecol Oncol* 64 (1):130-5. doi: 10.1006/gyno.1996.4532.

Mansfield, P., and A. A. Maudsley. 1977. "Medical imaging by NMR." *Br J Radiol* 50 (591):188-94. doi: 10.1259/0007-1285-50-591-188.

Maretty-Nielsen, K., N. Aggerholm-Pedersen, A. Safwat, P. H. Jorgensen, B. H. Hansen, S. Baerentzen, A. B. Pedersen, and J. Keller. 2014. "Prognostic factors for local recurrence and mortality in adult soft tissue sarcoma of the extremities and trunk wall: a cohort study of 922 consecutive patients." *Acta Orthop* 85 (3):323-32. doi: 10.3109/17453674.2014.908341.

Maricevich, M., R. Maricevich, H. Chim, S. L. Moran, P. S. Rose, and S. Mardini. 2014. "Reconstruction following partial and total sacrectomy defects: an analysis of outcomes and complications." *J Plast Reconstr Aesthet Surg* 67 (9):1257-66. doi: 10.1016/j.bjps.2014.05.001.

Marnitz, S., C. Kohler, M. Muller, K. Behrens, K. Hasenbein, and A. Schneider. 2006. "Indications for primary and secondary exenterations in patients with cervical cancer." *Gynecol Oncol* 103 (3):1023-30. doi: 10.1016/j.ygyno.2006.06.027.

Marth, C., F. Landoni, S. Mahner, M. McCormack, A. Gonzalez-Martin, and N. Colombo. 2017. "Cervical cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up." *Ann Oncol* 28 (suppl_4):iv72-iv83. doi: 10.1093/annonc/mdx220.

Mastrangelo, G., J. M. Coindre, F. Ducimetiere, A. P. Dei Tos, E. Fadda, J. Y. Blay, A. Buja, U. Fedeli, L. Cegolon, A. Frasson, D. Ranchere-Vince, C. Montesco, I. Ray-Coquard, and C. R. Rossi. 2012. "Incidence of soft tissue sarcoma and beyond: a population-based prospective study in 3 European regions." *Cancer* 118 (21):5339-48. doi: 10.1002/cncr.27555.

Mat Saad, A. Z., A. S. Halim, W. I. Faisham, W. S. Azman, and W. Zulmi. 2012. "Soft tissue reconstruction following hemipelvectomy: eight-year experience and literature review." *Scientific World Journal* 2012:702904. doi: 10.1100/2012/702904.

Mathes, S. J., and J. Bostwick, 3rd. 1977. "A rectus abdominis myocutaneous flap to reconstruct abdominal wall defects." *Br J Plast Surg* 30 (4):282-3. doi: 10.1016/0007-1226(77)90118-7.

Matsuo, K., R. S. Mandelbaum, C. L. Adams, L. D. Roman, and J. D. Wright. 2019. "Performance and outcome of pelvic exenteration for gynecologic malignancies: A population-based study." *Gynecol Oncol* 153 (2):368-375. doi: 10.1016/j.ygyno.2019.02.002.

Mavrogenis, A. F., K. Soultanis, P. Patapis, G. Guerra, N. Fabbri, P. Ruggieri, and P. J. Papagelopoulos. 2012. "Pelvic resections." *Orthopedics* 35 (2):e232-43. doi: 10.3928/01477447-20120123-40.

Mayerson, J. L., A. N. Wooldridge, and T. J. Scharschmidt. 2014. "Pelvic resection: current concepts." *J Am Acad Orthop Surg* 22 (4):214-22. doi: 10.5435/jaaos-22-04-214.

McArdle, A., D. A. Bischof, K. Davidge, C. J. Swallow, and D. C. Winter. 2012. "Vaginal reconstruction following radical surgery for colorectal malignancies: a systematic review of the literature." *Ann Surg Oncol* 19 (12):3933-42. doi: 10.1245/s10434-012-2503-3.

McCahill, L. E., R. Krouse, D. Chu, G. Juarez, G. C. Uman, B. Ferrell, and L. D. Wagman. 2002. "Indications and use of palliative surgery-results of Society of Surgical Oncology survey." *Ann Surg Oncol* 9 (1):104-12. doi: 10.1245/aso.2002.9.1.104.

McCarthy, A. S. E., M. J. Solomon, C. E. Koh, A. Firouzbakht, S. A. Jackson, and D. Steffens. 2019. "Quality of life and functional outcomes following pelvic exenteration and sacrectomy." *Colorectal Dis*. doi: 10.1111/codi.14925.

McCraw, J. B., F. M. Massey, K. D. Shanklin, and C. E. Horton. 1976. "Vaginal reconstruction with gracilis myocutaneous flaps." *Plast Reconstr Surg* 58 (2):176-83. doi: 10.1097/00006534-197608000-00006.

McGlone, T. P., W. A. Bernie, and D. W. Elliott. 1982. "Survival following extended operations for extracolonic invasion by colon cancer." *Arch Surg* 117 (5):595-9. doi: 10.1001/archsurg.1982.01380290055010.

McKnight, A. J., V. O. Lewis, L. D. Rhines, and M. M. Hanasono. 2013. "Femur-fibula-fillet of leg chimeric free flap for sacral-pelvic reconstruction." *J Plast Reconstr Aesthet Surg* 66 (12):1784-7. doi: 10.1016/j.bjps.2013.05.025.

McMahon, C. J., N. M. Rofsky, and I. Pedrosa. 2010. "Lymphatic metastases from pelvic tumors: anatomic classification, characterization, and staging." *Radiology* 254 (1):31-46. doi: 10.1148/radiol.2541090361.

Merimsky, O., Y. Kollender, M. Inbar, S. Chaitchik, and I. Meller. 1997. "Palliative major amputation and quality of life in cancer patients." *Acta Oncol* 36 (2):151-7. doi: 10.3109/02841869709109223.

Miles, W. K., D. W. Chang, S. S. Kroll, M. J. Miller, H. N. Langstein, G. P. Reece, G. R. Evans, and G. L. Robb. 2000. "Reconstruction of large sacral defects following total sacrectomy." *Plast Reconstr Surg* 105 (7):2387-94.

Miller, B., M. Morris, D. M. Gershenson, C. L. Levenback, and T. W. Burke. 1995. "Intestinal fistulae formation following pelvic exenteration: a review of the University of Texas M. D. Anderson Cancer Center experience, 1957-1990." *Gynecol Oncol* 56 (2):207-10. doi: 10.1006/gyno.1995.1033.

Milne, T., M. J. Solomon, P. Lee, J. M. Young, P. Stalley, J. D. Harrison, and K. K. Austin. 2014. "Sacral resection with pelvic exenteration for advanced primary and recurrent pelvic cancer: a single-institution experience of 100 sacrectomies." *Dis Colon Rectum* 57 (10):1153-61. doi: 10.1097/dcr.0000000000000196.

Mirabello, L., R. J. Troisi, and S. A. Savage. 2009. "Osteosarcoma incidence and survival rates from 1973 to 2004: data from the Surveillance, Epidemiology, and End Results Program." *Cancer* 115 (7):1531-43. doi: 10.1002/cncr.24121.

Miyamoto, Y., T. Akiyama, Y. Sakamoto, R. Tokunaga, M. Ohuchi, H. Shigaki, J. Kurashige, M. Iwatsuki, Y. Baba, N. Yoshida, and H. Baba. 2016. "Omental flap after pelvic exenteration for pelvic cancer." *Surg Today* 46 (12):1471-1475. doi: 10.1007/s00595-016-1348-y.

Moore, Keith L. 2018. *Clinically oriented anatomy*. Eight edition ed. Philadelphia: Wolters Kluwer.

Morris, J., R. Yang, M. Roth, J. Gill, R. Gorlick, Y. Lo, B. H. Hoang, E. Garfein, and D. S. Geller. 2017. "Mechanical analysis of the vascularized fibular graft prosthetic composite (VFGPC) for internal hemipelvectomy reconstruction." *J Surg Oncol* 115 (7):864-869. doi: 10.1002/jso.24593.

Nagarajan, R., D. R. Clohisy, J. P. Neglia, Y. Yasui, P. A. Mitby, C. Sklar, J. Z. Finklestein, M. Greenberg, G. H. Reaman, L. Zeltzer, and L. L. Robison. 2004. "Function and quality-of-life of survivors of pelvic and lower extremity osteosarcoma and Ewing's sarcoma: the Childhood Cancer Survivor Study." *Br J Cancer* 91 (11):1858-65. doi: 10.1038/sj.bjc.6602220.

Nakamura, T., A. Abudu, H. Murata, R. J. Grimer, S. R. Carter, R. M. Tillman, and L. Jeys. 2013. "Oncological outcome of patients with deeply located soft tissue sarcoma of the pelvis: a follow up study at minimum 5 years after diagnosis." *Eur J Surg Oncol* 39 (9):1030-5. doi: 10.1016/j.ejso.2012.12.019.

Nelson, G., J. Bakkum-Gamez, E. Kalogera, G. Glaser, A. Altman, L. A. Meyer, J. S. Taylor, M. Iniesta, J. Lasala, G. Mena, M. Scott, C. Gillis, K. Elias, L. Wijk, J. Huang, J. Nygren, O. Ljungqvist, P. T. Ramirez, and S. C. Dowdy. 2019. "Guidelines for perioperative care in gynecologic/oncology: Enhanced Recovery After Surgery (ERAS) Society recommendations-2019 update." *Int J Gynecol Cancer* 29 (4):651-668. doi: 10.1136/ijgc-2019-000356.

Nelson, R. A., and C. E. Butler. 2009. "Surgical outcomes of VRAM versus thigh flaps for immediate reconstruction of pelvic and perineal cancer resection defects." *Plast Reconstr Surg* 123 (1):175-83. doi: 10.1097/PRS.0b013e3181904df7.

Nie, Z., Q. Lu, and H. Peng. 2018. "Prognostic factors for patients with chondrosarcoma: A survival analysis based on the Surveillance, Epidemiology, and End Results (SEER) database (1973-2012)." *J Bone Oncol* 13:55-61. doi: 10.1016/j.jbo.2018.09.003.

Nishizawa, K., K. Mori, Y. Saruhashi, S. Takahashi, and Y. Matsusue. 2014. "Long-term clinical outcome of sacral chondrosarcoma treated by total en bloc sacrectomy and reconstruction of lumbosacral and pelvic ring using intraoperative extracorporeal irradiated autologous tumor-bearing sacrum: a case report with 10 years follow-up." *Spine J* 14 (5):e1-8. doi: 10.1016/j.spinee.2013.10.057.

Nisula, S., K. M. Kaukonen, S. T. Vaara, A. M. Korhonen, M. Poukkanen, S. Karlsson, M. Haapio, O. Inkinen, I. Parviainen, R. Suojaranta-Ylinen, J. J. Laurila, J. Tenhunen, M. Reinikainen, T. Ala-Kokko, E. Ruokonen, A. Kuitunen, and V. Pettila. 2013. "Incidence, risk factors and 90-day mortality of patients with acute kidney injury in Finnish intensive care units: the FINNAKI study." *Intensive Care Med* 39 (3):420-8. doi: 10.1007/s00134-012-2796-5.

O'Connor, M. I., and F. H. Sim. 1989. "Salvage of the limb in the treatment of malignant pelvic tumors." *J Bone Joint Surg Am* 71 (4):481-94.

O'Sullivan, B., A. M. Davis, R. Turcotte, R. Bell, C. Catton, P. Chabot, J. Wunder, R. Kandel, K. Goddard, A. Sadura, J. Pater, and B. Zee. 2002. "Preoperative versus postoperative radiotherapy in soft-tissue sarcoma of the limbs: a randomised trial." *Lancet* 359 (9325):2235-41. doi: 10.1016/s0140-6736(02)09292-9.

Ottaviani, G., and N. Jaffe. 2009. "The epidemiology of osteosarcoma." *Cancer Treat Res* 152:3-13. doi: 10.1007/978-1-4419-0284-9_1.

Pano, B., C. Sebastia, L. Bunesch, J. Mestres, R. Salvador, N. G. Macias, and C. Nicolau. 2011. "Pathways of lymphatic spread in male urogenital pelvic malignancies." *Radiographics* 31 (1):135-60. doi: 10.1148/rg.311105072.

Pano, B., C. Sebastia, E. Ripoll, P. Paredes, R. Salvador, L. Bunesch, and C. Nicolau. 2015. "Pathways of lymphatic spread in gynecologic malignancies." *Radiographics* 35 (3):916-45. doi: 10.1148/rg.2015140086.

Park, J. Y., H. J. Choi, S. Y. Jeong, J. Chung, J. K. Park, and S. Y. Park. 2007. "The role of pelvic exenteration and reconstruction for treatment of advanced or recurrent gynecologic malignancies: Analysis of risk factors predicting recurrence and survival." *J Surg Oncol* 96 (7):560-8. doi: 10.1002/jso.20847.

Parry, M. C., M. Laitinen, J. Albergo, L. Jeys, S. Carter, C. L. Gaston, V. Sumathi, and R. J. Grimer. 2016. "Osteosarcoma of the pelvis." *Bone Joint J* 98-b (4):555-63. doi: 10.1302/0301-620x.98b4.36583.

Pawlik, T. M., J. M. Skibber, and M. A. Rodriguez-Bigas. 2006. "Pelvic exenteration for advanced pelvic malignancies." *Ann Surg Oncol* 13 (5):612-23. doi: 10.1245/aso.2006.03.082.

Petruzziello, A., W. Kondo, S. B. Hatschback, J. A. Guerreiro, F. P. Filho, C. Vendrame, M. Luz, and R. Ribeiro. 2014. "Surgical results of pelvic exenteration in the treatment of gynecologic cancer." *World J Surg Oncol* 12:279. doi: 10.1186/1477-7819-12-279.

Pickard, A. S., M. P. Neary, and D. Cella. 2007. "Estimation of minimally important differences in EQ-5D utility and VAS scores in cancer." *Health Qual Life Outcomes* 5:70. doi: 10.1186/1477-7525-5-70.

Pillai, S., and S. Govender. 2018. "Sacral chordoma : A review of literature." *J Orthop* 15 (2):679-684. doi: 10.1016/j.jor.2018.04.001.

Platt, E., G. Dovell, and S. Smolarek. 2018. "Systematic review of outcomes following pelvic exenteration for the treatment of primary and recurrent locally advanced rectal cancer." *Tech Coloproctol* 22 (11):835-845. doi: 10.1007/s10151-018-1883-1.

Puchner, S. E., P. T. Funovics, C. Bohler, A. Kaider, C. Stihsen, G. M. Hobusch, J. Panotopoulos, and R. Windhager. 2017. "Oncological and surgical outcome after treatment of pelvic sarcomas." *PLoS One* 12 (2):e0172203. doi: 10.1371/journal.pone.0172203.

Pusic, A. L., and B. J. Mehrara. 2006. "Vaginal reconstruction: an algorithm approach to defect classification and flap reconstruction." *J Surg Oncol* 94 (6):515-21. doi: 10.1002/jso.20489.

Qiu, S. S., M. Jurado, and B. Hontanilla. 2013. "Comparison of TRAM versus DIEP flap in total vaginal reconstruction after pelvic exenteration." *Plast Reconstr Surg* 132 (6):1020e-7e. doi: 10.1097/PRS.0b013e3182a97ea2.

Ramamurthy, R., J. C. Bose, V. Muthusamy, M. Natarajan, and D. Kunjithapatham. 2009. "Staged sacrectomy--an adaptive approach." *J Neurosurg Spine* 11 (3):285-94. doi: 10.3171/2009.3.spine08824.

Reichardt, P., M. Leahy, X. Garcia Del Muro, S. Ferrari, J. Martin, H. Gelderblom, J. Wang, A. Krishna, J. Eriksson, A. Staddon, and J. Y. Blay. 2012. "Quality of Life and Utility in Patients with Metastatic Soft Tissue and Bone Sarcoma: The Sarcoma Treatment and Burden of Illness in North America and Europe (SABINE) Study." *Sarcoma* 2012:740279. doi: 10.1155/2012/740279.

Reynolds, J. J., R. Khundkar, S. Boriani, R. Williams, L. D. Rhines, N. Kawahara, J. P. Wolinsky, Z. L. Gokaslan, and P. P. Varga. 2016. "Soft Tissue and Bone Defect Management in Total Sacrectomy for Primary Sacral Tumors: A Systematic Review With Expert Recommendations." *Spine* (*Phila Pa 1976*) 41 Suppl 20:S199-s204. doi: 10.1097/brs.0000000000001834.

Rezk, Y. A., K. E. Hurley, J. Carter, F. Dao, B. H. Bochner, J. J. Aubey, A. Caceres, M. H. Einstein, N. R. Abu-Rustum, R. R. Barakat, V. Makker, and D. S. Chi. 2013. "A prospective study of quality of life in patients undergoing pelvic exenteration: interim results." *Gynecol Oncol* 128 (2):191-7. doi: 10.1016/j.ygyno.2012.09.030.

Rosen, G., B. Caparros, A. Nirenberg, R. C. Marcove, A. G. Huvos, C. Kosloff, J. Lane, and M. L. Murphy. 1981. "Ewing's sarcoma: ten-year experience with adjuvant chemotherapy." *Cancer* 47 (9):2204-13. doi: 10.1002/1097-0142(19810501)47:9<2204::aid-cncr2820470916>3.0.co;2-a.

Ross, D. A., R. F. Lohman, S. S. Kroll, A. W. Yasko, G. L. Robb, G. R. Evans, and M. J. Miller. 1998. "Soft tissue reconstruction following hemipelvectomy." *Am J Surg* 176 (1):25-9.

Roulet, S., L. R. Le Nail, G. Vaz, A. Babinet, V. Dumaine, A. Sallot, and P. Rosset. 2019. "Free fillet lower leg flap for coverage after hemipelvectomy or hip disarticulation." *Orthop Traumatol Surg Res* 105 (1):47-54. doi: 10.1016/j.otsr.2018.10.018.

Samant, M., E. I. Chang, J. Petrungaro, J. P. Ver Halen, P. Yu, R. J. Skoracki, and D. W. Chang. 2012. "Reconstruction of massive oncologic defects following extremity amputation: a 10-year experience." *Ann Plast Surg* 68 (5):467-71. doi: 10.1097/SAP.0b013e318232b096.

Sasikumar, A., C. Bhan, J. T. Jenkins, A. Antoniou, and J. Murphy. 2017. "Systematic Review of Pelvic Exenteration With En Bloc Sacrectomy for Recurrent Rectal Adenocarcinoma: R0 Resection Predicts Disease-free Survival." *Dis Colon Rectum* 60 (3):346-352. doi: 10.1097/dcr.0000000000000737.

Schoeller, T., G. M. Huemer, and G. Wechselberger. 2008. "The transverse musculocutaneous gracilis flap for breast reconstruction: guidelines for flap and patient selection." *Plast Reconstr Surg* 122 (1):29-38. doi: 10.1097/PRS.0b013e318177436c.

Schuck, A., S. Ahrens, M. Paulussen, M. Kuhlen, S. Konemann, C. Rube, W. Winkelmann, R. Kotz, J. Dunst, N. Willich, and H. Jurgens. 2003. "Local therapy in localized Ewing tumors: results of 1058 patients treated in the CESS 81, CESS 86, and EICESS 92 trials." *Int J Radiat Oncol Biol Phys* 55 (1):168-77. doi: 10.1016/s0360-3016(02)03797-5.

Scoccianti, G., V. Ranucci, F. Frenos, D. Greto, G. Beltrami, R. Capanna, and A. Franchi. 2016. "Soft tissue myxofibrosarcoma: A clinico-pathological analysis of a series of 75 patients with emphasis on the epithelioid variant." *J Surg Oncol* 114 (1):50-5. doi: 10.1002/jso.24250.

Senchenkov, A., S. L. Moran, P. M. Petty, J. Knoetgen, 3rd, R. P. Clay, U. Bite, S. A. Barnes, and F. H. Sim. 2008. "Predictors of complications and outcomes of external hemipelvectomy wounds: account of 160 consecutive cases." *Ann Surg Oncol* 15 (1):355-63. doi: 10.1245/s10434-007-9672-5.

Senchenkov, A., S. L. Moran, P. M. Petty, J. Knoetgen, 3rd, N. V. Tran, R. P. Clay, U. Bite, C. H. Johnson, S. A. Barnes, and F. H. Sim. 2009. "Soft-tissue reconstruction of external hemipelvectomy defects." *Plast Reconstr Surg* 124 (1):144-55. doi: 10.1097/ PRS.0b013e3181a80557.

Serlo, J. A., I. J. Helenius, M. Sampo, K. Vettenranta, U. M. Saarinen-Pihkala, S. M. Kivivuori, P. Riikonen, A. Kivioja, T. Bohling, M. Kallajoki, A. Ristimaki, K. Vasama, and M. Tarkkanen. 2013. "Ewing's sarcoma family of tumors in Finland during 1990-2009: a population-based study." *Acta Oncol* 52 (4):767-75. doi: 10.3109/0284186x.2012.728714.

Serlo, J., I. Helenius, K. Vettenranta, M. Perkkio, P. Riikonen, M. Sampo, and M. Tarkkanen. 2015. "Surgically treated patients with axial and peripheral Ewing's sarcoma family of tumours: A population based study in Finland during 1990-2009." *Eur J Surg Oncol* 41 (7):893-8. doi: 10.1016/j.ejso.2015.02.010.

Sforsini, Carlos; Wikinski, Jaime A. 2006. "Anatomical review of the lumbosacral plexus and nerves of the lower extremity." *Techniques in Regional Anesthesia and Pain Management* 10 (4):138-144.

Shao, Q. D., X. Yan, J. Y. Sun, and T. M. Xu. 2015. "Internal hemipelvectomy with reconstruction for primary pelvic neoplasm: a systematic review." *ANZ J Surg* 85 (7-8):553-60. doi: 10.1111/ ans.12895.

Sherman, C. E., M. I. O'Connor, and F. H. Sim. 2012. "Survival, local recurrence, and function after pelvic limb salvage at 23 to 38 years of followup." *Clin Orthop Relat Res* 470 (3):712-27. doi: 10.1007/s11999-011-1968-x.

Shin, K. H., B. T. Rougraff, and M. A. Simon. 1994. "Oncologic outcomes of primary bone sarcomas of the pelvis." *Clin Orthop Relat Res* (304):207-17.

Shin, K. J., S. H. Lee, K. S. Koh, and W. C. Song. 2018. "Anatomical Consideration for the Safe Elevation of the Deep Circumflex Iliac Artery in Flap Surgery." *Plast Reconstr Surg* 142 (1):193-201. doi: 10.1097/prs.0000000000004514.

Shukla, H. S., and L. E. Hughes. 1984. "The rectus abdominis flap for perineal wounds." *Ann R Coll Surg Engl* 66 (5):337-9.

Sindhar, S., D. Kallogjeri, T. S. Wildes, M. S. Avidan, and J. F. Piccirillo. 2019. "Association of Preoperative Functional Performance With Outcomes After Surgical Treatment of Head and Neck Cancer: A Clinical Severity Staging System." *JAMA Otolaryngol Head Neck Surg* 145 (12):1128-36. doi: 10.1001/jamaoto.2019.1035.

Sintonen, H. 2001. "The 15D instrument of health-related quality of life: properties and applications." *Ann Med* 33 (5):328-36. doi: 10.3109/07853890109002086.

Sole, C. V., F. A. Calvo, P. A. de Sierra, R. Herranz, L. Gonzalez-Bayon, and J. L. Garcia-Sabrido. 2014. "Multidisciplinary therapy for patients with locally oligo-recurrent pelvic malignancies." *J Cancer Res Clin Oncol* 140 (7):1239-48. doi: 10.1007/s00432-014-1667-6.

Solomon, M. J., K. K. Austin, L. Masya, and P. Lee. 2015. "Pubic Bone Excision and Perineal Urethrectomy for Radical Anterior Compartment Excision During Pelvic Exenteration." *Dis Colon Rectum* 58 (11):1114-9. doi: 10.1097/dcr.0000000000000479.

Solomon, M. J., K. G. Brown, C. E. Koh, P. Lee, K. K. Austin, and L. Masya. 2015. "Lateral pelvic compartment excision during pelvic exenteration." *Br J Surg* 102 (13):1710-7. doi: 10.1002/ bjs.9915.

Standring, Susan, Neil R. Borley, and Henry Gray. 2008. *Gray's anatomy : the anatomical basis of clinical practice*. Edited by Susan Standring, Neil R. Borley and Henry Gray. 40. ed., 150 years anniversary ed ed. Edinburgh: Churchill Livingstone.

Stein, M. J., A. Karir, M. Ramji, M. Allen, J. R. Bain, R. Avram, R. Boushey, R. Auer, and M. Jarmuske. 2019. "Surgical outcomes of VRAM versus gracilis flaps for the reconstruction of pelvic defects following oncologic resection()." *J Plast Reconstr Aesthet Surg.* doi: 10.1016/j. bjps.2018.12.044.

Stevenson, J. D., M. K. Laitinen, M. C. Parry, V. Sumathi, R. J. Grimer, and L. M. Jeys. 2018. "The role of surgical margins in chondrosarcoma." *Eur J Surg Oncol* 44 (9):1412-1418. doi: 10.1016/j.ejso.2018.05.033.

Stiller, C. A., A. Trama, D. Serraino, S. Rossi, C. Navarro, M. D. Chirlaque, and P. G. Casali. 2013. "Descriptive epidemiology of sarcomas in Europe: report from the RARECARE project." *Eur J Cancer* 49 (3):684-95. doi: 10.1016/j.ejca.2012.09.011.

Stoker, J. 2009. "Anorectal and pelvic floor anatomy." *Best Pract Res Clin Gastroenterol* 23 (4):463-75. doi: 10.1016/j.bpg.2009.04.008.

Stokke, J., L. Sung, A. Gupta, A. Lindberg, and A. R. Rosenberg. 2015. "Systematic review and meta-analysis of objective and subjective quality of life among pediatric, adolescent, and young adult bone tumor survivors." *Pediatr Blood Cancer* 62 (9):1616-29. doi: 10.1002/pbc.25514.

Talarczyk, M. R., J. H. Boehmler, K. Ljungquist, P. Tiwari, J. L. Mayerson, and M. Miller. 2013. "External hemipelvectomy pelvic ring stabilization: the unique application of chimeric lower extremity pedicled fillet flaps." *J Reconstr Microsurg* 29 (6):367-72. doi: 10.1055/s-0032-1333319.

Tashiro, K., M. Arikawa, Y. Fukunaga, F. Nakatani, E. Kobayashi, A. Kawai, and S. Miyamoto. 2019. "Free latissimus dorsi musculocutaneous flap for external hemipelvectomy reconstruction." *Microsurgery* 39 (2):138-143. doi: 10.1002/micr.30373.

Templeton, K. J., and E. B. Toby. 2001. "Free filet leg flap." *Clin Orthop Relat Res* (385):182-5.

Tham, N. L., W. R. Pan, W. M. Rozen, M. P. Carey, G. I. Taylor, R. J. Corlett, and M. W. Ashton. 2010. "The pudendal thigh flap for vaginal reconstruction: optimising flap survival." *J Plast Reconstr Aesthet Surg* 63 (5):826-31. doi: 10.1016/j.bjps.2009.02.060.

Toro, J. R., L. B. Travis, H. J. Wu, K. Zhu, C. D. Fletcher, and S. S. Devesa. 2006. "Incidence patterns of soft tissue sarcomas, regardless of primary site, in the surveillance, epidemiology and end results program, 1978-2001: An analysis of 26,758 cases." *Int J Cancer* 119 (12):2922-30. doi: 10.1002/ijc.22239.

Trojani, M., G. Contesso, J. M. Coindre, J. Rouesse, N. B. Bui, A. de Mascarel, J. F. Goussot, M. David, F. Bonichon, and C. Lagarde. 1984. "Soft-tissue sarcomas of adults; study of pathological prognostic variables and definition of a histopathological grading system." *Int J Cancer* 33 (1):37-42. doi: 10.1002/ijc.2910330108.

Tsagozis, P., M. K. Laitinen, J. D. Stevenson, L. M. Jeys, A. Abudu, and M. C. Parry. 2019. "Treatment outcome of patients with chondroblastic osteosarcoma of the limbs and pelvis." *Bone Joint J* 101-b (6):739-744. doi: 10.1302/0301-620x.101b6.Bjj-2018-1090.R1.

Tsiplova, K., E. Pullenayegum, T. Cooke, and F. Xie. 2016. "EQ-5D-derived health utilities and minimally important differences for chronic health conditions: 2011 Commonwealth Fund Survey of Sicker Adults in Canada." *Qual Life Res* 25 (12):3009-3016. doi: 10.1007/s11136-016-1336-0.

Tsuda, Y., S. Evans, J. D. Stevenson, M. Parry, T. Fujiwara, M. Laitinen, H. Outani, and L. Jeys. 2019. "Is the Width of a Surgical Margin Associated with the Outcome of Disease in Patients with Peripheral Chondrosarcoma of the Pelvis? A Multicenter Study." *Clin Orthop Relat Res* 477 (11):2432-2440. doi: 10.1097/corr.0000000000000926.

Unal, C., O. A. Yirmibesoglu, J. Ozdemir, and M. Hasdemir. 2011. "Superior and inferior gluteal artery perforator flaps in reconstruction of gluteal and perianal/perineal hidradenitis suppurativa lesions." *Microsurgery* 31 (7):539-44. doi: 10.1002/micr.20918.

Ungar, L., and L. Palfalvi. 2006. "Pelvic exenteration without external urinary or fecal diversion in gynecological cancer patients." *Int J Gynecol Cancer* 16 (1):364-8. doi: 10.1111/j.1525-1438.2006.00446.x.

Urh, A., P. T. Soliman, K. M. Schmeler, S. Westin, M. Frumovitz, A. M. Nick, B. Fellman, D. L. Urbauer, and P. T. Ramirez. 2013. "Postoperative outcomes after continent versus incontinent urinary diversion at the time of pelvic exenteration for gynecologic malignancies." *Gynecol Oncol* 129 (3):580-5. doi: 10.1016/j.ygyno.2013.02.024.

Valle, G., and G. Ferraris. 1969. "Use of the omentum to contain the intestines in pelvic exenteration." *Obstet Gynecol* 33 (6):772-5.

Valle, M., O. Federici, P. Ialongo, F. Graziano, and A. Garofalo. 2011. "Prevention of complications following pelvic exenteration with the use of mammary implants in the pelvic cavity: Technique and results of 28 cases." *J Surg Oncol* 103 (1):34-8. doi: 10.1002/jso.21716.

van Houdt, W. J., A. M. Griffin, J. S. Wunder, and P. C. Ferguson. 2018. "Oncologic Outcome and Quality of Life After Hindquarter Amputation for Sarcoma: Is it Worth it?" *Ann Surg Oncol* 25 (2):378-386. doi: 10.1245/s10434-017-5806-6.

van Wulfften Palthe, O. D., M. T. Houdek, P. S. Rose, M. J. Yaszemski, F. H. Sim, P. J. Boland, J. H. Healey, F. J. Hornicek, and J. H. Schwab. 2017. "How Does the Level of Nerve Root Resection in En Bloc Sacrectomy Influence Patient-Reported Outcomes?" *Clin Orthop Relat Res* 475 (3):607-616. doi: 10.1007/s11999-016-4794-3.

van Wulfften Palthe, O. D. R., S. J. Janssen, J. S. Wunder, P. C. Ferguson, G. Wei, P. S. Rose, M. J. Yaszemski, F. H. Sim, P. J. Boland, J. H. Healey, F. J. Hornicek, and J. H. Schwab. 2017. "What questionnaires to use when measuring quality of life in sacral tumor patients: the updated sacral tumor survey." *Spine J* 17 (5):636-644. doi: 10.1016/j.spinee.2016.11.004.

van Wulfften Palthe, O. D. R., I. Tromp, A. Ferreira, A. Fiore, J. A. M. Bramer, N. C. van Dijk, T. F. DeLaney, J. H. Schwab, and F. J. Hornicek. 2019. "Sacral chordoma: a clinical review of 101 cases with 30-year experience in a single institution." *Spine J* 19 (5):869-879. doi: 10.1016/j.spinee.2018.11.002.

Varga, P. P., Z. Szoverfi, and A. Lazary. 2014. "Surgical treatment of primary malignant tumors of the sacrum." *Neurol Res* 36 (6):577-87. doi: 10.1179/1743132814y.0000000366.

Vartanian, E. D., J. V. Lynn, D. P. Perrault, E. M. Wolfswinkel, A. M. Kaiser, K. M. Patel, J. N. Carey, P. C. Hsieh, and A. K. Wong. 2018. "Risk Factors Associated with Reconstructive Complications Following Sacrectomy." *Plast Reconstr Surg Glob Open* 6 (11):e2002. doi: 10.1097/gox.0000000000002002.

Verbruggen, S. W., and N. C. Nowlan. 2017. "Ontogeny of the Human Pelvis." *Anat Rec* (*Hoboken*) 300 (4):643-652. doi: 10.1002/ar.23541.

Vleeming, A., M. D. Schuenke, A. T. Masi, J. E. Carreiro, L. Danneels, and F. H. Willard. 2012. "The sacroiliac joint: an overview of its anatomy, function and potential clinical implications." *J Anat* 221 (6):537-67. doi: 10.1111/j.1469-7580.2012.01564.x.

Vos, M., D. J. Grunhagen, H. Kosela-Paterczyk, P. Rutkowski, S. Sleijfer, and C. Verhoef. 2019. "Natural history of well-differentiated liposarcoma of the extremity compared to patients treated with surgery." *Surg Oncol* 29:84-89. doi: 10.1016/j.suronc.2019.04.004.

Wakelin, S. J., C. W. Oliver, and M. H. Kaufman. 2004. "Hip disarticulation--the evolution of a surgical technique." *Injury* 35 (3):299-308. doi: 10.1016/s0020-1383(03)00063-9.

Wang, Y., W. Guo, D. Shen, X. Tang, Y. Yang, T. Ji, and X. Xu. 2017. "Surgical Treatment of Primary Osteosarcoma of the Sacrum: A Case Series of 26 Patients." *Spine* (*Phila Pa 1976*) 42 (16):1207-1213. doi: 10.1097/brs.0000000000002043.

Wang, Y., W. Liang, S. Qu, Y. Zhang, Z. Du, T. Ji, H. Qu, R. Gorlick, and W. Guo. 2019. "Assessment of patient experiences following total sacrectomy for primary malignant sacral tumors: A qualitative study." *J Surg Oncol* 120 (8):1497-1504. doi: 10.1002/jso.25756.

Ware, J. E., Jr., and C. D. Sherbourne. 1992. "The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection." *Med Care* 30 (6):473-83.

Wee, J. T., and V. T. Joseph. 1989. "A new technique of vaginal reconstruction using neurovascular pudendal-thigh flaps: a preliminary report." *Plast Reconstr Surg* 83 (4):701-9. doi: 10.1097/00006534-198904000-00018.

Wei, R., W. Guo, R. Yang, X. Tang, Y. Yang, T. Ji, and H. Liang. 2019. "Reconstruction of the pelvic ring after total en bloc sacrectomy using a 3D-printed sacral endoprosthesis with re-establishment of spinopelvic stability: a retrospective comparative study." *Bone Joint J* 101-b (7):880-888. doi: 10.1302/0301-620x.101b7.Bjj-2018-1010.R2.

Werne, S. 1953. "Two cases of hindquarter-amputation." *Acta Orthop Scand* 23 (2):90-9. doi: 10.3109/17453675308991202.

Westin, S. N., V. Rallapalli, B. Fellman, D. L. Urbauer, N. Pal, M. M. Frumovitz, L. M. Ramondetta, D. C. Bodurka, P. T. Ramirez, and P. T. Soliman. 2014. "Overall survival after pelvic exenteration for gynecologic malignancy." *Gynecol Oncol* 134 (3):546-51. doi: 10.1016/j.ygyno.2014.06.034.

Wheeless, C. R., Jr. 1989. "Neovagina constructed from an omental J flap and a split thickness skin graft." *Gynecol Oncol* 35 (2):224-6. doi: 10.1016/0090-8258(89)90048-6.

Wheeless, C. R., Jr., B. McGibbon, J. H. Dorsey, and G. P. Maxwell. 1979. "Gracilis myocutaneous flap in reconstruction of the vulva and female perineum." *Obstet Gynecol* 54 (1):97-102. doi: 10.1097/00006250-197907000-00022.

Whelan, J., A. McTiernan, N. Cooper, Y. K. Wong, M. Francis, S. Vernon, and S. J. Strauss. 2012. "Incidence and survival of malignant bone sarcomas in England 1979-2007." *Int J Cancer* 131 (4):E508-17. doi: 10.1002/ijc.26426.

Whelan, J. S., and L. E. Davis. 2018. "Osteosarcoma, Chondrosarcoma, and Chordoma." *J Clin Oncol* 36 (2):188-193. doi: 10.1200/jco.2017.75.1743.

WHO. 2020. accessed 24.6.2020. https://www.who.int/cancer/palliative/definition/en/.

Wirbel, R. J., M. Schulte, B. Maier, M. Koschnik, and W. E. Mutschler. 2000. "Chondrosarcoma of the pelvis: oncologic and functional outcome." *Sarcoma* 4 (4):161-8. doi: 10.1080/13577140020025878.

Wirbel, R. J., M. Schulte, and W. E. Mutschler. 2001. "Surgical treatment of pelvic sarcomas: oncologic and functional outcome." *Clin Orthop Relat Res* (390):190-205. doi: 10.1097/00003086-200109000-00022.

Woll, P. J., P. Reichardt, A. Le Cesne, S. Bonvalot, A. Azzarelli, H. J. Hoekstra, M. Leahy, F. Van Coevorden, J. Verweij, P. C. Hogendoorn, M. Ouali, S. Marreaud, V. H. Bramwell, and P. Hohenberger. 2012. "Adjuvant chemotherapy with doxorubicin, ifosfamide, and lenograstim for resected soft-tissue sarcoma (EORTC 62931): a multicentre randomised controlled trial." *Lancet Oncol* 13 (10):1045-54. doi: 10.1016/s1470-2045(12)70346-7.

Workman, M. L., D. F. Bailey, and B. L. Cunningham. 1992. "Popliteal-based filleted lower leg musculocutaneous free-flap coverage of a hemipelvectomy defect." *Plast Reconstr Surg* 89 (2):326-9.

Yamamoto, Y., H. Minakawa, and N. Takeda. 1997. "Pelvic reconstruction with a free fillet lower leg flap." *Plast Reconstr Surg* 99 (5):1439-41.

Yamamoto, Y., and T. Sugihara. 2003. "Pelvic reconstruction with a free fillet lower leg flap." *Plast Reconstr Surg* 111 (4):1475-6. doi: 10.1097/01.prs.0000049454.83097.18.

Yari, P., P. U. Dijkstra, and J. H. Geertzen. 2008. "Functional outcome of hip disarticulation and hemipelvectomy: a cross-sectional national descriptive study in the Netherlands." *Clin Rehabil* 22 (12):1127-33. doi: 10.1177/0269215508095088.

York, J. E., A. Kaczaraj, D. Abi-Said, G. N. Fuller, J. M. Skibber, N. A. Janjan, and Z. L. Gokaslan. 1999. "Sacral chordoma: 40-year experience at a major cancer center." *Neurosurgery* 44 (1):74-9; discussion 79-80.

Yu, E., P. P. Koffer, T. A. DiPetrillo, and T. J. Kinsella. 2016. "Incidence, Treatment, and Survival Patterns for Sacral Chordoma in the United States, 1974-2011." *Front Oncol* 6:203. doi: 10.3389/fonc.2016.00203.

Zang, J., W. Guo, R. Yang, X. Tang, and D. Li. 2015. "Is total en bloc sacrectomy using a posterior-only approach feasible and safe for patients with malignant sacral tumors?" *J Neurosurg Spine* 22 (6):563-70. doi: 10.3171/2015.1.Spine14237.

Zhang, H. Y., I. Thongtrangan, R. S. Balabhadra, J. A. Murovic, and D. H. Kim. 2003. "Surgical techniques for total sacrectomy and spinopelvic reconstruction." *Neurosurg Focus* 15 (2):E5.

Zoccali, C., J. Skoch, A. S. Patel, C. M. Walter, P. Maykowski, and A. A. Baaj. 2016. "Residual neurological function after sacral root resection during en-bloc sacrectomy: a systematic review." *Eur Spine J* 25 (12):3925-3931. doi: 10.1007/s00586-016-4450-3.

Zoucas, E., S. Frederiksen, M. L. Lydrup, W. Mansson, P. Gustafson, and P. Alberius. 2010. "Pelvic exenteration for advanced and recurrent malignancy." *World J Surg* 34 (9):2177-84. doi: 10.1007/s00268-010-0637-7.

ORIGINAL PUBLICATIONS

PUBLICATION
I

Clinical results and quality of life after reconstruction following sacrectomy for primary bone malignancy

Kiiski J, Kuokkanen HO, Kääriäinen M, Kaartinen IS, Pakarinen TK, Laitinen MK

ELSEVIER

EURAPS

JPRAS
An International Journal of
Surgical Reconstruction
www.JPRASurg.com

Clinical results and quality of life after reconstruction following sacrectomy for primary bone malignancy

Check for updates

Juha Kiiski [a,b,*], **Hannu O Kuokkanen** [a], **Minna Kääriäinen** [b], **Ilkka S Kaartinen** [b,c], **Toni-Karri Pakarinen** [d], **Minna K Laitinen** [d,e]

[a] Department of Plastic Surgery, Helsinki University Central Hospital, Helsinki, Finland
[b] Division of Plastic Surgery, Unit of Musculoskeletal Surgery, Tampere University Hospital, Tampere, Finland
[c] Department of Plastic and Reconstructive Surgery, Karolinska University Hospital, Stockholm, Sweden
[d] Division of Orthopaedics and Traumatology, Unit of Musculoskeletal Surgery, Tampere University Hospital, Tampere, Finland
[e] Department of Orthopaedics and Traumatology, Helsinki University Central Hospital, Helsinki, Finland

Summary *Background:* Sacrectomy is a rare and demanding surgical procedure that results in major soft tissue defects and spinopelvic discontinuity. No consensus is available on the optimal reconstruction algorithm. Therefore, the present study evaluated the results of sacrectomy reconstruction and its impact on patients' quality of life (QOL).
Methods: A retrospective chart review was conducted for 21 patients who underwent sacrectomy for a primary bone tumour. Patients were divided into groups based on the timing of reconstruction as follows: no reconstruction, immediate reconstruction or delayed reconstruction. QOL was measured using the EQ-5D instrument before and after surgery in patients treated in the intensive care unit.
Results: The mean patient age was 57 (range 22–81) years. The most common reconstruction was gluteal muscle flap (n = 9) and gluteal fasciocutaneous flap (n = 4). Four patients required free-tissue transfer, three latissimus dorsi flaps and one vascular fibula bone transfer. No free flap losses were noted. The need for unplanned re-operations did not differ between groups

---

(p = 0.397), and no significant differences were found for pre- and post-operative QOL or any of its dimensions.

Discussion: Free flap surgery is reliable for reconstructing the largest sacrectomy defects. Even in the most complex cases, surgery can be safely staged, and final reconstruction can be carried out within 1 week of resection surgery without increasing peri-operative complications. Sacrectomy does not have an immoderate effect on the measured QOL.

Introduction

The incidence of primary malignant sacral tumours is low, and these tumours often initially present with relatively mild and non-specific symptoms.[1] These tumours can progress to a large, advanced tumour. Depending on the histology, standard treatment in most cases is *en bloc* resection with or without adjuvant oncological treatment.[2,3] Advances in both medical imaging and surgical care have made most of these tumours resectable.

Hemi- and total sacrectomies result in complex bony and soft tissue defects with a possible disruption of the pelvic ring, spinopelvic discontinuity and inadequate soft tissue coverage. The reconstruction of these defects relies on the basic principles of surgical reconstruction as follows: providing spinopelvic stability, eliminating dead space and allowing tension-free wound closure. Because of the rarity of the sacrectomy procedure and the variability in reconstruction, no consensus has been reached on the optimal reconstruction method.[4] There is no concurrence on whether spinopelvic fixation is mandatory after a total sacrectomy[4]. The use of microvascular flaps for soft tissue or bone reconstruction is rare, probably because of the difficulties in finding proper donor vessels in this region.[4]

Previous studies of sacrectomy have focused on oncological outcome,[5,6] spinopelvic reconstruction[7] or soft tissue reconstruction;[8,9] however, only a limited number of studies have measured the effect of this complex and often disabling surgery on patient-reported outcome.[6,10,11] The present retrospective cohort study had two main objectives. The first was to evaluate whether the timing of the reconstruction affects surgical or oncological outcome. An urge for delaying tissue reconstruction emerged after an extremely complicated case was treated with prolonged sacrectomy. Previous studies of reconstruction after sacrectomy have not addressed the timing of reconstructive surgery in detail.[8,9,12] Second, we wanted to investigate the effect of this often mutilating surgery on patients' quality of life (QOL).

Methods

Selection criteria

Patients were identified from a prospectively maintained oncology database at Tampere University Hospital, Finland. The study was approved by the Institutional Review Board. All patients who underwent surgery for a primary bone tumour arising from the sacrum between 1 January 2008 and 30 June 2017 were included in the study. Patients with sacral metastasis, other malignancies affecting the sacrum (e.g. invasive rectal carcinoma), benign sacral lesions or bone biopsies (without intent for curative tumour resection) were excluded. Histology was confirmed in all patients by pre-operative biopsy. Pre-operative imaging studies were reviewed in a multidisciplinary team (MDT) meeting to determine the degree of tumour extension, nerve root involvement and surgical planning for both resection and reconstruction.

Variables and measurements

Data on patient demographics, surgical details, tumour characteristics, pre- or post-operative radiotherapy and/or chemotherapy and complications were collected from medical records. Complications were collected until death or the date last seen. Sacrectomies were classified as total sacrectomy, hemisacrectomy (sagittal osteotomy), partial sacrectomy (if part of the proximal sacrum could be saved) and extended sacrectomy (if lumbar vertebrae were resected *en bloc* with the tumour).[13] Patients were divided into three categories depending on the need for and timing of reconstruction. Patients who did not need soft tissue or spinopelvic reconstruction were classified as no reconstruction (NR). Patients who underwent soft tissue or bony reconstruction in a single stage operation were classified as immediate reconstruction (IR). Patients with planned staged resection and secondary reconstruction at a later date were classified as delayed reconstruction (DR).

The EQ-5D instrument was used to measure pre- and post-operative QOL. EQ-5D data were collected from a prospectively maintained intensive care unit (ICU) database on patients treated post-operatively in the ICU. Pre-operative data were recorded at the time of ICU admission. Post-operative EQ-5D data were collected at 6 months between 2008 and 2010 and at 12 months after 2010. The EQ-5D has been validated for measuring the health-related QOL of ICU patients[14] and comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. All dimensions are graded from 1 to 3, with a lower grade meaning a better quality. These dimensions are combined into an EQ-5D index (range 0 to 1, with 1 representing a better quality).

Surgical technique

In partial sacrectomies, resection is performed solely by a posterior approach. In these cases, one or both of the S3

nerve roots can be preserved. In the posterior approach, the anterior aspect of the sacrum is mobilised with blunt dissection. Resection of both S3 nerve roots results in sphincter incontinence. Incontinence causes post-operative faecal contamination of the wound and, therefore, either temporary or permanent colostomy is favoured. If permanent colostomy was chosen, a combined anterior-posterior approach was used. This approach started with a laparotomy to mobilise the sigmoid colon anteriorly, thus leaving the posterior part of the colon untouched and lying on the sacrum. If temporary colostomy was chosen, colostomy was performed leaving the dissected distal sigmoid colon in place. The procedure then proceeded from the posterior part. Dissecting down to the deep musculature, an osteotomy was performed through the sacrum and the tumour removed *en bloc* with the sigmoid colon and anal canal.

In sacrectomies resulting in spinopelvic discontinuity, spinopelvic fixation was performed by a spine surgeon in collaboration with an orthopaedic oncologist. A plastic surgeon was responsible for soft tissue coverage and vascularised bone reconstruction. The soft tissue reconstruction was planned depending on defect size, available local tissue and gluteal vessel patency. For medium-sized defects, regional gluteal muscle or fasciocutaneous flaps were most commonly used. The perineal and posterior abdominal walls were reconstructed using either autologous tissue or synthetic mesh. In the case of delayed reconstruction, the skin was closed directly if possible, thus leaving a dead space behind with appropriately sized drains. In three patients in whom the skin could not be closed, negative pressure wound therapy (NPWT) was applied to cover the wound and possible fixation material (Figure 1a–f).

Follow-up

Routine follow-up included the re-evaluation of patients every 3 months for the first 2 years, at 6 month intervals for the next 3 years and then annually thereafter. A chest radiograph was obtained to identify possible dissemination of disease. Spine and pelvic radiographs were obtained from bony reconstructions to identify possible reconstruction failures. Magnetic resonance imaging (MRI) was obtained to identify possible local recurrence (LR).

Statistical analysis

Kaplan-Meier curves were constructed to assess patient survival. Categorical variables were compared between groups by chi-square test. Continuous variables were compared between groups by the Kruskal-Wallis test. Pre-operative and post-operative EQ-5D scores were tested by the Wilcoxon signed-rank test. All statistical analyses were performed using SPSS Statistics 24.0 (IBM Armonk, NY, USA). A *p* value of <0.05 was considered significant.

Results

A total of 21 patients with a mean age of 57 (range 22–81) years were operated on during the study period. Indi-

cation for sacrectomy was chordoma in 15 patients, chondrosarcoma in four patients and high-grade dedifferentiated sarcoma in two patients. The patient demographics and their tumour characteristics and treatments are provided in Table 1. Five patients did not require any soft tissue or bone reconstruction (NR), 11 underwent IR, and five had a planned DR (Table 2). The mean follow-up was 38 (range 0–108) months.

Seventeen patients had R0 resection, and four had R1 resection (two patients with S3/4 resection, one with hemisacrectomy and one with extended sacrectomy). Four patients (19%) had LR: two patients with primary R0 resection and two patients with R1 resection. The mean time to LR was 23 (range 5–48) months. Three of the LRs occurred in chordoma and one in high-grade dedifferentiated sarcoma. All the LRs occurred in soft tissue, no bony recurrences were noted. The treatment of LR was excision in one patient, palliation in one patient and radiotherapy followed by denosumab administration in one patient, and the details on further treatment were missing for one patient. Three patients died because of disease progression, and one patient had a fatal post-operative intracranial haemorrhage on the first post-operative day. The overall disease-specific survival was 83% at 1 year and remained the same at 5 years (Figure 2).

Resection size, length of hospital stay, surgical time and peri-operative blood loss differed significantly between the reconstruction groups (Table 2). No significant difference was found between the reconstruction groups regarding tumour histology, number of unplanned re-operations, surgical margins, LR or survival. Surgical details are presented in Table 3. All the patients in the NR group had partial sacrectomy distal to S3/4. Patients whose sacrectomies were distal to S1/2 or who underwent less extensive hemisacrectomies were reconstructed immediately. Nine of the 11 patients in the IR group had only soft tissue reconstruction and two had spinopelvic fixation and soft tissue reconstruction. Resection volumes exceeding 2000 cc^3 or soft tissue resections more than 20 cm in width were considered large and required a free flap reconstruction. Resections of smaller volumes and lengths were considered moderate. All extended sacrectomies, total sacrectomies and hemisacrectomies demanding microvascular tissue transfer were reconstructed in two stages. All patients in the DR group planned to have a secondary reconstruction within a week of the resection. This occurred in four patients; but one patient postponed reconstruction to 14 days after the primary surgery due to a complicated ICU period.

A total of 20 soft tissue flap reconstructions were performed in 16 patients. The most commonly used flaps were gluteal muscle flaps, followed by gluteal fasciocutaneous flaps. In three cases, a latissimus dorsi (LD) free flap was used when free tissue transfer was required (Table 4). Recipient vessels for microvascular transfer were end-to-end to a branch of the internal iliac vessel (n = 1), end-to-side of the internal iliac vessel (n = 1), gluteal perforator vessel (n = 1) and a long saphenous vein arteriovenous loop from the groin (n = 1).

A spinopelvic instrument reconstruction was performed using double iliac screw fixation combined with posterior lumbar segmental fixation. Bone reconstruction was performed using a non-vascularised autologous fibula in four patients, vascularised fibula in one patient and a tibia

Figure 1 A. MRI of high-grade dedifferentiated sarcoma of the sacrum. B. Status after intra-lesional resection in another hospital before *en bloc* tumour resection. C. After *en bloc* resection of the L5 corpus, sacrum and medial parts of both ilea. Soft tissue resection extended inferior to the trochanter major of the right femur. D. Situation before reconstructive surgery after the removal of negative pressure wound therapy (NPWT). E. Healed LD free flap and pedicled vastus lateralis and ALT flap 1 month after wound healing and immediate rehabilitation. F. Post-operative radiograph.

Table 1 Surgical details of the patients. R0 = no ink on the margin, R1 = ink on the margin, IR = immediate reconstruction, NR = no reconstruction, DR = delayed reconstruction, VRAM flap = vertical rectus abdominis myocutaneous flap, LAP = lumbar artery perforator, LD = latissimus dorsi, NPWT = negative pressure wound therapy, ALT = anterolateral thigh, AKI = acute kidney injury, NSTEMI = non-ST elevation myocardial infarction, APR = abdominoperineal resection.

Patient	Age (years)/gender	Histology	Resection	Resection margin	Timing of the reconstruction	Reconstruction	Length of the first operation (hh:mm)	Length of the secondary reconstruction, DR group (hh:mm)	Length of stay, total/ICU (days)	Mesh	Complications	Peri-operative bleeding (ml)	Re-operations	Alive	Local recurrence	Follow-up (months)
1	48/F	Chordoma	S1/S2	R0	IR	Gluteal muscle flap and fasciocutaneous flap	8:05	-	14/1	Vypro	1. Ileus 2. Deep infection	3300	None	Y	N	108
2	56/F	Chordoma	S1/S2	R0	IR	Bilateral gluteus muscle flap	9:35	-	11/1	Parietex Compositum	Percutaneous seroma drainage	3500	None	Y	N	99
3	67/M	Chordoma	S1/S2	R0	IR	VRAM	15:40	-	43/7	Parietex Compositum (after VRAM flap loss)	1. AKI 2. Rhabdomyolysis 3. VRAM flap loss 4. NSTEMI 5. Wound dehiscence 6. Deep vein thrombosis 7. Deep infection	10,000	1. Bilateral gluteus musculocutaneous flap 2. Wound revision and direct closure	Y	N	36
4	64/M	Chordoma	Total	R0	DR	1. Spinopelvic fixation and NPWT 2. Free vascular fibula bone transfer and bilateral gluteus muscle flap	10:47	5:28	19/1	None	Mechanical complication of the spinopelvic fixation	3800	None	Y	N	78
5	23/M	HG sarcoma NOS	Hemisacrectomy	R1	DR	2. Pedicled LAP, distally based LD musculocutaneous flap and tibial allograft	10:40	6:32	22/1	Vypro	1. Deep vein thrombosis (pre-op) 2. Haematoma	5300	1. Haematoma evacuation	Y	N	72
6	74/M	Chordoma	S1/S2	R0	IR	Gluteal muscle flap	7:26	-	12/0	None	None	Unknown	None	Y	Y	60
7	65/M	Chondrosarcoma	Hemisacrectomy	R0	IR	Spinopelvic fixation, fibula autograft and bilateral gluteal muscle flap	8:25	-	25/1	Vypro	1. Iatrogenic contact burn 2. Wound dehiscence 3. Deep infection at 2 months	4000	1. Wound excision and direct closure 2. Wound debridement and direct closure 3. Wound debridement and NPWT	Y	N	49
8	22/M	HG sarcoma NOS	Extended	R1	DR	1. Spinopelvic fixation and NPWT 2. Pedicled vastus lateralis and ALT flap, microvascular LD flap and fibula bone autograft	13:19	7:10	53/15	None	1. Candida albicans septicaemia 2. Flap donor site wound dehiscence	3700	1. Wound debridement and direct closure	N	Y	8
9	57/F	Chordoma	S3/4	R0	NR	Direct closure	1:35	-	7/1	Prolene	None	200	None	Y	N	48
10	45/M	Chordoma	Total	R0	DR	1. Spinopelvic fixation 2. Microvascular LD flap and fibula autograft	12:28	8:18	60/7	Vicryl	1. Compartment syndrome 2. Deep infection	7000	1. Fasciotomy 2. Infection drainage 3. Removal of the spinopelvic fixation at 9 months	Y	N	49
11	81/M	Chordoma	S3/4	R1	IR	Regional fasciocutaneous flap	4:45	-	10/0	None	None	1700	None	N	Y	10
12	51/F	Chordoma	S3/4	R0	IR	Regional fasciocutaneous flap	5:45	-	11/1	Vypro	Deep infection	1700	None	Y	Y	36
13	69/F	Chordoma	S2/3	R0	IR	Bilateral gluteus muscle flap	4:51	-	14/1	Vypro	Anal incontinency	630	1. APR and colostomy at 2 months	Y	N	36
14	58/M	Chordoma	S1/2	R0	IR	Bilateral gluteus muscle flap	7:48	-	14/2	Vypro	None	3200	None	Y	N	34
15	63/M	Chondrosarcoma	Hemisacrectomy	R0	DR	1. Spinopelvic fixation, fibula autograft and NPWT 2. Microvascular LD flap	8:42	4:49	27/1	Optilene	None	3000	None	Y	N	24
16	58/M	Chondrosarcoma	Hemisacrectomy	R0	IR	Spinopelvic fixation, fibula autograft and bilateral gluteal muscle flap	9:55	-	3/2	Vypro	Brain haemorrhage	4000	1. Emergency craniotomy	N	N	0
17	63/F	Chondrosarcoma	Hemisacrectomy	R0	IR	Regional fasciocutaneous flap	7:20	-	16/1	Optilene	None	1900	None	Y	N	25
18	41/F	Chordoma	Coccyx	R0	NR	Direct closure	1:54	-	6/0	Vypro	None	100	None	Y	N	3
19	67/M	Chordoma	S3/4	R1	NR	Direct closure	2:41	-	7/0	None	None	555	None	Y	N	7
20	73/F	Chordoma	S3/4	R0	NR	Direct closure	2:39	-	30/0	None	Deep infection	910	1. Debridement	Y	N	1
21	41/F	Chordoma	S3/4	R0	NR	Direct closure	3:40	-	31/0	Prolene	Deep infection	500	1. Mesh removal and debridement 2. Debridement	Y	N	3

Table 2 Demographics and surgical details of the different reconstruction groups.

	No reconstruction (n = 5)	Immediate reconstruction (n = 11)	Delayed reconstruction (n = 5)	P-value*
Sex, F:M	4:1	5:6	0:5	0.043
Mean age (range)	55.8 (41-73)	62.7 (48-81)	43.4 (22-64)	0.164
Histology				0.061
Chordoma	5	8	2	
HG sarcoma NOS	0	0	2	
Chondrosarcoma	0	3	1	
Mean resection size, cm^{3}**	347.0 (88.4) n = 5	1252.3 (687.6) n = 9	2274.0 (2320.7) n = 2	0.007
Hospital stay, days	16.2 (13.1)	15.7 (10.5)	36.2 (18.9)	0.055
ICU stay, days	0 (0)	1.6 (1.9)	5.0 (6.1)	0.006
Surgical time, hh:mm				
Resection and immediate reconstruction	2:29 (0:48)	8:08 (3:01)	11:11 (1:47)	0.001
Delayed reconstruction surgery	–	–	6:27 (1:22)	
Peri-operative blood loss (ml)	453 (320)	3393 (2583)	4560 (1601)	0.004
Number of unplanned re-operations	0.60 (0.89)	0.64 (1.03)	1.20 (1.10)	0.397

Data are presented as mean (SD) unless otherwise noted. * Kruskal-Wallis and chi-square tests as appropriate. ** Four values were missing from the analysis.
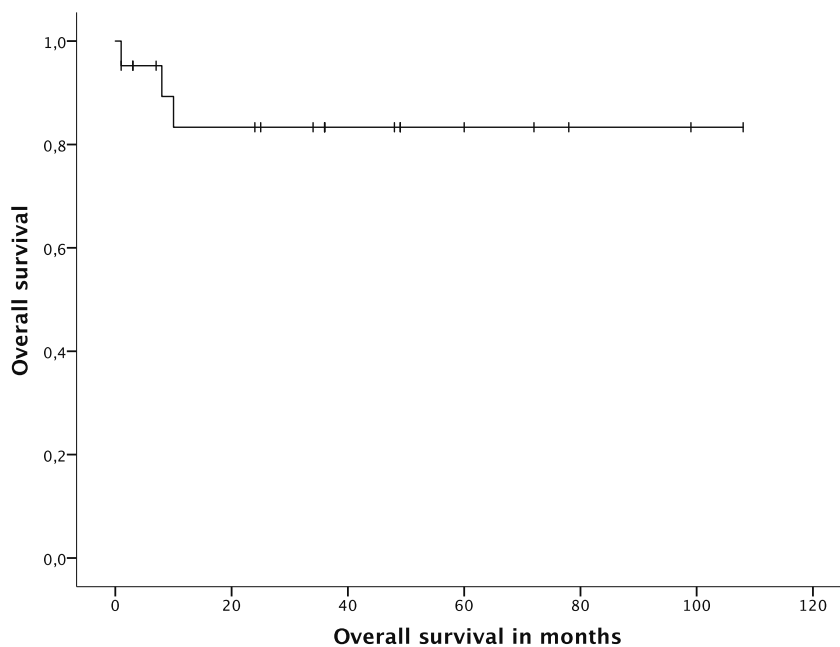
Figure 2 Kaplan-Meier curve of overall survival.

allograft in one patient. The bone graft was fixed to the host bone with additional cortical screws.

EQ-5D baseline data at ICU admission were available for 10 of the 14 patients treated in the ICU. Follow-up data were available for eight patients. Six of the 14 patients (43%) treated in the ICU had both pre-operative and post-operative EQ-5D data and were included in the analy-sis. No significant difference was found between the pre- and post-operative EQ-5D index or any of its dimensions (Table 5).

All complications during surgery, hospital stay and follow-up were recorded. Thirteen of the 21 patients (62%) had a total of 25 complications. The most common com-plication was post-operative infection (n = 8 patients), with

Table 3 Peri-operative details of the different reconstruction groups.

	No reconstruction	Immediate reconstruction	Delayed reconstruction	Total
Resection				
Extended	0	0	1	1
Total	0	0	2	2
Hemisacrectomy	0	3	2	3
S1/2 resection	0	5	0	5
S2/3 resection	0	1	0	1
S3/4 resection	4	2	0	6
Coccyx	1	0	0	1
Reconstruction				
Soft-tissue only	-	9	0	9
Spinopelvic fixation + auto/allograft bone + soft tissue flap	-	2	1	3
Spinopelvic fixation + vascular bone transfer + soft tissue flap	-	0	1	1
Spinopelvic fixation + autograft bone + soft tissue free flap with/without vascular bone flap	-	0	3	3
Mesh				
None	2	2	2	6
Absorbable	0	0	1	1
Semi-absorbable	1	7	1	9
Non-absorbable	2	2	1	5
Colostomy				
No colostomy	5	5	0	10
Loop sigmoideostomy	0	2	0	2
End sigmoideostomy	0	4	3	7

Table 4 Soft tissue flaps and vascular bone transfers in the immediate reconstruction (IR) and delayed reconstruction (DR) groups.

Flap	IR	DR
Gluteal muscle		
Unilateral	2	
Bilateral	6	1
Fasciocutaneous flap based on gluteal vessels	4	
VRAM	1	
LAP		1
LD free flap		3
Distally based LD		1
Vastus lateralis and ALT		1
Vascular fibula bone transfer		1
Total	13	8

VRAM flap = vertical rectus abdominis myocutaneous flap, LAP flap = lumbar artery perforator flap, LD flap = latissimus dorsi flap, ALT flap = anterolateral thigh flap

Table 5 EQ-5D index and dimensions for patients with full pre- and post-operative data.

	Pre-operative	Post-operative	P-value
EQ-5D index	0.81933	0.78933	0.600
Mobility	1.33	1.83	0.180
Self-care	1.00	1.33	0.157
Usual activities	1.17	1.50	0.317
Pain/discomfort	2.17	1.67	0.180
Anxiety/depression	1.17	1.00	0.317

five patients requiring surgical interventions to control the infection. Three patients had wound complications, two had venous thromboembolism and two required lower extremity fasciotomies due to compartment syndrome or rhabdomyolysis. Only one pedicled vertical rectus abdominis myocutaneous (VRAM) flap was lost. No other total or partial flap losses were noted in this study. All microvascular flaps survived completely.

Discussion

Algorithms have been proposed for the reconstruction of total[9,12] and partial sacrectomy defects[15], but they do not consider the duration of surgery or morbidity. Though these previous studies on reconstruction after sacrectomy provide useful steps for soft tissue coverage and bone reconstruction, they do not address the timing of reconstructive surgery in more detail. Sacral resection may result in heterogeneous bone and soft tissue defects depending on the size and location of the tumour. The factors that need to be addressed are the need for spinopelvic fixation due to pelvic instability, bone reconstruction, posterior abdominal wall reconstruction and the amount of soft tissue needed to fill the dead space and surface the defect. In such complicated cases, reconstruction requires expertise from many

different specialities[8,9]. The results of our study show that a planned two-stage reconstruction for the largest tumours is safe in a MDT setting and can be added to the reconstructive algorithm.

Interestingly, we did not have any LRs in bone; three of the LRs were in soft tissue and one was in the spinal canal. This emphasises the need for *en bloc* wide margin resection not only in bone but also in soft tissues[16]. An intra-operative computer navigation-assisted surgery can alleviate bone resection, but adequate soft tissue margins remain a challenge for orthopaedic oncologists[17]. The need for adequate soft tissue resection should not be limited by the reconstructive possibilities. The possibility of free flap or more complex reconstructions allows appropriate soft tissue resection without the hardship of a limited amount of local tissue.

The most commonly used flap for medium-sized defects in our series was a gluteal muscle flap. Later in the series, gluteal region fasciocutaneous flaps were also used. In most cases, part of the fasciocutaneous flap was de-epithelialised to fill the dead space. Our flap selection was in line with previous publications.[8,9,12,15] A major difference in our study from previous publications was the use of a VRAM flap. Pedicled VRAM has been widely used to reconstruct large perineal and sacral defects after sacrectomy.[8,9,12,15,18] Only one VRAM flap was used in our series; the flap was lost completely due to vascular compromise and multiple medical complications. For large defects in which regional gluteal muscle or a fasciocutaneous flap was insufficient, our primary flap choice was a microvascular LD flap. There are two main reasons for preferring an LD free flap over a VRAM flap. First, patients who underwent proximal, total or extended sacrectomy need a permanent colostomy; therefore, compromising the anterior abdominal wall integrity with flap harvest should be avoided. Although relatively rare, donor site bulging, abdominal hernias and infections are possible complications of VRAM flap use.[19] In addition to donor site problems, a reason for avoiding an abdominal flap was that the major reconstructions were carried out at a second stage. The use of an abdomen-based flap would not have been feasible in this setting because of the previous abdominal surgery performed in the week prior to the re-construction. Using an LD free flap, delayed reconstruction can be carried out in the prone or decubitus position without changing the position during the reconstructive surgery. For most cases, there were sufficient local recipient vessels for microvascular anastomosis. In one case, we used a long saphenous loop as a recipient vessel for microvascular anastomosis, as local vessels were unusable.[20] In our series, the use of free flaps was successful, as we did not have vascular compromise, take-backs or partial or total flap losses with free flaps.

There was great variation in the reconstruction of the posterior abdominal wall in this study. For most patients, the posterior abdominal wall was reconstructed with either non-absorbable synthetic mesh or semi-absorbable mesh. The role of mesh in posterior abdominal wall reconstruction is controversial. Synthetic meshes have been used to reconstruct sacral integrity.[21] We had only one case of deep infection that required mesh removal after 1 month. No intestinal fistulae or other intestinal complications directly related to the mesh were noted in this study. A combina-

tion of a posterior approach, gluteal flaps and acellular human dermal matrix for sacrectomy defect reconstruction is favoured over synthetic mesh to overcome infectious complications.[9,22,23] Other authors have favoured soft tissue reconstruction for perineal and sacral defects.[24,25] However, no studies have directly compared synthetic mesh, biological mesh and flap only for the reconstruction of sacral defects.

Total sacrectomy, extended sacrectomy and hemisacrectomy cause instability and discontinuity between the spine and pelvis. In the literature, there are multiple choices for reconstruction to facilitate early mobilisation and better ambulation, and spinopelvic fixation using double iliac screw fixation combined with posterior lumbar segmental fixation is one of the most common procedures.[7] Without iliolumbar ligamentous stability or other biological support, spinopelvic fixation will eventually fail in good survivors; therefore, vascularised or non-vascularised bone reconstruction is recommended in addition to spinopelvic fixation. The question of whether a bone graft should be vascularised is controversial. When considering bone reconstruction, some authors advocate the use of vascularised bone transfer,[26,27] whereas others have reported similar or better results with non-vascularised grafts.[28-30] In our series, we used vascularised bone graft, especially at the beginning, but with increasing evidence of good results in the literature, we changed to non-vascularised grafts without any problems.

After an extremely complicated case of sacrectomy (patient number 3) with multiple complications due to poor intra-operative homeostasis, excessive blood loss and kidney failure, we wanted to examine the possibility of staging the reconstructive surgery in difficult cases. The benefit of this planned delayed reconstruction is to allow the patient to recover from the combined anterior-posterior approach and avoid a prolonged time in the Mecca position. Patient homeostasis and coagulative status can be optimised for reconstruction during the week, and reconstruction can be carried out safely. This approach enables patients to recover longer than in the previously described staged sacrectomy approach.[33] An additional indication for converting planned IR to DR is unexpected difficulty during the tumour resection or anaesthesia resulting in excessive blood loss, hypothermia or any other kind of disruption of the patient's homeostasis. In this scenario, the reconstruction will be converted to a planned delayed operation rather than risking any additional deterioration of the patient's condition. This would be comparable to damage control surgery in many other indications.[31,32] For patients in whom the skin cannot be closed in the primary operation, the wound is covered with dressing for NPWT during the recovery period. The NPWT is changed once in the operating room and the wound washed out. In very long and complicated extended sacrectomies requiring free flaps, this planned DR is recommended and should be openly introduced to the reconstruction algorithms.

Our current algorithm for sacrectomies and subsequent reconstruction is as follows:

(1) Partial sacrectomy distal to S3/4 level: Most of these patients can be managed with primary closure of the wound. In patients with more extensive soft tissue

resection, reconstruction can be performed with local flaps, either a gluteal muscle flap or local gluteal fasciocutaneous flap.

(2) Partial sacrectomy above S3/4 level: This results in moderate-sized soft tissue defects. These defects can be reconstructed immediately with local gluteal muscle or gluteal fasciocutaneous flaps. A mesh is used for perineal or posterior abdominal wall closure if needed.

(3) Sagittal hemisacrectomy with moderate-sized soft tissue defect: The defect can be reconstructed immediately with a posterior-only approach. Bone fixation is carried out with double iliac screw fixation combined with sacral or posterior lumbar segmental fixation and fibula autograft. The soft tissue defect is reconstructed with local pedicled flaps from the gluteal region.

(4) Sagittal hemisacrectomies with large volume tissue defect: A posterior approach is used. Bone fixation is performed and the wound closed directly or with NPWT. After 1 week, a free flap is used to reconstruct the soft tissue and/or bone defect in a second surgery. If no local donor vessels are available, a long saphenous vein arteriovenous loop is used.

(5) Total sacrectomy or partial sacrectomy with large volume defect requiring a free flap: The surgery is planned in two stages. A combined anterior-posterior approach is used for resection. In a total sacrectomy, spinopelvic fixation is performed and the wound closed directly or with NPWT. After 1 week, a free flap is used to reconstruct the soft tissue and/or bone defect in a second surgery.

(6) Patients with unexpected difficulties during tumour resection: In the case of an unexpected difficulty during tumour resection or anaesthesia resulting in excessive blood loss, hypothermia or any other kind of disruption of the patient's homeostasis, the surgery is performed in two stages.

No significant decline was found in the EQ-5D index or any of its five dimensions. There was a trend towards reducing pain and discomfort, but the difference was not significant. However, a limited number of patients treated in the ICU had both pre-operative and post-operative QOL data available, and the statistical analysis was not able to demonstrate any difference regarding the EQ-5D or its dimensions. Some studies have reported the functional status of patients who underwent sacrectomy using MSTS,[10] PROMIS[11] or other scoring systems,[6] but these studies lack pre-operative comparisons.

The major limitations of this study are clearly its retrospective nature and limited number of patients, thus limiting the statistical analysis. However, malignant primary bone tumours in the sacrum are rare, and resections performed due to other malignancies make the results more heterogeneous; therefore, these patients were excluded. The number of patients in this study, though low, is in line with earlier reports.[8] In addition, though the study is retrospective, the QOL data were recorded in the ICU database prospectively.

Conclusion

Free flap reconstruction is feasible for reconstructing large sacrectomy defects, and the saphenous arteriovenous loop is an alternative recipient site if local vessels are not available. In the most complex cases, surgery can be staged safely and final reconstruction carried out within 1 week after ablative surgery without increasing peri-operative complications. We recommend considering planned DR for very long and complicated sacrectomies. Patients tolerate the functional deficit caused by sacrectomy, and the surgery does not have an immoderate effect on the measured QOL.

Acknowledgment

References

1. Varga PP, Szoverfi Z, Lazary A. Surgical treatment of primary malignant tumors of the sacrum. *Neurol Res* 2014;**36**:577-87.
2. York JE, Kaczaraj A, Abi-Said D, et al. Sacral chordoma: 40-year experience at a major cancer center. *Neurosurgery* 1999;**44**:74-9 discussion 79-80.
3. Bergh P, Gunterberg B, Meis-Kindblom JM, Kindblom LG. Prognostic factors and outcome of pelvic, sacral, and spinal chondrosarcomas: a center-based study of 69 cases. *Cancer* 2001;**91**:1201-12.
4. Reynolds JJ, Khundkar R, Boriani S, et al. Soft Tissue and Bone Defect Management in Total Sacrectomy for Primary Sacral Tumors: A Systematic Review With Expert Recommendations. *Spine (Phila Pa 1976)* 2016;**41**(Suppl 20):S199-204.
5. Arkader A, Yang CH, Tolo VT. High long-term local control with sacrectomy for primary high-grade bone sarcoma in children. *Clin Orthop Relat Res* 2012;**470**:1491-7.
6. Ji T, Guo W, Yang R, et al. What are the conditional survival and functional outcomes after surgical treatment of 115 patients with sacral chordoma. *Clin Orthop Relat Res* 2017;**475**:620-30.
7. Bederman SS, Shah KN, Hassan JM, et al. Surgical techniques for spinopelvic reconstruction following total sacrectomy: a systematic review. *Eur Spine J* 2014;**23**:305-19.
8. Miles WK, Chang DW, Kroll SS, et al. Reconstruction of large sacral defects following total sacrectomy. *Plast Reconstr Surg* 2000;**105**:2387-94.
9. Kim JE, Pang J, Christensen JM, et al. Soft-tissue reconstruction after total en bloc sacrectomy. *J Neurosurg Spine* 2015;**22**:571-81.
10. Kiatisevi P, Piyaskulkaew C, Kunakornsawat S, Sukunthanak B. What are the functional outcomes after total sacrectomy without spinopelvic reconstruction. *Clin Orthop Relat Res* 2017;**475**:643-55.
11. van Wulfften Palthe OD, Houdek MT, Rose PS, et al. How does the level of nerve root resection in en bloc sacrectomy influence patient-reported outcomes. *Clin Orthop Relat Res* 2017;**475**:607-16.
12. Maricevich M, Maricevich R, Chim H, et al. Reconstruction following partial and total sacrectomy defects: an analysis of outcomes and complications. *J Plast Reconstr Aesthet Surg* 2014;**67**:1257-66.
13. Li D, Guo W, Tang X, Ji T, Zhang Y. Surgical classification of different types of en bloc resection for primary malignant sacral tumors. *Eur Spine J* 2011;**20**:2275-81.

14. Angus DC, Carlet J. Surviving intensive care: a report from the 2002 brussels roundtable. *Intensive Care Med* 2003;**29**:368-77.

15. Garvey PB, Rhines LD, Feng L, Gu X, Butler CE. Reconstructive strategies for partial sacrectomy defects based on surgical outcomes. *Plast Reconstr Surg* 2011;**127**:190-9.

16. Varga PP, Szoverfi Z, Fisher CG, et al. Surgical treatment of sacral chordoma: prognostic variables for local recurrence and overall survival. *Eur Spine J* 2015;**24**:1092-101.

17. Jeys L, Matharu GS, Nandra RS, Grimer RJ. Can computer navigation-assisted surgery reduce the risk of an intralesional margin and reduce the rate of local recurrence in patients with a tumour of the pelvis or sacrum. *Bone Joint J* 2013;**95-b**:1417-24.

18. Glatt BS, Disa JJ, Mehrara BJ, et al. Reconstruction of extensive partial or total sacrectomy defects with a transabdominal vertical rectus abdominis myocutaneous flap. *Ann Plast Surg* 2006;**56**:526-30 discussion 30-1.

19. Horch RE, Hohenberger W, Eweida A, et al. A hundred patients with vertical rectus abdominis myocutaneous (VRAM) flap for pelvic reconstruction after total pelvic exenteration. *Int J Colorectal Dis* 2014;**29**:813-23.

20. Fudem GM, Marble KR. Latissimus dorsi free flap for sacral wound closure: the world's longest vein grafts for free tissue transfer. *Microsurgery* 1996;**17**:449-51.

21. Junge K, Krones CJ, Rosch R, Fackeldey V, Schumpelick V. Mesh reconstruction preventing sacral herniation. *Hernia* 2003;**7**:224-6.

22. Abhinav K, Shaaban M, Raymond T, et al. Primary reconstruction of pelvic floor defects following sacrectomy using Permacol graft. *Eur J Surg Oncol* 2009;**35**:439-43.

23. Dasenbrock HH, Clarke MJ, Bydon A, et al. Reconstruction of extensive defects from posterior en bloc resection of sacral tumors with human acellular dermal matrix and gluteus maximus myocutaneous flaps. *Neurosurgery* 2011;**69**:1240-7.

24. Kaartinen IS, Vuento MH, Hyoty MK, Kallio J, Kuokkanen HO. Reconstruction of the pelvic floor and the vagina after total pelvic exenteration using the transverse musculocutaneous gracilis flap. *J Plast Reconstr Aesthet Surg* 2015;**68**:93-7.

25. Diaz J, McDonald WS, Armstrong M, et al. Reconstruction after extirpation of sacral malignancies. *Ann Plast Surg* 2003;**51**:126-9.

26. Hilven PH, Bayliss L, Cosker T, et al. The vascularised fibular graft for limb salvage after bone tumour surgery: a multicentre study. *Bone Joint J* 2015;**97-b**:853-61.

27. Ogura K, Sakuraba M, Miyamoto S, et al. Pelvic ring reconstruction with a double-barreled free vascularized fibula graft after resection of malignant pelvic bone tumor. *Arch Orthop Trauma Surg* 2015;**135**:619-25.

28. Laitinen MK, Parry MC, Albergo JI, et al. Resection of the ilium in patients with a sarcoma: should the pelvic ring be reconstructed. *Bone Joint J* 2017;**99-b**:538-43.

29. Humail SM, Ghulam MK, Zaidi IH. Reconstruction of the distal radius with non-vascularised fibular graft after resection of giant cell tumour of bone. *J Orthop Surg (Hong Kong)* 2014;**22**:356-9.

30. Saini R, Bali K, Bachhal V, et al. En bloc excision and autogenous fibular reconstruction for aggressive giant cell tumor of distal radius: a report of 12 cases and review of literature. *J Orthop Surg Res* 2011;**6**:14.

31. Ball CG. Damage control surgery. *Curr Opin Crit Care* 2015;**21**:538-43.

32. Tadlock MD, Sise MJ, Riccoboni ST, et al. Damage control in the management of ruptured abdominal aortic aneurysm: preliminary results. *Vasc Endovascular Surg* 2010;**44**:638-44.

33. Ramamurthy R, Bose JC, Muthusamy V, Natarajan M, Kunjithapatham D. Staged sacrectomy-an adaptive approach. *J Neurosurg Spine* 2009;**11**:285-94.

PUBLICATION
II

Transverse myocutaneous gracilis flap reconstruction is feasible after pelvic exenteration: 12-year surgical and oncological results

Kiiski J, Räikkönen K, Vuento MH, Hyöty MK, Kallio J, Kuokkanen HO, Kaartinen IS

Transverse myocutaneous gracilis flap reconstruction is feasible after pelvic exenteration: 12-year surgical and oncological results

Juha Kiiski [a, *], Kim Räikkönen [b], Maarit H. Vuento [c], Marja K. Hyöty [d], Jukka Kallio [e], Hannu O. Kuokkanen [f], Ilkka S. Kaartinen [a, g]

[a] Department of Musculoskeletal Surgery and Diseases, Tampere University Hospital and University of Tampere, Faculty of Medicine and Life Sciences, Tampere, Finland
[b] University of Tampere, Faculty of Medicine and Life Sciences and University of Tampere, Faculty of Medicine and Life Sciences, Tampere, Finland
[c] Department of Gynecology and Obstetrics, Tampere University Hospital and University of Tampere, Faculty of Medicine and Life Sciences, Tampere, Finland
[d] Department of Gastroenterology, Tampere University Hospital and University of Tampere, Faculty of Medicine and Life Sciences, Tampere, Finland
[e] Department of Urology, Tampere University Hospital and University of Tampere, Faculty of Medicine and Life Sciences, Tampere, Finland
[f] Helsinki University Hospital, Department of Plastic Surgery, Finland
[g] Department of Reconstructive Plastic Surgery, Karolinska University Hospital, Stockholm, Sweden

ARTICLE INFO

ABSTRACT

Introduction: Pelvic exenteration (PE) is the only curative treatment for certain locally advanced intra-pelvic malignancies. PE has high morbidity, and optimal reconstruction of the pelvic floor remains undetermined.
Materials and methods: A retrospective chart review was performed at a tertiary university center to assess the surgical and oncological outcomes of 39 PE procedures over a 12-year period. The majority of patients (n = 25) underwent transverse musculocutaneous gracilis (TMG) flap reconstruction for pelvic floor reconstruction.
Results: The 1- and 5-year overall survival (OS) was 72% (95%CI 58%—86%) and 48% (95%CI 31%—65%), respectively. In multivariate analysis, lymph node metastasis (HR 3.070, p = 0.024) and positive surgical margins (HR 3.928, p = 0.009) were risk factors for OS. In this population, 71.8% of the patients had at least one complication. The complication rate was 65.4% and 84.6% for patients with versus without flap reconstruction, respectively (p = 0.191). The length of stay was longer for patients with a major complication 16,0 ± 5,9 days vs. 29,4 ± 14,8 days, p = 0,001, but complications did not affect OS.
Conclusion: For selected patients, PE is a curative option for locally advanced, residual, or recurrent intrapelvic tumors. Pelvic floor and vulvovaginal defects can reliably be reconstructed using TMG flaps. TMG flaps are favored in our institution over abdominal-based flaps because the donor site morbidity is reasonable and TMG does not interfere with enterostomy.
© 2019 Elsevier Ltd, BASO ~ The Association for Cancer Surgery, and the European Society of Surgical Oncology. All rights reserved.

Introduction

Complete *en bloc* surgical resection with clear margins is paramount for patient survival in advanced and recurrent pelvic malignancies [1]. Pelvic exenteration (PE) is a complex surgical procedure involving partial or total removal of the pelvic organs. Total pelvic exenteration (TPE) includes removal of the rectum, genital organs, and bladder. Anterior pelvic exenteration (APE) includes partial or total removal of the vagina, removal of the uterus and bladder. Posterior pelvic exenteration (PPE) includes partial or total removal of the vagina, removal of the uterus and rectum. Based on the extent of surgical resection, pelvic exenterations are

classified as type I (supralevator), type II (infralevator), or type III (infralevator with vulvectomy). PE was first described by Brunschwig in 1948 as a palliative procedure, but PE is now performed mainly in selected patients with curative intent [2,3].

PE has considerable morbidity, and the patient's quality of life is negatively affected by one or two permanent ostomies. Furthermore, the pelvic visceral anatomy is profoundly altered, and the integrity of the pelvic floor is weakened, creating a risk of postoperative complications and functional problems. In contemporary publications, the postoperative complication rates after PE range from 56% to 94% [1,4—7], while 5-year overall survival (OS) ranges from 22% to 62% [8—11]. The most important predictors of survival are clear surgical margins [1,8,12] and negative lymph node status [13].

Reconstruction after PE entails securing the pelvic floor, filling in the dead space, and forming a neovagina in selected patients who undergo total PE. Studies show that the results of autologous reconstruction are superior to those of synthetic mesh- or acellular dermal matrix-based solutions [14]. Myocutaneous flap reconstruction has a reduced major pelvic floor wound complication rate compared to primary closure after extensive pelvic floor resection [15]. Flaps based on the inferior epigastric artery are most commonly used for pelvic floor and vaginal reconstruction, including the vertical rectus abdominis musculocutaneous (VRAM) flap, transverse rectus abdominis musculocutaneous (TRAM) flap, or, more recently, the deep inferior epigastric artery perforator (DIEP) flap [15—17]. Abdominally-based flaps interfere with abdominal wall integrity; this is noteworthy because many PE patients require urinary diversion and/or end colostomy [1,9]. Pelvic floor reconstruction by transverse myocutaneous gracilis (TMG) flap was first described by Kolehmainen et al. [18]. TMG flap is often the most feasible local option for pelvic floor and vaginal reconstruction, and this option does not impair abdominal wall integrity [19].

This retrospective chart review was performed to evaluate oncological outcomes and complications related to PE and TMG flap reconstruction in a tertiary university center over a 12-year period.

Materials and Methods

Selection criteria

This was a retrospective cohort study of all patients who underwent PE surgery between January 1, 2005 and December 31, 2016 for an oncological indication at Tampere University Hospital. The study was approved by our institutional review board (ETL code R16582). Patients were identified from our electronic medical records and surgical database. Preoperative evaluation included a laboratory work-up, clinical examination of the patient, and magnetic resonance imaging to evaluate the size of the tumor and its relationship with the nearby organs. Whole body positron emission tomography-computed tomography (PET-CT) was used to exclude distant metastasis. All patients underwent curative intent surgery.

Variables and measurements

The following data were obtained: patient demographics, comorbidities, operative details, histopathological results, pre- and postoperative radiotherapy, chemotherapy, and complications. Complications were classified according to Clavien-Dindo classification [20]. Complications classified as 3b or higher were categorized as severe. All complications were collected from the date of exenteration to the date of last contact. Disease relapse (local relapse or metastasis) information was determined from medical records, and deaths were identified from the national population database. Disease-free survival (DFS) was measured from the date of exenteration to the date of recurrence, date of death or date of last contact. OS was measured from the date of exenteration to the date of death or date of last contact.

Surgical technique

All patients are evaluated with gynecologic oncologist and plastic surgeon prior the operation. Patients undergoing TPE receive sexual counselling from specialized nurse and are offered vaginal reconstruction.

The patient is placed in the dorsal lithotomy position. Colostomy and possible uretero-ileo-cutaneostomy locations, as well as TMG flap landmarks, are marked preoperatively. The pelvis is approached by a midline laparotomy incision. At laparotomy, the entire abdomen and pelvis are carefully examined for any evidence of metastatic or intraperitoneal cancer, and the lower para-aortic lymph nodes are sampled for frozen section analyses. If these are negative, a bilateral pelvic lymphadenectomy is performed, and an immediate frozen section analysis is performed to determine whether the operation should continue. The size and location of the tumor dictates the type (type I, II, or III) of exenteration that is required to obtain clear surgical margins.

Once the tumor has been resected, the reconstructive team starts the flap harvest while the oncology team performs urinary diversion. Our TMG flap harvest technique for pelvic floor and vagina reconstruction has been described in detail previously [19]. For unilateral reconstruction, a skin paddle that is approximately 8—10 cm by 20 cm is harvested with the gracilis muscle divided at the distal part near the knee joint. A bilateral TMG flap is used for vaginal reconstruction as well as in cases with extended perineal skin resection. In these cases, the skin island is approximately 6—7 cm by 20 cm. Reconstruction starts with distal skin incision and continued until muscular fascia. Fascia is opened over gracilis muscle and muscle is dissected all the way near knee joint. Anterior part of the proximal skin incision is carried out to muscle fascia. Vascular pedicle is identified under adductor muscle in it is dissected free from surrounding tissues and motor nerve is divided. Rest of the skin paddle and distal muscle insertion are incised to finalize the flap harvest. After flap harvest, a tunnel is created under the labia, and flaps are pulled through. The posterior and anterior parts of the skin island are de-epithelialized, and a neovagina is formed by suturing the skin paddles together, starting from the ventral portion of the neovagina. The posterior part of the de-epithelialized skin is sutured to Cooper's ligaments, and the distal portion of the muscles are sutured posteriorly to the pelvic floor through the laparotomy wound to fill the dead space and the pelvic floor defect and to prevent bowel herniation (Fig. 1a—h). Donor sites are closed directly with a suction drain. Key points of the reconstructive procedure are shown surgical video (Supplement 1).

Supplementary video related to this article can be found at https://doi.org/10.1016/j.ejso.2019.04.021.

Statistical analysis

Categorical variables were compared using a chi-square test. Continuous variables were compared using an independent sample t-test. DFS and OS were assessed with the Kaplan-Meier method, and statistical significance was determined using a log-rank test. Cox regression analysis was used to identify independent factors affecting survival. All statistical analyses were performed using SPSS Statistics 24.0 (IBM Armonk, NY, USA), and a p-value less than 0.05 was considered significant.

Fig. 1. PPE with most of the posterior and lateral walls resected (a) and after bilateral TMG flap reconstruction (b). Infralevator TPE (c), pelvic floor filling with de-epithelialized skin and muscle flap viewed from abdominal cavity (d) and vaginal reconstruction (e). PPE with posterior vaginal wall resection (f) with unilateral TMG flap reconstruction (g and h). PPE = posterior pelvic exenteration, TMG = transverse myocutaneous gracilis, TPE = total pelvic exenteration.

Results

During the 12-year study period, 38 women underwent a total of 39 exenteration operations. One patient underwent a first APE and then, two years later, underwent PPE after local recurrence. The mean patient age was 59.3 ± 12.2 years, and the mean follow-up was 35.1 (range 2.5–123) months. Table 1 shows the patients' demographic characteristics, comorbidities, and body mass index (BMI) values.

Of the 39 patients, 26 (66.7%) underwent TPE, 11 (28.2%) underwent PPE, and 2 (5.1%) underwent APE. The mean surgical time was 428 ± 56 min for TPE and 374 ± 49 min for combined APE and PPE (p = 0.032). The mean length of stay was 22.5 days for the TPE group and 15.5 days for the combined PPE and APE groups (p = 0.024). The length of stay was 16.0 ± 5.9 days for patients without severe complications and 29.4 ± 14.8 days for patients with severe complications (p = 0.001). While 15 (38.5%) patients had a

primary surgical procedure, 24 (61.5%) had a secondary salvage procedure after previously failed primary therapy. A total of 29 (74.4%) patients had pre-operative radiotherapy, and 1 (2.6%) patient had post-operative radiotherapy. Table 2 lists the primary locations and histology of the tumors. Nine (23.1%) patients had local lymph node metastasis.

We found that 27 (69.2%) patients underwent flap reconstruction for pelvic floor and/or vaginal reconstruction. Of these, 17 (43.6%) had bilateral TMG flap reconstruction, 9 (23.1%) had unilateral TMG flap reconstruction, and 1 (2.6%) had TRAM flap reconstruction; 12 (30.8%) patients had no flap reconstruction for the pelvic floor defect (Fig. 2). Out of 26 patients who underwent TPE, 12 (46,2%) had vaginal reconstruction. Bilateral TMG flap was used for all vaginal reconstructions in the TPE group.

The 1- and 5-year DFS of all patients was 58% (95%CI 43%–74%) and 45% (95%CI 28%–68%), respectively, and the 1- and 5-year OS of all patients was 72% (95%CI 58%–86%) and 48% (95%CI 31%–65%), respectively. Factors affecting OS in univariate analysis were BMI over 30 (p = 0.028), lymph node metastasis (p = 0.048), and positive surgical margins (p = 0.001) (Table 4). When these were applied to multivariate analysis, only positive surgical margins (p = 0.009) and lymph node metastasis (p = 0.027) were significant factors that contributed to OS (Table 4). The mean OS for patients with negative surgical margins was 84 months (95%CI 64–105 months) versus 17 months (95%CI 7.8–27 months) for patients with positive surgical margins (p < 0.001) (Fig. 3a). The 1-year OS of patients with intralesional surgical (R2) resection (n = 3) was 33% (OS range, 10–15 months). The mean OS was 20 months (95%CI 12–29 months) for patients with lymph node metastasis and 77 months (95%CI 58–97 months) for patients without lymph node metastasis (p = 0,039) (Fig. 3b).

There was a total of 49 complications in 28 (71.8%) patients. The complication rate was 65.4% and 84.6% for patients with versus without flap reconstruction, respectively (p = 0.191). Prior

Table 1
The demographic characteristics, comorbidities, body mass index values, tumor types, and radiotherapy status of 39 patients who underwent pelvic exenteration.

	Mean	Range
Age	59,3	30–78
Body mass index	26,2	16,0–38,0
	N	%
Diabetes	4	10,3
Chronic heart disease	2	5,1
Chronic pulmonary diasease	1	2,6
Primary tumor	15	38,5
Tumor recurrence	24	61,5
Radiotherapy		
Pre-operative	29	74,4
Post-operative	1	2,6
None	9	23,0

Table 2

Tumor histology and primary location of the tumor in 39 patients who underwent pelvic exenteration.

Histology	N	%
Adenocarinoma	20	51,3
Spinocellular ca	12	30,8
Melanoma	5	12,8
Cystadenocarcinoma	2	5,1
Primary location		
Cervix	12	30,8
Vagina	7	17,9
Vulva	6	15,4
Uterus	5	12,8
Rectum	5	12,8
Ovary	3	7,7
Urethra	1	2,6

radiotherapy, BMI, diabetes, and age did not affect the complication rate. A total of 12 patients (30.8%) had at least one severe complication, and the most common complications were infection (43,6%) and local wound dehiscence (33,3%) (Table 3). There was one complication that was directly flap-related, a minor edge necrosis of a TMG flap that was treated with excision and direct closure. The most severe complication of each patient according to Clavien-Dindo classification is shown in Table 3.

Discussion

PE remains the only curative alternative for certain locally advanced, residual, or recurrent tumors of the pelvic organs, especially those involving the female reproductive organs. Even though a majority of the patients in this series experienced surgical or medical complications, the 5-year OS rate approached 50% with no perioperative mortality.

Careful patient selection, planning, and a multidisciplinary team approach are paramount for successful PE. Patient age was not

Fig. 2. Exenterations and their reconstructions. TPE = total pelvic exenteration, PPE = posterior pelvic exenteration, APE = anterior pelvic exenteration. TMG = transverse myocutaneous gracilis flap, TRAM = transverse rectus abdominis flap.

associated with an increased risk of complications or with OS, highlighting the importance of individualized decision making for this patient group [10,21]. Patients require close follow-up in the post-operative period, as complications are common after PE. Patients also required interventions by multiple specialties during the post-operative period. The overall length of stay of 22.5 days for TPE was similar to that in other cohorts [1,13,22].

PE can be performed for curative intent in patients who present with advanced or recurrent pelvic malignancies. Our 5-year OS of 48% was comparable to that in larger patient cohorts [2,4]. BMI affected OS in univariate analysis but not in multivariate analysis. Obesity has not been shown to affect recurrence or OS in patients who undergo PE for a gynecological indication [23]. In multivariate analysis, only negative surgical resection margins (R0) and negative lymph node status had a positive effect on patient survival. Both negative surgical margins [1,9,13,24] and negative lymph node status [13,24] have been shown to be predictive for survival.

There was a tendency toward a lower complication rate in the flap reconstruction, cohort, although this did not reach statistical significance. Flap closure is superior to primary closure for pelvic floor defects following oncologic resection [15]. Reconstruction after PE has three main goals: securing the pelvic floor in order to prevent perineal herniation of the bowel; filling in the dead space; and forming a vagina, either partially or entirely. A variety of methods have been described, ranging from free skin and bowel grafts to local flaps, muscle flaps, and myocutaneous flaps [25,26]. Of these alternatives, only vascularized fasciocutaneous or myocutaneous flaps can achieve all three of these goals. Both mesh and acellular dermal matrix have been used previously to support the pelvic floor, but these are associated with increased infection rate and fistulas [14]. Furthermore, autologous reconstruction is needed for patients who want to be able to have intercourse.

The TMG flap is conveniently located in the upper thigh, providing a pliable flap with a width of 6—10 cm and a length up to 26 cm, and, together with the gracilis muscle, has enough bulk to fill in the pelvic floor. It can be raised as a unilateral or bilateral flap, depending on the reconstructive requirements and the amount of expendable tissue. We found that TMG flaps are versatile tool for pelvic floor and vaginal reconstruction after PE. Bilateral TMG reconstruction is indicated for TPE patients who wish to have vaginal reconstruction and PPE patients whos vaginal resection included, not only posterior wall of the vagina, but resection extended to the lateral wall. Bilateral TMG flaps are also required for some patients who undergo concomitant radical vulvectomy. Remaining of the defects can be reliably reconstructed with unilateral TMG flap. Horizontally oriented skin paddle in TMG flap was reliable with only one minor skin edge necrosis in this series. Reconstructing the pelvic floor and vagina with a unilateral or bilateral TMG flap has been our preferred choice since 2011 [19]. Vaginal reconstruction was offered to all patients with TPE and was performed on 12 patients.

TMG flaps have two additional advantages over abdominal-based flaps (VRAM/TRAM or DIEP flaps). First, patients undergoing TPE required urinary diversion and colostomy through the abdominal wall. Harvesting the flap from the abdomen is associated with significant donor site morbidity as it weakens the anterior abdominal wall resulting abdominal wound complication rate up to 48% [16]. Some prefer gracilis flap over abdominal flap when bilateral ostomies are needed [27]. However, there is no clear evidence that use of abdominal flap would increase abdominal herniation risk [15,28] Second, harvesting the TMG flaps and reconstruction of the pelvic floor can be performed while the urologist performs urinary diversion. Our mean surgical time of 428 min was comparable to the 335—725 min reported for reconstructions with abdominal-based flaps in previously published
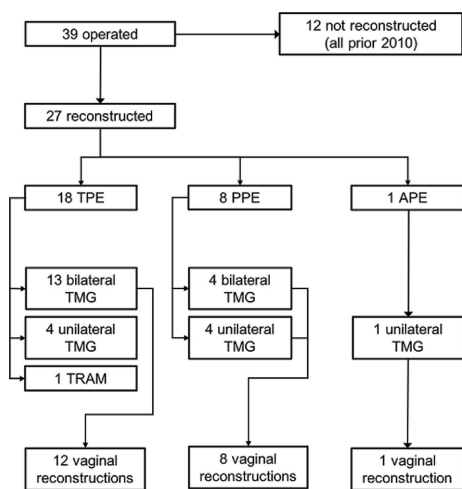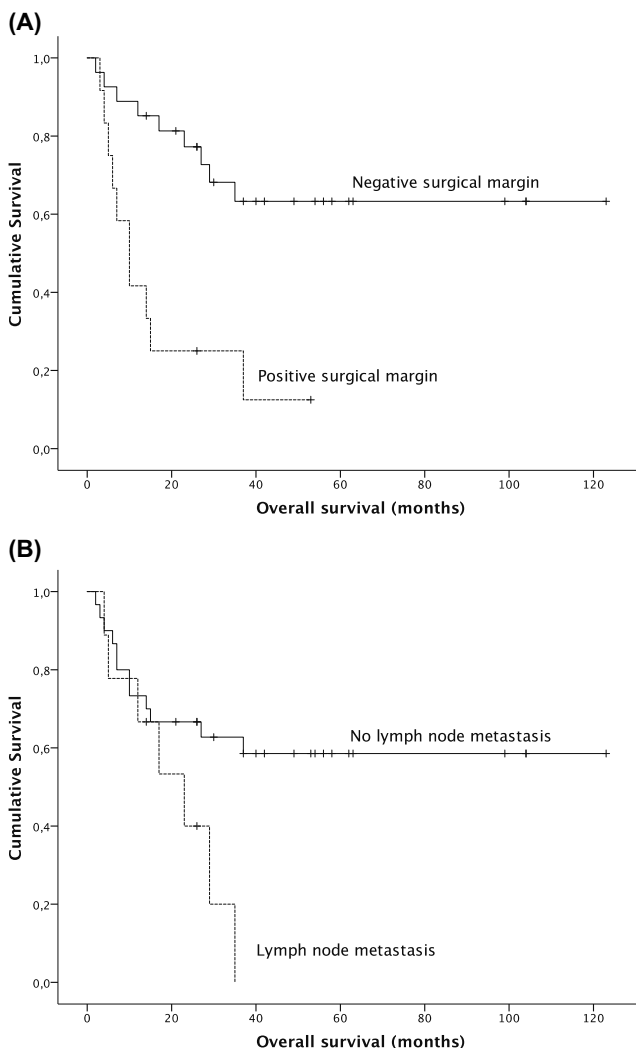
(A)

(B)

Fig. 3. Kaplan-Maier plots showing overall survival (OS) in patients with R0 or R1/2 resection margins (A) with or without lymph node metastasis (B).

series [17,29]. There are no prospective studies comparing thigh or abdominal based flaps for pelvic floor and vaginal reconstruction. No differences were detected on outcomes or complications when thigh and abdominal flaps were compared in meta-analysis or recent retrospective studies [15,27,30].

Our overall complication rate of 71.8% was similar to the rates in previous publications [1,9,13]; notably, earlier reports did not always define complication severity. Here we stratified complication severity using the Clavien-Dindo classification. In our cohort, the majority of complications were minor complications, and the severe complication rate was 30,8%. Severe complications prolonged the length of stay but did not affect the DFS or OS. The most common complications were infectious complications, and the majority of these were managed with antimicrobial treatment. Wound dehiscence was the most common operatively-managed complication. There were three post-operative decubital ulcers. We were not able to retrace the timing of these ulcers nor could we determine whether proper preventive measures failed or whether the decubital ulcer risk was disregarded during post-operative care. There was only one direct flap-related complication with partial flap loss in this cohort. Our flap-related complication rate was lower than in series that used abdominal-based flap reconstruction

Table 3
Complications (number and percentage) and the grade of the most severe complication in 39 patients who underwent pelvic exenteration.

Complication	n	%
Infection	17	43,6%
Wound dehiscence	13	33,3%
Enteral fistula	3	7,7%
Postoperative decubital ulcer	3	7,7%
Acute kidney injury	2	5,1%
Pelvic evisceration	1	2,6%
Urinary fistula	1	2,6%
Urinary incontinence	1	2,6%
Cardiac insufficiency	1	2,6%
Hernia/bulging	1	2,6%
Thromboembolic complication	1	2,6%
Flap loss		
Partial	1	2,6%
Total	0	0%

Clavien-Dindo grade	n	%
1	4	10,3%
2	8	20,5%
3a	4	10,3%
3b	10	25,6%
4a	2	5,1%

[16,17].

One limitation of this study was its retrospective nature. Although the number of patients who underwent PE during the 12-year study period was comparable to the number in some earlier reports [5,13], the heterogeneity of the tumor location and histology limited its statistical power for detecting risk factors for complications as well as histology-specific survival. No patient-reported outcome measures were available for this patient cohort.

In conclusion, in carefully selected patients who are treated by an experienced multidisciplinary team, PE is a possible curative option for recurrent gynecological, urological, and gastrointestinal cancers. Clear surgical margins are paramount for survival and should be the goal in every case. Pelvic floor and vulvovaginal defects can be reconstructed with TMG flaps without additional morbidity.

Conflict of interest

None of the authors have conflict of interest to declare.

References

[1] Zoucas E, Frederiksen S, Lydrup ML, Mansson W, Gustafson P, Alberius P. Pelvic exenteration for advanced and recurrent malignancy. World J Surg 2010;34:2177—84.
[2] Brown KGM, Solomon MJ, Koh CE. Pelvic exenteration surgery: the evolution of radical surgical techniques for advanced and recurrent pelvic malignancy. Dis Colon Rectum 2017;60:745—54.
[3] Brunschwig A. Complete excision of pelvic viscera for advanced carcinoma; a one-stage abdominoperineal operation with end colostomy and bilateral ureteral implantation into the colon above the colostomy. Cancer 1948;1: 177—83.
[4] Knight S, Lambaudie E, Sabiani L, Mokart D, Provansal M, Tallet A, et al. Pelvic exenterations for gynecologic cancers: a retrospective analysis of a 30-year experience in a cancer center. Eur J Surg Oncol 2018;44:1929—34.
[5] Petruzziello A, Kondo W, Hatschback SB, Guerreiro JA, Filho FP, Vendrame C, et al. Surgical results of pelvic exenteration in the treatment of gynecologic cancer. World J Surg Oncol 2014;12:279.
[6] Hagemans JAW, Rothbarth J, Kirkels WJ, Boormans JL, van Meerten E, Nuyttens J, et al. Total pelvic exenteration for locally advanced and locally recurrent rectal cancer in the elderly. Eur J Surg Oncol 2018;44:1548—54.
[7] Westin SN, Rallapalli V, Fellman B, Urbauer DL, Pal N, Frumovitz MM, et al. Overall survival after pelvic exenteration for gynecologic malignancy. Gynecol Oncol 2014;134:546—51.
[8] Steffens D, Solomon MJ, Young JM, Koh C, Venchiarutti RL, Lee P, et al. Cohort study of long-term survival and quality of life following pelvic exenteration. BJS Open 2018;2:328—35.
[9] Berek JS, Howe C, Lagasse LD, Hacker NF. Pelvic exenteration for recurrent gynecologic malignancy: survival and morbidity analysis of the 45-year experience at UCLA. Gynecol Oncol 2005;99:153—9.
[10] Radwan RW, Evans MD, Davies M, Harris DA, Beynon J. Pelvic exenteration for advanced malignancy in elderly patients. Br J Surg 2016;103:e115—9.
[11] Schmidt AM, Imesch P, Fink D, Egger H. Indications and long-term clinical outcomes in 282 patients with pelvic exenteration for advanced or recurrent cervical cancer. Gynecol Oncol 2012;125:604—9.
[12] Smith B, Jones EL, Kitano M, Gleisner AL, Lyell NJ, Cheng G, et al. Influence of tumor size on outcomes following pelvic exenteration. Gynecol Oncol 2017;147:345—50.
[13] Maggioni A, Roviglione G, Landoni F, Zanagnolo V, Peiretti M, Colombo N, et al. Pelvic exenteration: ten-year experience at the European institute of oncology in Milan. Gynecol Oncol 2009;114:64—8.
[14] Goldberg GL, Sukumvanich P, Einstein MH, Smith HO, Anderson PS, Fields AL. Total pelvic exenteration: the Albert Einstein college of medicine/Montefiore medical center experience (1987 to 2003). Gynecol Oncol 2006;101:261—8.
[15] Devulapalli C, Jia Wei AT, DiBiagio JR, Baez ML, Baltodano PA, Seal SM, et al. Primary versus flap closure of perineal defects following oncologic resection: a systematic review and meta-analysis. Plast Reconstr Surg 2016;137: 1602—13.
[16] Berger JL, Westin SN, Fellman B, Rallapali V, Frumovitz M, Ramirez PT, et al. Modified vertical rectus abdominis myocutaneous flap vaginal reconstruction: an analysis of surgical outcomes. Gynecol Oncol 2012;125:252—5.
[17] Qiu SS, Jurado M, Hontanilla B. Comparison of TRAM versus DIEP flap in total vaginal reconstruction after pelvic exenteration. Plast Reconstr Surg 2013;132:1020e—7e.
[18] Kolehmainen M, Suominen S, Tukiainen E. Pelvic, perineal and genital reconstructions. Scand J Surg 2013;102:25—31.
[19] Kaartinen IS, Vuento MH, Hyoty MK, Kallio J, Kuokkanen HO. Reconstruction of the pelvic floor and the vagina after total pelvic exenteration using the transverse musculocutaneous gracilis flap. J Plast Reconstr Aesthet Surg 2015;68:93—7.
[20] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205—13.
[21] Huang M, Iglesias DA, Westin SN, Fellman B, Urbauer D, Schmeler KM, et al. Pelvic exenteration: impact of age on surgical and oncologic outcomes. Gynecol Oncol 2014;132:114—8.
[22] Guo Y, Chang E, Bozkurt M, Park M, Liu D, Fu JB. Factors affecting hospital length of stay following pelvic exenteration surgery. J Surg Oncol 2018;117: 529—34.
[23] Iglesias DA, Westin SN, Rallapalli V, Huang M, Fellman B, Urbauer D, et al. The effect of body mass index on surgical outcomes and survival following pelvic exenteration. Gynecol Oncol 2012;125:336—42.
[24] Park JY, Choi HJ, Jeong SY, Chung J, Park JK, Park SY. The role of pelvic exenteration and reconstruction for treatment of advanced or recurrent gynecologic malignancies: analysis of risk factors predicting recurrence and survival. J Surg Oncol 2007;96:560—8.
[25] Fowler JM. Incorporating pelvic/vaginal reconstruction into radical pelvic surgery. Gynecol Oncol 2009;115:154—63.
[26] Salom EM, Penalver MA. Pelvic exenteration and reconstruction. Cancer J 2003;9:415—24.
[27] Stein MJ, Karir A, Ramji M, Allen M, Bain JR, Avram R, et al. Surgical outcomes of VRAM versus gracilis flaps for the reconstruction of pelvic defects following oncologic resection. J. Plast. Reconstr. Aesthet. Surg. 2019;72:565—71.
[28] Nelson RA, Butler CE. Surgical outcomes of VRAM versus thigh flaps for immediate reconstruction of pelvic and perineal cancer resection defects. Plast Reconstr Surg 2009;123:175—83.
[29] Ferron G, Gangloff D, Querleu D, Frigenza M, Torrent JJ, Picaud L, et al. Vaginal reconstruction with pedicled vertical deep inferior epigastric perforator flap (diep) after pelvic exenteration. A consecutive case series. Gynecol Oncol 2015;138:603—8.
[30] Block LM, Hartmann EC, King J, Chakmakchy S, King T, Bentz ML. Outcomes analysis of gynecologic oncologic reconstruction. Plast Reconstr Surg Glob Open 2019;7:e2015.

PUBLICATION
III

Soft tissue reconstruction after pelvic amputation: The efficacy and reliability of free fillet flap reconstruction

Kiiski J, Laitinen MK, Le Nail LR, Kuokkanen HO, Peart F, Rossert P, Bourdais-Sallot A, Jeys LM, Parry MC

■ **ONCOLOGY**

Surgical and oncological outcomes after hindquarter amputation for pelvic sarcoma

WHO WILL BENEFIT FROM THE PROCEDURE?

J. Kiiski,
M. C. Parry,
L-R. Le Nail,
V. Sumathi,
J. D. Stevenson,
I. S. Kaartinen,
L. M. Jeys,
M. K. Laitinen

From Royal Orthopaedic Hospital, The Royal Orthopaedic Hospital NHS Foundation Trust, Birmingham, UK

Aims
Survival rates and local control after resection of a sarcoma of the pelvis compare poorly to those of the limbs and have a high incidence of complications. The outcome for patients who need a hindquarter amputation (HQA) to treat a pelvic sarcoma is poor. Our aim was to evaluate the patient, tumour, and reconstructive factors that affect the survival of the patients who undergo HQA for primary or recurrent pelvic sarcoma.

Methods
We carried out a retrospective review of all sarcoma patients who had undergone a HQA in a supraregional sarcoma unit between 1996 and 2018. Outcomes included oncological, surgical, and survival characteristics.

Results
A total of 136 patients, with a mean age of 51 (12 to 83) underwent HQA, 91 for a bone sarcoma and 45 for a soft tissue sarcoma. The overall survival (OS) after primary HQA for a bone sarcoma was 90.7 months (95% confidence interval (CI) 64.1 to 117.2). In patients undergoing a secondary salvage HQA it was 90.3 months (95% CI 58.1 to 122.5) (p = 0.727). For those treated for a soft tissue sarcoma (STS), the mean OS was 59.3 months (95% CI 31.1 to 88.6) for patients with a primary HQA, and 12.5 months (95% CI 9.4 to 15.5) for those undergoing a secondary salvage HQA (p = 0.038). On multivariate analysis, high histological grade (hazard ratio (HR) 2.033, 95% CI 1.127 to 3.676; p = 0.018) and a diagnosis of STS (HR 1.653, 95% CI 1.027 to 2.660; p = 0.039) were associated with a poor prognosis. The 30-day mortality for patients with curative intent was 0.8% (1/128). For those in whom surgery was carried out with palliative intent it was 33.3% (2/6) (p = 0.001). In total, 53.7% (n = 73) of patients had at least one complication with 23.5% (n = 32) requiring at least one further operation. Direct closure was inferior to flap reconstruction in terms of complete primary wound healing (60.0% (3/5) vs 82.0% (82/100); p = 0.023).

Conclusion
In carefully selected patients HQA is associated with satisfactory overall survival, with a low risk of perioperative mortality, but considerable morbidity. However, caution must be exercised when considering the procedure for palliation due to the high incidence of early postoperative mortality.

Cite this article: *Bone Joint J* 2020;102-B(6):788–794.

Introduction

Sarcomas are rare malignant mesenchymal tumours which constitute approximately 1% of all malignancies[1] and 5% to 15% of all tumours of the pelvis.[2-4] Tumours arising in the pelvis present a unique challenge to orthopaedic oncologists due to the absence of natural anatomical barriers, the close proximity of vital neurovascular structures, and the high mechanical demands placed on any pelvic reconstruction following the excision of the tumour.

Most osseous and soft tissue sarcomas (STS) of the pelvis are now managed by limb salvage surgery, principally by internal pelvic resection.[5-9] However, in cases of advanced disease or where the ability to achieve clear margins at resection are compromised by limb salvage surgery, hindquarter amputation (HQA) may still be considered. HQA may also be considered in patients in whom the limb would be rendered useless after tumour resection as palliation for the treatment of
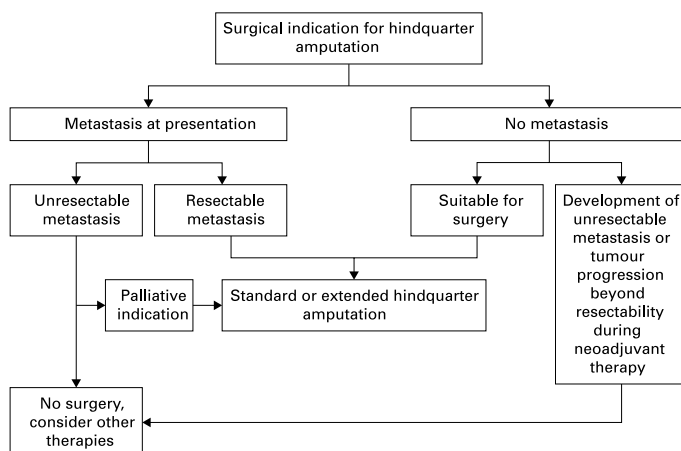
Fig. 1

Algorithm diagram for hindquarter amputation.

intractable pain or to aid nursing care in the case of advanced disease. While no absolute criteria exist, the consensus among orthopaedic oncologists is that involvement by tumour of two of the three critical structures around the pelvis, the iliac vessels, the hip joint, and the sciatic nerve, warrants consideration of HQA.[10] These anatomical considerations should not be considered in isolation, and consideration should also be given to the patients' age, comorbidities, and their willingness to undergo life-changing ablative surgery.[10,11]

Although considerable advances have been made in their treatment, the prognosis for patients with a primary pelvic sarcoma continues to be worse than that of patients with a sarcoma of the limbs as tumours often present late, by which time they have achieved a significant size, and have often metastasized.[12-14] Poor prognostic factors for patients undergoing pelvic resection for a primary malignancy include age, tumour volume, surgical margin, and metastasis at presentation.[6,15] Results are more often based on limb salvage procedures, and papers reporting the outcomes of HQA often describe relatively small numbers of patients[16-18] or, due to the rarity of the procedure, they include benign conditions such as infection. They may also include patients who have been treated over a long period, during which time pelvic imaging, whole-body staging, or the indications for internal pelvic resection have changed.[17,19,20] Thus, the factors that affect disease specific and overall survival (OS) after HQA have not been clearly described.

The aims of this study were firstly to evaluate specific patient and tumour characteristics that correlate with the most significant benefit from HQA in the era of limb salvage surgery, taking into consideration advances in treatment, diagnostics, and multidisciplinary management. Secondly, to evaluate if the method of reconstruction after HQA had any effect on overall or disease-specific survival, or on the incidence of complications.

Methods

Following institutional review board approval, we carried out a retrospective review of all patients undergoing HQA between January 1996 and August 2018 in a single tertiary referral centre for sarcoma. Patients were identified from a prospectively maintained database which records all patient contacts as well as details of demographics, tumour characteristics, surgical resection, and complications. The study period was selected on the basis that during this time, all patients with the most common indications for HQA (primary malignant tumours of bone and STS) were managed in a comparable way by multidisciplinary team discussion and the use of modern chemotherapy and radiotherapy regimens, where indicated. A minimum 12 months' follow-up and complete histopathology records were required for all surviving patients. Patients who underwent HQA for diagnoses other than sarcoma were excluded.

HQA was classified as extensile if the bone resection extended medial to the sacroiliac joint, to include the sacral ala, sacral or lumbar vertebrae, or the abdominal wall. Primary curative surgery was defined as treatment which aimed to cure, that is, in patients who had not undergone any surgery to the primary tumour and who did not have metastatic disease. Secondary salvage surgery was defined as treatment in which previous limb-salvage surgery had failed because of local recurrence (LR). Palliative surgery was considered only in patients who surgery would not cure, such as those presenting with inoperable metastatic disease. Patients who presented with synchronous metastases, but whose metastases were resected before or after HQA, were considered be of curative intent. Primary healing was defined as a lack of a need for any revision surgery or local wound therapy over a one-month period following the index procedure. Partial flap loss was defined as the need for any surgical debridement of the wound due to partial or total necrosis of the flap.

Table I. Patient demographics.

Characteristics	Patients
Eligible patients, n	136
Male, n (%)	80 (58.8)
Mean age, yrs (range)	51 (12 to 83)
Bone sarcoma, n (%)	91 (66.9)
Total hemipelvis	30 (22.1)
Ilium	17 (12.5)
Acetabulum	17 (12.5)
Pubic or ischial bone	3 (2.2)
Proximal femur	24 (17.6)
Soft tissue sarcoma, n (%)	45 (33.0)
Thigh	24 (17.6)
Gluteal	17 (12.5)
Groin	4 (2.9)
Histology	
Chondrosarcoma	56 (41.2)
Osteosarcoma	28 (20.6)
Ewing's sarcoma	2 (1.5)
Parosteal osteosarcoma	1 (0.7)
Periosteal osteosarcoma	1 (0.7)
Undifferentiated pleomorphic sarcoma, n (%)	23 (16.9)
Leiomyosarcoma	6 (4.4)
Angiosarcoma	2 (1.5)
Myxoid liposarcoma	4 (2.9)
Synovial sarcoma	4 (2.9)
Malignant peripheral nerve sheet tumour	3 (2.2)
Triton tumour	2 (1.5)
Fibrosarcoma	2 (1.5)
Extraskeletal chondrosarcoma	1 (0.7)
Liposarcoma	1 (0.7)
Mean size, cm (range)	16.2 (5 to 49)
Mean tumour volume, cm³ (range)	2,944 (100 to 39,700)
Mean closest margin, mm (range)	8.5 (0 to 120)
Positive surgical margin (R1/2), n (%)	
Bone	17 (18.7)
STS	14 (31.1)
Surgical attempt, n (%)	
Primary surgical procedure	83 (61.0)
Secondary surgical procedure	53 (39.0)
Extent of amputation, n (%)	
Standard	92 (67.6)
Extended	40 (29.4)
Missing	4 (2.9)
Preoperative chemotherapy, n (%)	
Bone	15 (16.9)
STS	7 (16.3)
Preoperative radiotherapy, n (%)	
Bone	2 (2.3)
STS	14 (27.3)
Indication for surgery, n (%)	
Curative	128 (94.1)
Palliative	6 (4.4)
Missing	2 (1.5)
Alive at latest follow-up	57 (41.9)
Local recurrence	36 (26.5)
Metastasis	67 (49.3)

STS, soft tissue sarcoma.

During the period of study, all patients underwent pelvic MRI and CT scanning to evaluate the extent of local disease and systemic staging depending on the histology of the primary tumour. The histology and imaging studies were reviewed in a supraregional sarcoma Multidisciplinary Team (MDT) meeting where the tumour type, staging, indication for neoadjuvant therapy, and operative management were discussed (Figure 1). The decision to undertake HQA was based on the underlying diagnosis, the staging of the patient, the volume of the tumour, the projected achievable margins had limb salvage been contemplated, and the wishes of the patient and their family. Patients received counselling from the special limb fitting services prior to amputation.

The cohort consisted of 136 patients, with a mean age of 51 (12 to 83) years who underwent HQA during the study period. In total, 59% (n = 80) of the patients were male. Most underwent HQA to treat a sarcoma of bone (66.9%, n = 91). In 83 patients (61%) HQA was intended to be curative while in the other 53 (39%) it was for secondary salvage following tumour recurrence or failed limb-salvage surgery. The intent was curative in 128 (94.1%), palliative in six (4.4%), and unavailable in two (1.5%). Patient demographics are summarized in Table I.

Statistical analysis. Median and mean values with ranges were calculated for continuous variables. Overall survival was measured from the date of HQA to the date of death or date of last follow-up. Local recurrence-free survival (LRFS) was measured from the date of the HQA to the date of local recurrence, date of death or date of last follow-up. Kaplan-Meier curves were constructed to assess overall survival and LRFS and the log-rank test was used to test the statistical significance. Cox proportional hazard model was used to assess factors affecting the overall survival. We calculated the 95% confidence interval (CI) for relative risks. The Mann-Whitney U test and chi-squared test were used to test the statistical significance for continuous and categorical variables, respectively. A p-value < 0.05 was considered statistically significant. All statistical analyses were carried out using SPSS Statistics 24.0 (IBM, Armonk, New York, USA).

Results

Patient-related outcomes. The mean overall survival for patients with a primary bone sarcoma was 90.7 months (95% CI 64.1 to 117.2) for primary curative surgery, and 90.3 months (95% CI 58.1 to 122.5) for secondary salvage surgery (p = 0.727, log-rank test) (Figure 2a). The mean tumour volume for primary and salvage groups was 3,748 cm³ (SD 2,738) and 1,519 cm³ (SD 1,795), respectively (p < 0.001, Mann-Whitney U test). For patients undergoing HQA as treatment of a STS with primary curative intent, the mean overall survival was 59.3 months (95% CI 31.1 to 88.6), compared with 12.5 months (95% CI 9.4 to 15.5) for patients undergoing secondary salvage surgery (p = 0.038, log-rank test) (Figure 2b). The mean tumour volume for primary and salvage groups was 3,318 cm³ (SD 2,536) and 2,227 cm³ (SD 2,017), respectively (p = 0.162, Mann-Whitney U test). The one-, three-, and five-year overall survival are presented in Table II. On multivariate analysis, factors associated with a poor prognosis for overall survival included HQA as treatment for STS (hazard ratio (HR) 1.653;
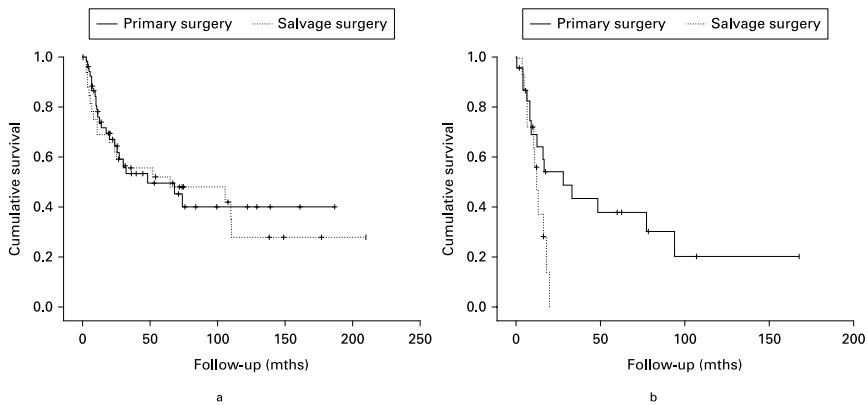
Fig. 2

a) Survival after hindquarter amputation for bone sarcoma as a primary surgical procedure and salvage surgical procedure after local recurrence. b) Survival after hindquarter amputation as a primary surgical procedure and salvage surgical procedure for soft tissue sarcoma after local recurrence.

Table II. One-, three-, and five-year osteosarcoma. Log-rank test for mean survival time.

Variable	1-yr OS, % (95% CI)	3-yr OS, % (95% CI)	5-yr OS, % (95% CI)	p-value
Tumour location				0.008
Bone	71.5 (62.0 to 80.8)	52.5 (41.5 to 63.5)	47.2 (35.6 to 58.8)	
Soft-tissue	62.1 (31.9 to 62.5)	27.5 (12.0 to 43.0)	24.0 (9.1 to 38.9)	
Histology				
Chondrosarcoma (CS)	77.8 (66.6 to 89.9)	64.0 (50.3 to 77.7)	20.2 (4.5 to 35.9)	N/A
Osteosarcoma	64.3 (45.9 to 82.7)	36.7 (18.1 to 55.3)	32.1 (13.7 to 50.5)	0.017 vs CS
UPS	66.6 (46.2 to 87.0)	41.6 (15.9 to 67.3)	31.2 (4.9 to 57.5)	0.100 vs CS
Other	56.4 (37.0 to 75.8)	20.2 (4.5 to 35.9)	20.2 (4.5 to 35.9)	< 0.001 vs CS
Grade				
Grade 1	100	100	100	N/A
Grade 2	94.7 (84.7 to 100)	66.0 (43.9 to 88.1)	52.0 (27.3 to 76.7)	0.010 vs grade 3
Grade 3	60.3 (50.5 to 70.1)	38.0 (27.4 to 48.6)	34.6 (24.0 to 45.2)	0.018 vs grade 3
Closest margin				0.017
> 1 mm	79.4 (69.8 to 89.0)	48.8 (36.1 to 61.5)	46.2(33.3 to 59.1)	
≤ 1 mm	55.9 (43.2 to 68.6)	41.4 (28.1 to 54.7)	34.1 (20.8 to 47.4)	
Sex				0.183
Female	69.0 (56.7 to 81.3)	52.3 (38.6 to 66.0)	49.5 (35.4 to 63.6)	
Male	68.3 (57.5 to 79.1)	39.4 (27.1 to 51.7)	32.9 (20.6 to 45.2)	
Timing of the surgery				0.257
Primary	72.6 (62.6 to 82.6)	48.9 (36.9 to 60.9)	42.5 (30.0 to 55.0)	
Salvage	62.1 (48.6 to 75.6)%	39.5 (25.4 to 53.6)	36.8 (22.7 to 50.9)	
Extent of the surgery				0.302
Standard	67.7 (58.3 to 77.1)	39.6 (28.0 to 51.2)	35.9(24.3 to 47.5)%	
Extended	69.9 (55.6 to 84.2)	61.9 (46.6 to 77.2)	52.0 (35.5 to 68.5)	
Tumour volume				
< 1,000 cm³	70.3 (54.8 to 85.8)	51.4 (34.2 to 68.6)	41.7 (24.6 to 58.8)	N/A
1,000 to 1,999 cm³	69.4 (51.8 to 87.0)	44.9 (22.0 to 67.8)	33.7 (8.0 to 59.4)	0.453 vs < 1,000 cc
2,000 to 3,999 cm³	64.3 (46.5 to 82.1)	41.5 (22.7 to 60.3)	41.5 (22.7 to 60.3)	0.649 vs < 1,000 cc
> 4,000 cm³	66.6 (48.6 to 84.6)	35.7 (14.7 to 56.7)	35.7 (14.7 to 56.7)	0.379 vs < 1,000 cc

CI, confidence interval; CS, chondrosarcoma; N/A, not applicable; OS, overall survival; UPS, undifferentiated pleomorphic sarcoma.

95% CI 1.027 to 2.660; p = 0.039) and high grade histological subtypes, including both bone and soft tissue (HR 2.033; 95% CI 1.127 to 3.676; p = 0.018).

The incidence of local recurrence in patients undergoing HQA was 25.3% (23/91) for a bone sarcoma and 28.9% (13/45)

for a STS. LRFS was 96.5% (95% CI 93 to 100) at one year and 61.5% (95% CI 48 to 75) at five years for patients with a bone sarcoma, and 87.5% (95% CI 77 to 98) at one year and 43.1% (95% 19 to 67) at five years for those with a STS (p = 0.216). None of the variables investigated, including tumour grade,

Table III. Number (%) of flaps used, flap loss rate, and primary healing rate. Complete flap survival was defined as complete flap survival without any need for flap revision or wound necrosis. Primary healing was defined as no need for any takeback to theatre and no prolonged local wound therapy.

Flap	n (%)	Complete flap survival, n (%)	Reoperation, n (%)	Primary healing, n (%)
Posterior gluteal flap	50 (36.8)	39 (78.0)	11 (22.0)	32 (64.0)
Anterior thigh flap	42 (30.9)	36 (85.7)	9 (21.4)	31 (73.8)
Fillet flap	6 (4.4)	5 (83.3)	2 (33.3)	4 (66.7)
Direct closure / skin only	5 (3.7)	3 (60.0)*	2 (40.0)	3 (60.0)
VRAM flap	2 (1.5)	2 (100)	0 (0.0)	1 (50.0)
Unknown reconstruction	31 (22.8)	22 (71.0)	8 (27.6)	18 (58.0)
Total	136 (100)	107 (78,6)	32 (23.9)	89 (65.4)

*p < 0.05.
VRAM, vertical rectus abdominis.

Table IV. Number (%) of complications.

Complication	Bone	STS	Total	p-value
Wound dehiscence, n (%)	29 (32.6)	8 (17.8)	37 (27.6)	0.082
Infection, n (%)	21 (23.6)	9 (20)	30 (22.1)	0.916
Pulmonary embolism, n (%)	2 (2.2)	1 (2.2)	3 (2.2)	1.000
In-hospital death, n (%)	1 (1.1)	2 (4.4)	3 (2.2)	0.211
Clostridium difficile infection, n (%)	2 (2.2)	0 (0)	2 (1.5)	0.316
Other medical complication, n (%)	2 (2.2)	0 (0)	2 (1.5)	0.316
Ureter injury, n (%)	1 (1.1)	0 (0)	1 (0.7)	0.480
Retained foreign body, n (%)	1 (1.1)	0 (0)	1 (0.7)	0.480

STS, soft tissue sarcoma.

extent of the HQA, margin, or tumour volume had a significant effect on LRFS.

In six patients, the indication for HQA was palliative. Three underwent HQA for a bone sarcoma and three for treatment of a STS. The median tumour volume was 5,600 cm^3 (IQR 2,197 to 7,971), which was significantly greater than in patients undergoing HQA with curative intent (1,736 cm^3 (IQR 720 to 3,356)) (chi-squared test, p = 0.019). The margins achieved at HQA were significantly closer (chi-squared test, p = 0.020): four patients had intralesional margins. The median overall survival was 2.4 months (95% CI 0.0 to 6.1): two of the six (33.3%) died while still in hospital, within two weeks of surgery. The 30-day mortality was 0.8% for patients undergoing surgery with curative intent and 33% for those with palliative intent (Log-rank, p = 0.001).

Flap-related outcomes. Soft tissue reconstruction in most of the patients was carried out using a local posterior gluteal flap or an anterior thigh flap. The contralateral vertical rectus abdominis musculocutaneous flap was used in two patients (1.5%). Overall, 4.4% (n = 6) of patients had a massive soft tissue defect after HQA which needed free flap reconstruction. All free flaps were microvascular fillet flaps from amputated limbs. Flap description was insufficient in 22.8% (n = 31) of the cases. Wound closure was direct in five patients. The incidence of complete wound healing was lower in those who underwent direct wound closure than in those in whom the defect was reconstructed using either a local or free flap (60.0% (3/5) vs 82.0% 82/100), chi-squared test, p = 0.023). In two cases (1.5%), flap loss required secondary flap reconstruction. There were no other significant differences between the method of local or free flap used for reconstruction and flap-related complications, flap survival, reoperation, or primary healing rate (Table III).

Most patients (53.7%) had at least one complication: 23.5% required reoperation for their management. Tumour origin (soft-tissue/bone), preoperative radiotherapy, chemotherapy, the chosen reconstructive flap, and treatment intent did not affect the rate of complications. The results for flap survival and complications are summarized in Tables III and IV.

Discussion

HQA remains a mainstay of treatment for locally advanced sarcomas arising from, or involving, the pelvis, despite advances in the management of pelvic tumours and the increasing use of limb salvage surgery. We have shown that despite the relatively high incidence of postoperative complications, HQA remains a safe surgical option in terms of postoperative mortality, with a 30-day mortality of less than 1%.

We have also shown that histological diagnosis and tissue of origin has an effect on the overall survival after HQA, in that those with a STS fare worse than those with a bone sarcoma. The overall five-year survival of patients with a bone sarcoma (47.2%) was higher than that of patients with a STS, (24.0%). This reinforces the findings of others who have shown that HQA can be a long-term cure for a sarcoma of bone.[21,22] It may also reflect the variation in the types of tumour seen in the pelvis. The pelvis is a common site for chondrosarcomas, the treatment of which is almost entirely surgical. In cases of STS, for the tumour to have grown to such a volume that HQA is required, in itself an independent factor relating to a poor outcome, the presence of undetected metastases is extremely likely. This may, in part, explain the poor survival of patients undergoing HQA for a STS of the pelvis.

Primary and secondary salvage surgery had similar survival rates. By contrast, the overall survival of patients undergoing salvage HQA for a recurrent STS was especially poor (12.5 months, 95% CI 9.4 to 15.5). This is significantly worse than the overall survival after recurrence of a soft tissue sarcoma of the limbs[23] and may be explained by the difficulty in attaining clear margins of the recurrent disease even with ablative surgery.[24] Tumour volume itself did not have a significant effect on overall survival, but may have an effect on the margins achieved at the time of HQA. For sarcomas of bone, the smaller tumour volume in the salvage surgery group may partly explain the favourable outcomes seen in this group. The same is not true for the salvage STS group and may be a function of the poor prognosis associated with advanced recurrence in STS.

The relatively large number of patients with a diagnosis of chondrosarcoma, osteosarcoma, and undifferentiated pleomorphic sarcoma (UPS) allowed a subset analysis of overall survival in these tumour types. Patients with a chondrosarcoma had better five-year survival than those with an osteosarcoma, as previous publications have shown.[25,26] In addition to STS,

only a resection margin of 1 mm and a grade 3 tumour were prognostic for poorer survival in the univariate model. In the multivariate model only grade 3 histology and location of a soft tissue tumour remained poor prognostic factors.

In our series, palliation was the indication for HQA in six patients. Though anecdotal evidence exists that in selected cases, patients benefit from this massive surgery,[19] the outcome of these patients remain poor. Our 30-day mortality of 0.8% (1/128) for patients operated on with an intent to cure is lower than that previously published.[19,20,27-29] However, 33% (2/6) of patients undergoing palliative HQA died within two weeks of the operation. The median survival in this group was only 2.4 months (95% CI 0.0 to 6.1). As the likelihood of achieving any benefit after such radical surgery is likely to come within months of the procedure, the indication for HQA as a palliative procedure must be called into question. It appears from our results that none of the patients who underwent palliative HQA survived long enough to benefit from the operation. There is no clear evidence that palliative major proximal amputation reduces pain though, in selected cases, it has been reported that palliative amputation can improve a patient's quality of life.[30] There are no comparative studies of major proximal amputation and surveillance or other means of palliation in the literature. Therefore, on the basis of these results, HQA solely for palliation should be considered with extreme caution and only considered when all other interventions with a lower morbidity are lacking and patient is suffering intolerably. Patients and their families should be carefully counselled on the nature and likely outcomes of the planned procedure.

Most patients (53.7%, 73/136) included in this study suffered at least one complication after HQA and nearly one-third needed secondary operations. The incidence of complications has remained unchanged over time and is comparable to our own previous studies and those of others.[19,20,29] It is noteworthy however, that only 1.5% (n = 2) of patients suffered flat failure requiring secondary surgery for wound closure. This is lower than that reported elsewhere.[31] We have shown that direct closure of the defect following HQA is associated with a high risk of secondary wound complications. On this basis, we would advocate local or free flap reconstruction wherever possible. Extended HQA has been shown to increase complications, while age, sex, histology, grade, or intent of the operation have not been associated with wound complication.[29] However, in our study, we were unable to associate any of these factors with the risk of flap failure.

The retrospective design of this study presents unavoidable limitations. We were not able to evaluate the functional outcome or health-related quality of life of these patients. The database used for the study does not include systematically collected patient reported outcome measures or functional status. Complications were not prospectively collected and as a result, it was not possible to classify them reliably according to the Clavien-Dindo classification.[32] However, because of the comprehensive nature of the database used at our hospital, it was possible to identify complications that needed secondary surgical procedures.

This study does, however, have several strengths. Firstly, the cohort includes all sarcoma patients who underwent HQA in

a high-volume supraregional sarcoma unit over a period of 21 years. Secondly, outcome data were available for all patients and no patients were lost to follow-up. Thirdly, the patient cohort was relatively homogeneous when compared to those in the available literature, as the study population excluded all non-sarcoma-related diagnoses. All patients included in this study were managed through a single MDT: there was, therefore, consistency in the preoperative assessment and postoperative evaluation of patient and tumour related factors. Imaging and histology were reviewed in an MDT meeting and the indications for limb-salvaging pelvic resection remained consistent throughout the study period.

In conclusion, therefore, while HQA is a drastic, disfiguring, and life-changing procedure, it is a reasonable option for patients undergoing primary treatment of a pelvic sarcoma, especially those of bony origin. For those with recurrent disease, it also has a role in selected patients for improving overall survival. However, caution must be exercised when considering HQA for recurrent soft tissue sarcomas involving the pelvis as the overall survival is significantly worse than that seen bone sarcomas of the pelvis. The notion held by the surgeon that there is nothing else that can be done apart from a drastic limb sacrificing procedure must be tempered by the poor overall survival seen in specific subgroups. Indeed, when considering HQA for palliation of disseminated pelvic sarcoma, the survival from the procedure is so poor that the role of HQA must be questioned. However, in carefully selected patients, particularly those with a primary, localized sarcoma of bone, HQA, where indicated, is associated with satisfactory survival and a low risk of perioperative mortality. The incidence of postoperative wound complications is high but the incidence of flap failure requiring secondary flap reconstruction is low.

Take home message

- Survival is similar after salvage hindquarter amputation in bone sarcoma, but inferior in soft tissue sarcoma, when compared to primary hindquarter amputation.
- Hindquarter amputation has low perioperative mortality, but relatively high postoperative morbidity with wound complications and infections being the most common complications.
- Palliative hindquarter amputation should be critically evaluated considering high 30-day mortality rate.

Twitter

Follow J. Kiiski @JuhaKii
Follow J. D. Stevenson @MrJDStevenson
Follow L. M. Jeys @leejeys
Follow M. K. Laitinen @MinnaLaitinen2

References

1. **Zahm SH**, **Fraumeni JF Jr**. The epidemiology of soft tissue sarcoma. *Semin Oncol.* 1997;24(5):504–514.

2. **Toro JR**, **Travis LB**, **Wu HJ**, **Zhu K**, **et al**. Incidence patterns of soft tissue sarcomas, regardless of primary site, in the surveillance, epidemiology and end results program, 1978-2001: an analysis of 26,758 cases. *Int J Cancer.* 2006;119(12):2922–2930.

3. **Mastrangelo G**, **Coindre JM**, **Ducimetière F**, **et al**. Incidence of soft tissue sarcoma and beyond: a population-based prospective study in 3 European regions. *Cancer.* 2012;118(21):5339–5348.

4. **Ottaviani G**, **Jaffe N**. The epidemiology of osteosarcoma. *Cancer Treat Res.* 2009;152:3–13.

5. **Nakamura T**, **Abudu A**, **Murata H**, **et al**. Oncological outcome of patients with deeply located soft tissue sarcoma of the pelvis: a follow up study at minimum 5 years after diagnosis. *Eur J Surg Oncol.* 2013;39(9):1030–1035.

6. **Puchner SE**, **Funovics PT**, **Böhler C**, **et al**. Oncological and surgical outcome after treatment of pelvic sarcomas. *PLoS One*. 2017;12(2):e0172203.

7. **Mayerson JL**, **Wooldridge AN**, **Scharschmidt TJ**. Pelvic resection: current concepts. *J Am Acad Orthop Surg*. 2014;22(4):214–222.

8. **Kawai A**, **Healey JH**, **Boland PJ**, **et al**. Prognostic factors for patients with sarcomas of the pelvic bones. *Cancer*. 1998;82(5):851–859.

9. **Zhang Y**, **Guo W**, **Tang X**, **et al**. En bloc resection of pelvic sarcomas with sacral invasion: a classification of surgical approaches and outcomes. *Bone Joint J*. 2018;100-B(6):798–805.

10. **O'Connor MI**, **Sim FH**. Salvage of the limb in the treatment of malignant pelvic tumors. *J Bone Joint Surg Am*. 1989;71-A(4):481–494.

11. **Wedemeyer C**, **Kauther MD**. Hemipelvectomy- only a salvage therapy? *Orthop Rev (Pavia)*. 2011;3(1):e4.

12. **Mahmoud O**, **Tunceroglu A**, **Chokshi R**, **et al**. Overall survival advantage of chemotherapy and radiotherapy in the perioperative management of large extremity and trunk soft tissue sarcoma; a large database analysis. *Radiother Oncol*. 2017;124(2):277–284.

13. **Song WS**, **Cho WH**, **Jeon DG**, **et al**. Pelvis and extremity osteosarcoma with similar tumor volume have an equivalent survival. *J Surg Oncol*. 2010;101(7):611–617.

14. **Wan ZH**, **Huang ZH**, **Chen LB**. Survival outcome among patients with Ewing's sarcoma of bones and joints: a population-based cohort study. *Sao Paulo Med J*. 2017;136(2):116–122.

15. **Farfalli GL**, **Albergo JI**, **Ritacco LE**, **et al**. Oncologic and clinical outcomes in pelvic primary bone sarcomas treated with limb salvage surgery. *Musculoskelet Surg*. 2015;99(3):237–242.

16. **Couto AG**, **Araújo B**, **Torres de Vasconcelos RA**, **et al**. Survival rate and perioperative data of patients who have undergone hemipelvectomy: a retrospective case series. *World J Surg Oncol*. 2016;14(1):255.

17. **Baliski CR**, **Schachar NS**, **McKinnon JG**, **Stuart GC**, **Temple WJ**. Hemipelvectomy: a changing perspective for a rare procedure. *Can J Surg*. 2004;47(2):99–103.

18. **Ham SJ**, **Schraffordt Koops H**, **Veth RP**, **et al**. External and internal hemipelvectomy for sarcomas of the pelvic girdle: consequences of limb-salvage treatment. *Eur J Surg Oncol*. 1997;23(6):540–546.

19. **Grimer RJ**, **Chandrasekar CR**, **Carter SR**, **et al**. Hindquarter amputation: is it still needed and what are the outcomes? *Bone Joint J*. 2013;95-B(1):127–131.

20. **Apffelstaedt JP**, **Driscoll DL**, **Spellman JE**, **et al**. Complications and outcome of external hemipelvectomy in the management of pelvic tumors. *Ann Surg Oncol*. 1996;3(3):304–309.

21. **Sherman CE**, **O'Connor MI**, **Sim FH**. Survival, local recurrence, and function after pelvic limb salvage at 23 to 38 years of followup. *Clin Orthop Relat Res*. 2012;470(3):712–727.

22. **Lex JR**, **Evans S**, **Stevenson JD**, **et al**. Dedifferentiated chondrosarcoma of the pelvis: clinical outcomes and current treatment. *Clin Sarcoma Res*. 2018;8(1):23.

23. **Daigeler A**, **Zmarsly I**, **Hirsch T**, **et al**. Long-term outcome after local recurrence of soft tissue sarcoma: a retrospective analysis of factors predictive of survival in 135 patients with locally recurrent soft tissue sarcoma. *Br J Cancer*. 2014;110(6):1456–1464.

24. **Laitinen MK**, **Parry MC**, **Le Nail LR**, **et al**. Locally recurrent chondrosarcoma of the pelvis and limbs can only be controlled by wide local excision. *Bone Joint J*. 2019;1-B(3):266–271.

25. **Tsagozis P**, **Laitinen MK**, **Stevenson JD**, **et al**. Treatment outcome of patients with chondroblastic osteosarcoma of the limbs and pelvis. *Bone Joint J*. 2019;101-B(6):739–744.

26. **Parry MC**, **Laitinen M**, **Albergo J**, **et al**. Osteosarcoma of the pelvis. *Bone Joint J*. 2016;98-B(4):555–563.

27. **van Houdt WJ**, **Griffin AM**, **Wunder JS**, **Ferguson PC**. Oncologic Outcome and Quality of Life After Hindquarter Amputation for Sarcoma: is it Worth it? *Ann Surg Oncol*. 2018;25(2):378–386.

28. **Karakousis CP**, **Emrich LJ**, **Driscoll DL**. Variants of hemipelvectomy and their complications. *Am J Surg*. 1989;158(5):404–408.

29. **Senchenkov A**, **Moran SL**, **Petty PM**, **et al**. Predictors of complications and outcomes of external hemipelvectomy wounds: account of 160 consecutive cases. *Ann Surg Oncol*. 2008;15(1):355–363.

30. **Daigeler A**, **Lehnhardt M**, **Khadra A**, **et al**. Proximal major limb amputations—a retrospective analysis of 45 oncological cases. *World J Surg Oncol*. 2009;7(1):15.

31. **Senchenkov A**, **Moran SL**, **Petty PM**, **et al**. Soft-tissue reconstruction of external hemipelvectomy defects. *Plast Reconstr Surg*. 2009;124(1):144–155.

32. **Dindo D**, **Demartines N**, **Clavien PA**. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240(2):205–213.

Author information:
J. Kiiski, MD, Plastic Surgeon
I. S. Kaartinen, MD, PhD, Plastic Surgeon
Department of Musculoskeletal Surgery and Diseases, Tampere University Hospital and University of Tampere, Faculty of Medicine and Life Sciences, Tampere, Finland.

M. C. Parry, BSc, MBChS, MD, FRCS, Consultant in Orthopaedic Oncology and Reconstructive Surgery
V. Sumathi, MD, FRCPath, Consultant Pathologist
J. D. Stevenson, MBChB BMedSci, FRCS, Consultant in Orthopaedic Oncology and , Arthroplasty Surgeon
L. M. Jeys, DSc, FRCS, Professor, Consultant in Orthopaedic Oncology and Reconstructive Surgery
Royal Orthopaedic Hospital, The Royal Orthopaedic Hospital NHS Foundation Trust, Birmingham, UK.

L-R. Le Nail, MD, PhD, Orthopaedic Surgeon, Orthopaedic Surgery Department, University Hospital of Tours, Medical University of Tours, Tours, France.

M. K. Laitinen, MD, PhD, Orthopaedic Surgeon, Helsinki University Hospital, Department of Orthopaedics, Helsinki, Finland; University of Helsinki, Helsinki, Finland.

Author contributions:
J. Kiiski: Designed the study, Collected and analyzed the data, Prepared the manuscript.
M. C. Parry: Collected and analyzed the data, Prepared the manuscript.
L-R. Le Nail: Collected and analyzed the data, Prepared the manuscript.
V. Sumathi: Collected and analyzed the data, Prepared the manuscript.
J. D. Stevenson: Collected and analyzed the data, Prepared the manuscript.
I. S. Kaartinen: Prepared the manuscript.
L. M. Jeys: Designed the study, Collected and analyzed the data, Prepared the manuscript.
M. K. Laitinen: Designed the study, Collected and analyzed the data, Prepared the manuscript.