Pelvic exenteration complications

STATEMENT OF ORIGINALITY

The work presented in this thesis is, to the best of my knowledge and belief, original except as acknowledged in the text. I hereby declare that I have not submitted this material, either in full or in part, for a degree at this or any other institution.

Dr Kilian Brown
7th March 2017

ACKNOWLEDGEMENTS

I would like to thank and acknowledge my primary supervisor Professor Michael Solomon for his guidance and support. As the founder and head of the Royal Prince Alfred Hospital Pelvic Exenteration unit, the work within this thesis would not have been possible without his expertise nor his constant encouragement. I would also like to acknowledge and thank Dr Cherry Koh, my co-supervisor, for the extraordinary effort she has put into guiding me and helping me to develop skills in clinical research over several years.

I would like to acknowledge the surgeons, fellows, registrars, nursing and allied health staff at the Pelvic Exenteration Unit at Royal Prince Alfred Hospital whose clinical work has culminated in the outcomes reported in this thesis. I must also thank the staff at the Surgical Outcomes Research Centre, both past and present, and particularly Madhu Prasad, Ken Ly, Lindy Masya and Rachael Roberts for all their assistance.

I would like to thank my family and friends for their support and encouragement.

Most importantly I would like to acknowledge and thank the patients who agreed to participate in the studies within this thesis at a very difficult and daunting time.
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PUBLICATIONS ARISING FROM THIS THESIS

Journal articles:

Brown KGM, Solomon MJ, Latif E, Koh CE, Vasilaras A, Eisinger E, Sved P. Urological complications after cystectomy as part of pelvic exenteration are higher than that after cystectomy for primary bladder malignancy. *Journal of Surgical Oncology*. Accepted for publication 9th November 2016


Conference presentations:

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Additional publications relevant to this thesis but not forming part of it:

INTRODUCTION

Pelvic exenteration surgery was first described in 1948 by Alexander Brunschwig in New York as a palliative procedure for unsalvageable cervical carcinoma and involves multi-visceral resection of pelvic tumours. In 2016, pelvic exenteration is well established as a potentially curative option for locally advanced and recurrent pelvic tumours of the gastrointestinal, gynaecological or urological tract, where en bloc multi-visceral resection is performed with the aim of achieving clear resection margins. Interestingly, the first published report of total pelvic exenteration in Australia was performed at Royal Prince Alfred Hospital, Sydney, in 1956 by a gynaecologist J. Cameron Loxton who spent three months with Dr Brunschwig in New York.

While the survival advantage of pelvic exenteration is confirmed, such radical resections may be associated with significant morbidity. A systematic review of contemporary literature by Yang and colleagues reported outcomes of pelvic exenteration of rectal cancer and documented a 53% median complication (range 37 – 100%) and median mortality rate of 2.5% (range 0 – 25%). Potential morbidity following pelvic exenteration depends on the extent of resection necessary for complete oncological clearance, i.e. which organs, neurovascular structures, soft tissues or bones are excised, and the subsequent reconstruction required. In patients requiring en bloc cystectomy for tumours involving the bladder, for example, urinary diversion is commonly achieved by construction of an ileal or colonic conduit. Major conduit-related complications include uretero-enteric anastomotic stricture or leak, fistulae or septic episodes. Repair or reconstruction of major pelvic vessels may be required in selected patients following excision of tumours involving the common or external iliac vessels, and can be associated with postoperative deep vein or graft thrombus, haemorrhage or compartment syndrome, however the literature is limited in reported outcomes of this subset of patients. As increasingly radical and potentially morbid resections are performed at the periphery of
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the pelvis in pursuit of cure, such as high sacrectomy and lateral neurovascular excision, it is important to investigate postoperative morbidity with a view to reducing it.

This thesis aimed to report the incidence of complications in particular subgroups of patients undergoing pelvic exenteration and identify factors which may predict these outcomes. Other postoperative outcomes including length of stay, oncological outcomes and survival were investigated. In chapter one the evolution of pelvic exenteration surgery over the 20th and 21st centuries is presented and provides an introduction and historical background for the thesis including a review of current literature. The study presented in chapter two investigated the incidence and risk factors for postoperative complications associated with urinary diversion (a major source of morbidity in exenteration patients) and compared patients who had urinary diversion as part of a pelvic exenteration with those who underwent cystectomy alone for primary bladder malignancy. Chapter three includes two studies which investigated the outcomes of lateral pelvic compartment exenteration, in terms of morbidity and survival, and explored the safety and feasibility of common or external iliac vessel resection and reconstruction. In chapter four, two novel surgical techniques which attempt to reduce morbidity associated with vascular reconstruction and high sacral resection (developed by the candidate’s primary supervisor, MJS) are presented. In chapter 4.1 a spiral saphenous vein graft technique for major pelvic vessel reconstruction during exenteration is presented. The existing literature reporting use of the spiral graft technique is reviewed and successful use for reconstruction of the common and external iliac artert and vein in a pelvic exenteration patient is reported. Chaper 4.2 presents a novel technique for en bloc resection of locally recurrent rectal cancer that invades the high sacral bone, where only the involved sacral segment is mobilised and excised en bloc, allowing preservation of uninvolved distal and contralateral sacral bone and nerve roots. The aim of this technique is to achieve complete oncological resection (i.e. a clear posterior bony margin) while maintaining structural
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stability of the pelvis and minimising neurological deficit associated with traditional sacral resection. Both techniques described in chapter 4 are the subject of ongoing investigation.

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CHAPTER 1

Pelvic exenteration surgery: the evolution of radical surgical techniques for advanced and recurrent pelvic malignancy

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Accepted for publication, Diseases of the Colon & Rectum, 29\textsuperscript{th} December 2016
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Abstract

Pelvic exenteration was first described by Alexander Brunschwig in 1948 in New York as a palliative procedure for recurrent carcinoma of the cervix. Due to initially high rates of morbidity and mortality, the practice of this ultra-radical operation was largely confined to a small number of American centres for most of the 20th century. The post-World War II era saw advances in anaesthesia, blood transfusion and intensive care medicine which would facilitate the evolution of more radical and heroic abdominal and pelvic surgery. In the last three decades pelvic exenteration has continued to evolve into one of the most important treatments for locally advanced and recurrent rectal cancer. This review aimed to explore the evolution of pelvic exenteration surgery and identify the pioneering surgeons, seminal papers and novel techniques which have led to its current status of as the procedure of choice for locally advanced and recurrent rectal cancer.
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Introduction

Pelvic exenteration (PE) refers to radical multi-visceral resection of locally advanced or recurrent tumours of the pelvis. En bloc resection of all contiguously involved anatomical structures is performed with a view to achieving complete oncological (R0) resection. The primary justification of such radical surgery is the reasonable chance of cure which is now achievable in up to 63% of patients\textsuperscript{1-4}. R0 resection is the most important factor in predicting survival and quality of life (QoL) after surgery\textsuperscript{5,6} and has therefore become the holy grail of PE.

PE was first described in 1948 as a palliative procedure for recurrent carcinoma of the cervix, and has since evolved into one of the most important modalities for locally advanced and recurrent rectal cancer\textsuperscript{2}. In the late 1940s and early 1950s, the survival outcomes were poor with operative mortality rates as high as 23-35%\textsuperscript{7,8}. Due to these poor early outcomes the second half of the 20\textsuperscript{th} century saw few centres practicing exenteration surgery in any meaningful numbers. Advances in anaesthesia, blood transfusion, medical imaging, intensive care medicine, patient selection and surgical techniques have allowed increasingly radical ‘higher and wider’ resections to be undertaken safely\textsuperscript{9}. As a result, long term survival has become achievable with acceptable morbidity in selected patients at specialised units.

This review aimed to trace the history of radical pelvic surgery from its first description in 1948 and identify the key steps in its technical evolution, including the pioneering surgeons, seminal papers and novel techniques, which have led to the current status of PE as a potentially curative option for locally advanced and recurrent rectal cancer.
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**1948: the Pioneers of Pelvic Exenteration**

In the 1930s and 40s the prognosis for cervical cancer was poor. Irradiation by radium and deep X-ray therapy was the primary treatment, and local progression was common, with a cure rate of only 20-30%\(^\text{10}\). Up to 42% of women who died from cervical cancer did so with disease still confined to the pelvis\(^\text{11}\). Terminal patients suffered from intractable pain, bowel obstruction and pyelonephritis or uraemia from ureteric obstruction. At this time palliative procedures for refractive pelvic pain included neurosurgical cordotomy, prefrontal lobotomy or alcohol injection into nerve roots\(^\text{12,13}\). The second World War saw significant advances in anaesthesia (particularly blood transfusion), antimicrobial therapy and management of critically ill patients, allowing increasingly radical surgery to become feasible. The first description of PE for these patients was published by Alexander Brunschwig at the Memorial Hospital (later Memorial Sloan Kettering Cancer Centre), New York, in 1948 in which he described a ‘procedure of desperation since all other attempts to control the disease had failed’\(^\text{7}\).

Brunschwig was a general surgeon with an interest in all areas of surgical oncology. Prior to describing PE, he was the first surgeon to report the single stage radical pancreaticoduodenectomy in 1937\(^\text{14}\), also known as Whipple’s procedure (Whipple had described radical pancreaticoduodenectomy as a two-stage procedure in 1935)\(^\text{15}\). Brunschwig had previously made several ‘desultory’ attempts at a three-stage operation for locally advanced rectosigmoid tumours in the 1930s, but never published his results as the ‘complications were serious and survival periods brief’\(^\text{16}\). Around the same time, Eugene Bricker had been independently performing exenteration-like procedures for rectal cancer at the Ellis Fischel Cancer Centre in Missouri from 1940 onwards, but due to poor outcomes and the interruption of World War II he did not publish at the time\(^\text{17}\).

*The original operation*
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In his original paper Brunschwig clearly stated the palliative intent of the procedure, and the only selection criteria were that disease must be confined to the pelvis\(^7\). Broadly, the operative approach was similar to that used today (figure 1). The patient was placed in the Trendelenburg position and dissection started at the aortic bifurcation and was carried down over the iliac arteries, ligating and dividing the ovarian vessels and resecting all iliac nodes. Bilaterally the internal iliac artery and vein were ligated and divided near their origin to enter a plane lateral to the vessels and the pelvic mass was retracted medially. The dissection was carried anteriorly, incising the peritoneal reflection over the anterior wall of the bladder to allow its mobilisation from the pubic symphysis. Both ureters were divided proximal to tumour and individually implanted into the sigmoid colon before it was transected distal to the ureters but proximal to the pelvic tumour\(^18\). The posterior dissection followed the concavity of the sacrum to finally allow complete isolation and mobilisation of the pelvic viscera. The abdominal wound was then closed with the end of the sigmoid incorporated as a stoma (a ‘wet colostomy’) at the inferior extent of the midline incision before the perineal approach was commenced (figure 1B).

The patient was repositioned in the lithotomy position and an elliptical incision was made around the introitus and anus between the tip of the coccyx and the clitoris. The dissection was carried superiorly and laterally, levator ani muscles divided at their attachment to the bony pelvis and the specimen was delivered ‘en masse’ via the perineal wound.

In Brusnchwig’s original series of 22 patients undergoing total PE, the intraoperative and postoperative mortality rates were 0 and 23% (5 patients) respectively, which he defended as

\textit{‘not considered excessive and would compare favourable with the mortalities attendant upon the initial attempts at gastrectomy for cancer, total pneumonectomy, pancreaticoduodenectomy, combined abdominoperineal resection of the colon, and so on\(^7\)’}
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Richard Boronow, a trainee of Brunschwig’s recalled working with him in New York, reminiscing that ‘Dr Brunschwig would do two exenterations – then start his office hours at 2:00 in the afternoon!’\(^1\). While some surgeons were enthusiastic about the new ultraradical procedure, many were critical and some considered it ‘a thoughtless form of mutilation, with limited chance of success for palliation, much less cure’\(^1\).

1950s and 1960s: Beyond cervical cancer

In the 1950s, Brunschwig, Bricker, and other pioneering surgeons went on to apply the new radical approach to malignancies arising from other pelvic viscera including the rectum. Brunschwig’s original 1948 series included the case of a man with advanced sigmoid cancer invading the trigone of the bladder, a segment of ileum and the vermiform appendix which were resected en bloc\(^2\). The patient remained disease free and well at 14 months follow up. Thompson and Howe reported the first case of complete pelvic evisceration for locally advanced rectal cancer in 1950\(^3\), the same year that Brintnall and Flocks presented a series of nine patients requiring ‘en masse pelvic viscerectomy’ for rectal or sigmoid carcinoma, of which 3 died in the postoperative period\(^4\).

In the following decades various units (mostly in America) gradually applied the new concept of ultra radical pelvic resection to cancer of the vulva\(^5\), ovary\(^6,7\), prostate\(^8,9\) and pelvic sarcomas\(^10\) including embryonal rhabdomyosarcoma of the vagina in infants and children\(^11,12\). The first non-malignant indication for PE was radiation necrosis of the pelvic viscera in 1951, which remained a relatively common reason for surgery while early radiation techniques including intra-cervical radium persisted\(^13\). The indications for PE were influenced by technology and refined surgical techniques over the following decades. The need for PE for cervical cancer declined, partly due to development of the cervical smear which allowed earlier recognition and the improvements in radiation therapy during the technological revolution from the 1960s onwards. Within a few years the
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less radical ‘partial exenteration’ for anteriorly invading cervical tumours without rectal involvement had been described\(^{31}\), as was an extended PE with en bloc small bowel resection for involved loops\(^{32}\).

Both Brunschwig and Bricker had traditionally performed the entire operation with a single surgical team by completing the abdominal approach first, before re-positioning the patient in the lithotomy position to commence the perineal dissection. The synchronous two team abdominoperineal PE used by most exenteration units today was adapted from rectal cancer surgery in 1959 by Schmitz and colleagues in Chicago\(^{33}\). The second half of the 20\(^{th}\) century saw the rise of surgical specialisation, driven in part by World War II from which many surgeons returned home with experience in thoracic, reconstruction and orthopaedic surgery. Surgical subspecialisation ensued and drove the development of multi disciplinary surgical units, which would utilise the new subspecialist surgeon (plastic & reconstructive, urological, orthopaedic, vascular and neurosurgical) for various phases of the procedure, and undoubtedly contributed to improvements in morbidity and mortality (table 1).

**Urinary diversion**

One of the early challenges in refining the PE procedure was feasible reconstruction of the urinary system. Brunschwig’s ‘wet colostomy’ with ureteric implantation into the proximal colon was unsatisfactory and quickly superseded. After failed attempts to fashion a continent abdominal urinary reservoir from isolated sigmoid colon and caecum, Bricker described the ileal conduit in 1950\(^{34}\) which remains the workhouse of urinary diversion in 2016 (figure 2).

A number of units soon described significant postoperative complications associated with urinary diversion, in particular the development of urinary fistulas\(^{8,35}\). Brunschwig showed that in patients who survived greater than five years after exenteration ‘the most frequent subsequent cause of death is the deterioration of the diverted urinary tract’\(^{36}\). He advocated for the early use of temporary or
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permanent nephrostomy tubes, with ‘constant surveillance’ of the urinary diversion, and a low threshold for emergency nephrostomy for diversion of the urinary tract\textsuperscript{36}.

Today, en bloc cystectomy is required in 20-53\% of patients undergoing PE\textsuperscript{2,37-39} and postoperative urological complications remain a major source of morbidity with longer hospital stays and increased mortality\textsuperscript{37}. Compared to cystectomy alone for primary urological malignancy, urinary diversion may be associated with significantly higher urological morbidity in the context of irradiated, redo surgery and is reported between 9 and 24\%, with 7 – 16\% rate of urinary leaks (table 2)\textsuperscript{37-42}. Techniques for continent urinary diversion which were developed in the 1980s have generally been avoided in PE patients at most centres due to concerns about higher complication rates, however recently some units have developed experience with these techniques which may be feasible in selected patients\textsuperscript{43}. The technique of perineal urethrectomy to achieve a more antero-inferior margin in the male has recently been described\textsuperscript{44}.

**1970s: Perineal Reconstruction**

In the 1970s focus turned to the high rate of septic complications following exenteration, particularly fistulas and abscesses, which were noted to arise in the irradiated empty pelvis in up to 15\% of patients\textsuperscript{45}. Surgical techniques were developed to address these problems and included the use of greater omentum to suspend the small bowel and urinary conduit out of the pelvic cavity and fill the dead space and at some units were associated with reduced fistula rates\textsuperscript{46,47}. The use of locoregional myocutaneous flaps for perineal reconstruction was a significant advance in exenteration surgery which allowed both closure of large perineal defects not amenable to primary closure as well as transposition of healthy tissue into the pelvis to reduce perineal and septic complications\textsuperscript{48,49}. These flaps are rotated into position in the perineum on their vascular pedicle and include the gracilis flap (which was the first myocutaneous flap described in 1976, figure 3)\textsuperscript{50}, while other more commonly
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used flaps are the rectus abdominus based on the inferior epigastric vessels\textsuperscript{51}, and gluteus maximus flap\textsuperscript{52}, due to their robustness and greater bulk.

The 1970s also saw major technological advances leading to the development of intensive care units with mechanical ventilation and invasive monitoring, which contributed to the steady improvement in postoperative morbidity and mortality after radical cancer surgery. Early experiences with routine admission to an intensive care unit after PE in 1980, utilising ventilator support, ‘mini dose’ heparin and cardiac monitoring contributed to lower rates of respiratory and cardiac failure, thromboembolic events and mortality\textsuperscript{53} and has become the standard of care for all PE patients.

1980s: Composite Pelvic Bone Resection

Brunschwig and Barber published the first series of PE with composite bony resection in 1969 which included 28 patients (of 925 PEs) with en bloc resection of the pubis, ischium or sacrum\textsuperscript{54}. Eight patients (29\%) died in the operative period and only four patients (15\%) survived more than five years. Although techniques for sacral resections for chordomas evolved in the orthopaedic literature over the following years\textsuperscript{55}, these poor initial outcomes discouraged any further investigation of composite pelvic bone resection during PE over the next 20 years.

The concept of sacrectomy was revisited in the 1980s by Wanebo and colleagues who described abdomino-prone sacral resection in 11 patients for recurrence of rectal cancer in the posterior pelvis (figure 4)\textsuperscript{56}. After an initial abdominal phase with pelvic dissection and mobilization of involved organs, the patient was repositioned for prone en bloc sacrectomy and clear resection margins were achieved in all patients with two postoperative deaths. Takagi et al utilized this technique in a prone completion sacrectomy following abdominoperineal total PE for en bloc resection of the involved sacrum\textsuperscript{57}. The work of Wanebo and Takagi prompted interest in the role of composite sacral
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resection for recurrent rectal cancer and set the scene for various units to undertake these radical
resections in the 1990s and 2000s (table 3), producing contemporary morbidity rates of 40 to 91%,
mortality less than 5% and 28 – 46% 5-year survival\textsuperscript{58-62}.

More recently several units have developed alternative techniques for en bloc sacral resection which
avoid the traditional complete sacrectomy in an attempt to minimize morbidity. Hemisacrectomy,
resection of the anterior cortex of the sacrum to preserve nerve roots and segmental sacrectomy have
been proposed as alternative techniques however this literature is largely limited to case reports\textsuperscript{63-66}.
The technique of abdomino-lithotomy sacrectomy to resect the lower sacrum (below S3) en bloc has
recently been described\textsuperscript{67}.

**Lateral pelvic sidewall excision**

Tumour involvement of the lateral pelvic sidewall has traditionally been considered an absolute
contraindication to curative surgery at most units, largely due to the technical difficulty of achieving
a clear resection margin safely where the tumour abuts or involves major neurovascular structures or
lateral pelvic bone. However, as early as 1949 Brunschwig described ‘resection of the great veins of
the lateral pelvic wall’ in order to gain clearance of laterally extending gynaecological tumours\textsuperscript{68}. In
1967 Barber and Brunschwig reported a series of 55 patients undergoing PE with radical en bloc
common or external iliac vessel excision\textsuperscript{69}, of which only 5 patients had vessel reconstruction using a
graft as;

\textit{‘The precarious condition of the patient, as well as the fact that the procedure is often carried out in a
grossly contaminated and frequently previously heavily irradiated field and often with visible
radiation changes in the large vessel, precluded the use of any type of graft in most instances’}\textsuperscript{69}

The three patients with arterial excision alone all died within 30 days of surgery with gangrene of the
ipsilateral lower limb, none of the eight patients with arterial and venous resection were alive at 5
years and of 45 patients with venous excision alone were 5 surviving at 5 years. Due to these poor
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early outcomes the contemporary literature is limited and patients with involvement of the sidewall, and particularly the common or external iliac vasculature, are generally not candidates for curative surgery.\textsuperscript{70-75}

Despite the lower rates of R0 resection as well as poorer survival outcomes for patients with lateral pelvic sidewall invasion (table 4)\textsuperscript{70,76,77}, Wanebo reported composite resection of the ilium or ischium for laterally invasive tumours in five patients of which four survived between 3 and 6 years in 1987\textsuperscript{78}. More recently, en bloc resection of the pelvic side wall for advanced and recurrent rectal cancer involving lateral neurovascular structure has been described and has produced encouraging oncological and survival outcomes (table 4)\textsuperscript{79}. Similar techniques have been reported in the gynaecological literature for cervical cancer\textsuperscript{80}.

A small number of contemporary units have developed experience with ‘higher and wider’ lateral resections for tumour involvement of the common and external iliac vessels\textsuperscript{81,82}, and extending to the sciatic nerve and ischial bone\textsuperscript{83,84}. These early studies have reported R0 resection rates of 38-58% in patients undergoing vascular excision and reconstruction, no perioperative mortality, and 96-100% long term graft patency\textsuperscript{81,82}. These emerging reports may justify further investigation of more radical vascular excision and reconstruction in selected PE patients in the future.

Conclusion

Radical pelvic cancer surgery has evolved since PE was first described in 1948 and it now represents a potentially curative treatment for patients with locally advanced or recurrent pelvic tumours. Technical aspects of the procedure have been modified and refined over six decades, with notable developments including intestinal urinary conduits, composite pelvic bone techniques, lateral neurovascular excision and perineal reconstruction with myocutaneous flaps. Improved techniques,
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advances in technology and critical care medicine have driven reductions in morbidity and mortality and improved survival rates over this time and understanding surgical anatomy has expanded the safety of wide excisions so that the paradigm is not ‘what can be exenterated’ but ‘what should be exenterated’. There remain unanswered questions around the repeated use of radiation and intraoperative brachytherapy, postoperative chemotherapy, synchronous metastatectomy, repeat exenteration for re-recurrent rectal cancer and the future role of laparoscopic and robotic surgery in exenteration.

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Table 1. Selected series reporting outcomes of pelvic exenteration surgery over seven decades

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<tr>
<th>Author</th>
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<th>R0 (%)</th>
<th>Mortality (%)</th>
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<td>84 (PRC)**</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>72 (RRC)**</td>
<td></td>
</tr>
<tr>
<td>Harris</td>
<td>2016</td>
<td>Multicentre</td>
<td>533</td>
<td>59</td>
<td>-</td>
<td>-</td>
<td>28</td>
</tr>
</tbody>
</table>

*requiring hospitalization or reoperation, **3-year overall survival, OS overall survival -not reported, RRC recurrent rectal cancer, PRC primary rectal cancer
Pelvic exenteration complications

**Table 2.** Selected series reporting results of urinary reconstruction during pelvic exenteration

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Location</th>
<th>No. patients</th>
<th>Reconstruction (%)</th>
<th>Overall urological morbidity (%)</th>
<th>Urinary fistula/leak (%)</th>
<th>R0 (%)</th>
<th>Mortality (%)</th>
<th>Overall Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrigley</td>
<td>1976</td>
<td>Minnesota, USA</td>
<td>34</td>
<td>100 0 0</td>
<td>25</td>
<td>25</td>
<td>-</td>
<td>12</td>
<td>-</td>
</tr>
<tr>
<td>Fallon</td>
<td>1979</td>
<td>Iowa, USA</td>
<td>43</td>
<td>77 17 5</td>
<td>14 (early) 14 (late)</td>
<td>14</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Orr</td>
<td>1982</td>
<td>Alabama, USA</td>
<td>115</td>
<td>84 16 0</td>
<td>-</td>
<td>9</td>
<td>9</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Russo</td>
<td>1999</td>
<td>New York, USA</td>
<td>47</td>
<td>94 2 4</td>
<td>17</td>
<td>4</td>
<td>89</td>
<td>2</td>
<td>53% at 17 months median follow up</td>
</tr>
<tr>
<td>Hovvaneaeghel</td>
<td>2004</td>
<td>Marseille, France</td>
<td>124</td>
<td>41 3 56</td>
<td>9</td>
<td>8</td>
<td>-</td>
<td>8</td>
<td>-</td>
</tr>
<tr>
<td>Goldberg</td>
<td>2006</td>
<td>New York, USA</td>
<td>103</td>
<td>63 0 37</td>
<td>-</td>
<td>14</td>
<td>-</td>
<td>1</td>
<td>47% (5yr)</td>
</tr>
<tr>
<td>Stocchi</td>
<td>2006</td>
<td>Cleveland, USA</td>
<td>82*</td>
<td>43 36 0</td>
<td>-</td>
<td>7</td>
<td>-</td>
<td>2</td>
<td>19% (5yr)</td>
</tr>
<tr>
<td>Stotland</td>
<td>2009</td>
<td>Toronto, Canada</td>
<td>126</td>
<td>75 5 20</td>
<td>24</td>
<td>9</td>
<td>-</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Teixeira</td>
<td>2012</td>
<td>Sydney, Australia</td>
<td>74</td>
<td>64 36 0</td>
<td>-</td>
<td>16</td>
<td>70</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

- not reported, *20 patients (24%) did not undergo urological reconstruction
Pelvic exenteration complications

**Table 3.** Selected series reporting results of en bloc sacrectomy for locally advanced or recurrent rectal cancer

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Location</th>
<th>Patients</th>
<th>Highest sacral level</th>
<th>Blood loss, median, ml</th>
<th>Operating time, median hrs</th>
<th>R0 (%)</th>
<th>Mortality (%)</th>
<th>Morbidity (%)</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wanebo</td>
<td>1981</td>
<td>New York, USA</td>
<td>11</td>
<td>S1/2</td>
<td>11.5 units transfused*</td>
<td>11*</td>
<td>100**</td>
<td>18</td>
<td>-</td>
<td>30**</td>
</tr>
<tr>
<td>Takagi</td>
<td>1983</td>
<td>Nagoya, Japan</td>
<td>5</td>
<td>S2/3</td>
<td>7400*</td>
<td>9.7*</td>
<td>-</td>
<td>0</td>
<td>40</td>
<td>-</td>
</tr>
<tr>
<td>Temple</td>
<td>1992</td>
<td>Calgary, Canada</td>
<td>9/11‡</td>
<td>S1/2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>9</td>
<td>36*</td>
<td>18</td>
</tr>
<tr>
<td>Magrini</td>
<td>1996</td>
<td>Rochester, USA</td>
<td>14/16‡</td>
<td>S2/3</td>
<td>3350</td>
<td>12.5</td>
<td>69</td>
<td>0</td>
<td>69</td>
<td>48 (2-yr)</td>
</tr>
<tr>
<td>Wanebo</td>
<td>1999</td>
<td>Providence, USA</td>
<td>53</td>
<td>L5/S1</td>
<td>-</td>
<td>74</td>
<td>8</td>
<td>36</td>
<td>-</td>
<td>31</td>
</tr>
<tr>
<td>Zacherl</td>
<td>1999</td>
<td>Vienna, Austria</td>
<td>12</td>
<td>S1/2</td>
<td>17.4 units transfused*</td>
<td>8.6*</td>
<td>100</td>
<td>0</td>
<td>42</td>
<td>21.7*</td>
</tr>
<tr>
<td>Gonzalez</td>
<td>2003</td>
<td>Denver, USA</td>
<td>41/45‡</td>
<td>-</td>
<td>-</td>
<td>73</td>
<td>4</td>
<td>56</td>
<td>-</td>
<td>31 (DF)</td>
</tr>
<tr>
<td>Melton</td>
<td>2006</td>
<td>New York, USA</td>
<td>29</td>
<td>S2/3</td>
<td>5 units transfused</td>
<td>-</td>
<td>62</td>
<td>4</td>
<td>59</td>
<td>33 (DS)</td>
</tr>
<tr>
<td>Akasu</td>
<td>2007</td>
<td>Tokyo, Japan</td>
<td>44</td>
<td>S2</td>
<td>3208</td>
<td>12.5</td>
<td>55</td>
<td>2</td>
<td>61</td>
<td>28</td>
</tr>
<tr>
<td>Sagar</td>
<td>2009</td>
<td>Leeds, UK</td>
<td>40</td>
<td>S2/3</td>
<td>3 units transfused</td>
<td>-</td>
<td>50</td>
<td>2.5</td>
<td>60</td>
<td>55.6 DF***</td>
</tr>
<tr>
<td>Ferenschild</td>
<td>2009</td>
<td>Rotterdam, Netherlands</td>
<td>25</td>
<td>S3</td>
<td>6500</td>
<td>8</td>
<td>77</td>
<td>0</td>
<td>68</td>
<td>32</td>
</tr>
<tr>
<td>Bhangu</td>
<td>2012</td>
<td>London, UK</td>
<td>30</td>
<td>S1/2</td>
<td>1725</td>
<td>9.5</td>
<td>68</td>
<td>0</td>
<td>50</td>
<td>76 (3-yr)</td>
</tr>
<tr>
<td>Milne</td>
<td>2014</td>
<td>Sydney, Australia</td>
<td>79/100‡</td>
<td>S1/2</td>
<td>4500</td>
<td>11.9</td>
<td>72</td>
<td>0</td>
<td>74</td>
<td>45***</td>
</tr>
<tr>
<td>Bosman</td>
<td>2014</td>
<td>Eindhoven, Netherlands</td>
<td>86</td>
<td>S2</td>
<td>6823 RRC* 3506 PRC*</td>
<td>-</td>
<td>56</td>
<td>5</td>
<td>-</td>
<td>24 PRC</td>
</tr>
<tr>
<td>Colibaseanu</td>
<td>2014</td>
<td>Rochester, USA</td>
<td>30</td>
<td>L4/5</td>
<td>2663</td>
<td>-</td>
<td>93</td>
<td>0</td>
<td>76</td>
<td>28 RRC</td>
</tr>
<tr>
<td>Khaled</td>
<td>2014</td>
<td>Toronto, Canada</td>
<td>19</td>
<td>S1/2</td>
<td>5000</td>
<td>10.4</td>
<td>100</td>
<td>5</td>
<td>79</td>
<td>77*</td>
</tr>
<tr>
<td>Uehara</td>
<td>2015</td>
<td>Nagoya, Japan</td>
<td>32</td>
<td>S1/2</td>
<td>2653</td>
<td>16.5</td>
<td>77</td>
<td>0</td>
<td>91</td>
<td>76 (3-yr)</td>
</tr>
</tbody>
</table>
Pelvic exenteration complications

*mean, **patients undergoing curative surgery, ***patients with R0 resection, ‡ numerator is number of patients with rectal cancer and denominator is number of patients undergoing surgery, DF disease-free, DS disease-specific, OS overall survival -not reported, RRC recurrent rectal cancer, PRC primary rectal cancer
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Table 4. Selected series reporting results of lateral pelvic sidewall excision during pelvic exenteration

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Location</th>
<th>No. patients</th>
<th>Vascular reconstruction</th>
<th>Blood loss, median, ml</th>
<th>Operating time, median hrs</th>
<th>R0 (%)</th>
<th>Mortality (%)</th>
<th>Morbidity (%)</th>
<th>Overall survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barber</td>
<td>1967</td>
<td>New York, USA</td>
<td>55</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>35</td>
<td>-</td>
<td>11% (5yr)*</td>
</tr>
<tr>
<td>Yamada</td>
<td>2001</td>
<td>Kagoshima, Japan</td>
<td>17/60†</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>-</td>
<td>0% (5yr)</td>
</tr>
<tr>
<td>Moore</td>
<td>2004</td>
<td>New York, USA</td>
<td>12/119†</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>17</td>
<td>9</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Austin</td>
<td>2009</td>
<td>Sydney, Australia</td>
<td>36</td>
<td>8</td>
<td>6.6 units transfused</td>
<td>9</td>
<td>53</td>
<td>0</td>
<td>70</td>
<td>69% at 19 months mean follow up</td>
</tr>
<tr>
<td>Solomon</td>
<td>2015</td>
<td>Sydney, Australia</td>
<td>200</td>
<td>23</td>
<td>3500</td>
<td>10.25</td>
<td>67</td>
<td>0.5</td>
<td>82</td>
<td>35% (5yr)</td>
</tr>
</tbody>
</table>

* 35 patients with excision of iliac vein only, †numerator is patients with lateral sidewall excision, denominator is all patients undergoing surgery, -not reported
Pelvic exenteration complications

**Figure 1 (A)** Diagram showing levels of transection of the ureters (U) and colon (C) and incision encompassing the vulva and anus (PW) from Alexander Brunschwig’s original paper. (B) Diagram showing conditions at end of operation indicating areas of peritonectomy (shaded area, P, P', PI', PI'”). The midline colostomy is shown with both ureters (U, U’) implanted into the colon a short distance above colostomy. Copyright © 1948 American Cancer Society. Reproduced with permission from John Wiley & Sons Ltd.
Pelvic exenteration complications

**Figure 2** Diagram from Bricker’s original paper on urinary diversion\(^{34}\) demonstrating the evolution of various intestinal reconstruction techniques including bilateral ureteric anastomosis to an isolated segment of sigmoid colon (A), terminal ileum with caecal reservoir (B), caecum with terminal ileum for urinary drainage tract (C) and the contemporary ileal conduit (D). Copyright © 1950 Surgical Clinics of North America. Reproduced with permission from Elsevier.
Pelvic exenteration complications

**Figure 3** Diagram of the gracilis myocutaneous flap for reconstruction of the perineum after pelvic exenteration as described by McCraw and colleagues in 1976. Copyright © 1976 Plastic & Reconstructive Surgery. Reproduced with permission from Wolters Kluwer.
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Figure 4 Diagrams from Wanebo’s first description of abdomino-prone sacral resection showing the extent of resection required for recurrence of rectal cancer in the posterior compartment (A), lines of transection of the sacrum from the posterior approach (B), the operative defect after sacral resection (C) and rotational skin flaps for wound closure (D)\textsuperscript{56}. Copyright © 1981 J.B Lippincott Company. Reproduced with permission from Wolters Kluwer.
Urological complications after cystectomy as part of pelvic exenteration are higher than that after cystectomy for primary bladder malignancy

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Accepted for publication, Journal of Surgical Oncology November 9\textsuperscript{th} 2016
Pelvic exenteration complications

Abstract

Background: Total cystectomy and subsequent reconstruction of the urinary tract may be required for primary malignancy of the bladder, or in the context of multi-visceral resection for more advanced pelvic tumours. Complications following urinary diversion are a major source of morbidity, particularly in pelvic exenteration (PE) patients.

Methods: All patients who underwent radical cystectomy alone or during PE at a single tertiary referral centre between 2008 and 2014 were reviewed. Postoperative urological complications were collected and compared between groups.

Results: 231 patients underwent en bloc cystectomy (98 cystectomy alone, 133 as part of a PE). Postoperative urological complications occurred in 33% of the cystectomy alone group and 59% of the PE group (P<0.001). PE for recurrence had higher complications than PE for primary malignancy (67% vs. 48%, P=0.035). Urological leaks occurred in 3, 6 and 14% of patient who had cystectomy alone, PE for primary malignancy and PE for recurrence. Major blood loss and previous pelvic radiotherapy independently predicted conduit-associated complications in PE patients (P=0.002 and 0.035).

Conclusions: Urological complications of cystectomy, particularly urine leaks and sepsis, are more common in patients undergoing PE compared to those with cystectomy alone. Prior pelvic radiotherapy, the extent of surgical resection and major blood loss may contribute to urological morbidity.

Keywords: Cystectomy; pelvic exenteration; ileal conduit; urine leak; urinary diversion

Introduction

The most common indication for radical cystectomy is a primary malignancy of the urinary tract such as those arising from the bladder, prostate or urethra. However, a radical cystectomy may also be required as part of an extended radical resection or pelvic exenteration (PE) for more advanced
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malignancies of the pelvis, whether primary or recurrent. In any case, subsequent reconstruction of
the urinary tract is required. While an ileal conduit is generally preferred, colonic conduits, wet
colostomies or even orthotopic bladder are also options depending on the local surgical expertise
and clinical situation.

The oncological role of PE for locally advanced and recurrent pelvic malignancies arising from the
anorectum, gynaecological or urological systems is now well established\(^1\text{-}^3\). Depending on the
anatomic location of the tumour or recurrence or the anticipated bladder function, an en bloc
cystectomy may be required in 20\text{-}53\% of all patients undergoing a PE\(^3\text{-}^6\). Morbidity associated
with cystectomy and its reconstruction can be considerable but in the setting of re-operative surgery
where multi-visceral en bloc resection is required in an irradiated field, as is commonly the case in
PE surgery for locally recurrent cancer, this morbidity is even more marked\(^7\text{-}^8\). Several exenteration
units have published urine leak rates in excess of 15\% after conduit formation and this contrasts
sharply against the urine leak rates in contemporary urological literature where a leak rate of <5\% is
generally reported following conduit formation for a primary urological malignancy\(^4\text{-}^8\text{-}^14\). Whether
this disparity reflects true differences in complication rates between a more radical versus a less
radical operation, primary versus re-operative surgery or whether this difference reflects
institutional differences in complication rates or selection bias is unclear. The aim of this study was
to compare urological complication rates between that of radical cystectomy or cystoprostatectomy
alone for a primary urological malignancy and radical cystectomy or cystoprostatectomy as a part
of a PE; as well as to identify factors that may inform and predict these urological complications
which may impact on future surgical decision making.

Methods
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The study was conducted as part of a program of research exploring clinical and patient reported outcomes in PE surgery in Australia, funded in part through the Priority-Driven Collaborative Cancer Research Scheme by Cancer Australia and The Cancer Council Australia (ID 570860) and approved by the Royal Prince Alfred Hospital Human Research Ethics Committee.

The study cohort included all patients who underwent radical cystectomy or total cystoprostatectomy either alone (non-PE group) or as part of a PE (PE group) at a single tertiary referral centre between 2008 and 2014 (inclusive). PE was defined as resection of the rectum/recurrent rectal cancer with en bloc resection of greater than 50% of two or more major unrelated organs and/or major pelvic neurovascular sidewall structures or bone. Patients who had partial cystectomy or who did not have reconstruction of the urinary tract after cystectomy (e.g. those with end-stage renal failure) were excluded. In female patients who underwent radical cystectomy for isolated bladder malignancy, an abdominal hysterectomy and/or bilateral salpingo-oophorectomy was typically performed depending on previous gynaecological surgery and patient and surgeon preference. This was not considered pelvic exenteration (i.e. was not performed for tumour involvement) and these patients were included in the cystectomy alone group.

PE patients were routinely staged using CT scan of the chest, abdomen and pelvis in addition to an MRI of the pelvis and a PET-CT scan. The decision to perform a cystectomy or cystoprostatectomy is made at a PE multi-disciplinary team (MDT) meeting. Indications for en bloc cystectomy were usually for contiguous tumour involvement or anticipated poor urinary function either as a result of high sacrectomy or small residual bladder capacity. Patients undergoing cystectomy alone routinely had a CT scan of the abdomen, chest and pelvis. Bone scintigraphy or pelvic MRI were performed in selected patients where there was concerns about bony metastases or local invasion of adjacent
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organs. Pathology and imaging were reviewed at a urological tumour MDT meeting where the
decision to proceed to surgery was made.

The method of reconstruction (i.e. ileal conduit, colonic conduit or orthotopic neobladder) was
dependent on surgeon and patient preference. In PE patients, the choice of reconstruction also
depended on the availability of healthy and non-irradiated small bowel as well as whether or not
there had been a pre-existing colostomy. Neobladder reconstruction was not generally offered to PE
patients. The surgical technique used for conduit construction has been previously described\(^4,15\). In
brief, an isolated segment of ileum or colon was used to form the conduit with proximal ureter from
outside the irradiated field where possible. The Bricker technique\(^16\) was used for uretero-enteral
anastomoses over infant feeding tubes which were secured to the wall of the conduit or urostomy
bag to prevent migration. The technique for orthotopic neobladder has also been previously
described and in brief, approximately 50 cm of distal ileum was harvested, preserving the terminal
ileum, and detubularised at the anti-mesenteric border. A Hautmann orthotopic neobladder was
fashioned with continuous 3-0 absorbable sutures\(^17\). The Bricker technique was also used in these
patients and the ileo-urethral anastomosis was sewn over a 20 Fr urinary catheter.

Data for the cystectomy alone group were retrospectively collected from medical records.
Data for PE patients were derived from a prospectively maintained electronic database
supplemented by additional data collection from patient medical records. Cardiac comorbidities
included ischaemic heart disease, valvular disease, cardiomyopathy and arrhythmias. Vascular
comorbidities included thromboembolic, cerebrovascular or peripheral vascular disease, or history
of dissection or aneurysm. A urine leak has previously been defined as the presence of creatinine
rich effluent from abdominal drains or wound sites, and/or radiological evidence of contrast
extravasation from the conduit itself or ureteric anastomosis\(^15\).
Statistical analysis was performed using SPSS software (IBM SPSS Statistics Version 22.0, IBM Corp., Armonk, NY). The chi square test was used to compare groups and identify univariate predictors of complications. Fisher’s exact test was used where samples contained less than five patients. Continuous variables were analysed using the independent samples t-test or median test for nonparametric data. P values were considered significant if less than 0.05.

Results

Over the study period, a total of 231 patients required en bloc cystectomy or cystoprostatectomy. Of these, 98 underwent cystectomy or cystoprostatectomy alone and 133 underwent cystectomy or cystoprostatectomy as part of a PE. During the same time period, there were 304 PEs performed (44% requiring en bloc cystectomy). The median age of the study cohort was 65 (range 15 – 94) and 173 (75%) were male. A total of 111 patients (48%) had a postoperative complication related to urinary diversion and the median length of hospital stay was 23 days (range 9-189). Table 1 compares baseline patient characteristics between cystectomy or cystoprostatectomy alone patients and patients who underwent PE.

Indications for cystectomy or cystoprostatectomy alone included transitional cell carcinoma (84%) or squamous cell carcinoma (3%) of the bladder, sarcoma (3%), neuroendocrine tumours (2%) and non-cancer indications (8%). In this group twenty (20%) and 14 (14%) patients had previously had pelvic radiotherapy and chemotherapy respectively. The majority (91%) had an ileal conduit formed for urinary reconstruction while the remaining 9% had an orthotopic neobladder. There were no colonic conduits in this group. Of 26 female patients in the cystectomy group, 14 patients (54%) also underwent hysterectomy with bilateral salpingo-oophorectomy at the time of surgery, 3 (12%) underwent oophorectomy, 2 (8%) underwent hysterectomy, 1 (4%) underwent vaginectomy. The
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median length of stay of patients undergoing cystectomy alone was 18 days (range 9-116) during which time 32 patients (33%) had a complication related to the urinary diversion.

In the PE group, 48 (36%) patients had their operation for primary malignancy, 84 (63%) for recurrent malignancy and one (1%) for chronic pelvic sepsis following a perforated rectal tumour (Table 2). 54 patients (41%) in this group had neoadjuvant chemotherapy and 124 patients (93%) had previously had pelvic radiotherapy, of whom 55 (45%) had this as part of a planned neoadjuvant regime. An ileal conduit was formed in 108 (81%) of PE patients, while the remaining 25 patients (19%) had a colonic conduit. Orthotopic neobladders were not performed in PE patients. En bloc radical sacrectomy was performed due to posterior tumour invasion in 80 patients (60%), while 23 (17%) required radical excision of pubic bone in order to achieve clearance of the tumour anteriorly. The perineum was reconstructed using a regional myocutaneous flap in 53 PE patients (40%), while primary closure was possible in the remaining 80 patients (60%).

Patients who underwent cystectomy or cystoprostatectomy alone had a higher median age than those undergoing PE (72 vs. 61 years, P < 0.001), a lower rate of previous pelvic radiotherapy (20% vs. 93%, P < 0.001) as well as a higher rates of cardiac comorbidity (32% vs. 15%, P = 0.003), diabetes mellitus (26% vs. 12%, P = 0.007) and renal impairment (41 vs. 15%, P < 0.001) (Table 1). The median length of hospital stay for patients who had cystectomy or cystoprostatectomy alone and PE was 18 and 28 days respectively (P < 0.001).

The overall rate of postoperative complications associated with urinary diversion was 33% in the cystectomy or cystoprostatectomy alone group and 59% in patients undergoing PE (48% for primary vs. 67% for recurrent malignancy, P = 0.035) (Table 3). The most common conduit-associated complication in all groups was postoperative urinary tract infection (UTI), which was
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more common in patients who had PE for recurrent malignancy compared to those undergoing
cystectomy alone or PE for primary malignancy (50%, 21% and 26%, P < 0.001). There was no
difference in the rate of UTI between patients undergoing cystectomy alone and PE for primary
malignancy (26% vs. 21%, P = 0.534). UTI was associated with an increased median length of stay
in PE patients (P = 0.002) but not in patients who had cystectomy alone (P = 0.202). Urine leaks
occurred in 3, 6 and 14% of patient who had cystectomy alone, PE for primary malignancy and PE
for recurrence. The difference was not statistically significant between cystectomy alone and
primary PE groups (P = 0.395). Median time from surgery to diagnosis of a urine leak was 11 days
(range 2 - 63). The leak was managed conservatively in 4 (22%) patients. Eleven patients required
radiological intervention (percutaneous nephrostomy tube placement) (61%) and three needed a
reoperation (17%).

A total of 10 patients required return to theatre for operations involving the urinary conduit, of
which seven patients had had PE for recurrent malignancy (table 4). The reason for return to theatre
was intraabdominal haemorrhage complicated by an ischaemic conduit (three patients), urine leak
(three patients) and urostomy dehiscence (one patient). The remaining three patients required return
to theatre for non-urological reasons (e.g. enterocutaneous fistula) during which the conduit was
inadvertently injured during mobilization requiring repair.

Univariate analysis of factors that predicted development of a complication associated with urinary
diversion are summarised in table 5. Previous pelvic radiotherapy and greater than 5000 mL
intraoperative blood loss independently predicted postoperative conduit-associated complications in
PE patients (P = 0.035 and 0.002, respectively). There were no predictors of complications
identified in patients with PE for primary malignancy. In patients undergoing PE for recurrent
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malignancy, more than 5000 mL intraoperative blood loss predicted development of a postoperative complication (P = 0.038).

In the pelvic exenteration group, diabetes, preoperative hypoalbuminaemia and greater than 5000 mL intraoperative blood loss were factors associated with postoperative urological leaks, however this association did not reach statistical significance (P = 0.084, 0.073, 0.081).

**Discussion**

Urinary diversion after PE may be associated with higher rates of postoperative complications compared to patients undergoing cystectomy alone, however the literature in this area remains sparse\(^3\text{-}\text{6}\). This study reports the outcomes of 231 consecutive patients who underwent urinary diversion performed by the same urology unit between 2008 and 2014. The main findings of this study are that urinary diversion after PE is associated with higher complication rates, particularly when the indication is for recurrent malignancies. This difference in complication rates was found despite the cystectomy alone group being older and having higher rates of underlying cardiovascular disease, diabetes and renal impairment. Patients in the PE group had a higher rate of urine leaks and were also more likely to return to theatre either for a conduit related complication or during which the conduit is inadvertently injured, causing an intra-operative complication. High urine leak rates after PE have been previously reported\(^4,\text{8}\text{-}\text{11}\) and results of this study confirm a true difference in complication rates between these two groups of patients.

The rate of postoperative conduit-associated complications was 33\%, 48\%, 67\% in the cystectomy, primary malignancy PE and recurrent malignancy PE groups, respectively (P < 0.001). Although previously published series have reported complication rates between 17\% and 24\%\(^7,\text{8}\) these did not report rates of urinary tract infection (UTI), which was the most common complication in this
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study, occurring in 40% of PE patients (21% for primary, 50% for recurrent malignancy) and most likely accounts for the disparately higher complication rate. Although low grade urosepsis managed conservatively would not traditionally be considered a major postoperative complication and is therefore not often reported, in this series it was common and prolonged the length of stay in PE patients and therefore remains a significant source of morbidity in this group of patients at our unit. Goldberg and colleagues documented a UTI or pyelonephritis in 36% of patients with urological reconstruction after PE, a result that is more consistent with the current study however this rate may be underestimated by the retrospective nature of their series. Interestingly, the rate of postoperative UTI was similar in patients undergoing cystectomy alone and PE for primary malignancy (26% vs. 21%, P = 0.534).

Reported rates of postoperative urine leaks in pelvic exenteration patients range between 12-16%\textsuperscript{4,10,11,15}. These figures are considerably higher than the rate of urine leaks reported in patients undergoing radical cystectomy alone (usually less than 5%)\textsuperscript{12}. It has been demonstrated that urine leaks after PE are a considerable source of morbidity that increase length of hospital stay and may convey a survival disadvantage in this group of patients\textsuperscript{4}. In the current series 11% of pelvic exenteration patients developed a postoperative urine leak. The rate of urine leaks was high after PE for recurrence (14%), but lower in both PE for primary disease (6%) and cystectomy alone (3%). As with postoperative UTI, there was no statistically significant difference in the rate of urine leaks between the PE for primary malignancy and cystectomy alone group (P = 0.395). These results suggest that it is not simply the magnitude of the resection itself that contributes to urological morbidity but the fact that it is a major re-operative operation that is more relevant in increasing post-operative complications.
No patient or operative factors have been consistently shown to predict urological complications in PE patients, although cardiac disease, diabetes, major intraoperative blood loss, previous radiotherapy as well as type of urinary reconstruction have been implicated in this study. Reports of high rates of urological complications after preoperative radiotherapy were not replicated in a contemporary exenteration series by Stotland and colleagues. Although a statistically significant association was identified between preoperative radiotherapy and urological complications in the current series (P = 0.035), almost all patients (93%) had received radiotherapy previously and therefore a small group of non-irradiated patients for comparison prevents any definite conclusions. Patients who had major intraoperative blood loss (> 5000ml) were more likely to experience a postoperative urological complication after PE. The increased risk of urological complication may be driven by a combination of pelvic irradiation and tissue hypoperfusion that is less common in the cystectomy patients. Interestingly there was no difference in complication rates between patients with colonic conduit or ileal conduits in the PE group. Most colonic conduits were fashioned because of the unsuitability (radiation and dense adhesions) of the ileum.

Although this is the first study to compare urological outcomes in PE and cystectomy patients, there are limitations with the data. This includes retrospective data collection in the cystectomy group and small numbers in particular comparator groups (e.g. non-irradiated PE patients) which makes definite conclusions about predictors of urological complications difficult.

In conclusion, patients undergoing urinary diversion for cystectomy performed in the context of PE are at substantially higher risk of postoperative urological complications compared to those with cystectomy alone. Urine leaks and sepsis are significantly higher in this group of patients and are associated with a longer hospital stay. Prior pelvic radiotherapy, the extent of surgical resection and major intraoperative blood loss may contribute to urological morbidity.
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References


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**Table 1.** Baseline information for patients undergoing urinary diversion in non-PE and PE groups

<table>
<thead>
<tr>
<th></th>
<th>Non-PE (N=98)</th>
<th>PE (N=133)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median (range)</td>
<td>72 (41-94)</td>
<td>61 (15-86)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>72 (73)</td>
<td>101 (76)</td>
<td>0.669</td>
</tr>
<tr>
<td>Female</td>
<td>26 (27)</td>
<td>32 (24)</td>
<td></td>
</tr>
<tr>
<td>Previous pelvic radiotherapy</td>
<td>20 (20)</td>
<td>124 (93)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy</td>
<td>14 (14)</td>
<td>54 (41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>31 (32)</td>
<td>20 (15)</td>
<td>0.003</td>
</tr>
<tr>
<td>Vascular</td>
<td>22 (22)</td>
<td>19 (14)</td>
<td>0.100</td>
</tr>
<tr>
<td>Diabetes</td>
<td>25 (26)</td>
<td>16 (12)</td>
<td>0.007</td>
</tr>
<tr>
<td>Other malignancy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urological</td>
<td>14 (14)</td>
<td>15 (11)</td>
<td>0.477</td>
</tr>
<tr>
<td>Non-urological</td>
<td>12 (12)</td>
<td>10 (8)</td>
<td>0.217</td>
</tr>
<tr>
<td>Preoperative albumin &lt; 35 g/L</td>
<td>7 (7)</td>
<td>10 (8)</td>
<td>0.936</td>
</tr>
<tr>
<td>Preoperative GFR &lt; 60 ml/min/1.73m²</td>
<td>40 (41)</td>
<td>15 (11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urinary reconstruction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ileal conduit</td>
<td>89 (91)</td>
<td>108 (81)</td>
<td></td>
</tr>
<tr>
<td>Colonic conduit</td>
<td>0 (0)</td>
<td>25 (19)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Neobladder</td>
<td>9 (9)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Intraoperative blood loss &gt; 5000ml</td>
<td>NA</td>
<td>45 (34)</td>
<td></td>
</tr>
<tr>
<td>Length of stay, days, median (range)</td>
<td>18 (9-116)</td>
<td>28 (9-189)</td>
<td>&lt;0.001†</td>
</tr>
</tbody>
</table>

Numbers in parentheses are percentage unless otherwise indicated
NA: data not available
* Test is chi square unless otherwise indicated
† Median Test
†† Fisher’s exact test
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Table 2. Origin of cancer in 133 patients undergoing urinary diversion during PE

<table>
<thead>
<tr>
<th></th>
<th>Primary, N (%)</th>
<th>Recurrent, N (%)</th>
<th>Total (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal</td>
<td>37 (28)</td>
<td>60 (45)</td>
<td>97</td>
</tr>
<tr>
<td>Anal SCC</td>
<td>2 (2)</td>
<td>11 (8)</td>
<td>13</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>2 (2)</td>
<td>2 (2)</td>
<td>4</td>
</tr>
<tr>
<td>Bladder</td>
<td>2 (2)</td>
<td>1 (1)</td>
<td>3</td>
</tr>
<tr>
<td>Prostate</td>
<td>1 (1)</td>
<td>2 (2)</td>
<td>3</td>
</tr>
<tr>
<td>Colon</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>2</td>
</tr>
<tr>
<td>Gynaecological</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>0 (0)</td>
<td>2 (2)</td>
<td>2</td>
</tr>
<tr>
<td>Ovarian</td>
<td>0 (0)</td>
<td>2 (2)</td>
<td>2</td>
</tr>
<tr>
<td>Uterine</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1</td>
</tr>
<tr>
<td>Vaginal melanoma</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1</td>
</tr>
<tr>
<td>Vulval SCC</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>1</td>
</tr>
<tr>
<td>Adenocarcinoma of unknown primary</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1</td>
</tr>
<tr>
<td>Rectal melanoma</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>1</td>
</tr>
<tr>
<td>Neuroendocrine tumour</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>1</td>
</tr>
<tr>
<td>Non-cancer</td>
<td></td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>
Pelvic exenteration complications

Table 3. Postoperative complication rates after urinary diversion during cystectomy alone or pelvic exenteration for primary or recurrent cancer

<table>
<thead>
<tr>
<th></th>
<th>Non-PE (N=98)</th>
<th>PE – primary malignancy (N=48)</th>
<th>PE – recurrent malignancy (N=84)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-PE vs. PE</td>
<td>Non-PE vs. primary PE vs. recurrent PE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UTI</td>
<td>25 (26)</td>
<td>10 (21)</td>
<td>42 (50)</td>
<td>0.027†</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Urine leak</td>
<td>3 (3)</td>
<td>3 (6)</td>
<td>12 (14)</td>
<td>0.025</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.017</td>
</tr>
<tr>
<td>Ureteric stricture</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>3 (4)</td>
<td>0.139</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.153</td>
</tr>
<tr>
<td>Abdominal collection</td>
<td>7 (7)</td>
<td>10 (21)</td>
<td>22 (26)</td>
<td>0.001†</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.002†</td>
</tr>
<tr>
<td>Postoperative haemorrhage</td>
<td>1 (1)</td>
<td>3 (6)</td>
<td>4 (5)</td>
<td>0.143</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.119</td>
</tr>
<tr>
<td>Return to theatre</td>
<td>1 (1)</td>
<td>2 (4)</td>
<td>7 (8)</td>
<td>0.047</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.033</td>
</tr>
<tr>
<td>Any conduit-related complication</td>
<td>32 (33)</td>
<td>23 (48)</td>
<td>56 (67)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001†</td>
</tr>
</tbody>
</table>

*Test is Fisher’s exact test unless otherwise indicated, † Chi square test, PE pelvic exenteration, UTI urinary tract infection

Table 4. Details of ten patients requiring return to theatre involving the urinary conduit

<table>
<thead>
<tr>
<th>Primary Operation</th>
<th>Day</th>
<th>Reason for return to theatre</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-PE</td>
<td>3</td>
<td>Urine leak</td>
<td>Anastomoses resutured and omental patch</td>
</tr>
<tr>
<td>PE</td>
<td>7</td>
<td>Urine leak</td>
<td>Foley catheter eroded blind end of conduit. Primarily repaired.</td>
</tr>
<tr>
<td>PE</td>
<td>10</td>
<td>Urine leak</td>
<td>Hole in blind end of conduit. Resected with linear stapler.</td>
</tr>
<tr>
<td>PE</td>
<td>0</td>
<td>Haemorrhage and ischaemic conduit</td>
<td>Complete conduit revision</td>
</tr>
<tr>
<td>PE</td>
<td>3</td>
<td>Haemorrhage and ischaemic conduit</td>
<td>Ischaemic segment of conduit resected and reconstructed with small bowel</td>
</tr>
<tr>
<td>PE</td>
<td>1</td>
<td>Haemorrhage</td>
<td>Iatrogenic damage to conduit during dissection</td>
</tr>
<tr>
<td>PE</td>
<td>35</td>
<td>Enterocutaneous fistula</td>
<td>Iatrogenic damage to conduit during dissection. Conduit revised.</td>
</tr>
<tr>
<td>PE</td>
<td>83</td>
<td>Enterocutaneous fistula</td>
<td>Small bowel used to extend conduit to allow mobilisation. One ureter re-implanted onto the extension</td>
</tr>
<tr>
<td>PE</td>
<td>8</td>
<td>Incarcerated small bowel hernia</td>
<td>Iatrogenic damage to conduit near urostomy during dissection. Urostomy resited.</td>
</tr>
<tr>
<td>PE</td>
<td>10</td>
<td>Urostomy dehiscence</td>
<td>Stoma revised</td>
</tr>
</tbody>
</table>
Table 5. Univariate predictors of postoperative conduit-related complications comparing non-PE and PE patients

<table>
<thead>
<tr>
<th>Patient had a conduit-related complication*</th>
<th>Non-PE (N=98)</th>
<th>PE (N=133)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;70</td>
<td>0.764</td>
<td>0.863</td>
</tr>
<tr>
<td>Gender</td>
<td>0.811</td>
<td>0.214</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>0.373</td>
<td>0.631</td>
</tr>
<tr>
<td>Vascular</td>
<td>0.614</td>
<td>0.097</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.615</td>
<td>0.417</td>
</tr>
<tr>
<td>Urological malignant</td>
<td>0.745</td>
<td>0.960</td>
</tr>
<tr>
<td>Urological non-malignant</td>
<td>0.740†</td>
<td>0.675†</td>
</tr>
<tr>
<td>Other malignancy</td>
<td>0.575†</td>
<td>0.529</td>
</tr>
<tr>
<td>Previous pelvic radiotherapy</td>
<td>0.777</td>
<td>0.035†</td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy</td>
<td>0.376†</td>
<td>0.397</td>
</tr>
<tr>
<td>Reconstruction type</td>
<td>0.468†</td>
<td>0.331</td>
</tr>
<tr>
<td>Preoperative Albumin &lt; 35 g/L</td>
<td>0.595†</td>
<td>0.526†</td>
</tr>
<tr>
<td>Preoperative GFR &lt; 60 ml/min/1.73m²</td>
<td>0.681</td>
<td>0.510</td>
</tr>
<tr>
<td>Intraoperative blood loss &gt; 5000ml</td>
<td>NA</td>
<td>0.002</td>
</tr>
</tbody>
</table>

* Test is chi square unless otherwise indicated
NA: data not available
† Fisher’s exact test
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CHAPTER 3.1

Lateral pelvic compartment excision during pelvic exenteration

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Published in British Journal of Surgery:

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Abstract

Background: Pelvic exenteration involving the lateral compartment remains a relative or absolute contraindication in most units. Initial exenteration experience in our unit revealed a 21% clear margin rate (R0) which improved to 53% with early results adopting a novel technique for en bloc resection of the iliac vessels and other sidewall structures. The objective of this study was to report morbidity and oncological outcomes in 200 consecutive exenterations involving the lateral compartment.

Methods: Patients undergoing pelvic exenteration between 1994 and 2014 were eligible for review. 200 patients with en bloc resection of the lateral compartment were included.

Results: R0 resection was achieved in 66% of patients undergoing surgery for cancer (197 patients) and 69% of planned curative resections. For patients with colorectal cancer, a clear resection margin was associated with a significant overall survival benefit (P=0.030). Median overall and disease-free survival in this group was 41 and 27 months, respectively. The overall 1-, 3- and 5-year survival rates were 86%, 46% and 35%, respectively. No predictors of survival were identified on univariate analysis other than margin status and operative intent. Excision of the common or external iliac vessels or sciatic nerve did not confer a survival disadvantage.

Conclusion: The continuing evolution of radical techniques of pelvic exenteration has seen the improvement in R0 margin status (the “holy grail” of pelvic exenteration) from 21 to 66% over a 20-year period by adopting routinely a more lateral anatomic plane. 5-year overall survival rates are comparable to more centrally-based tumours.
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Introduction

Pelvic exenteration offers potentially curative treatment to patients with locally advanced and recurrent tumours of the pelvis. Contemporary literature demonstrates acceptable morbidity and quality of life associated with these radical multi-visceral resections, which confer overall 5-year survival up to 65%. As a result, exenteration is now accepted as a safe and feasible option for this group of patients with otherwise incurable disease. Increasingly more radical resections are being successfully undertaken in order to achieve clear resection margins, which is considered the most important predictor of survival. Despite this, the role of pelvic exenteration in the management of tumours involving the lateral sidewall of the pelvis remains controversial. Due to proximity to the pelvic bone and major neurovascular structures, achieving en bloc excision with a clear lateral resection margin is technically challenging, particularly in the setting of previous surgery and radiotherapy. This group of patients have been shown to have poorer survival when compared to those with tumours involving the other compartments of the pelvis. As a result, extensive pelvic sidewall involvement has traditionally been considered a contraindication to surgery and this group of patients remain precluded from a curative operation in many units.

A previously described radical approach to advanced primary or recurrent pelvic malignancies involving the pelvic sidewall has demonstrated the oncological feasibility of exenteration in this group of patients without increased morbidity. This technique involves en bloc resection of pelvic sidewall structures including the internal iliac vessels, piriformis and obturator internus muscles, ischium, and sacrotuberous and sacrospinous ligaments. The objective of this study is to report the postoperative and oncological outcomes of 200 consecutive patients undergoing pelvic exenteration with en bloc lateral iliac vessel excision at a single centre.

Patients & Method
Pelvic exenteration complications

Patients who had a pelvic exenteration at Royal Prince Alfred Hospital between 1994 and 2014 were eligible for review. 200 patients with en bloc resection of the lateral compartment defined by at least a complete resection of all or a significant part of the internal iliac vessel system as part of their operation were identified from a prospective electronic database and included in this study. All patients underwent thorough clinical review and preoperative imaging in order to confirm resectability of the locally recurrent or advanced tumour, the patient’s fitness for surgery and the presence of irresectable metastatic disease. All patients were reviewed at a specialised exenteration multi-disciplinary team (MDT) meeting, attended by a radiologist, oncologist, and colorectal, orthopaedic, vascular, plastic and urological surgeons. Pre-operative PET-CT and MRI were used to assess the extent of lateral tumour invasion into the sidewall which guided the extent of dissection. CT or MR angiography and venography was performed in patients where tumour closely approximated the common or external iliac vessels to further assess involvement. If en bloc resection of the vessels with subsequent reconstruction was anticipated the patient was reviewed clinically by a vascular surgeon and further investigations (such as venous Doppler studies of the lower limbs assessing suitability for harvesting) conducted as required.

Surgical Procedure

A detailed anatomical understanding of the lateral pelvic sidewall and lumbosacral triangle is critical when considering the operative approach to laterally extending pelvic tumours (paper under peer review). A technique for dissection and en bloc resection of the iliac vessels and other sidewall structures to achieve clear lateral resection margins has been described\textsuperscript{16} and is summarised in this section. Similar techniques have been reported in the gynaecological literature.\textsuperscript{17}

After division of adhesions and mobilisation of small bowel loops from the pelvis, the common and external iliac artery (CIA, EIA) and vein (CIV, EIV) are dissected starting proximally at the apex of
Pelvic exenteration complications

the Triangle of Marcille and the bifurcation of the aorta and inferior vena cava and proceeding
distally to the origin of the internal iliac artery (IIA) and vein (IIV). At this point ureterolysis is
performed with a cuff of alveolar tissue to preserve blood supply. If en bloc ureterectomy is
indicated the ureter is divided proximal to the point of involvement by the tumour. After the EIA
and EIV are dissected, the internal iliac artery (IIA) and vein (IIV) are ligated and divided at their
origins. Where the tumour encases or adheres to the common iliac vessels, part or all of the
involved vessel is excised en bloc with the tumour to gain a clear margin, which is done in
preference to attempting to dissect the vessel free of tumour. Techniques for repair or reconstruction
of the common and external iliac vessels using autologous and synthetic grafts have been
previously described\textsuperscript{18,19} and should be performed immediately to minimise the risk of
compartment syndrome and thrombosis.

Suture ligation of the IIA and IIV at their origins allows partial devascularisation of the pelvic
viscera and allows access to their branches and tributaries which are then dissected, ligated and
divided. Mobilisation and gentle medial retraction of the tumour mass is then possible and gives the
surgeon access to a lateral plane of dissection. By dissecting laterally to the internal iliac vessels,
the deep pelvic fascia covering the lumbosacral trunk and sacral nerve roots on the piriformis
muscle are exposed. The piriformis muscle, sciatic nerve distal to the ischial spine, obturator
internus and levator muscles are dissected free from the bony pelvic sidewall and, if required, the
ischium and sacrotuberous and sacrospinous ligaments can be resected using energy devices and an
osteotome. If sacrectomy is required, it can be performed via an anterior abdominal approach if the
level of division is below S3 or otherwise completed in the prone position according to established
principles.\textsuperscript{20-24}

Data Collection
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Medical records of included patients were reviewed and the data extracted included patient demographics, details of their cancer, operation details, pathological analysis findings, resection margin status, postoperative complications, length of stay and survival data. Major complications were defined as those requiring re-operative or radiological intervention or which prolonged the expected length of hospital stay. Resection margins were categorised as microscopically clear of malignant cells (R0), microscopically involved (R1) or macroscopically involved (R2).

Statistical analysis was completed using SPSS software (IBM SPSS Statistics Version 22.0, IBM Corp., Armonk, NY). Kaplan-Meier survival curves were used to estimate patient survival outcomes, which were compared using the log-rank test to identify univariate predictors of survival. Patient with non-colorectal malignancy were excluded from the survival analysis. A significant P value was defined as less than 0.05.

The study was conducted as part of a program of research exploring clinical and patient reported outcomes in pelvic exenteration surgery in Australia, funded in part through the Priority-Driven Collaborative Cancer Research Scheme by Cancer Australia and The Cancer Council Australia (ID 570860) and approved by the Royal Prince Alfred Hospital Human Research Ethics Committee.

Results

Of 398 pelvic exenterations during the study period, en bloc iliac vessel excision was performed in 200 cases (50%). 120 patients (60%) were male and the median age was 60 years (range 15-83). 77 patients (39%) in the series had radiotherapy prior to surgery either as neoadjuvant therapy or during treatment of their primary tumour in some cases of recurrence. Demographic and operation details of 200 patients in this series are summarised in Table 1. There were 183 curative operations (92%) and 93 patients (47%) had a bladder-sparing procedure. The majority of patients had a pelvic
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Exenteration for locally recurrent rectal cancer (100, 50%) or advanced primary rectal cancer (32, 16%) while squamous cell carcinoma of the anus and gynaecological malignancies accounted for 10% and 6%, respectively (Table 2). Three patients had a non-cancer indication for surgery; including chronic pelvic sepsis secondary to a previously perforated primary rectal tumour, diverticular mass thought to be malignant disease and pelvic fibromatosis.

103 patients (52%) had a total cystectomy, which was performed en bloc with subsequent urinary diversion in the form of an ileal or colonic conduit (77% and 23%, respectively). One patient on haemodialysis for end stage kidney disease did not have urinary reconstruction. Resection of the sciatic nerve was required in 27 patients (14%) in this series and ischium in 22 (11%). One or both of the common or external iliac artery or vein were resected en bloc with the tumour in 29 patients (15%), of which 23 had repair or reconstruction of the vessel while six were ligated without reconstruction due to presumed collateral circulation from preoperative occlusion by thrombus or local tumour compression.

Morbidity

Overall a postoperative complication occurred in 164 patients (82%). The major and minor complication rates were 28% and 79%, respectively, and are summarised in Table 3. Sepsis was the most common postoperative complication and occurred in 100 patients (50%). Where sources of sepsis were identified, these were recorded as urological (31%), intra-abdominal (14%), wound-related (12%), intravenous line-related (5%) and pulmonary (3%). The most common reasons for reintervention were drainage of pelvic collections (13%) and percutaneous nephrostomy tube insertion or conduit revision for urological leaks following urinary diversion (14%). In 47 patients with a flap, seven required return to theatre for debridement following flap breakdown (5%). The most common minor complication was urinary retention, which occurred in 26% of patients with a
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bladder-sparing procedure. Other minor complications included motor neurological deficit (17%),
cardiac arrhythmia (18%) and atelectasis (16%).

Of the 29 patients who had en bloc resection of the common or external iliac, six required
reintervention (21%). Three patients required laparotomy or angiography and stent insertion for
abdominopelvic haematomas, although only two of these cases were due to dehiscence of the
vascular graft. Two patients had thrombosis of the reconstructed vessel requiring thrombectomy in
one patient and a venous and arterial bypass in another. One patient required lower limb fasciotomy
on day 1 for compartment syndrome.

Margin status and survival

The overall rate of clear resection margins was 66% in patients undergoing surgery for cancer (197
patients). This increased to 69% in those who had an operation with curative intent. Margin status
rates for tumours according to their origin are presented in Table 4. Notably, clear resection margins
were achieved in 66% of patients with a planned curative resection of locally recurrent rectal
cancer.

For patients undergoing pelvic exenteration for colorectal cancer, a clear resection margin was
associated with a significant overall survival benefit ($P=0.030$) (Figure 1). Median overall survival
in this group was 41 months. The overall 1-, 3- and 5-year survival rates were 86%, 46% and 35%,
respectively. The median overall survival was 29 months in patients with R1 margin status and 17
months in patients with R2 margins. A clear resection margin also conferred a significant increase
in disease-free survival ($P=0.014$), with a median of 27 months in this group. One patient died
within 30 days of surgery (<1% mortality). No predictors of overall survival were identified on
univariate analysis other than margin status and intent of the procedure (Table 5). Patients with
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primary and recurrent tumours did not have a significantly different disease-free (P=0.393) or overall survival (P=0.334, Figure 2). Patients requiring excision of the common or external iliac vessels, ischial bone, or sciatic nerve did not have a survival disadvantage (P = 0.580, 0.201, 0.780, respectively).

The median overall survival of patients with locally recurrent rectal cancer was 35 months. For patients with clear resection margins, median overall survival was 45 months (P=0.010) and disease-free survival was 27 months (P=0.006). In this subgroup the overall 3- and 5-year survival rates were 45% and 34%.

Median follow up time of the study cohort was 3.2 years (range 0 – 18.5 years).

Discussion

Pelvic malignancies involving the lateral pelvic sidewall have previously been associated with lower clear resection margin rates and poorer survival compared to central, anterior and posterior tumours. Two recent Delphi studies carried out internationally among experts have confirmed that extensive pelvic sidewall involvement is considered a relative contraindication to curative surgery at many units and debate continues about the role of lateral iliac vessel resection. This study reports the results of 200 consecutive cases of pelvic exenteration over 20 years with en bloc iliac vessel resection for locally advanced or recurrent cancer of the pelvis. R0 resection was achieved in 69% of patients who had an operation with curative intent. For colorectal cancer, this translated to a median overall survival of 41 months, a 3-year survival rate of 46% and a 5-year survival rate of 35%. These encouraging results improve on our units earlier experience with en bloc iliac (53% R0 resection) and support the use of this radical technique at specialised multi-
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disciplinary exenteration units in selected patients who should not be precluded from curative resection.

The exenteration literature is limited regarding outcomes of patients undergoing surgery for tumours involving the pelvic sidewall. Moore and colleagues at Memorial Sloan-Kettering Cancer Centre reported R0 margins in 36% of tumours involving the lateral pelvic compartment and 19% in cases where pelvic sidewall involvement was suspected on preoperative imaging. Moore and colleagues at Memorial Sloan-Kettering Cancer Centre reported R0 margins in 36% of tumours involving the lateral pelvic compartment and 19% in cases where pelvic sidewall involvement was suspected on preoperative imaging. Yamada and coworkers reported a 5-year survival of 0% in laterally invasive recurrence of rectal cancer and our institution contributed to a multicentre study that similarly demonstrated a survival disadvantage where there was lateral compartment involvement. The current series presents improved results from experience with this technique that are comparable to reports in contemporary exenteration literature of median overall survival between 28 and 45 months and 5-year survival between 17 and 65%.

In a consensus statement developed by The Beyond TME Collaborative, encasement of the external or common iliac vessels requiring en bloc excision and reconstruction was considered a relative contraindication to surgery by 78% of experts. In addition, various reviews have considered external or common iliac vessel involvement an absolute contraindication to surgery. However, two recent studies have reported acceptable morbidity and R0 resection rates of 58% and 38% in patients with excision and reconstruction of major pelvic vessels (paper accepted for publication). These encouraging reports in addition to the current series, which did not demonstrate a survival disadvantage after common or external iliac vessel excision, represent emerging literature which questions previously considered “irresectable” tumours for which curative resection may be possible in selected patients. It is possible that attempting to dissect the tumour off an involved vessel increases the likelihood of an involved lateral margin and for this reason it has been our
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approach to plan a more radical en bloc excision based on preoperative imaging in these patients. Similarly, more lateral excisions involving en bloc resection of the sciatic nerve and ischial bone did not affect patient survival in this series. The St. Marks group recently reported initial outcomes of a modified technique for sidewall resection via an initial trans-gluteal approach to the sciatic notch with the patient prone. This approach does not allow an initial abdominal exploration to assess local invasion, metastatic disease or adhesiolysis and mobilisation of small bowel however clear resection margins were achieved all six patients in the series and further investigation of this technique is warranted.

MRI is the imaging modality of choice for determining tumour resectability and guiding the extent of dissection during preoperative planning. Dresen and colleagues studied the accuracy of MRI in determining invasion of pelvic structures and confirmed its role in this setting with a negative predictive value of 93-100%, although the authors did report difficulty in determining pelvic sidewall involvement in some cases with diffuse post-operative or -radiotherapy fibrotic changes. Georgiou and co-workers reported similar findings with the sensitivity of MRI being lower in the lateral compartment (89.3%) when compared to other pelvic compartments. Therefore MRI is critical for identifying planes for planned dissection however care must be taken when assessing the extent of pelvic sidewall invasion and should be interpreted by an experienced radiologist. This reinforces the need for a specialised MDT.

Conclusion

The continuing evolution of radical techniques of pelvic exenteration for advanced and recurrent pelvic malignancy has seen the improvement in R0 margin status (the “holy grail” of pelvic exenteration) from 21 to 68% over a 20 year period by adopting routinely a more lateral anatomic plane defined within the Triangle of Marcille.
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Acknowledgements

The authors thank Rachael Roberts and Ken Ly for assistance with data collection.

References

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**Figure 1.** Kaplan-Meier overall survival plot of patients undergoing pelvic exenteration for colorectal cancer (R0 vs R1/R2 resection, P = 0.030)

![Kaplan-Meier overall survival plot of patients undergoing pelvic exenteration for colorectal cancer (R0 vs R1/R2 resection, P = 0.030)](image)

**Figure 2.** Kaplan-Meier overall survival plot (primary vs. recurrent colorectal cancer, P = 0.334)

![Kaplan-Meier overall survival plot (primary vs. recurrent colorectal cancer, P = 0.334)](image)
Table 1. Demographic information for patients undergoing pelvic exenteration with lateral iliac resection (N=200)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>120 (60)</td>
</tr>
<tr>
<td>Female</td>
<td>80 (40)</td>
</tr>
<tr>
<td>Age, median (range), years</td>
<td>60 (15-83)</td>
</tr>
<tr>
<td>Resection intent</td>
<td></td>
</tr>
<tr>
<td>Curative</td>
<td>183 (92)</td>
</tr>
<tr>
<td>Palliative</td>
<td>17 (9)</td>
</tr>
<tr>
<td>Resected sidewall structures</td>
<td></td>
</tr>
<tr>
<td>Ureter</td>
<td>63 (32)</td>
</tr>
<tr>
<td>Piriformis muscle</td>
<td>10 (5)</td>
</tr>
<tr>
<td>Obturator muscle</td>
<td>27 (14)</td>
</tr>
<tr>
<td>Sciatic nerve</td>
<td>27 (14)</td>
</tr>
<tr>
<td>Femoral nerve</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Obturator nerve</td>
<td>29 (15)</td>
</tr>
<tr>
<td>Internal iliac vessels</td>
<td>200 (100)</td>
</tr>
<tr>
<td>Common/External iliac vessels</td>
<td>29 (15)</td>
</tr>
<tr>
<td>Urinary conduit (N=102)</td>
<td></td>
</tr>
<tr>
<td>Ileal</td>
<td>79 (40)</td>
</tr>
<tr>
<td>Colonic</td>
<td>23 (12)</td>
</tr>
<tr>
<td>Bone resection (N=132)</td>
<td></td>
</tr>
<tr>
<td>Sacrectomy</td>
<td>107 (54)</td>
</tr>
<tr>
<td>Ischium</td>
<td>22 (11)</td>
</tr>
<tr>
<td>Pubis</td>
<td>17 (9)</td>
</tr>
<tr>
<td>Reconstruction (N=47)</td>
<td></td>
</tr>
<tr>
<td>VRAM Flap</td>
<td>44 (22)</td>
</tr>
<tr>
<td>Gracilis flap</td>
<td>2 (1)</td>
</tr>
<tr>
<td>V-Y flap</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Margin status‡</td>
<td></td>
</tr>
<tr>
<td>R0</td>
<td>126 (69)</td>
</tr>
<tr>
<td>R1</td>
<td>52 (28)</td>
</tr>
<tr>
<td>R2</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Blood loss, median (range), L</td>
<td>3.5 (0.0-25.0)</td>
</tr>
<tr>
<td>Length of operation, median (range), min</td>
<td>615 (165-1200)</td>
</tr>
<tr>
<td>Length of ICU admission, median (range), day</td>
<td>2 (0-27)</td>
</tr>
<tr>
<td>Length of stay, median (range), day</td>
<td>25 (5-189)</td>
</tr>
</tbody>
</table>

‡ n = 183 patients undergoing a curative resection
Table 2. Origin of cancer (N=200)

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>Primary (%)</th>
<th>Recurrent (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal</td>
<td>32 (16)</td>
<td>100 (50)</td>
<td>132</td>
</tr>
<tr>
<td>Anal SCC</td>
<td>1 (1)</td>
<td>18 (9)</td>
<td>19</td>
</tr>
<tr>
<td><strong>Gynaecological</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovarian</td>
<td>1 (1)</td>
<td>4 (2)</td>
<td>5</td>
</tr>
<tr>
<td>Uterine</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1</td>
</tr>
<tr>
<td>Cervical</td>
<td>0 (0)</td>
<td>4 (2)</td>
<td>4</td>
</tr>
<tr>
<td>Vaginal melanoma</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1</td>
</tr>
<tr>
<td>Endometrial</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Sarcoma</strong></td>
<td></td>
<td></td>
<td>15</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colon</td>
<td>6 (3)</td>
<td>4 (2)</td>
<td>10</td>
</tr>
<tr>
<td>Bladder</td>
<td>3 (2)</td>
<td>1 (1)</td>
<td>4</td>
</tr>
<tr>
<td>Prostate</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>2</td>
</tr>
<tr>
<td>Neuroendocrine tumour</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>2</td>
</tr>
<tr>
<td>Perineal melanoma</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Non-cancer</strong></td>
<td>-</td>
<td>-</td>
<td>3</td>
</tr>
</tbody>
</table>
Table 3. Postoperative mortality and morbidity for pelvic exenteration and lateral iliac resection (N=200)

<table>
<thead>
<tr>
<th>Complication</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Major Complications</strong></td>
<td></td>
</tr>
<tr>
<td>Wound/Flap</td>
<td></td>
</tr>
<tr>
<td>Wound dehiscence</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Flap dehiscence</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Partial flap necrosis</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Full flap necrosis</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Sacral osteomyelitis</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Pulmonary embolus</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>6 (3)</td>
</tr>
<tr>
<td>Vascular graft thrombosis</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Thrombophlebitis</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Compartment syndrome</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Gastrointestinal (reoperation)</td>
<td></td>
</tr>
<tr>
<td>Enterocutaneous fistula</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Small bowel obstruction</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Pelvic collection</td>
<td>26 (13)</td>
</tr>
<tr>
<td>Ischaemic ileostomy</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Anastomotic leak</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Urological</td>
<td></td>
</tr>
<tr>
<td>Urological leak</td>
<td>14 (14)*</td>
</tr>
<tr>
<td>Renal calculi</td>
<td>1 (1)</td>
</tr>
<tr>
<td><strong>Minor Complications</strong></td>
<td></td>
</tr>
<tr>
<td>Wound/Flap</td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>29 (15)</td>
</tr>
<tr>
<td>Minor wound dehiscence</td>
<td>20 (10)</td>
</tr>
<tr>
<td>Minor flap dehiscence</td>
<td>9 (5)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td></td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>36 (18)</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>16 (8)</td>
</tr>
<tr>
<td>Respiratory</td>
<td></td>
</tr>
<tr>
<td>Atelectasis</td>
<td>31 (16)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>15 (8)</td>
</tr>
<tr>
<td>Pulmonary oedema</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Gastrointestinal (conservative)</td>
<td></td>
</tr>
<tr>
<td>Enterocutaneous fistula</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Small bowel obstruction</td>
<td>10 (5)</td>
</tr>
<tr>
<td>Pelvic collection</td>
<td>33 (17)</td>
</tr>
</tbody>
</table>
Pelvic exenteration complications

<table>
<thead>
<tr>
<th>Category</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged ileus</td>
<td>29 (15)</td>
</tr>
<tr>
<td>Neurological</td>
<td></td>
</tr>
<tr>
<td>Sensory deficit</td>
<td>21 (11)</td>
</tr>
<tr>
<td>Motor deficit</td>
<td>34 (17)</td>
</tr>
<tr>
<td>Renal/urological</td>
<td></td>
</tr>
<tr>
<td>Urinary retention</td>
<td>25 (26)†</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>9 (5)</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Postoperative transfusion</td>
<td>12 (6)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>100 (50)</td>
</tr>
</tbody>
</table>

* N = 102 patients with urinary conduit
† N = 97 patients with bladder-sparing operation
Pelvic exenteration complications

Table 4. R0 rates for lateral iliac resection by origin of cancer (N=197)

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>R0 (%)</th>
<th>R1/R2 (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary rectal cancer</td>
<td>26 (81)</td>
<td>6 (19)</td>
<td>32</td>
</tr>
<tr>
<td>Recurrent rectal cancer</td>
<td>62 (62)</td>
<td>38 (38)</td>
<td>100</td>
</tr>
<tr>
<td>Anal SCC</td>
<td>11 (58)</td>
<td>8 (42)</td>
<td>19</td>
</tr>
<tr>
<td>Gynaecological</td>
<td>9 (75)</td>
<td>3 (25)</td>
<td>12</td>
</tr>
<tr>
<td>Other</td>
<td>23 (68)</td>
<td>11 (32)</td>
<td>34</td>
</tr>
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</table>

Table 5. Univariate predictors of survival of patients with colorectal cancer

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall survival</th>
<th>Disease-free survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 60</td>
<td>0.241</td>
<td>0.759</td>
</tr>
<tr>
<td>Male vs. female sex</td>
<td>0.913</td>
<td>0.799</td>
</tr>
<tr>
<td>Curative intent</td>
<td>0.012</td>
<td>NA</td>
</tr>
<tr>
<td>Primary vs. recurrent tumour</td>
<td>0.334</td>
<td>0.393</td>
</tr>
<tr>
<td>R0 margin</td>
<td>0.030</td>
<td>0.014</td>
</tr>
<tr>
<td>Blood loss &gt; 5000ml</td>
<td>0.141</td>
<td>0.833</td>
</tr>
<tr>
<td>Major complication</td>
<td>0.152</td>
<td>0.400</td>
</tr>
<tr>
<td>Bladder-sparing operation</td>
<td>0.536</td>
<td>0.963</td>
</tr>
<tr>
<td>Sacrectomy</td>
<td>0.128</td>
<td>0.054</td>
</tr>
<tr>
<td>Common/external iliac excision</td>
<td>0.580</td>
<td>0.733</td>
</tr>
<tr>
<td>Ischial bone resection</td>
<td>0.201</td>
<td>0.918</td>
</tr>
<tr>
<td>Sciatic nerve excision</td>
<td>0.780</td>
<td>0.773</td>
</tr>
</tbody>
</table>

NA = not applicable.
Pelvic exenteration complications

CHAPTER 3.2

Outcomes following en bloc iliac vessel excision and reconstruction during pelvic exenteration

Kilian G.M. Brown\textsuperscript{a,b}, Cherry E. Koh\textsuperscript{a,b,c}, Michael J. Solomon\textsuperscript{a,b,c,d,*}, Raffi Qasabian\textsuperscript{e}, David Robinson\textsuperscript{e}, Steven Dubenec\textsuperscript{e}

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Published in Diseases of the Colon & Rectum:
Pelvic exenteration complications

Abstract

**Background:** Advanced pelvic cancers involving the lateral pelvic compartment, and particularly the iliac vasculature, are difficult to manage. Common or external iliac vessel involvement has traditionally been considered a contraindication for curative surgery.

**Objective:** To investigate pathological and surgical outcomes particularly postoperative morbidity of pelvic exenteration with en bloc major iliac vascular excision and reconstruction.

**Design:** A case series.

**Setting:** A quaternary referral centre for pelvic exenteration in Sydney, Australia.

**Patients:** Patients undergoing en bloc iliac vessel excision as part of their pelvic exenteration for a locally advanced pelvic malignancy.

**Main outcome measures:** Over the study period, 336 patients underwent pelvic exenteration. 21 patients (6.3%) underwent en bloc vascular excision of 29 vessels for tumour involvement. 24 vessels required reconstruction. The primary outcomes were postoperative complications and pathological outcomes. Survival rates were estimated using Kaplan-Meier technique.

**Results:** Operating time for patients who underwent vascular excision and reconstruction was longer but this did not reach significance (631 vs. 531 minutes, p=0.052). Mean blood loss was significantly higher in the vascular excision and reconstruction group (6.8 vs 3.4L, p<0.001).

Patients who required en bloc vascular excision were less likely to have R0 margins compared to patients who did not (38% vs. 78%, p<0.001). There was no intra-operative or 30-day mortality. Overall graft patency and limb loss at one year was 96% and 0%, respectively. 52% of patients had at least one vascular related complication. Median overall and disease free survival were 34 and 26 months, respectively.

**Limitations:** This study is limited by a relatively small number of heterogeneous patients.
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**Conclusion**: En bloc vascular resection and reconstruction for contiguous tumour involvement is feasible and safe in selected patients. Advanced pelvic tumours involving iliac vessels should not be precluded from curative surgery in specialised institutions.
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Introduction

Pelvic exenteration is an established procedure for patients with locally advanced or recurrent pelvic cancers where no other possibility of cure exists. Because of the magnitude of the procedure, surgery is generally offered when clear resection margins are likely. Pelvic side wall involvement and high sacral involvement have traditionally been considered contraindications for surgery. However, with improved surgical technique, many units with an exenteration interest have pushed the boundaries of “resectability” and redefined what in their experience constitutes “resectable disease”.

In exenterative surgery, the lateral compartment typically poses the most challenge to the surgeon because of the major vascular and neural structures within that compartment. Either intended resection of or unintended injury to either of these can have disastrous surgical or functional consequences to the patient. Not surprisingly, extensive pelvic side wall involvement is typically considered an absolute contraindication for curative surgery.\(^1\)\(^-\)\(^d\) Because of technical difficulties in achieving R0 resection, tumours with pelvic side wall involvement typically have a worse prognosis compared to central or posterior recurrences.\(^5\)\(^,\)\(^6\) Previous authors have demonstrated the feasibility of en bloc vascular excision and reconstruction in conjunction with radical excisions of pelvic tumours. However, this experience is limited even within institutions with a subspecialty interest in recurrent pelvic malignancies.\(^7\)\(^,\)\(^8\)

Due to the limited literature reporting pelvic exenteration with en bloc vascular excision and reconstruction, it remains unclear, firstly, whether or not iliac vessel involvement should be considered a contraindication for surgery, and secondly, if major vascular reconstruction contributes to patient morbidity. The aims of this study are to report the surgical outcomes and complications of
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patients who underwent en bloc vascular excision and reconstruction as part of their pelvic exenteration. Pathology is also reviewed to determine R0 rates.

Materials and Methods

Patient Sample

Patients who underwent pelvic exenteration for locally advanced or recurrent pelvic tumours between 1995 and 2013 at Royal Prince Alfred Hospital, Sydney, were identified from a prospectively maintained electronic database and formed the study cohort. The decision to perform excision and reconstruction of the common or external iliac vessels was based on the patient's clinical status and pre-operative imaging, reviewed at a pelvic exenteration multi-disciplinary team (MDT) meeting. All patients underwent CT of the chest, abdomen and pelvis and MRI of the pelvis. Over the course of this series positron emission tomography (PET) was increasingly utilised and is now a routine part of preoperative staging to rule out the presence of metastatic disease. Where imaging suggested involvement of pelvic vascular structures further assessment included CT or MR angiogram and duplex ultrasound studies of the lower limbs to assess extent of involvement of the vasculature, local tumour compression and to identify vessels suitable for autologous grafting.

Operative Procedure

Preoperative MRI was used to guide the extent of pelvic sidewall excision. If necessary, the rectum, ureter, sciatic nerve, piriformis, obturator internus or ischium were also excised en bloc in order to achieve clear resection margins. Surgical technique for tumours involving the lateral compartment of the pelvis has been previously described. The internal iliac vessels, which can generally be sacrificed during pelvic exenteration, were resected en bloc with the specimen without reconstruction after which the common and external iliac artery and vein were assessed for tumour involvement. Where there was infiltration of the vessel wall or a plane could not be developed
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between it and the encasing tumour, en bloc resection of all or part of the vessel was performed in order to achieve an R0 resection. If the involved common or external iliac vessel could not be excised without functional sequelae (e.g. chronically occluded iliac vein with established collaterals) subsequent reconstruction was performed to restore vessel continuity and blood flow to the lower extremity.

Technique for reconstruction depends on the extent of resection required and therefore the ensuing defect. Where only a cuff of the vessel wall is excised, repair was performed either primarily or using a patch repair. Where a segment of the vessel was excised, an interposition conduit graft was used for reconstruction. Both synthetic (polytetrafluoroethylene, PTFE) and autologous grafts (commonly superficial femoral or great saphenous veins) were used. Autologous graft material was preferred, when available, due to lower thrombogenicity and risk of infection. In selected cases where the common or external iliac vein was thrombosed from tumour compression pre-operatively, vessel excision was performed without reconstruction. Where local vessel reconstruction was not possible, options for reconstruction include extra-anatomical bypass using a femoral-femoral cross-over bypass graft or, in the case of a vein, the contralateral great saphenous vein used for cross-over. These techniques were not necessary in this cohort as a primary reconstruction modality.

Full-length compression stockings were applied postoperatively and prophylactic antibiotics were continued for five days. Limb vascular observations were performed every four hours for the first three post-operative days and these were then gradually reduced if no graft-related complications developed. Lower limb arterial and venous duplex ultrasonography was also performed routinely in hospital. Patients received subcutaneous heparin for the duration of hospital stay, which was changed to subcutaneous low molecular weight heparin following discharge if there had been a
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postoperative thrombotic complication and where warfarin therapy was contraindicated. Patients were routinely followed up clinically by both the colorectal and vascular surgeons. Patients also routinely underwent 6 monthly duplex follow up to assess graft patency. For patients who underwent arterial reconstruction, ankle brachial indexes were also included as part of their duplex assessment.

Data Collection and Analysis

After ethical approval was granted by the Sydney Local Health District (RPAH Zone) human research ethics committee data was collected from medical records. Margin status was defined as R0 (margins clear of malignant cells), R1 (microscopically involved margins) and R2 (macroscopically involved margin). Demographics, clinical characteristics and outcomes were compared for patients with and without vascular excision and reconstruction using the Mann-Whitney U test for non-normally distributed data, while the Chi-square test (categorical variables) and independent-samples t-test (continuous variables) were used for normally distributed data. The survival outcomes were calculated using Kaplan-Meier curves with the log-rank test for comparison of these curves. Statistical analysis was performed using SPSS software (IBM SPSS Statistics Version 22.0, IBM Corp., Armonk, NY).

Results

Of 336 patients who underwent pelvic exenteration in the study period, excision of the internal iliac vessels was required in 164 patients (49%) to achieve complete tumour resection. 21 patients (6.3%) underwent 29 en bloc excisions of an external or common iliac vessel for tumour involvement. Demographic and clinical characteristics for these 21 patients are summarised in Table 1. The median age was 58 years (range 36 - 79) and 57% of patients were female. Involvement of pelvic vascular structures was identified on preoperative imaging in 16 patients,
Pelvic exenteration complications while it was an intraoperative finding in 5 cases. Table 2 includes details of common and external iliac reconstructions performed in this series. Ten (48%), 3 (14%) and 8 (38%) patients had en bloc excision of vein, artery and both vein and artery, respectively. 21 vessel reconstructions were performed using interposition grafts (16 autologous, 5 synthetic), two had patch repair of the vessel and one was repaired primarily. The vessel could be excised without reconstruction in 5 patients because of pre-operative thrombotic occlusion. Mean intra-operative blood loss was 6.8L (range 1.0-16.0L) and the mean length of hospital stay was 30 days (range 4 - 80).

Clear resection margins (R0) were achieved in 38% of vascular patients vs. 78% of non-vascular reconstruction patients (p<0.001). On pathological analysis, there was tumour invasion or encasement of the vessel wall in 22 (76%) of the 29 excised vessels. Eight (38%) patients had R0 resection margins, while 11 and two patients had R1 and R2 margins, respectively. Of the 11 patients with R1 margins, 6 had involved margins at superior, distal or posterior margins away from the site of the iliac excision. Only seven were related to an involved lateral margin even more lateral to iliac vessel and in 4 of these 7, an even wider excision was precluded by bone (ilium or L5 vertebrae) or soft tissue through the sciatic notch. Of the two patients with R2 resection margins, both had localised tumour perforation with an abscess cavity that was not appreciable on pre-operative imaging and both had involved margins at the tumour cavity which was away from the iliac vessel itself.

The median overall and disease-free survival of patients undergoing en bloc excision of the common or external iliac vessels was 34 and 26 months, respectively.

Morbidity and Mortality
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There was no operative or 30-day mortality in patients undergoing vascular excision and reconstruction and overall patency and limb loss at one year was 96% and 0%, respectively. 17 (81%) patients had at least one postoperative complication (Table 3) although eight patients had a single minor complication that either did not prolong hospitalisation or only required medical management. Vascular specific complications occurred in 11 of 21 patients (52%). Of these 11 patients, five that required reintervention. The median time to reintervention was 2 days (range 0 - 24). Of those who underwent reintervention, one patient required evacuation of an abdominopelvic haematoma due to presumed bleeding from an autologous arterial graft anastomosis, however there was no active bleeding seen on intraoperative inspection of the vascular anastomosis. Another patient developed compartment syndrome in the leg ipsilateral to the arterial and venous reconstruction and underwent fasciotomy on day 1 after surgery. One patient haemorrhaged from dehiscence of a synthetic arterial graft due to secondary infection from an infected pelvic collection on day 24 and underwent emergency angiography and stent grafting. There were two patients that required reoperation for graft thrombosis. One underwent venous thrombectomy and insertion of an IVC filter for a thrombosed autologous venous graft. The second patient was found to have a pulseless, paralysed leg distal to the vascular reconstruction with paraesthesia and pain. Duplex ultrasound demonstrated thrombosis of the synthetic arterial graft and venous thrombosis distal to the point of ligation (without reconstruction). This patient underwent right common iliac artery and vein embolectomy with subsequent arterial femoral-femoral PTFE crossover graft and left great saphenous vein to right common femoral vein bypass graft. The other patients with vascular specific complications had a wound abscess at the vein harvest site (1), deep vein thrombosis at a site other than the reconstruction (2) and thrombosis of a venous reconstruction (3). Thrombosis of a venous graft occurred in five patients at a median of 2 days after surgery (range 0 - 9). Complications associated with arterial reconstructions (graft thrombosis, infection, dehiscence, compartment syndrome) occurred in 4 patients after a median time of 3.5 days (range 0 – 24).
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Compared to 315 exenteration patients who did not undergo external or common iliac vessel excision and reconstruction, mean intra-operative blood loss was significantly higher in patients who had vascular reconstruction (6.8 vs. 3.4L, p<0.001), and mean operating time was longer (but did not reach statistical significance, 631 vs. 531 min, p = 0.052). However, this did not translate to a difference in mean length of hospital stay (30 vs. 28 days, p = 0.597). There was also no difference in the rate of complications between groups (p = 0.130) or the median number of complications per patient (1 vs. 1, p = 0.859).

Discussion

This study reports outcomes of 21 patients who underwent en bloc excision and reconstruction of iliac vasculature during pelvic exenteration and contributes to existing reports that major vascular excision and reconstruction is feasible and safe. Not surprisingly, vascular excision and reconstruction is associated with a longer operating time and higher blood loss but importantly, there was no operative mortality. Vascular specific complications however, occurred in just over half the patients and 50% of these were significant enough to require a repeat intervention. Although the R0 rates were lower compared to patients that did not require vascular excision, 38% of patients who would have been otherwise palliated now stand a chance of cure. As much as we are encouraged by the improved R0 results from this study, the R0 rates remain considerably lower than that of patients who did not require en bloc vascular excision and even better surgical techniques as well as better patient selection are needed to improve surgical and oncological outcomes.

Traditionally, extensive tumour involvement of the pelvic sidewall or encasement of the common or external iliac vessels have been considered absolute contraindications to surgery. Within our
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unit, we have developed considerable experience with pelvic side wall excision including that of the internal iliac vessels but en bloc common or external iliac excision remains uncommon because these tumours are typically “higher” and “wider” and there are often other features on pre-operative staging that would preclude curative surgery. Therefore, this cohort of 21 patients represent a selected group of patients in a specialised centre. What the results of this study has demonstrated is that clear resection margins can be achieved in selected patients by en bloc resection of pelvic vascular structures during exenteration surgery (38% in the current series), and that major vascular reconstruction can be performed safely.

Median overall and disease-free survival of patients undergoing resection of tumours with common or external iliac vessel involvement was 34 months and 26 months, respectively. Although heterogeneous tumour biology within this relatively small patient sample prevents any certain conclusions about long term survival, these outcomes are comparable to the large pelvic exenteration series which report overall median survival in the range of 21-43 months.11-15 Further investigation of long term survival rates in this group of patients is warranted. Even with these early results in a highly selected patient group, what this case series demonstrates is that involvement of the iliac vasculature by itself should not be an absolute contraindication for consideration of surgery.

An approach to tumours involving the lateral pelvic sidewall has previously been described and early results with this technique included R0 resection in 53% of patients.8 A more recent series of 200 consecutive patients undergoing pelvic exenteration with lateral compartment involvement demonstrated R0 resection in 66% of patients (paper under peer review). In the current series, clear resection margins were achieved in 38% of patients with en bloc vascular resection and reconstruction compared to 78% in patients without vascular reconstruction (p<0.001). The lower
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R0 resection rate as well as the higher volume of blood loss and longer operation duration reflects the technically challenges that the pelvic sidewall presents to the operating surgeon and the more radical surgery that is required in this subgroup of patients. When the site of the involved margins were reviewed, what is clear is that it is invariably not the iliac vessel itself which determined the resection margins although it did increase the complexity of the procedure. What is clear on closer pathologic assessment of these specimens is that these are invariably extensive tumours with “higher” and “wider” involvement of other structures. It is possible also that the use of intraoperative radiation therapy (IORT) in patients with involved or close resection margins could reduce local recurrence, particularly those with R1, however this is not available at our institution. A recent case series by Abdelsattar and colleagues reported 12 patients who underwent radical resection of locally advanced and recurrent colorectal cancer involving the aorta or iliac vessels. The current series results are comparable to the Mayo Clinic experience, which reported 0% mortality at 30 days and a 75% morbidity rate.

The reconstruction technique for pelvic vascular structures after oncological resection is not well described. Small series and case reports have described reconstruction of iliac vasculature in the context of trauma, isolated nodal recurrence of colon cancer, and arterial graft infection, however there are few published reports of major vessel reconstruction in the setting of pelvic exenteration. Twenty-one (72%) vessel reconstructions in this series required an interposition graft of which 16 were autologous grafts (most were the superficial femoral vein). Given the lack of guidelines for these patients, it is preferred that established vascular principles are adhered to, including the use of autologous graft material in preference to synthetic material where possible, in order to reduce the risk of graft thrombosis or infection. This is particularly important during pelvic exenteration, where the operative field may be contaminated by multiple bowel resections. Despite this, the current series includes a significant number of vascular complications and five patients...
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required reintervention, most of which were in the first week of the postoperative period. In the past
our unit’s practice was to clamp the involved iliac vessels proximally and distally to gain
haemostatic control, complete en bloc tumour resection and commence vascular reconstruction
once the specimen was delivered. However, this practice has changed after a patient who developed
postoperative compartment syndrome requiring multiple right leg fasciotomies and skin grafting. It
is now preferred to reconstruct any involved vasculature immediately after they are divided even
before the specimen is delivered as long as there is adequate access for the vascular team to perform
their procedure. Abdelsattar and colleagues reported no graft-related complications, however in
their series there was only one venous reconstruction and reconstructions tended to involve larger
vessels (including the aorta) with higher flow rates, which may reduce the likelihood of distal
anastomosis thrombosis and graft failure. The use of anti-coagulation after venous reconstruction
can be helpful to prevent graft thrombosis but in exenteration patients, the use of anti-coagulation is
limited by concerns of ongoing ooze from the large raw surgical bed that can result in a large pelvic
haematoma. The seemingly high vascular specific complication rate may seem alarming at first.
However, these outcomes are comparable to contemporary series of vascular reconstruction during
sarcoma surgery where postoperative morbidity ranges from 36 - 71% and major wound healing
complications are reported in up to 68%. Reintervention rates vary from 8 to 50% and limb
salvage range from 84 – 100%.

In order to minimise morbidity, patients with extensive vascular involvement should undergo
thorough preoperative assessment by a specialist vascular surgeon and be considered at a specific
exenteration MDT meeting where likelihood of R0 resection is discussed and the sequence of
surgical specialities planned meticulously. Preoperative thromboembolic disease should be assessed
by clinical review and optimised by anticoagulation and IVC filter insertion where appropriate.
Duplex ultrasonography should be routinely performed to assess local vessel compression by the
Pelvic exenteration complications
tumour, detect venous thrombosis and assess lower limb luminal diameters for potential harvest and
grafting. A high index of suspicion should be maintained in the immediate postoperative period
with four hourly clinical limb assessments and duplex ultrasound studies of the lower limbs distal to
the graft such that graft-related complications are detected early and disastrous complications
avoided. Extended antibiotic prophylaxis should be administered where graft reconstruction has
been performed concomitantly with bowel resection. The use of spiral great saphenous autologous
grafts tailored to the resected vessel diameter is currently being tested in our unit as an alternative to
the superficial common femoral vein. 26

The limitations of this study are the highly selective nature of this series. The heterogeneous tumour
biology within this relatively small patient sample limits our ability to draw definite conclusions
about long term survival. There are also practical limitations in follow up for interstate and
international patients that could have led to potential under reporting of complications following
discharge, however most patients within this sample are enrolled in our main prospective quality of
life study which would have capture ongoing health service utilisation and therefore complications
or readmissions after discharge.

Conclusion
En bloc vascular resection and reconstruction is safe and feasible when performed at specialised
institutions albeit the accompanying morbidity rates. Ongoing studies are required to clarify
indications but within the confines of this early experience, these results are encouraging and in our
opinion, iliac vasculature involvement by itself should not constitute absolute contraindication for
an attempt at curative surgery although case selection is paramount.
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Acknowledgements

The authors thank Lindy Maysa and Rachael Roberts for assistance with data collection.

References


Pelvic exenteration complications

**Table 1.** Demographic information for patients undergoing vascular excision and reconstruction (n=21)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n</th>
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<tbody>
<tr>
<td><strong>Age</strong></td>
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<td>&lt;70</td>
<td>19</td>
</tr>
<tr>
<td>&gt;70</td>
<td>2</td>
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<tr>
<td><strong>Gender</strong></td>
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<tr>
<td>Male</td>
<td>9</td>
</tr>
<tr>
<td>Female</td>
<td>12</td>
</tr>
<tr>
<td><strong>Resection intent</strong></td>
<td></td>
</tr>
<tr>
<td>Curative</td>
<td>17</td>
</tr>
<tr>
<td>Palliative</td>
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<tr>
<td><strong>Cancer presentation</strong></td>
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</tr>
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</tr>
<tr>
<td>Primary</td>
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<tr>
<td>Recurrent</td>
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</tr>
<tr>
<td>Re-recurrent</td>
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</tr>
<tr>
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</tr>
<tr>
<td>Leiomyosarcoma (recurrent)</td>
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</tr>
<tr>
<td>Squamous cell carcinoma</td>
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</tr>
<tr>
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</tr>
<tr>
<td>Retroperitoneal sarcoma</td>
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</tr>
<tr>
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<tr>
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</tr>
<tr>
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</tr>
<tr>
<td>Prior &gt; 2 years</td>
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<td><strong>Chemotherapy</strong></td>
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</tr>
<tr>
<td>No</td>
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<tr>
<td><strong>Previous thromboembolic disease</strong></td>
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<tr>
<td>No</td>
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</tr>
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<td><strong>Preoperative anticoagulation</strong></td>
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</tr>
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<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>No</td>
<td>16</td>
</tr>
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<td><strong>Margin status</strong></td>
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</tr>
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<td>R0</td>
<td>8</td>
</tr>
<tr>
<td>R1</td>
<td>11</td>
</tr>
<tr>
<td>R2</td>
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</tr>
<tr>
<td><strong>Blood loss, mean (range), L</strong></td>
<td>6.8 (1.0-16.0)</td>
</tr>
<tr>
<td><strong>Length of operation, mean (range), min</strong></td>
<td>631 (220-1145)</td>
</tr>
<tr>
<td><strong>Length of stay, mean (range), day</strong></td>
<td>30 (4-80)</td>
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### Table 2. Details of vessel excision and reconstruction

<table>
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<tr>
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<th>Arterial (n=11)</th>
<th>Venous (n=18)</th>
<th>Total (n=29)</th>
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</tr>
<tr>
<td>Primary repair</td>
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</tr>
<tr>
<td>Patch</td>
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<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Interposition graft</td>
<td>10</td>
<td>11</td>
<td>21</td>
</tr>
<tr>
<td>Ligation without reconstruction</td>
<td>1</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>Reconstruction material†</strong></td>
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<td></td>
</tr>
<tr>
<td>Synthetic</td>
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</tr>
<tr>
<td>PTFE</td>
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</tr>
<tr>
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<td>18</td>
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<tr>
<td>GSV</td>
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</tr>
<tr>
<td>IIV</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Vessel involvement by tumour</strong></td>
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<td></td>
</tr>
<tr>
<td>Wall involvement</td>
<td>10</td>
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</tr>
<tr>
<td>No involvement</td>
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<td>5</td>
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<tr>
<td>Missing</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

† n = 23 interposition grafts or patch repairs (i.e. not primary repair)

SFV, superficial femoral vein; GSV, great saphenous vein; IIA, internal iliac artery; IIV, internal iliac vein; PTFE, polytetrafluoroethylene
Pelvic exenteration complications

**Table 3. Postoperative Complications for Pelvic Exenteration with Vascular Reconstruction (n=21)**

<table>
<thead>
<tr>
<th>Complication</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>7</td>
<td>33</td>
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<tr>
<td>Stoma</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Neurological</td>
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<td>19</td>
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<tr>
<td>Cardiovascular</td>
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<td>24</td>
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<tr>
<td>Respiratory</td>
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<td>5</td>
</tr>
<tr>
<td>Sepsis</td>
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<td>33</td>
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<tr>
<td>Vascular</td>
<td>11</td>
<td>52</td>
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<tr>
<td>Thrombosis of reconstructed vessel</td>
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</tr>
<tr>
<td>Arterial†</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Venous§</td>
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<td>36</td>
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<tr>
<td>Graft infection‡</td>
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<td>4</td>
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<tr>
<td>Deep vein thrombosis*</td>
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<td>10</td>
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<tr>
<td>Pelvic haematoma</td>
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<td>10</td>
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<tr>
<td>Wound healing complication</td>
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<tr>
<td>Compartment syndrome</td>
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<tr>
<td><strong>Reoperation (n=5)</strong></td>
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<tr>
<td>Thrombectomy</td>
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<tr>
<td>Evacuation pelvic haematoma</td>
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<td></td>
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<tr>
<td>Graft stent insertion</td>
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<td></td>
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<tr>
<td>Fasciotomy</td>
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</table>

†n = 10 arterial reconstructions
§n = 14 venous reconstructions
‡n = 23 interposition grafts or patch repairs (i.e. not primary repair)
*At site other than graft (i.e. not thrombosis of reconstructed vessel)
Pelvic exenteration complications

CHAPTER 4.1

Spiral saphenous vein graft for major pelvic vessel reconstruction during exenteration surgery

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Published Annals of Vascular Surgery:

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Abstract

This article describes a great saphenous vein spiral graft technique for reconstruction of iliac vessels following en bloc resection during pelvic exenteration. Use of different size syringes as a scaffold allows the surgeon to construct autologous vascular interposition conduits of variable diameter to match the luminal size of the vessel requiring reconstruction. Autologous vascular grafts are preferred in exenteration surgery where the operative field is commonly contaminated by concomitant bowel resection, which carries an increased risk of graft infection.

Keywords: Pelvic exenteration; Vascular Reconstruction; Interposition graft; common iliac artery reconstruction
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**Introduction**

Multi-visceral en bloc resection with a view to clear resection margins is a key oncological principle in the management of locally advanced or recurrent cancers. Where there is contiguous tumour involvement of a major abdominal or pelvic vessel, en bloc vascular resection is performed with subsequent vessel reconstruction. Vascular reconstruction can be challenging in the presence of bowel and bladder resection where the operative field may be contaminated. The use of a synthetic vascular conduit in these circumstances is suboptimal because of the potential for graft infection, which can result in disastrous complications. However, this often proves necessary due to the major discrepancies in luminal circumference that autologous options may present and the additional concerns with leg oedema as a result of harvesting in post radiotherapy pelvises. This article describes a simple but effective spiral autologous graft technique that is used in our unit for the reconstruction of iliac vessels following pelvic exenteration.

**Case Presentation**

Figure 1 is a coronal MRI view of a 36-year-old man that shows a large retroperitoneal leiomyosarcoma. The patient presented with a sensation of abdominal fullness, distension and a palpable abdominal mass. There was compression flattening of the right psoas muscle and encasement of the right common iliac artery (CIA) and vein (CIV) and the right ureter. The tumour measured 14.2 cm by 9.9 cm axially and the superior mesenteric artery (SMA) lay centrally within the lesion. No bony invasion was evident and no metastases were identified. The case was reviewed at a specialised MDT (multi-disciplinary team) meeting and it was decided to proceed with surgical resection of the tumour with a plan for likely en bloc excision and reconstruction of the right CIA and CIV.
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At laparotomy, the terminal ileum was adherent to and invaded by the tumour requiring en bloc resection of approximately 50cm of small bowel with the tumour. The sigmoid mesentery was intimately involved and was divided along the margin of the tumour, requiring resection of that segment of sigmoid colon. The SMA and ileocolic vessels were able to be dissected free of the tumour, while the right CIA and CIV were involved and to be removed en bloc with the specimen. The right ureter was also divided and a right nephrectomy performed.

Bilateral GSV (great saphenous vein) harvest was performed and two spiral grafts were constructed using the technique described below (fig. 2) while the abdominal dissection was carried out. For reconstruction of the right CIA, a GSV spiral graft was constructed using a 5ml syringe and another for the right CIV using a 10ml syringe. The involved vessels were clamped and divided, allowing delivery of the specimen and reconstruction using the previously prepared interposition spiral grafts was performed. Figures 3 and 4 are intraoperative photographs showing the right CIV and CIA spiral interposition grafts in situ. After vascular reconstruction was complete and vessel clamps removed a high anterior resection was performed. Postoperatively, the patient had full-length compression stockings applied and was commenced on heparin (5000 units TDS). Lower limb circulation observations were performed four hourly in the immediate postoperative period to identify early limb ischaemia. Anticoagulation with warfarin was commenced postoperatively and prophylactic antibiotics were continued for five days.

The patient experienced prolonged ileus postoperatively and required 13 days of total parenteral nutrition. He was discharged from hospital on day 21 after an otherwise unremarkable recovery and no concerns from a vascular perspective. At 5 months the patients ileostomy was reversed and duplex ultrasound confirmed that both arterial and venous spiral grafts were patent with no stenosis. Locally recurrent disease was demonstrated in the small bowel mesentery on a PET scan at 6
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months. The recurrent tumour was resected requiring small bowel resection and anastomosis leaving the patient disease free. Since the patient had patent grafts and no limb symptoms warfarin was ceased and low dose aspirin commenced.

**GSV Harvest and Spiral Graft Construction**

The length of GSV required can be accurately calculated by previously described methods according the formula $2\pi r^1$ and is based on estimated luminal diametres on preoperative imaging. It has been our practice to harvest a longer section of GSV than is required and trim the conduit to the exact length required at laparotomy. The graft is prepared by ligating all tributaries. The harvested vein is incised longitudinally and all valves are excised. The rectangular patch is wrapped around a syringe in a spiral fashion and the cut edges are sutured together using 5.0 or 6.0 polypropylene suture to form a cylindrical interposition vascular conduit (fig. 2). Depending on the size of the vessel being reconstructed, the diameter of the conduit can be tailored by using different size syringes as a scaffold. For reconstruction of a CIA, a 3 or 5 ml syringe with an approximate 5 mm diameter is used as a scaffold while reconstruction of a CIV typically requires either a 5 ml or a 10 ml syringe. Alternatively a chest tube can be used as the scaffold. The conduit can then be trimmed to form a cylindrical tube graft. Proximal and distal anastomoses are performed with 5.0 or 6.0 polypropylene sutures. For tumours involving both iliac artery and vein, bilateral GSV harvest is performed and two spiral grafts are constructed using the technique described.

In order to maintain patency of the venous graft, a temporary arterio-venous fistula can be fashioned in the groin. A tributary of the GSV and common femoral artery are anastomosed in an end-to-side fashion using 7-0 polypropylene suture. A 3.0 nylon suture is left lying around the fistula as a landmark for subsequent reversal at a later stage if required. Warfarin is used for a period of six months and then change to low dose aspirin if patency is maintained.
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Ethical approval was granted by Sydney Local Health District (RPAH Zone) human research ethics committee and patient consent was obtained for the use of clinical imaging and photographs.

**Discussion**

Autologous grafts remain the preferred choice for vascular reconstruction primarily due to their low thrombogenicity and resistance to infection. However, there are limitations to the use of autologous grafts as there are few vessels that can be readily sacrificed without significant functional sequelae. As far as vascular reconstruction is concerned, GSV is the workhorse of all autologous grafts and has been used successfully for vascular reconstruction after resection of lower limb tumours, however its use for reconstruction of the pelvic vasculature is limited by major discrepancies in luminal calibre. Due to the lack of vessels of similar calibre that are suitable for autologous grafting surgeons have used biological alternatives such as bovine pericardium or even synthetic grafts for cancer resections involving the portal vein, aorta and inferior vena cava. Autologous grafts are preferred, particularly in pelvic exenteration, because of the high prevalence of septic complications following these procedures where the operative field is typically contaminated by gastrointestinal or genitourinary organisms. While bovine pericardium is of low thrombogenicity, it is costly. Synthetic graft material is manufactured in specific sizes and custom-designed grafts are expensive. In addition, the use of synthetic grafts in contaminated fields increases the risk of graft infection and failure. Autologous peritoneo-fascial grafts have also been used as a biological alternative for major venous reconstruction with low graft-related morbidity and may be a suitable option for reconstruction of pelvic vasculature.

Patients referred for consideration of pelvic exenteration are discussed at a MDT meeting comprising of colorectal, vascular, orthopaedic, urological surgeons as well as medical and
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radiation oncologists and a senior radiologist. Tumour resectability is determined with pre-operative MRI, which also guides decision-making about the extent of pelvic sidewall resection required. Tumours with suspected contiguous common or external iliac artery or vein involvement are further assessed using CT or MR angiography or venography to confirm vessel involvement. These patients also routinely undergo duplex mapping of their great saphenous and femoral venous systems to determine suitability as an autologous vascular graft. An operative approach to tumours involving the lateral pelvic sidewall with en bloc iliac vessel resection has previously been described\(^7\) and contiguously involved common or external iliac vessels are excised en bloc with the tumour. The method of vessel reconstruction used is dependent on vascular surgeon preference, availability of lower limb vessels for grafting and the luminal diameter of the vessel requiring reconstruction. Where possible, the GSV is harvested and grafts constructed on a back table prior to delivery of the specimen, however this often proves difficult due to limited access to the limb when operating in the pelvis at the same time.

Chiu and colleagues originally described the spiral vein graft in 1974 for the reconstruction of the superior vena cava\(^8\). More recently the versatility of this technique has been demonstrated in its use for reconstruction of the aorta\(^1\) and portal vein\(^9\). In our experience with common iliac reconstruction, the GSV spiral graft is useful in that it is autologous, can be tailored to suit vessels with different diameters by use of different size syringes as scaffolds and avoids harvest of the superficial femoral vein (SFV)\(^10\). A SFV autologous graft has been routinely used by our unit in the past, however this then relies solely on the profunda veins for deep venous drainage of the lower limb and carries a greater concern for leg oedema following harvest, particularly in the setting of previous or neoadjuvant preoperative radiotherapy as well as prior resection of primary cancers. Abdelsattar and colleagues\(^5\) recently reported the use of synthetic interposition grafts, femoral-femoral bypass and primary anastomosis for reconstruction of the aortioiliac axis after resection of
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colorectal cancer. Similar techniques have been described in case reports\textsuperscript{11,12}, however these do not offer the advantage of an exactly matched luminal size of the graft with the vessel requiring reconstruction.

**Conclusion**

The autologous GSV spiral graft allows the surgeon to construct a conduit of specific diameter by use of different size syringes as scaffolds for the reconstruction of a vessel of a particular diameter. The use of an autologous graft may reduce the risk of graft thrombosis and infection in a contaminated operative field.

**References**


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Figure 1. Magnetic resonance imaging view of a patient with a retroperitoneal leiomyosarcoma.

Figure 2. Construction of the GSV spiral graft. The rectangular patch is wrapped around a syringe in a spiral fashion and cut edges are sutured together.
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**Figure 3.** In situ GSV spiral graft (arrows) reconstruction of the right CIV. The left CIV is visible, as are the left CIA and left ureter (vessel loops).

**Figure 4.** In situ GSV spiral graft (arrows) reconstruction of the right CIA overlying the reconstructed right CIV.
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CHAPTER 4.2

Posterior high sacral segmental disconnection prior to anterior en bloc exenteration for recurrent rectal cancer

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Published in Techniques in Coloproctology:
Pelvic exenteration complications

Abstract
This article describes a novel technique for en bloc resection of locally recurrent rectal cancer that invades the high sacral bone (above S3). The involved segment of sacrum is mobilised with osteotomes during an initial posterior approach before an anterior abdominal phase where the segment of sacral bone is delivered with the specimen. This allows en bloc resection of the involved sacrum while preserving uninvolved distal and contralateral sacral bone and nerve roots. The goal is to obtain a clear bony margin and offer a chance of cure while improving functional outcomes by maintaining pelvic stability and minimising neurological deficit.
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Introduction

Achieving complete oncological (R0) resection is the most important predictor of long-term survival in patients undergoing curative surgery for recurrent rectal cancer. The ongoing evolution of surgical techniques for ‘higher and wider’ multivisceral resections has been driven by surgeons seeking the ultimate goal of R0 resection, which is now the key consideration when deciding what constitutes ‘resectable’ disease. High sacral bone involvement remains controversial, and although en bloc high sacrectomy has been shown to be safe and oncologically feasible in several specialist centres, concerns remain about pelvic instability and the need for subsequent reconstruction, as well as postoperative neurological deficits associated with sacrifice of sacral nerve roots. This article describes a novel technique for en bloc resection of the involved segment of the sacral bone and nerve roots only, rather than the traditional sacral amputation, with a view to preserving uninvolved distal and contralateral sacral bone and nerve roots.

Case Presentation

A 51-year-old man was referred to our unit with locally recurrent rectal cancer causing left sided intractable sciatica and weakness of ankle plantar flexion. He had previously undergone a staged anterior resection for rectal cancer and resection of a single liver metastasis after which he remained disease free for seven years. Pelvic MRI demonstrated isolated recurrence at the high rectal anastomosis extending posteriorly and laterally with invasion of the left sacrum from mid-S1 to S2/3 levels (fig. 1), encasement of the left S1 and S2 nerve roots and involving the left piriformis muscle and internal iliac vessels. The left L5 was not involved nor were any of the right sacral nerve roots. The patient was reviewed at the pelvic exenteration multi-disciplinary team meeting and, given that high total sacrectomy was the only alternative, after neoadjuvant chemoradiotherapy he proceeded to surgery with a plan to resect the involved S1-S3 vertebrae of the left hemisacrum and left sided nerve roots en bloc with the rectum and left pelvic sidewall. The aim was to preserve the left L5, S3 and S4
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nerves as well as all right sacral nerve roots to preserve the majority of lower limb motor as well as bladder function.

Informed consent was obtained from all individual participants included in the study including the patient.

**Technique**

The technique includes an initial posterior prone approach followed by an abdominal approach.

*Posterior phase*

The patient was placed in the prone position and a dorsal longitudinal skin incision made from the level of L3 to S4 in the midline. Subperiosteal dissection was carried out bilaterally over L5 and continued on the dorsal aspect of the sacrum to S3, mobilising the gluteus maximus muscle at its attachment. Dissection continued further laterally on the left to expose the lateral margin of the sacrum. A wide laminectomy over the left hemisacrum was performed from S1 to S3. The left S1 and S2 nerve roots were individually ligated and divided medial to the tumour while the L5 root was able to be preserved.

With careful reference to preoperative imaging and anatomical landmarks (i.e. sacral foramina and the median sacral crest) partial thickness transverse osteotomies were performed with an osteotome at a level just distal to the superior end plate of S1 and through the middle of the body of S3 (fig. 1). At this point intraoperative radiography was used to confirm the appropriate sacral levels. The osteotomy was extended vertically in the midline, deep to the remaining cauda equina, and a further longitudinal osteotomy was performed laterally through the sacrum. After again confirming osteotomy sites with intraoperative radiography and reference to preoperative MRI, completion of the
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osteotomy was performed carefully, stopping when the anterior cortical bone of the sacrum was breeched to prevent injury to iliac vasculature and other presacral structures. This then enabled the involved bony segment to become mobile with only some remaining anterior sacral soft tissue. Hence, the involved left S1-S3 segment of sacral bone containing tumour was mobile, ready for the completion and delivery via the anterior approach and thus maintaining the mechanical integrity of the sacrum. Given the lack of proximal vascular control, this phase of the operation required meticulous dissection to avoid inadvertent injury to internal iliac and presacral vasculature.

Abdominal phase

The patient was turned and placed in the modified Lloyd-Davies position and a midline laparotomy performed. This phase of the operation has been previously described\textsuperscript{4-6}. In summary, the residual left colon was transected proximal to the neorectum and bilateral ureterolysis performed. The left pelvic sidewall was dissected\textsuperscript{6}, with ligation and division of the anterior division of the left internal iliac artery (preserving the superior gluteal artery) and internal iliac vein and its tributaries. L5 was identified, dissected free and protected and the S1 nerve root was transected to free the L5 nerve root throughout its course. The presacral fascia was incised and the posterior osteotomies identified and joined circumferentially (fig. 2). A redo ultra-low anterior resection was performed and the specimen (fig. 3) was delivered through the abdominal wound.

Postoperatively the patient had a complete left S1-2 nerve root palsy and normal motor function in the right lower limb. He was able to mobilise independently at the time of discharge on day 23 after surgery. Pathological examination of the specimen demonstrated complete oncological resection.

Discussion
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More recent experiences with high sacrectomy at specialised centres have produced encouraging oncological and survival outcomes in patients with locally advanced or recurrent rectal cancer\textsuperscript{4,5}, who were traditionally excluded from curative surgery\textsuperscript{2,7}. High sacral bone involvement should not represent an absolute contraindication to surgery, however the procedure may carry significant morbidity, particularly when S1 and S2 nerve roots are sacrificed\textsuperscript{4,8}.

Modified approaches to traditional sacral amputation have been developed with a view to reducing morbidity and improving function while still achieving a safe resection margin. These include sacrectomy via the abdominal approach to avoid a prone phase in selected patients, hemisacrectomy with preservation of contralateral sacral nerves, and resection of the anterior cortical plate only of the sacrum to preserve the nerve roots and posterior bone\textsuperscript{9-12}. The technique described in this report may be useful as a less morbid alternative to high sacral amputation in selected patients with focal involvement of the high sacrum. Resecting only the involved segment allows preservation of distal and contralateral sacral nerve roots and also maintains sacropelvic stability. By doing the prone phase first followed by the abdominal phase (with specimen delivery from the front) a smaller ‘segmental sacrectomy’ is possible without complete amputation, where the size of the specimen would prevent removal through the smaller sacrectomy.

The main limitation of this technique is that the posterior approach must be done first, with limited vascular control, to allow delivery of the specimen. Furthermore, determination of the osteotomy sites to achieve complete oncological resection is based on preoperative MRI and requires specialised multi-disciplinary team input. This approach should therefore be considered only in highly selected patients at specialised centres with expertise in reoperative pelvic surgery and composite sacral resection.
References


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**Figure 1.** Axial (A) and sagittal (B) magnetic resonance imaging views of a patient with recurrent rectal cancer involving the left sacrum at S1 and S2 levels. Osteotomy sites are shown (white lines).
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**Figure 2.** Anterior view of the bony sacral defect after delivery of the specimen during the abdominal phase. Left common and external iliac veins are seen with blue vessel loops. Divided ends of the left internal iliac vein and artery are seen.

**Figure 3.** Tumour involving sacral bone (horizontal arrow), nerve roots and neorectum. The left internal iliac artery is also visualised (vertical arrow)
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**THESIS DISCUSSION**

Pelvic exenteration involves en bloc resection of multiple pelvic organs, often with excision of neurovascular and bony tissues at the periphery of the pelvis with complex reconstruction, and may be associated with significant postoperative morbidity. While patients who underwent pelvic exenteration under pioneering surgeons in the 1950s and 1960s experienced remarkably high rates of morbidity and mortality (chapter 1), contemporary literature suggests that pelvic exenteration offers a chance of cure to patients who would otherwise be palliated, and can be performed with acceptable morbidity and quality of life\(^1\,^2\). This thesis aimed to investigate rates of postoperative complications in patients who underwent radical pelvic surgery at the pelvic exenteration unit at Royal Prince Alfred Hospital, Sydney, since the unit was established in 1994. The major findings presented in chapter 2 are that the rate of urinary conduit-associated complications, especially urinary leaks and sepsis, are higher after pelvic exenteration than after cystectomy alone for primary bladder malignancy. Several factors may contribute to the higher rate of urological morbidity, including a history of pelvic irradiation, major intraoperative blood loss, cardiac disease, diabetes mellitus, as well as the type of urinary reconstruction. Chapter 3 found that en bloc lateral pelvic compartment excision allows complete oncological resection in 69% of patients undergoing planned curative surgery with acceptable postoperative morbidity (major and minor complication rates were 28% and 79%, respectively) and demonstrated that en bloc excision and reconstruction of the common or external iliac vessels is feasible, with no intraoperative or 30-day mortality, 96% overall graft patency at 1 year and 0% limb loss in a group of 21 patients. Chapter 4 described two novel techniques developed at the RPA exenteration unit (spiral saphenous vein graft for reconstruction of major pelvic vessels and segmental sacrectomy for tumours with high sacral involvement) in an attempt to reduce postoperative morbidity.
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In contemporary literature, en bloc cystectomy is required in 20-53% of patients undergoing pelvic exenteration\textsuperscript{3-5}. Russo and colleagues reported a urological morbidity rate of 17% in a cohort of 47 patients who underwent urinary diversion in the context of pelvic exenteration\textsuperscript{6}, which included two patients with urine leakage from the uretero-ileal anastomosis. Similar experiences have been reported by other centres with urological morbidity rates between 9 and 24% for ileal or colonic conduit reconstruction, and urinary leak rates between 7 and 16% (chapter 1, table 1)\textsuperscript{4,7-9}. The study presented in chapter 2 reported an overall conduit-related complication rate of 59% after exenteration (48% for patients with primary malignancies and 67% for patients with recurrent tumours, \textit{P}=0.035). This rate would appear higher than those published by other exenteration units, however most studies have not included rates of urinary tract infection or urosepsis which occurred in 21 and 50% of patients who had pelvic exenteration for primary and recurrent tumours, respectively, in this thesis. Khan and colleagues recently presented a series of 60 patients undergoing urinary reconstruction in the context of pelvic exenteration for rectal cancer, reporting a postoperative urological morbidity of 55% and a urinary tract infection rate 37%, figures which are more consistent with the results of our study\textsuperscript{10}. Other recent series by Goldberg and Tan have documented rates of urinary tract infections of 25 and 36%, respectively\textsuperscript{8,11}.

It remains unclear which patient or operative factors may predict urological morbidity. Preoperative pelvic radiation therapy has been associated with higher rates of urological morbidity following exenteration in gynaecological literature\textsuperscript{12}, however in a series of 126 patients with en bloc resection of urological organs (including 80% with a urinary conduit), Stotland and colleagues found no association between radiotherapy and urological morbidity (\textit{P} = 0.61)\textsuperscript{13}. In this thesis major blood loss and prior pelvic radiotherapy independently predicted conduit-associated complications after pelvic exenteration (\textit{P}= 0.002 and 0.035), and cardiac disease, diabetes, as well as type of urinary reconstruction have been implicated.
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Urinary leaks remain a major challenge in pelvic exenteration patients, with implications for length of stay and possibly long term patient survival. In this thesis the rate of postoperative urinary leak was 3% in cystectomy patients and 11% in pelvic exenteration patients (6% for primary tumours, 14% for recurrent tumours). A higher incidence of urinary leaks after pelvic exenteration surgery is in keeping with recent literature, with rates up to 20% documented by other authors (chapter 1, table 1). Interestingly, there was no difference in the rate of urine leaks between the PE for primary malignancy and cystectomy alone group (P = 0.395) in this thesis. It is likely that the higher morbidity after exenteration carried out for recurrent cancer reflects the more advanced disease and the more complex nature of treatment (radiotherapy and major re-operative surgery), rather than the extent of the resection alone. Small numbers of patients with urinary leaks prevented identification of any significant predictors of urinary leaks.

In the ongoing pursuit of clear margins, some specialised units have developed experience with even ‘higher and wider’ lateral resections for tumour involvement of the common and external iliac vessel, and extending to the sciatic nerve and ischial bone (chapter 3). Abdelsattar and colleagues at the Mayo clinic reported R0 resection in 7 of 12 patients undergoing en bloc resection and reconstruction of the aorta or iliac vessels with no 30-day mortality, 75% morbidity and 100% graft patency at 4 years. Chapter 3.2 presented a series of 21 patients requiring common or external iliac vessel resection and reconstruction which produced an R0 resection rate of 38% and a median overall survival of 34 months. Postoperative complications related to the vascular reconstruction were significant, occurring in 52% of patients with 24% of patients returning to theatre. However, importantly the overall graft patency at 1 year was 96%, limb loss was 0% and there was no intraoperative or 30-day mortality. These series represent selected subgroups of patients at specialized units and suggest that radical vascular excision and reconstruction may be performed
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safely in this setting. Improved surgical techniques and patient selection are critical if such radical resections are to adopted routinely. Investigation of vascular reconstruction techniques after iliac vessel excision is ongoing and includes the novel use of saphenous vein spiral grafts (chapter 4.1) and bovine pericardium.

Recently several specialised exenteration units have demonstrated the feasibility of high sacrectomy (above the S3 vertebrae)\textsuperscript{14,15}. If the level of sacral transection is below the level of the sacroiliac joint (below S3), the sacrectomy is performed trans-abdominally using osteotomes\textsuperscript{16}, giving better access to the pelvic sidewall and control of the iliac vasculature, and permits a more lateral dissection of the sciatic nerve as it traverses lateral to the greater sciatic foramen. For more proximal sacral bone involvement the patient is turned prone after the abdominoperineal phase for traditional prone sacrectomy. In contemporary literature high sacrectomy, although still controversial, has been shown to produce 5-year survival rates between 38 and 43% (chapter 1, table 2).

In an attempt to reduce the morbidity associated with nerve sacrifice and pelvic instability after traditional sacrectomy, several new techniques have been developed including abdominal sacrectomy\textsuperscript{16}, hemisacrectomy\textsuperscript{17}, and resection of the anterior cortical plate only of the sacrum\textsuperscript{18}. A novel technique for tumours invading high sacral bone described in chapter 4.2 involves posterior mobilisation of the involved sacral segment with osteotomes followed by a completion abdominal approach where the segment of sacral bone is excised en bloc with the pelvic mass. This minimises nerve root sacrifice and preserves mechanical integrity of the pelvis.
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The majority of pelvic exenteration patients will require both a permanent colostomy and urostomy and experience loss of sexual function, with many undergoing prolonged periods of rehabilitation. Furthermore, major bony or neurovascular resections may impair lower limb function and therefore limit mobilisation. The potential morbidity associated with this radical surgery which has been investigated in this thesis has obvious implications for postoperative QoL which, in addition to any anticipated survival benefit, must be weighed against the QoL and survival that can be expected when a palliative approach is adopted. As increasingly radical resections are performed, including high sacrectomy, lateral neurovascular excision and hemipelvectomy, it becomes increasingly important to establish what constitutes an ‘acceptable’ postoperative QoL from an individual patient’s perspective. While survival advantages of pelvic exenteration have been confirmed, contemporary literature reporting QoL after pelvic exenteration is limited. This represents a gap in the literature and requires further investigation to improve patient selection and surgical decision making.

References

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Chapter 1 titled “Pelvic exenteration surgery: the evolution of radical surgical techniques for advanced and recurrent pelvic malignancy” has been submitted for publication. The nature of the candidate’s contribution is as follows:
- Study concept and design
- Manuscript preparation and drafting
- Final approval of manuscript

The nature of contribution by the co-authors is as follows:
Prof Michael Solomon – study concept and design, preparation of manuscript, final approval of manuscript
Dr Cherry Koh - study concept and design, critical revision of manuscript, final approval of manuscript

Chapter 2 titled “Urological complications after cystectomy as part of pelvic exenteration are higher than that after cystectomy for primary bladder malignancy” has been submitted for publication. The nature of the candidate’s contribution is as follows:
- Study concept and design
- Data collection and analysis
- Data interpretation
- Manuscript preparation and drafting
- Final approval of manuscript

The nature of contribution by the co-authors is as follows:
Prof Michael Solomon – study concept and design, data interpretation, critical revision of manuscript, final approval of manuscript
Dr Edward Latif – study concept and design, data collection, critical revision of manuscript, final approval of manuscript
Dr Cherry Koh – study concept and design, data interpretation, critical revision of manuscript, final approval of manuscript
Dr Arthur Vasilaras – study concept and design, critical revision of manuscript, final approval of manuscript
Dr David Eisinger – study concept and design, critical revision of manuscript, final approval of manuscript
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A/Prof Paul Sved – study concept and design, data interpretation, critical revision of manuscript, final approval of manuscript

Chapter 3.1 titled “Lateral pelvic compartment excision during pelvic exenteration” has been published. The nature of the candidate’s contribution is as follows:

- Study concept and design
- Data collection and analysis
- Data interpretation
- Manuscript preparation and drafting
- Final approval of manuscript

The nature of contribution by the co-authors is as follows:

Prof Michael Solomon - study concept and design, data analysis, data interpretation, manuscript preparation and drafting, final approval of manuscript
Dr Cherry Koh - study concept and design, data collection and analysis, data interpretation, manuscript preparation and drafting, final approval of manuscript
Dr Peter Lee - study concept and design, data interpretation, critical revision of manuscript, final approval of manuscript
Dr Kirk Austin - study concept and design, data interpretation, critical revision of manuscript, final approval of manuscript
Ms Lindy Masya - data collection, data interpretation, critical revision of manuscript, final approval of manuscript

Chapter 3.2 titled “Outcomes following en bloc iliac vessel excision and reconstruction during pelvic exenteration” has been published. The nature of the candidate’s contribution is as follows:

- Study concept and design
- Data collection and analysis
- Data interpretation
- Manuscript preparation and drafting
- Final approval of manuscript

The nature of contribution by the co-authors is as follows:

Dr Cherry Koh - study concept and design, data collection and analysis, data interpretation, manuscript preparation and drafting, final approval of manuscript
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Dr David Robinson - study concept and design, data interpretation, critical revision of manuscript, final approval of manuscript
Dr Steven Dubenec - study concept and design, data interpretation, critical revision of manuscript, final approval of manuscript

Chapter 4.1 titled “Spiral saphenous vein graft for major pelvic vessel reconstruction during exenteration surgery” has been published. The nature of the candidate’s contribution is as follows:

- Study concept and design
- Data collection and analysis
- Data interpretation
- Manuscript preparation and drafting
- Final approval of manuscript

The nature of contribution by the co-authors is as follows:
Dr Cherry Koh - study concept and design, data collection and analysis, data interpretation, manuscript preparation and drafting, final approval of manuscript
Prof Michael Solomon - study concept and design, data interpretation, critical revision of manuscript, final approval of manuscript
Dr Ian Choy - study concept and design, data interpretation, critical revision of manuscript, final approval of manuscript
Dr Steven Dubenec - study concept and design, data interpretation, critical revision of manuscript, final approval of manuscript

Chapter 4.2 titled “Posterior high sacral segmental disconnection prior to anterior en bloc exenteration for recurrent rectal cancer” has been published. The nature of the candidate’s contribution is as follows:

- Study concept and design
- Data collection and analysis
- Data interpretation
- Manuscript preparation and drafting
- Final approval of manuscript

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Prof Michael Solomon - study concept and design, data interpretation, critical revision of manuscript, final approval of manuscript
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Dr Peter Lee - study concept and design, data interpretation, critical revision of manuscript, final approval of manuscript
Dr Paul Stalley - study concept and design, data interpretation, manuscript preparation and drafting, final approval of manuscript

Candidate’s signature:

Dr Kilian Brown

7th March 2017
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**Declaration by co-authors:**

The undersigned certify that the above declaration accurately reflects the nature of the candidate's contribution to the work presented in this thesis and the contribution of each of the co-authors.

There are no other authors of the publications. Conflicts of interest and sources of funding have been disclosed to the editor of the academic journals.

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Dr Arthur Vasilaras  
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Dr David Eisinger  
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A/Prof Paul Sved  
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Ms Lindy Masya  
Dr David Robinson  
Dr Paul Stalley  
Dr Steven Dubeneck
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Dr Ian Choy

Dr Edward Latif
APPENDIX 2: Additional publications relevant to this thesis but not forming part of it

Clinical algorithms for the diagnosis and management of urological leaks following pelvic exenteration

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Published in European Journal of Surgical Oncology:

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Abstract

Background: Urine leak following pelvic exenteration for locally advanced pelvic malignancy is a major complication leading to increased mortality, morbidity and length of stay. We reviewed our experience and developed a diagnostic and management algorithm for urine leaks in this patient population.

Methods: Consecutive patients who underwent en bloc cystectomy and conduit formation as part of pelvic exenteration at a single quaternary referral centre from 1995 to 2012 were reviewed. Patients with urine leak were identified. Medical records were reviewed to extract data on diagnosis and management and a suggested clinical algorithm was developed.

Results: Of 325 exenterations, there were 102 conduits, of which 15 patients (15%) developed a conduit related urine leak. Most (14/15) patients were symptomatic. Diagnosis was made by drain creatinine studies (12/15) and/or imaging (15/15). Management comprised of conservative management, radiologic urinary diversion, early surgical revision and late surgical revision in 3, 11, 2 and 1 patients respectively. Important lessons from our 17 year experience include a high index of suspicion in a patient who is persistently septic despite appropriate treatment, the importance of regular drain creatinine studies, CT (computer tomography) with delayed images (CT intravenous pyelogram) when performing a CT for investigation of sepsis and early aggressive management with radiologic urinary diversion to facilitate early healing.

Conclusion: Urine leak after pelvic exenteration is a complex problem. Conservative management usually fails and early diagnosis and intervention is the key. It is hoped that our algorithms will facilitate diagnosis and subsequent management of this group of patients.
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Introduction

The management of locally advanced and recurrent pelvic malignancy is challenging\(^1\)-\(^3\). Extensive multi-visceral resection is often required in order to achieve clear resection margins (R0 resection), which is now well established as the single most important predictor of long-term survival\(^4\). In patients where there is involvement of the trigone of the bladder or where the anticipated urinary function is likely to be poor, en bloc cystectomy is indicated with urinary diversion in the form of ileal or colonic conduit\(^5\). Recent large exenterative series suggest that this may be necessary in 30-50% of all patients undergoing curative resection for locally advanced or recurrent pelvic cancer\(^6\),\(^7\). Leakage of urine from a newly formed conduit is a major postoperative complication. In an earlier study from our institution, a conduit related urine leak rate of 16% was reported\(^6\), which is a disparately different result from that within contemporary urological literature, where rates of 2-6% are reported\(^8\),\(^9\). This is likely to be attributable to our cohort of patients having re-operative pelvic surgery with multi-visceral resection in an extensively irradiated field. However, this experience is not unique to our institution as high leak rates have also been reported following pelvic exenteration for urological and gynaecological cancer\(^10\)-\(^12\). Urological leaks are a considerable source of morbidity following pelvic exenteration, leading to increased resource consumption as necessitated by prolonged in and outpatient management, as well as a shorter median survival\(^6\). In view of our experience with the management of urine leaks, the lack of consensus in appropriate management and an increasing interest in exenterative radical resection\(^13\), it was felt that a suggested diagnostic and management algorithm may facilitate the management of this complex problem. With this in mind we reviewed our experience with a view to develop a suggested clinical algorithm for the diagnosis and management of urine leaks after pelvic exenteration surgery.

Patients and Methods
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Patients who underwent pelvic exenteration surgery for locally advanced or recurrent pelvic malignancies (including rectal cancer, SCC and sarcoma) at Royal Prince Alfred Hospital, between December 1995 and September 2012 were identified. Operations were considered exenterative when there was en bloc resection of at least one adjacent organ, as defined by Heriot and coworkers. Those who had an ileal or colonic conduit and subsequently developed a postoperative urine leak formed the study cohort. A urine leak was defined as the presence of creatinine rich effluent from abdominal drains or wound sites, and/or evidence of contrast extravasation from the conduit or ureteric anastomosis identifiable on imaging. Urine leaks with contrast extravasation arising from the ureteroenteric anastomosis were considered ‘anastomotic leaks’, whereas contrast extravasation from anywhere else on the conduit (e.g., the distal conduit staple line) were considered ‘conduit leaks’.

Patient medical records were reviewed for preoperative urological history, type of conduit, cause of leak, diagnosis, and subsequent investigations and management. Urine leaks were identified as early or late according to time to diagnosis and categorised as controlled or uncontrolled based on the patient’s drain and urine output volumes. The choice of day 6 as the cut off point for early versus late leak diagnosis was based on a study by Hensle et al and because it would fit in with our general approach to management in that leaks within a week of surgery will be considered for early surgical revision. The first suspicion of a urine leak was noted, and from this the delay to diagnosis was estimated; defined as the period of time between initial suspicion and diagnosis. Complications following image-guided investigations or interventions such as sepsis were recorded. Sepsis was defined as proof of bacteraemia or clinical suspicion of sepsis, as well as the signs and symptoms of the systemic inflammatory response syndrome. Persistent urosepsis is defined as sepsis of the urinary tract that does not resolve despite an appropriate course and duration of treatment including antibiotics and general supportive measures. For the purposes of this study, conservative
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management refers to any supportive management that did not require any radiologic or surgical intervention. Radiologic urinary diversion refers to any radiological interventions including the insertion of percutaneous nephrostomies for urinary diversion or percutaneous drain insertion whereas surgical intervention (early or late) refers to patients who required operative interventions such as conduit revision.

Ethics approval for this study was granted by the Sydney Local Health District (RPAH Zone) human research ethics committee.

**Surgery**

The decision to perform en bloc cystectomy and form a urinary conduit was based on preoperative discussions at a multidisciplinary exenteration meeting. The choice of reconstruction was at the discretion of the operating surgeon at the time of surgery, depending on evidence of radiation injury to small bowel and whether or not there was an established colostomy. Conduits were constructed according to standard technique. In summary, the isolated ileal or colonic segment was stapled closed at the blind abdominal end, the ureteroenteric anastomoses were constructed using the Bricker technique over ureteric catheters\(^{17}\) and a Brooke (end) or Turnbull (loop) stoma created. Depending on the surgeon, ureteric catheters were sutured in place to the stoma or within the conduit to prevent migration. At least one intra-abdominal drain was placed in each patient, and antibiotics were administered routinely for 5 days. Drain fluid creatinine analyses were routinely performed on day 2 and repeated regularly between every 5 to 7 days and as clinically indicated. Contrast radiology of the urinary tract was performed largely to confirm urinary leaks in the presence of clinical suspicion, although routine imaging was also performed in selected patients depending on surgeon preference. Imaging modalities included computer tomography intravenous pyelogram (CT IVP), CT conduitogram, “stentogram” and nephrostogram. A CT conduitogram is a
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contrast study of the conduit where the contrast is directly administered into the conduit via a Foley catheter whereas a “stentogram” is a fluoroscopic examination of the urinary tract that involves administration of contrast via the externally draining surgically placed ureteric catheters.

Fluoroscopic screening is carried out as the contrast is being excreted naturally from the renal pelvis into the conduit. A nephrostogram (CT or fluoroscopic) is a contrast study whereby the renal pelvis is directly cannulated for contrast examination. This is usually performed at the time of insertion of percutaneous nephrostomy.

Statistical analysis on this cohort of patients was not done because of the descriptive nature of this study and the small number of patients within the cohort.

Results

There were 325 patients who underwent a pelvic exenteration during the study period, 102 (31%) of who had an ileal or colonic conduit formed for urinary diversion. Of these, 18 developed a urine leak, however, three patients were excluded for non-conduit related leaks. One had a contained bladder leak (after partial cystectomy) and two had ureteric leaks from inadvertent ureteric injury. Of the 15 included cases (15% of all conduits), 12 were male with a median age of 62 (IQR = 56-66 years). 11 urine leaks were from ileal conduits (14% of all ileal conduits) and 4 were colonic (17% of colonic conduits). 7 patients (8% of conduits) had a urine leak from the ureteroenteric anastomosis, while 8 (9%) leaked from the conduit itself. In five cases there was an identifiable cause for the urine leak: due to an ischaemic conduit in one case, stomal stenosis of an existing ileostomy in another, two were iatrogenic from inadvertent perforation from a conduit catheter and one early leak was thought to be related to the technical construction of the ureteroenteric anastomosis. Table 1 summarises patient demographics.
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**Diagnosis**

The most common clinical manifestations of urine leak were sepsis (8 patients), increased drain output (6), leakage from the sacral wound (5) and decreased urine output (4). Of the four patients who had decreased urine output, three also had an increase in drain output or significant wound discharge. One patient had an asymptomatic urine leak, detected on routine stentogram on day 11 postop to check anastomotic integrity. The median time from operation to diagnosis of urine leak was 12 days (IQR = 9-37 days), and using our definition of 6 days as a cut off, two patients were considered to have an early leak, while 13 patients had late leaks.

The initial diagnosis of a urine leak was made on the basis of abdominal drain creatinine in 11 patients, and 10 of these were confirmed by imaging within 3 days. In the remaining 4 patients, two had their abdominal drains removed prior to leak diagnosis, one did not have drain creatinine studies ordered and another was diagnosed by routine stentogram.

In total, the site of leak was confirmed in 13 patients, 3 by CT IVP and 10 by CT conduitogram. In the remaining two cases the site of leak was not confirmed until a nephrostogram was performed at the time of percutaneous nephrostomy tube insertion. Imaging or radiological intervention related complications occurred in seven patients and were all sepsis related requiring intravenous antibiotics. Delay in diagnosis occurred in only one patient who did not undergo drain fluid creatinine analysis despite the suggestive nature of the percutaneously inserted drain fluid effluent. The delay in diagnosis was 10 days in this patient.

**Management**
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Of 15 patients diagnosed with a urine leak, three were managed conservatively. Two had small, contained urine leaks where management involved prolonged drainage by the conduit catheter and the ureteric stents inserted at the time of exenteration. One of these patients had an asymptomatic leak detected on routine screening stentogram, which resolved spontaneously a week later on repeat stentogram. A third patient was non-compliant with treatment and medical recommendations, and was therefore also treated conservatively despite initial plans for surgical conduit revision.

Two patients with early urine leaks underwent early surgical revision. In one patient, the leak resolved following repair of the conduit at the site of leak. The second patient had an iatrogenic conduit leak as a result of a Foley conduit catheter perforating the staple line at the blind end of the conduit. The catheter was inserted by the bedside to facilitate urinary drainage from an oedematous conduit. The site of perforation by conduit catheter was repaired and both ureteroenteric anastomoses were also reinforced but this patient went on to develop urine leak from a second site at the right ureteroenteric anastomosis 24 hours later, which required ongoing urinary diversion in the form of percutaneous nephrostomy.

Eleven patients were managed radiologically which involved a combination of percutaneous nephrostomy for urinary diversion, percutaneous drainage or trans-conduit drainage for conduit leaks if needed. This included the patient who developed a leak from a second site following early surgical revision. The leak resolved in seven of these patients who had nephrostomy tubes inserted for a median duration of 40 days (IQR = 21-57 days). One patient’s leak did not settle with drainage and underwent a late operative revision where the conduit was excised and refashioned. Three failed to heal despite prolonged drainage and developed progressive disease whilst they were in hospital. All were palliated with long term drainage. In one patient, palliative management involved ongoing drainage of the collection system by ureteric stents and percutaneous drainage with a drain,
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while the other two patients had permanent percutaneous nephrostomy tubes placed following ureteric lumen occlusion with a combination of sclerosis and coil embolisation.

Discussion

The purpose of this study was to review our experience with urine leaks after pelvic exenteration so as to develop a possible clinical algorithm for the diagnosis and management of this challenging problem (Figures 1 & 2). While we report relatively small numbers of postoperative urine leaks, this represents one of the largest series in the literature. Surprisingly, the urological literature in this area is limited, and lacks comprehensive guidelines for the management of this problem, particularly in our subset of patients where extensive multi-visceral resection has been performed in multiple compartments of the pelvis in the setting of high doses of prior radiation therapy. Within the literature, urine leaks after urological surgery often spontaneously resolve with external drainage. However we have not found this to be the case in pelvic exenteration patients. This may be related in part to the extensive surgery and a history of prior radiotherapy, although small numbers would limit our ability to draw this conclusion.

Factors that contributed to or caused a urine leak were identified in five patients, including an ischaemic conduit, unrecognised stomal stenosis of a prior ileostomy used for an ileal conduit, technical error and two cases of conduit perforation related to the use of conduit catheters. Awareness of these factors should prompt early suspicion and be points of caution in all patients with urinary diversions. Conduit drainage using conduit catheters should be performed using a multiply fenestrated catheter that has been secured in place to avoid inward migration of the catheter and prevent catheter-related erosion or damage to the conduit as the conduit decompresses. Where there is a delay in diagnosis, urine leaks tend to be less likely to heal spontaneously and have historically been associated with high morbidity. Routine drain fluid creatinine studies should be
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performed on day 2 after surgery to ensure early detection of urine leaks and it is recommended that this be repeated regularly and in the presence of signs such as high drain output, persistent urinary sepsis, low urine output or wound discharge. Many exenteration patients drain large amounts of fluid via abdominal drains due to extensive lymphadenectomy and disrupted lymphatic drainage. This may mask an underlying leak unless a high index of suspicion is maintained. In one case, a delay to diagnosis occurred because of high drain output attributed to a lymphocele. Thus, drain fluid creatinine analysis should be performed routinely and repeated regularly in this population and a high index of suspicion should be maintained. Sepsis was another common presentation in our series, and in several of these cases, an original diagnosis of urinary tract infection was made. Although it is common following the formation of a conduit, persistent urinary sepsis is suspicious and patients should be further investigated. In this setting, drainage effluent should be cultured to identify bacterial infection and guide choice of antibiotic therapy.

The use of routine imaging in postoperative assessment of patients with urinary diversions is debatable. The decision to perform imaging will be an individual surgeons preference, and although contemporary urological literature does not support the use of routine imaging of the urinary tract, the utility of this in an exenteration population is unclear. For the investigation of persistent urinary sepsis or a positive drain creatinine study, the use of CT IVP visualising the renal collecting system is preferred. This not only demonstrates pelvic collections, but also confirms the diagnosis of a leak, the site of a leak as well as demonstrating the relational anatomy. Should a CT IVP fail to confirm or diagnose a leak despite clinical suspicion, a CT conduitogram or a stentogram are useful second and third line investigations. Following nephrostomy tube insertion, a nephrostogram can be performed to diagnose the site of a leak, and in some cases a conduitoscopy may be necessary to confirm this as seen with the current study. However, conduitoscopy should be performed judiciously as the irrigating fluid during conduitoscopy can disperse at the time of the
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procedure. In our experience, this has not been a concern as this investigation is typically reserved for when the site of leak remains unclear despite aforementioned investigations or when the leak remains uncontrolled and is therefore performed late.

There are several management options in the approach to postoperative urine leaks. Early in our exenterative practice the management of urine leaks was more conservative with prolonged drainage and an observation-based approached. However, it became apparent that this patient population is different and that a more aggressive, interventional approach is needed. There is no consensus within the urological literature about the classification of urine leaks: Schmidt et al defined early urine leaks as those occurring within 10 days following surgery, while Hensle et al defined an early leak as within 6 days postoperation. We have chosen to classify urine leaks based on a cutoff of 6 days as this fits in with our surgical approach whereby a leak within a week of surgery is generally considered a technical error and patients are likely to benefit from early revision. Of note, most patients were diagnosed late, where the surgical window of opportunity is frequently lost and in this case maximal urinary diversion of urine should be achieved by insertion of bilateral percutaneous nephrostomy tubes. A driving force behind the evolution in leak management in our institution relates to the observation that drainage with percutaneous nephrostomy often results in a very prolonged inpatient admission (median of 40 days, IQR = 21-57 days). Thus, surgical revision should be considered where possible, although the number of patients who required surgical revision was small and would limit our ability to draw this conclusion.

In our opinion ongoing sepsis from a urine leak, albeit controlled, is an adverse prognostic indicator akin to anastomotic bowel leaks. The increased risk of local recurrence after bowel anastomotic leaks is well described. Although small numbers within this study precludes statistical analysis, the rapid disease progression in three patients with urine leaks in this series is alarming despite only
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having microscopically involved margins. It may be that ongoing pelvic sepsis and proinflammatory cytokines play a role in accelerated tumour cell growth and proliferation\textsuperscript{30,31}.

For interventions involving the urinary tract, particularly during the insertion of percutaneous nephrostomy tubes, there is known risk of sepsis and thus antibiotic cover is recommended. At the Memorial Sloan-Kettering Cancer Center, Russo and colleagues recommend single dose IV gentamicin during ureteric stent removal in exenteration patients\textsuperscript{21}. In our series 7 (47\%) patients developed sepsis following image-guided investigation or intervention, of which three occurred following an investigation alone (for example conduitogram). We would therefore extend Russo and colleagues’ recommendation to include all radiologic examinations of the urinary tract.

Based on our experience, the suggested diagnostic (figure 1) and management (figure 2) algorithms were developed with the aim of providing some recommendations for the management of this complex problem. This is a heterogeneous group of patients and the approach to a postoperative urine leak will vary widely following considerations of various other clinical and patient factors.

Clinical algorithms for the diagnosis and management of urine leaks following pelvic exenteration surgery were developed in view of the considerable experience that our institution has developed in managing this complex problem. Central to the management of these patients is the maintenance of a high index of suspicion and to further investigate patients with persistent urinary sepsis, increased drain outputs or wound discharge especially in the setting of decreased urine output. An early aggressive approach to management with consideration for early surgical revision or radiologic urinary diversion will expedite resolution of urine leakage thereby reducing morbidity
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References


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**Figure 1.** Clinical algorithm for the diagnosis of urine leaks

**Figure 2.** Clinical algorithm for the management of urine leaks
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**Table 1.** Summary characteristics of patients with urinary leaks following surgery

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%) patients with leak</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;70</td>
<td>12 (80)</td>
</tr>
<tr>
<td>&gt;70</td>
<td>3 (20)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12 (80)</td>
</tr>
<tr>
<td>Female</td>
<td>3 (20)</td>
</tr>
<tr>
<td><strong>Conduit</strong></td>
<td></td>
</tr>
<tr>
<td>Ileal</td>
<td>11 (73)</td>
</tr>
<tr>
<td>Anastomotic leak</td>
<td>5</td>
</tr>
<tr>
<td>Conduit leak</td>
<td>6</td>
</tr>
<tr>
<td>Colonic</td>
<td>4 (27)</td>
</tr>
<tr>
<td>Anastomotic leak</td>
<td>2</td>
</tr>
<tr>
<td>Conduit leak</td>
<td>2</td>
</tr>
<tr>
<td><strong>Timing</strong></td>
<td></td>
</tr>
<tr>
<td>Early leak (≤ 6 days)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Late leak (&gt; 6 days)</td>
<td>13 (87)</td>
</tr>
</tbody>
</table>
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#### Table 2. Case details of patients with urinary leaks after surgery

<table>
<thead>
<tr>
<th>Patient</th>
<th>Prior Surgery</th>
<th>Radiotherapy</th>
<th>Exenteration</th>
<th>Final Histology</th>
<th>Leak Diagnosis (Day)</th>
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<tbody>
<tr>
<td>1</td>
<td>APR</td>
<td>+</td>
<td>Total</td>
<td>AC</td>
<td>37</td>
</tr>
<tr>
<td>2</td>
<td>LAR, APR</td>
<td>-</td>
<td>+</td>
<td>A,C,LL,P</td>
<td>34</td>
</tr>
<tr>
<td>3</td>
<td>Hartmann’s</td>
<td>+</td>
<td>-</td>
<td>A,C,P</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>Primary pelvic exenteration</td>
<td>-</td>
<td>+</td>
<td>A,C,LL</td>
<td>AC</td>
</tr>
<tr>
<td>5</td>
<td>Primary pelvic exenteration</td>
<td>+</td>
<td>-</td>
<td>A,C</td>
<td>AC</td>
</tr>
<tr>
<td>6</td>
<td>AR</td>
<td>+</td>
<td>-</td>
<td>A,C</td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td>APR</td>
<td>+</td>
<td>-</td>
<td>A,C,P</td>
<td>52</td>
</tr>
<tr>
<td>8</td>
<td>Primary pelvic exenteration</td>
<td>+</td>
<td>-</td>
<td>Total</td>
<td>AC</td>
</tr>
<tr>
<td>9</td>
<td>ULAR</td>
<td>+</td>
<td>-</td>
<td>A,C,LL,P</td>
<td>63</td>
</tr>
<tr>
<td>10</td>
<td>ULAR</td>
<td>+</td>
<td>-</td>
<td>Total</td>
<td>AC</td>
</tr>
<tr>
<td>11</td>
<td>Primary pelvic exenteration</td>
<td>+</td>
<td>-</td>
<td>A,C,LL,P</td>
<td>Anal SCC</td>
</tr>
<tr>
<td>12</td>
<td>Hartmann’s</td>
<td>+</td>
<td>+</td>
<td>A,C,P</td>
<td>34</td>
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<tr>
<td>13</td>
<td>Radical hysterosalpingooophorectomy</td>
<td>+</td>
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<td>A,C</td>
<td>Cervical SCC</td>
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<tr>
<td>14</td>
<td>Partial exenteration</td>
<td>+</td>
<td>-</td>
<td>A,C,RL,P</td>
<td>Embryonal rhabdomyosarcoma</td>
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<tr>
<td>15</td>
<td>APR</td>
<td>+</td>
<td>-</td>
<td>Total</td>
<td>AC</td>
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</table>