



Evolution of pelvic exenteration surgery— resectional trends and survival outcomes over three decades



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ABSTRACT

Objective: To examine the changes in exenterative surgery over three decades analysing oncological outcomes and whether changes in surgical approach have led to improved patient outcomes.

Background: Advances in surgical technology, perioperative care and pattern of disease recurrence have coincided with an evolutionary change in exenterative surgery.

Methods: A review of a prospectively maintained databases of pelvic exenteration surgery from 1988 to 2018 at two high volume specialised institutions. The total cohort was divided into three major time points (1988–2004, 2005–2010 and 2011 to 2018) to allow comparative analysis. Primary endpoints were overall survival in primary and recurrent disease at each time point. Secondary endpoints included anastomotic leak, blood transfusion, ileus, wound infection rates and evolution of case complexity. Data were analysed using R with a $p < 0.05$ considered significant.

Results: Six hundred and seventy patients underwent exenterative surgery. In 2011–2018 there was an increase in resection of recurrent malignancy with a continuous increase in GI malignancies resected over each time period ($p < 0.001, < 0.01$) and a reduction in gynaecological malignancy ($p < 0.001$). A significant increase in sacrectomy, pelvic sidewall resection and ileal conduit reconstruction was observed ($p < 0.01, < 0.001$). In 2005–2010 patients had increased rates of ileus and anastomotic leak ($p < 0.05$). Patients undergoing resection for primary disease had improved overall survival at time points 1988–2004 and 2011–2018 compared to those with recurrent disease ($p = 0.007, < 0.001$). Overall survival was significantly improved in patients with primary versus recurrent disease ($p = 0.022$).

Conclusion: There has been a significant improvement in survival in patients undergoing pelvic exenteration surgery from primary disease. Case complexity has increased without significant morbidity.

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Introduction

Achieving a complete resection with clear margins for pelvic malignancy has been well documented in the literature as the most important prognostic factor [1,2]. Pelvic exenteration is a procedure that allows en bloc multivisceral resection of contiguous locally advanced or recurrent pelvic malignancy. First

described in the literature in 1948, it involves the resection of pelvic viscera in non disseminated pelvic lesions where radial margins are difficult to achieve due to tumour growth in close relation to or involving adjacent organs with reconstruction of gastrointestinal and genito-urinal tracts where necessary [3]. To date, survival data suggests long term survival in greater than 50% of patients after exenterative surgery for rectal, gynaecological and urological malignancy [4]. Due to the radical nature of the resection and reconstruction process there are inherently increased rates of morbidity and mortality when compared to standard isolated organ resection [5,6]. Mortality rates in excess of 20% have been outlined with perioperative morbidity ranging from

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approximately 30–80% [7–10].

With the advent of neoadjuvant therapies, patient optimisation strategies, advances in surgical techniques, imaging and technology; pelvic exenteration surgery has been largely adapted since first inception. Improved oncological and patient post-operative outcomes have been reported with such adaptations [11]. The development and application of total mesorectal excision (TME) surgery and use of radiation for rectal cancer has coincided with a significant decline in the incidence of local pelvic recurrence over the last decade from 30% to rates as low as 5–10% [12–15]. Furthermore, local failure and pattern of disease recurrence has also changed with diminishing central and TME component recurrences. Similar patterns have been recognised in gynaecological malignancy with improved multidisciplinary treatment. These numerous recent changes have led to the evolutionary customisation of exenteration surgery and reconstructive techniques for curative rather than palliative intent [16,17].

Such advances have taken place in a carefully coordinated approach with improved oncological and procedural outcomes reported to be possibly related to surgeon and hospital volume [18]. Moreover, the development of specialist centres has produced good oncological and patient outcomes for extended radical resection for rectal cancers beyond the TME plane [19,20]. The PelvEX collaborative highlighting outcomes in such centres globally has recently reported a 3-year overall survival of 56.4% in patients with clear margins [21]. Despite these improved figures exenteration surgery is not commonly practiced and slow to be adopted into many surgical units. This is possibly due to many studies such as PelvEX reporting short term oncological outcomes and also the lack of reported data highlighting changes in the evolution of exenteration surgery over a prolonged period of time. Furthermore, with such marked adaptations in approach and technique there have been scant studies reporting associated oncological outcomes with such customisation of surgery over time. The authors propose that it is imperative that such changes in resection and reconstructive technique are not at the patients detriment. Therefore the primary aims of this study was to examine the changes in patterns of resection in exenterative surgery over three decades analysing oncological outcomes in different histological subtypes of pelvic malignancies in primary and recurrent disease. Changes in primary pathology excised with exenteration surgery, compartments resected, case complexity measured by resection and reconstructive patterns and patient complications are reported throughout the study period to assess whether changes in surgical approach over time have led to improved patient outcomes.

Methods

A review of a prospectively maintained databases was undertaken to assess the outcome of patients who had undergone pelvic exenteration surgery. The primary objectives were to analyse changes in resections performed in exenteration surgery and assess oncological and patient outcomes. Two tertiary referral centres with specialist experience in the surgical management of advanced rectal cancer and similar surgical approaches to exenterative surgery were included. These institutions were Christchurch Hospital (Christchurch, New Zealand) and Peter MacCallum Cancer Centre (Melbourne, Australia). All patients were routinely discussed at a dedicated colorectal cancer multidisciplinary meeting. The diagnosis of all cancers was based on preoperative radiological imaging and clinical assessment. Data were prospectively collected at individual institutions. Patient demographics (age, sex), neoadjuvant & adjuvant regimen, use of intraoperative radiotherapy (IORT), surgical intent, type of surgery including extended resections and the

need for bony resection or flap reconstruction and complications were recorded. Histopathological assessment included lymph node positivity, presence of lympho-vascular invasion (LVI) and degree of differentiation. Centralised data were evaluated independently and analysed at the Peter MacCallum Cancer Centre, Melbourne, Australia.

Definitions

The total cohort was divided into three major time points to allow for equal cohort numbers over each decade of surgery for comparative analysis. The cohorts were divided in those operated on from 1988 to 2004, 2005–2010 and 2011 to 2018 respectively. Patients analysed included those who underwent resection for pathologies of the gastrointestinal tract (GIT), gynaecological, squamous cell carcinoma (SCC) and Other (Melanoma, Prostate, Sarcoma, GIST, Chordoma) and had surgically resected organs recorded prospectively. Type of exenteration performed was defined by the seven intrapelvic compartments demonstrating the organs that are included in each compartment to allow for more accurate documentation of changes in resectional patterns over the study period. They were classified as Anterior above peritoneal reflection (PR), Anterior below PR, Central, Posterior, Lateral, Inferior and Peritoneal Reflection [22]. Overall survival (OS) was defined as the time from the date of surgery to the date of death from any cause. Resection of primary disease was defined as newly diagnosed malignant process requiring up front pelvic exenteration based on clinical and radiological assessment. Recurrent disease was defined as newly diagnosed disease of similar histological characteristics as previously resected tumour with a R0 margin. Histopathological evaluation considered a R0 resection as a circumferential resection margin (CRM) of >1 mm R1 resection was the presence of microscopic residual disease defined as a CRM of ≤1 mm, whereas R2 resection was the presence of macroscopic residual disease. Complexity of exenteration was defined by type of organs resected or the requirement of organ reconstruction. Complications were compiled prospectively. A wound infection is defined by the US Centre for Disease Control and Prevention (CDC) as surgical site infection (SSI) [23]. This is further defined as superficial incisional SSI (recorded as grade1) deep incisional SSI (grade 2) organ/space SSI (grade3). Ileus was defined as functional obstruction of the gastrointestinal tract and especially the small intestine that is marked by the absence of peristalsis, is usually accompanied by abdominal pain, bloating, and sometimes nausea and vomiting, and typically occurs following abdominal surgery. Anastomotic leakage was defined as a defect of the intestinal wall at the anastomotic site to a communication between the intra- and extraluminal compartments [24].

Endpoints

The primary endpoints were overall survival in primary and recurrent disease and by histological subtype at each time point. Secondary endpoints included complication rates of anastomotic leak, blood transfusion requirement, ileus and wound infection rates and evolution of case complexity.

Statistical analysis

Data were analysed using R (version 3.0.3; R Development Core Team 2009). Baseline characteristics were summarised using descriptive statistics, with the mean and standard deviation (SD) used for categorical variables and the median and range for continuous variables. Comparison of outcomes between two

groups was performed using paired *t*-test and one-way Anova was used to analyse the means of three or more factors within the study with a *p*-value of less than 0.05 ($p < 0.05$) considered significant. Univariate and multivariate analysis was performed to examine the impact of one or multiple factors on outcome. The Kaplan-Meier method was used to estimate the OS curves for each histological subtype and in primary and recurrent disease and associated 95% confidence intervals were reported. Univariate analysis of possible prognostic variables on OS was assessed using the log-rank test (or exact log-rank test for small group numbers).

Results

Patients were divided into three time points dependent on timing of exenterative surgery, 1988–2004 ($n = 193$), 2005–2010 ($n = 250$) and 2011–2018 ($n = 265$, Table 1, Fig. 1). A significantly increased number of males underwent exenteration surgery in the latest time period. Age, ASA scores and co-morbidities remained similar throughout all time points. A significant increase in resections performed for recurrent disease was observed in 2011–2018 ($p < 0.01$). The number of node positive tumours (N1 & N2) resected have significantly increased over time ($p > 0.05$). There has been an increase in sacrectomy and prostatectomy over time with significant reduction in anal, ovarian and uterine resections. Furthermore a significant increase in lateral, central and central with posterior compartments were resected with a similar decrease in central with inferior compartment resection ($p < 0.01$).

From 1988 to 2004, a significant proportion of patients ($n = 142$) underwent exenterative surgery for primary disease compared to those with recurrent disease ($n = 51$). A significant similar pattern was observed from 2005 to 2010 ($n = 183$, $n = 67$ respectively) ($p < 0.01$). There was a change in 2011–2018 with a significantly higher proportion of patients undergoing exenterative surgery for recurrent disease ($n = 150$) rather than primary disease ($n = 115$, $p < 0.001$).

Throughout the study period there was a significant increase in exenteration surgery performed for GI related malignancies over each time point (1988–2004 $n = 135$, 2005–2010 $n = 161$, 2011–2018 $n = 225$, $p < 0.01$, Fig. 2). There was no statistical increase in patients undergoing exenterative surgery for SCC and other malignancies at each time point ($p = 0.6872$, $p = 0.6319$ respectively). There was a significant decrease in exenterative surgery being performed for patients with gynaecological related malignancies in 2005–2010 ($n = 99$) and 2011–2018 ($n = 10$, $p < 0.001$).

Case complexity has increased over the study period. There has been a significant increase in patients undergoing sacrectomy in 2011–2018 ($n = 60$, $p < 0.01$, Fig. 3). Urinary diversion and reconstruction with ileal conduit has also significantly increased in the latest time period ($n = 81$, $p < 0.001$). Similarly a significantly increased proportion of patients in 2011–2018 had pelvic sidewall resection performed ($n = 34$, $p < 0.001$). The number of patients undergoing flap reconstruction of the perineum remained similar throughout each time point ($p = 0.142$).

Complications were recorded prospectively within the database during the study period. There were a significant increase in patients with postoperative ileus during 2005–2010 time point compared to other time points ($p < 0.001$, Table 2). 25% of patients ($n = 52$) experienced post-operative ileus compared to 18% in 1988–2004 and 17% in 2011–2018. Of the total cohort, 20% of patients developed post-operative ileus. In patients undergoing a GI anastomosis a significantly higher proportion of patients experienced an anastomotic leak during 2005–2010 and 2011–2018 time

periods compared to 1988–2004 (5%, 6% respectively, $p = 0.006$). Of patients that had a gastro-intestinal anastomosis performed ($n = 127$) the anastomotic leak rate for the total cohort was 6%. The overall wound infection rate for the cohort was 19%. Wound infection rates were significantly higher in 2011–2018 ($n = 50$, $p < 0.001$). Superficial wound infections were significantly higher during this time period with less deep organ spaced infection (14% & 1% respectively). Deep organ space infections were highest in 1988–2004 and 2005–2010. Blood transfusion requirement was significantly lower in 2005–2010 compared to other time points ($p < 0.01$, Table 2). Mean transfusion was 0.943 of a unit (range 0–27units).

Overall survival for patients with primary and recurrent disease undergoing exenterative surgery was recorded during each time period and also for the total cohort. Patients with primary disease undergoing resection had a significantly improved survival in 1988–2004 and 2011–2018 than those undergoing operative intervention for recurrent disease ($p = 0.007$, $p < 0.001$, Fig. 4). There was no significant difference in survival observed in those with primary versus recurrent disease during 2005–2010 ($p = 0.484$). Within the total cohort those with primary resected disease had significantly improved survival than those with recurrent disease ($p = 0.022$). With regards to neoadjuvant therapies, 51% of patients received preoperative radiotherapy with 57% of patients receiving adjuvant chemotherapy.

Survival probability for each major histological subtype undergoing exenteration at each time point was measured. Those patients with gastrointestinal malignancy undergoing exenteration in 2011–2018 had significantly improved survival compared to those undergoing surgery in 1988–2004 and 2005–2010 ($p < 0.01$, Fig. 5). A similar pattern was observed in patients with gynaecological malignancy having a significantly improved survival when undergoing resection in 2011–2018 compared to those in 1988–2004 and 2005–2011 ($p < 0.05$). Patients with SCC and other malignancy (Melanoma, Prostate, Sarcoma, GIST, Chordoma) did not display any difference in survival when operated in each time point ($p = 0.793$, $p = 0.667$).

Discussion

This large international combined series from established centres, specialising in pelvic exenterative surgery, presents good outcomes and describes the evolution of this technique for locally advanced pelvic tumours. Surgical intervention to treat locally advanced pelvic tumours has steadily been gaining momentum. During the course of the last three decades, this study demonstrates advances in the operative strategies implemented and the types of pathology encountered. There was a tendency towards performing exenterative surgery for recurrent disease during the latter years of this study (2011–2018) compared with the preceding time points. The increasing complexity of the pathology encountered is also reflected by the expanding number of surgical components performed. This correlation is demonstrated by the increasing number of sacrectomy, ileal conduits and lateral pelvic sidewall dissections performed.

These increasing trends might mirror overcoming the surgical learning curve and therefore the technical challenges of the operative interventions evolve with increasing familiarity of the procedures. As surgeons become more comfortable with the techniques of exenterative surgery, the boundaries have been pushed, performing more radical surgery including cystectomy, sacrectomy and now lateral pelvic side wall resections. The complexity management of the disease has also increased (recurrent versus primary) and an increasing willingness to perform exenterative surgery on higher risk patients (less ASA 1 & 2

Table 1
Patient demographics, co-morbidities, tumour characteristics and organ/compartments resected.

	1988–2004		2005–2010		2011–2018		Total	
n	193	29%	212	32%	265	40%	670	
Gender								
Male	66	34%	67	32%	142	54%	275	41%
Female	127	66%	145	68%	99	37%	371	55%
Unknown					24	9%	24	4%
Age								
Mean (SD)	62.9 (13.5)		62.4 (13.0)		60.8 (12.9)		61.9 (13.1)	
Median (Range)	64.8 (26.4–111.0)		64.7 (22.1–89.2)		61.9 (19.0–87.0)		63.6 (19.0–111.0)	
ASA Grade								
1	11	5.60%	25	11.79%	16	6.03%	52	7.76%
2	108	55.90%	104	49%	102	38.49%	314	46.86%
3	57	29.50%	63	29.71%	58	21.88%	178	26.56%
4	5	2.59%	5	2.35%	6	2.26%	16	2.38%
x	11	5.60%	15	7.07%	59	22.26%	85	12.68%
Co-morbidity								
MI	15	7.77%	11	5.18%	16	6.03%	42	6.26%
Stroke	7	3.62%	8	3.77%	6	2.26%	21	3.13%
PVD	2	1%	2	0.94%	3	1.13%	7	1.04%
Asthma	11	5.60%	14	6.60%	8	3.01%	33	4.92%
COPD	16	8.20%	6	2.83%	3	1.13%	25	3.73%
Renal failure	6	3.10%	7	3.30%	5	1.88%	18	2.68%
Diabetes	22	11.39%	22	10.37%	21	7.92%	65	9.70%
Psychiatric disorder	12	6.21%	12	5.66%	9	3.39%	33	4.92%
Smoker	23	11.91%	31	14.62%	24	9.05%	78	11.64%
Tumour								
Primary	142	74%	166	78%	115	43%	423	63%
Recurrent	51	26%	46	22%	150	57%	247	37%
T								
0	105	54%	109	51%	9	3%	223	33%
1	2	1%	0	0%	4	2%	6	1%
2	6	3%	7	3%	18	7%	31	5%
3	20	10%	22	10%	84	32%	126	19%
4	60	31%	73	34%	92	35%	225	34%
X	0	0%	1	0%	58	22%	59	9%
N								
0	158	82%	161	76%	122	46%	441	66%
1	25	13%	30	14%	42	16%	97	14%
2	10	5%	17	8%	36	14%	63	9%
X	0	0%	4	2%	65	25%	69	10%
M								
0	181	94%	196	92%	225	85%	602	90%
1	12	6%	16	8%	39	15%	67	10%
Organs Resected								
Colon	29	15%	51	24%	52	20%	132	20%
Rectum	148	73%	140	66%	180	68%	468	70%
Anus	75	39%	40	19%	31	12%	146	22%
Small intestine	26	13%	43	20%	65	25%	134	20%
Vagina	49	25%	37	17%	50	19%	136	20%
Uterus	59	31%	73	34%	53	20%	185	28%
Ovaries FP tbes	66	34%	101	48%	41	15%	208	31%
Prostate	29	15%	31	15%	65	25%	125	19%
Bladder	54	28%	50	24%	78	29%	182	27%
Sacrum	30	16%	24	11%	60	23%	114	17%
Compartments Resected								
Central	6	3%	7	3%	38	14%	51	8%
central with posterior	29	15%	20	9%	70	26%	119	18%
anterior above PR with anterior below PR	25	13%	46	22%	24	9%	95	14%
central with anterior below PR	66	34%	89	42%	62	23%	217	32%
anterior below PR	5	3%	8	4%	21	8%	34	5%
anterior above PR with anterior below PR	4	2%	7	3%	10	4%	21	3%
lateral	3	2%	4	2%	34	13%	41	6%
central inferior	55	28%	31	15%	6	2%	92	14%

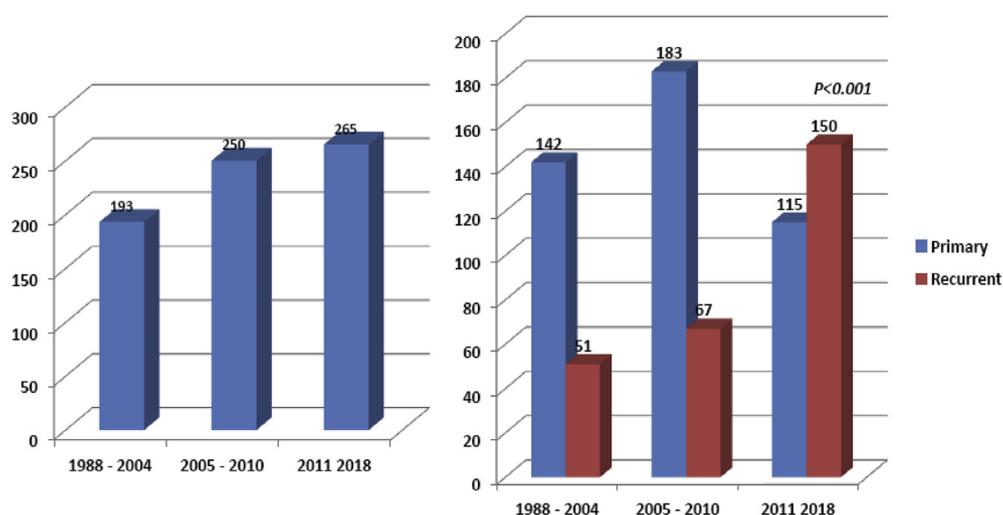


Fig. 1. Total patient cohort at each time point and resection of primary or recurrent disease: There was a significantly higher proportion of primary diagnosed malignancy undergoing pelvic exenteration in 1988–2004 and 2005–2010 ($p < 0.01$). In 2011–2018 there has been a significant shift in resection of recurrent malignancy compared to primary disease ($P < 0.001$).

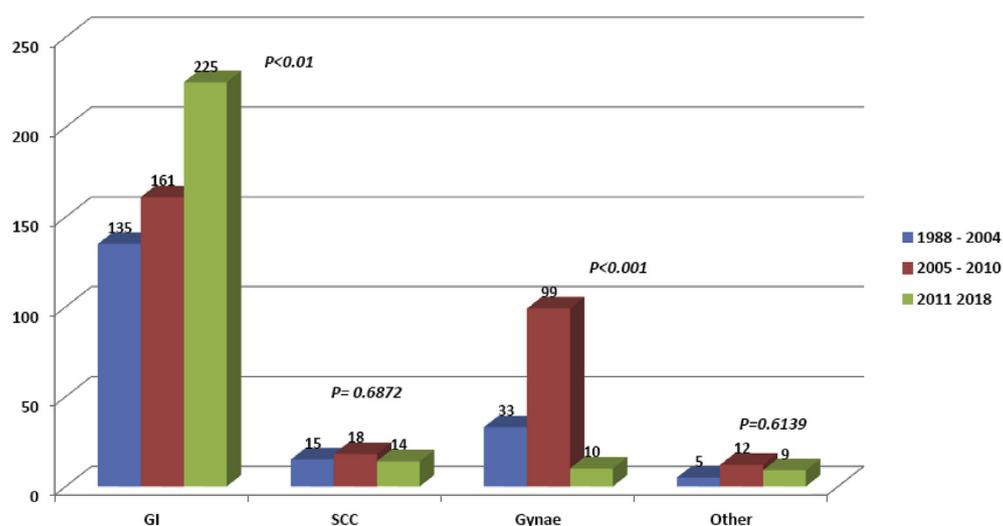


Fig. 2. Primary pathology resected: there has been a continuous increase in GI malignancies resected over each time period ($p < 0.01$). There has been a similar amount SCC and Other malignancies (Melanoma, Prostate, Sarcoma, GIST, Chordoma) resected at each time point during the study period ($p = 0.687$, $p = 0.61$ respectively). Gynaecological related malignancies have significantly reduced from 2005 to 2010 time point to 2011–2018 ($p < 0.001$).

patients).

The surgery has also become more bespoke, with the aim to improve patient's quality of life. During this study period, there has been an increasing trend towards sphincter preserving surgery, reflected by the downward trend in resecting the anus (39%–12%) as exenterative surgery has evolved. This might explain the slight increase in anastomotic leak rate between 2005 and 2010 (5%) compared with 1988–2004, which corresponds with the initial downward trend in resecting the anus. As this technique has evolved and further reduction in resecting the anus, the anastomotic leak rate has decreased to the baseline. Other efforts to improve patient's quality of life are reflected in the development of techniques to resect the prostate en bloc and leave the bladder insitu and functioning [25]. This strategy has been enabled by the development in the techniques for radical prostate surgery in prostate cancer.

The increasing familiarity and expertise in exenterative surgery might also be reflected in the decrease utilisation of blood transfusion in the middle period of this study. However, the adoption of expanding operative complexity, particularly with increasing pelvic side wall dissection and sacrectomy between 2010 and 2018, may also explain the increase in blood transfusion requirements during this time period, similar to the initial period (1988–2004).

This current study also reports a significant overall survival in patients undergoing exenteration surgery for primary compared to recurrent disease. This improved survival was observed in patients undergoing resection in 1988–2004 and 2011–2018 and further borne out in the total cohort despite no difference in survival observed in patients operated within 2005–2010. This observation could be reflected on the fact that there has been improved patient selection over the last decade despite the significant increase in

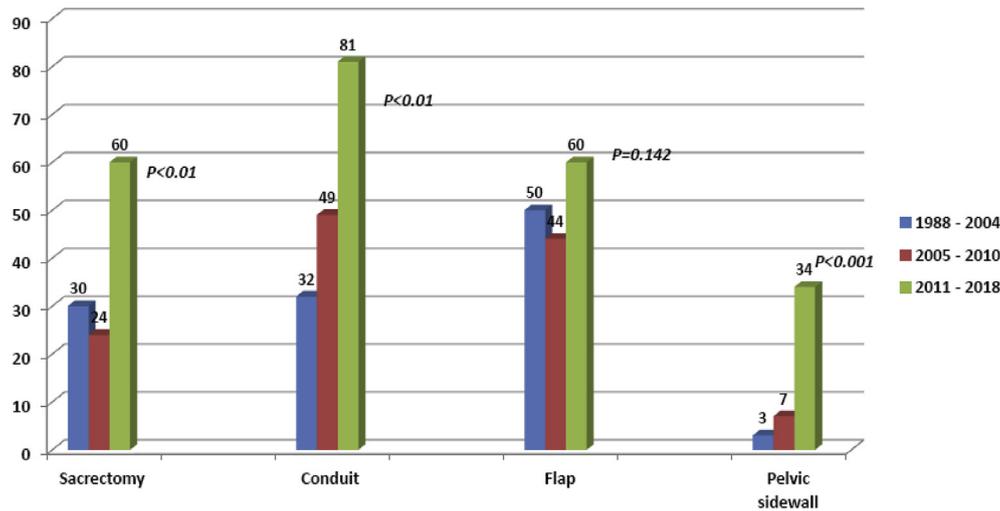


Fig. 3. Case complexity outlined by boney and sidewall resection and reconstruction. Throughout the study period there has been a significant increase in sacrectomy and pelvic sidewall resection ($p < 0.01$ and < 0.001 respectively). Patients undergoing flap reconstruction has remained similar throughout the study period ($p = 0.142$). Ileal conduit reconstruction has significantly increased in the most recent time point 2011–2018 ($p < 0.01$).

Table 2

Complications encountered during each time point and total cohort: Patients undergoing pelvic exenteration surgery during 2005–2010 had significantly increased rates of ileus compared to other time points ($p < 0.001$). There were also increased rates of anastomotic leak during this time period. Incidence of total wound infections were significantly lower in 2005–2010 time point ($p < 0.001$). Blood transfusion requirement was significantly higher during 1984–2004 and 2011–2018 time points ($p < 0.01$).

Complications	1988 –2004	2005 –2010	2011 –2018	Total cohort	P Value
Ileus					
No	159	160	197	516	0.001
Yes	34	52	44	130	
Anastomotic Leak					
No	98%	95%	99%	94%	P = 0.006
Yes	2%	5%	1%	6%	
Wound Infection					
No	150	173	191	514	P < 0.001
Grade 1	11	14	37	62	
Grade 2	25	19	10	54	
Grade 3	7	6	3	16	
Transfusion					
Mean (SD)	1.68	0.943	1.67	1.41	P < 0.01
Median (Range)	(5.88)	(3.24)	(3.24)	(4.19)	
	0 (0–55)	0 (0–27)	0 (0–20)	0 (0–55)	

patients with recurrent disease undergoing surgery within the two units. Throughout all time points there has been increased numbers of patients with GI pathology being resected however within the 2005–2010 period there was a significant increase in operative intervention in patients with gynaecological related malignancy followed by a significant decline in the last decade. The authors postulate that this significant increase could potentially lead to worse survival in patients undergoing resection within the primary malignancy group during this time point. The decline in gynaecological exenterative procedures performed in the latest time period is due to better patient selection as a result of greater understanding of oncological outcomes in gynaecological malignancy reported in the literature. Moreover, due to the fact that a major proportion of gynaecological related malignancies are SCC

in nature they are known to be associated with increased local recurrence rates. The authors also believe that improved pre-operative staging of gynaecological cancers in both centres with the utilisation of PET CT in the last decade has led to a consequential reduction in patients undergoing attempted curative exenterative surgery. Finally, the decrease in gynaecological exenteration performed within such colorectal units may also be due to the development of specialty trained gynaecological oncology surgeons that now undertake operative interventions in such patients. The literature to date has documented inferior survival in patients with gynaecological malignancy undergoing exenterative surgery than primary organ resection or resection of other pathologies. A study by Westin et al. reported five-year overall survival after pelvic exenteration was 40% in patients with gynaecological malignancy [26]. The authors report that survival outcomes have not significantly improved despite improvements in technique and patient selection undergoing exenteration. Moreover, they state that non-modifiable factors associated with gynaecological malignancy at the time of exenteration are associated with poor survival. These outcomes have been mirrored in other studies [27,28] A recent study reported an overall survival of 40.7% and cumulative 5-year overall survival of 38% in patients under exenterative surgery for primary and recurrent cervical carcinoma. In contrast patients undergoing exenterative surgery for GI related malignancies have superior overall oncological and survival outcomes. This analysis documents a sustained increase in survival at each time point in patients undergoing intervention for primary and recurrent disease with an overall 5 year survival of greater than 75% or primary resected malignancy in the latest time point. These findings are reflected in other smaller studies analysing survival outcomes in primary and recurrent disease. Ferenschild et al. report overall 5-year survival for primary locally advanced rectal cancer, recurrent rectal cancer, and cervical cancer was 66%, 8%, and 45% respectively [29]. Furthermore a more recent study comparing outcomes in rectal cancer patients under exenteration surgery highlight a significant reduced disease free survival in patients with recurrent rectal cancer compared to those with primary locally advanced disease [30]. Recurrent rectal cancer patients continued to have significant worse DFS even after patients with

Primary v Recurrent Disease

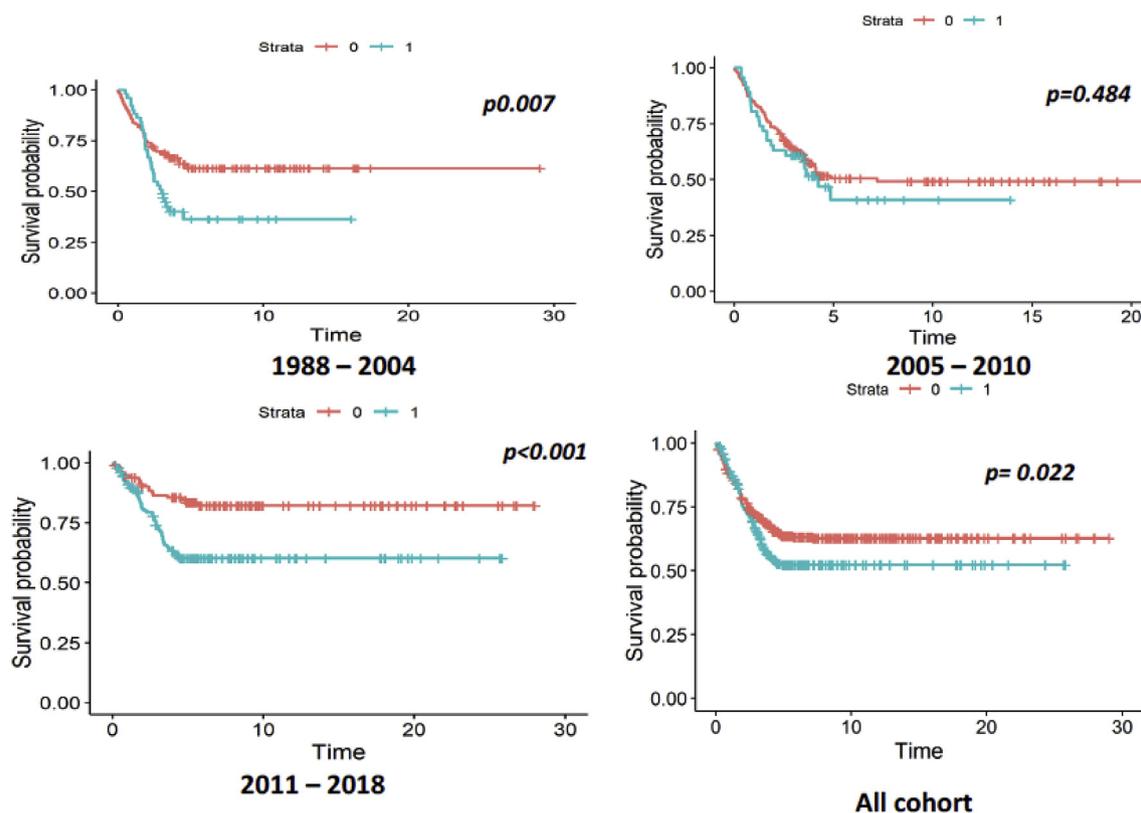


Fig. 4. Overall survival in primary (Red) and recurrent disease (Green): Patients undergoing resection for primary disease had significantly improved overall survival at time points 1988–2004 and 2011–2018 compared to those with recurrent disease ($p = 0.007$, $p < 0.001$ respectively). Overall survival for the total cohort was significantly improved in patients undergoing resection for primary disease versus recurrent disease ($p = 0.022$).

R1 resections were excluded. A study examining outcomes of 40 consecutive exenterations over a nine year period for locally advanced versus locally recurrent colorectal malignancy reported that 5-year overall survival was significantly inferior in recurrent disease as opposed to upfront advanced disease (58.7% vs. 11.8%, $P = 0.022$) [31]. Similar to cotemporary work from the PelvEX collaborative group and other centres, the authors report worse outcomes in recurrent disease and the importance of achieving an RO resection [1,30,32,33].

The five year survival probability of each primary pathology was analysed at each time point to assess survival outcomes. The analysis demonstrates that patients operated on during this current time point (2011–2018) had significantly improved five year survival in GI malignancy compared to other time points. There was no change in survival in those operated in 1988–2004 and 2005–2010. Moreover patients with SCC and Other malignancy had similar five year survivals regardless of time point of operation. Interestingly however the current study documents improved survival in patients undergoing exenteration for gynaecological malignancy during 2011–2018. With a significant reduction in the number of patients in the time point the authors postulate that improved patient selection for curative intent is likely to be the underlying reason for such a significant improved survival.

There are limitations to this study, which need to be considered. Firstly, interpretations of these results are limited somewhat by the

degree of heterogeneity, both within each and between centres. This includes the degree of heterogeneity of the patient populations, pathology, variations in the treatment strategies and surgical technique. It is also important to acknowledge that the data is collected over a long time period (1988–2018), which may also introduce a degree of inherent bias, given the evolving treatment strategies over time, which have been described. Changes in adjuvant and neoadjuvant treatment strategies in rectal cancer such as radiation oncology have influenced outcomes over the study period. However, there is a previous collaborative history with a high degree of consistency of approach across the centres included in this study [34,35].

Conclusion

Pelvic exenterative surgery has undergone dramatic changes over the last three decades with its indications now expanding to include significantly increased cases of recurrent disease. Despite increased case complexity over time there has been no significant change in the associated complication profile. Patients undergoing upfront exenteration for primary disease continue to have improved survival compared to those undergoing resection of recurrent malignancy. Finally patients with GI and gynaecological primaries have seen significant improved survival in the last decade.

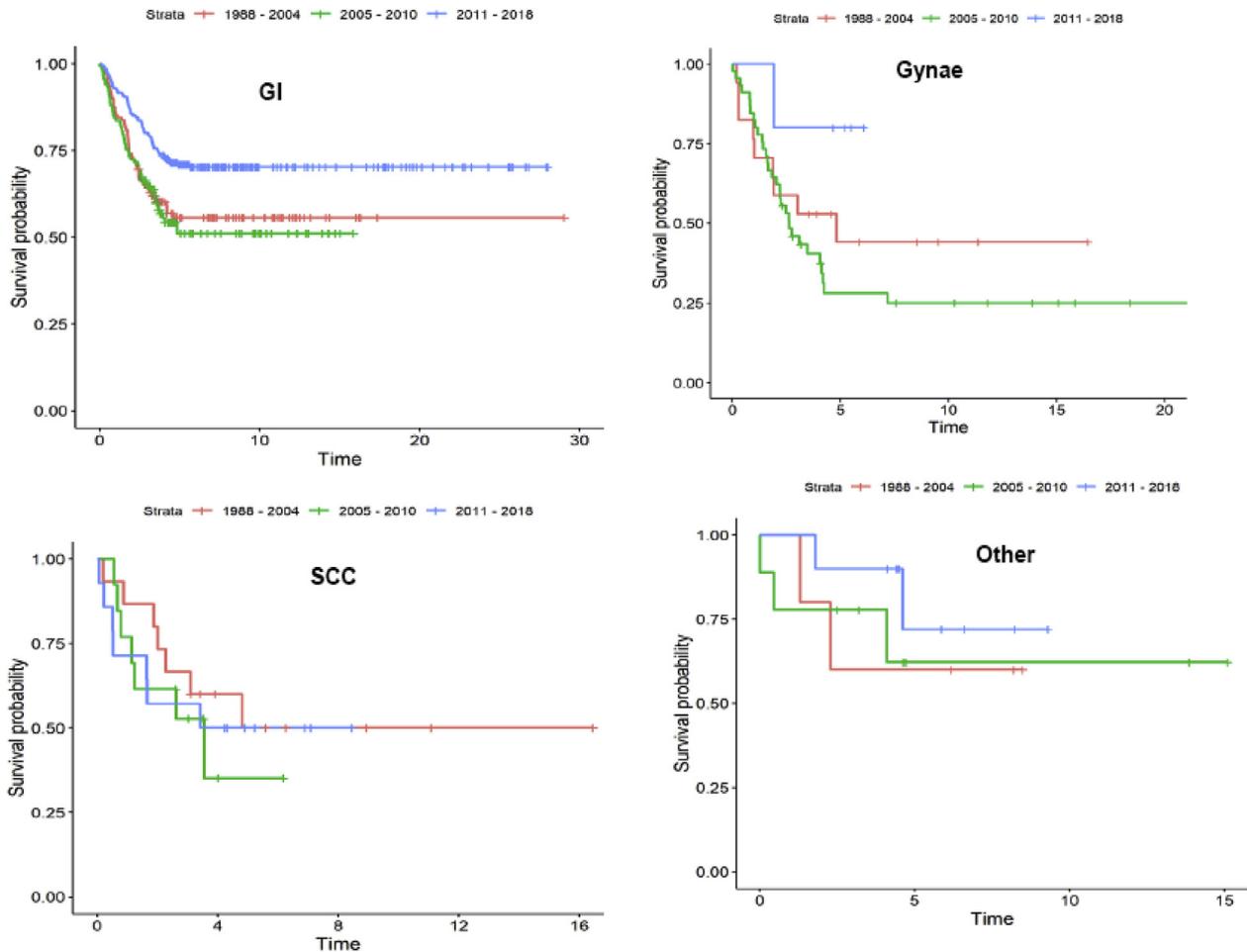


Fig. 5. Overall survival in each histological subtype at each time point. Patients undergoing pelvic exenteration with GI and SCC diagnosed malignancy had significant overall improved survival in 2011–2018 compared to other time points ($p < 0.01$ and $p < 0.05$ respectively). SCC and other malignancy (Melanoma, Prostate, Sarcoma, GIST and Chordoma) did not have improved survival at each time point.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejso.2019.07.015>.

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