Clinics of Oncology

Resview Article ISSN: 2640-1037 | Volume 8

Postoperative Management of Pelvic Exenteration: Strategies for Optimizing Clinical Outcomes

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Received: 18 June 2025
Accepted: 30 June 2025
Published: 05 July 2025
J Short Name: COO

Keywords:

Pelvic Exenteration; Perioperative Management; Perioperative Care; Patient outcomes; Multidisciplinary Approach

Citation:

Reitan Ribeiro, Postoperative Management of Pelvic Exenteration: Strategies for Optimizing Clinical Outcomes. Clin Onco. 2025; 8(5): 1-5

1. Abstract

Pelvic exenteration remains the cornerstone treatment of respectable locally advanced pelvic malignancies patients who have already received radiation. It represents one of the most challenging procedures in oncologic surgery due to its extensive and complex nature, with significant morbidity involved. The complexity of the surgery necessitates a comprehensive and multidisciplinary approach to perioperative management to mitigate complications and enhance patient outcomes. This article aims to synthesize current evidence and expert recommendations on postoperative strategies that contribute to the optimization of clinical outcomes in patients undergoing pelvic exenteration. We conducted a thorough review of the literature, focusing on postoperative management strategies on pain control, urinary function, infection prevention, diet optimization, thrombopenia's prophylaxis and rehabilitation. By integrating evidence-based perioperative management, multidisciplinary expertise and patient-centred care, it is possible to significantly impact the recovery trajectory and quality of life of patients subjected to this rigorous surgical intervention. This article contributes to the ongoing dialogue on enhancing perioperative care, offering insights that could enhance clinical practice and future research in the field of oncologic pelvic surgery.

2. Introduction

As important as the quality of execution of a complex procedure is the postoperative care that these procedures require for a satisfactory outcome. Pelvic exenteration, with its variations, is one of the largest and most complex procedures used in oncology. Although its mortality rate has been decreasing over time [1-3], its complications remain relevant, especially as more complex urinary, intestinal, and vaginal reconstructions are offered to patients [4].Enhanced recovery after surgery (ERAS) protocols plays an important role in improving postoperative outcomes [5]. However, information on specific postoperative care in pelvic exenteration is relatively limited, and standardizing care is difficult due to the particularities of patients undergoing this surgery and the variations in terms of extent and reconstruction. Therefore, the experience of services still carries significant weight in decision-making regarding postoperative management.Our objective is to review recommendations regarding the main postoperative care for patients undergoing total superelevated pelvic exenteration.

3. Methodology

We conducted a systematic search in the PubMed, Embase, and Cochrane Library databases, using a combination of keywords and MeSH terms related to "pelvic exenteration", "proctosigmoidectomy", "radical cystectomy", "radical hysterectomy", "perioperative""postoperative", "complications", "clinical outcomes", "diet", "physiotherapy", "thrombosis prophylaxis""thrombosis", "infection", "renal insufficiency", "fistula", and "rehabilitation". Data filters were applied to include studies published in the last fifteen years, reflecting the most recent practices and technologies. The search was complemented by a manual review of the references of selected articles to identify additional relevant studies.The inclusion criteria were: articles published in English, with perioperative management strategies in adult patients undergoing pelvic exenteration or major abdominal surgery involving one of the three organs of interest (rectum, uterus, and bladder), articleswith quantitative or qualitative data on clinical outcomes associated with different perioperative management strategies.Articles that did not provide specific data on postoperative management, case reports, editorials, comments, or non-systematic reviews, and articles that studied pediatric populations were excluded from the recommendations. Although these articles may have been used for discussion and better clinical understanding.Data Extraction and Analysis: Two independent reviewers performed data extraction, including information on authors, year of publication, study design, study population, examined postoperative management interventions, and main reported outcomes. Discrepancies were resolved by consensus or by a third reviewer. The extracted data were synthesized qualitatively, highlighting postoperative management strategies associated with better clinical outcomes. The synthesis focused on identifying patterns and divergences in evidence, as well as gaps in current knowledge.

This systematic review study does not involve primary patient data, therefore ethical approval was not required. All analyzed data are derived from previously published and publicly available studies.

4. Results and Discussion

The management of postoperative care, with a focus on a multidisciplinary approach to complications and early rehabilitation, is essential to optimize surgical outcomes. Despite ongoing advances in surgical technique, the 30-day perioperative morbidity remains relatively high, with rates ranging from 27% to 41.5% for pelvic exenteration due to colorectal, gynecological, or urological malignancies [6].

5. Pain Management

Different societies [7] recommend that multimodal analgesia be offered for the treatment of postoperative pain. This means using a variety of medications and analgesic techniques combined with non-pharmacological interventions. Intraoperative anesthetictechniques focused on opioid-sparing are known to accelerate postoperative recovery, decreasing symptoms of paralytic ileus and reducing hospital stays [8]. The use of epidural catheters, spinal anesthesia, and direct muscle block of the abdominal wall (transversus abdominis plane block - TAP block) also leads to a reduced need for intravenous and oral opioids postoperatively. When an epidural catheter is used, it should be managed by the anesthesiologist for at least 24-48 hours postoperatively, thus reducing cardiovascular and gastrointestinal morbidity [9,10].The composition of analgesia can vary greatly between services. However, there is a consensus, with a strong recommendation, that acetaminophen and/or non-steroidal anti-inflammatory drugs (NSAIDs) be provided to adults as part of multimodal analgesia for the management of postoperative pain in patients without contraindications [7].A meta-análise de 60 estudos constatou que há uma diminuição no consumo de morfina em 24 horas quando paracetamol, AINEs ou inibidores da COX-2 são administrados além da morfina PCA após cirurgia, sem diferença clara entre eles. Em relação a náuseas e vômitos, houve uma redução significativa com AINEs em comparação com o placebo, mas não para paracetamol ou inibidores da COX-2, nem para AINEs em comparação com paracetamol ou inibidores da COX-2. Com base em seis estudos (n = 695), 2,4% dos participantes que receberam um AINE experimentaram sangramento relacionado à cirurgia em comparação com 0,4% com placebo.Outra meta-análise investigou a correlação entre o uso de anti-inflamatórios não esteroides (AINEs) e a ocorrência de fístula anastomótica após cirurgias gastrointestinais. Foram incluídos 24 estudos, totalizando 31.877 pacientes, e os resultados indicaram uma associação significativa entre o uso de AINEs e vazamento anastomótico (OR 1,73; IC 95% = 1,31-2,29, P <0,0001). Análises adicionais mostraram que os AINEs não seletivos, mas não os inibidores seletivos da ciclo-oxigenase-2, estavam significativamente associados ao vazamento anastomótico. Entretanto, outra meta-análise com uma população homogênea de pacientes com câncer colorretal, incluindo 10.868 pacientes, concluiu que a taxa de fístula após a cirurgia colorretal não aumentou em pacientes que usaram AINEs para analgesia pós-operatória em comparação com não usuários. Isso se manteve não significativo após a estratificação para ressecções anteriores baixas e uso de AINEs seletivos ou não para COX-2. Assim, a associação de AINEs com a ocorrência de fístulas permanece controversa.A meta-analysis [11] of 60 studies found that there is a decrease in 24-hour morphine consumption when paracetamol, NSAIDs, or COX-2 inhibitors are administered in addition to PCA morphine after surgery, with no clear difference between them. Regarding nausea and vomiting, there was a significant reduction with NSAIDs compared to placebo, but not for paracetamol or COX-2 inhibitors, nor for NSAIDs compared

to paracetamol or COX-2 inhibitors. Based on six studies (n = 695), 2.4% of participants who received an NSAID experienced surgery-related bleeding compared to 0.4% with placebo.Another meta-analysis [12] investigated the correlation between the use of non-steroidal anti-inflammatory drugs (NSAIDs) and the occurrence of anastomotic leakage after gastrointestinal surgeries. A total of 24 studies, including 31,877 patients, were included, and the results indicated a significant association between NSAID use and anastomotic leakage (OR 1.73; 95% CI = 1.31-2.29, P <0.0001). Additional analyses showed that non-selective NSAIDs, but not selective COX-2 inhibitors, were significantly associated with anastomotic leakage. However, another meta-analysis with a homogeneous population of colorectal cancer patients, including 10,868 patients, concluded that the rate of fistula after colorectal surgery did not increase in patients who used NSAIDs for postoperative analgesia compared to non-users. This remained non-significant after stratification for low anterior resections and the use of selective or non-selective COX-2 NSAIDs. Thus, the association of NSAIDs with the occurrence of fistulas remains controversial.A special concern regarding the use of NSAIDs is the renal function of patients undergoing pelvic exenteration. A Cochrane meta-analysis [13] analyzed the effect of non-steroidal anti-inflammatory drugs (NSAIDs) in the perioperative period on postoperative renal function in patients with normal renal function. Twenty-six studies with a total of 8,835 participants were identified. The results indicated that the use of NSAIDs had uncertain effects on the risk of postoperative acute kidney injury (AKI) and may slightly increase serum creatinine (SCr) levels. Additionally, there were no reliable conclusions regarding the impact of NSAIDs on the need for renal replacement therapy (RRT), mortality, or length of hospital stay.These results highlight the need for caution in the use of NSAIDs for postoperative pain control in patients, and their use should be balanced with the associated risks. In our departments, we prefer their use in patients with normal renal function only in cases wherepain control with other methods is insufficient and for a short period, typically reducing their use to only 2-3 days.Regarding the use of opioids, although the general recommendation is to prefer oral over intravenous administration of opioids for postoperative analgesia, the oral route is often partially or completely compromised in the first days for patients undergoing pelvic exenteration. Therefore, it is recommended [7] that postoperative systemic analgesia be administered through patient-controlled analgesia (PCA) via intravenous route, and in these cases, a basal dose of opioids should not be used.Thus, analgesia options should be individualized, taking into account individual pain sensitivity, the type of incision performed, the presence of ostomies or drains, and the comorbidities of each patient.

6. Preservation of Urinary Function

The preservation of urinary function is crucial in patients undergoing pelvic exenteration. While the most obvious concern may seem to be urinary reconstruction and its complications, the maintenance of renal/tissue perfusion and diuresis often precedes the complications of reconstructions and may be even more relevant since renal failure, besides being serious in itself, greatly increases the incidence of practically all other complications in abdominal surgeries [14].A meta-analysis [14] of 18,473 patients revealed that patients with intraoperative oliguria have twice the risk of postoperative Acute Kidney Injury (AKI). Intraoperative oliguria was also associated with a fourfold increase in the demand for postoperative renal replacement therapy and in-hospital mortality (HR: 1.83, 95% CI: 1.24–2.69, P=0.002). On the other hand, reversing oliguria as a goal of intraoperative resuscitation and blind volume expansion can result in fluid overload, contributing to a higher risk of AKI [15] and increased postoperative complications [16]. It is important to note that all major surgeries are performed in a physiological antidiuretic state [17], and therefore it is common to observe a more flexible approach to intraoperative oliguria [18], especially when there are no other signs of hypoperfusion present [19]. This is due to the necessary preanesthetic fasting, which is aggravated by the use of narcotic and anesthetic agents and by the manipulation of visceraand peritoneum [20]. There is also reflex vasoconstriction, mediated by the neuroendocrine response, surgical trauma, blood loss, insensible fluid losses, and mechanical ventilation. Therefore, according to Mendes et al. [17], knowledge about the renal response to surgery and anesthesia, the adequacy of volume replacement, preferably guided by dynamic parameters, and attentive care during and after surgical stress are much more powerful weapons than any single parameter to minimize the risk of postoperative kidney injury.The same care regarding hydration should be given postoperatively, but the hemostasis mechanisms require a different approach from intraoperative care. Although anuria is abnormal and should be taken seriously, oliguria, however, can be a normal and expected occurrence as a result of judicious fluid management in the perioperative period [21]. Mizota et al. [22] suggest 0.3 ml/kg/h as the urine output threshold for increased risk of acute kidney injury in major abdominal surgeries.Oral hydration provides an improved method of fluid delivery postoperatively. It is recommended that patients receive 25 to 35 ml/kg of water per day during the recovery period [23], although this is an ambitious goal in the first days post-pelvic exenteration due to the ileus observed in most patients. Moreover, even this volume, which seems adequate, may be insufficient in patients with an ileostomy. Considering patients with adequate perfusion, the American Society for Enhanced Recovery (ASER) recommends the use of buffered isotonic crystalloids for the treatment of hypovolemia in patients undergoing colorectal surgical procedures [21], and the same can be extrapolated to patients undergoing other major surgeries like pelvic exenteration. Restrictions on the use of starch solutions are based on extrapolations from critical care literature

[21]. It is suggested that the same hemodynamic monitoring used intraoperatively be extended into the postoperative period as much as possible to guide fluid replacement [21].

7. Urinary Complications

Urinary tract infection (UTI) can occur in up to 40% of patients, and fistulas in up to 16%, making these the two most common urinary complications [24]. Urinary catheters help prevent stenosis of the uretero-ileal or uretero-colonic anastomosis, and double J catheters oreven external catheters that allow for individual output measurement can be used. These can be removed 3 to 4 weeks postoperatively after the adequate functioning of urine output and normalization of renal function.In cases of suspected urinary fistula, biochemical analysis of the drain output (creatinine or urea measurement), computed tomography (with an emphasis on the late phase), or even pyelography if ureteral catheters or nephrostomies are positioned can be employed. The need for surgical intervention should be individualized and reserved for refractory cases. Management with interventional radiology or prolonged urinary catheters is the preferred approach for late fistulas, occurring more than 6 days postoperatively [25].

8. Antibiotic Prophylaxis and Infections

In patients undergoing pelvic exenteration, the rate of surgical wound infection is estimated to be between 30% and 43% [3,26], while the rate of pelvic abscess can vary from 6% to 20% (3-5), making infectious complications one of the most important causes of morbidity and delays in hospital discharge. Therefore, some centers [27] recommend the use of extended prophylaxis for up to 5 days.The choice of antibiotic used for prophylaxis should take into account the three possible routes of contamination: urological, gynecological, and colorectal. Thus, Cefazolin combined with Metronidazole or Cefoxitin alone are the two initial options that cover all three sites simultaneously [28]. Although the use of Ceftriaxone as part of prophylaxis in colorectal surgery is common, we suggest reserving this antibiotic for a potential need to treat an infectious condition.In general, it is recommended that antimicrobials be initiated 60 minutes before the surgical incision (120 minutes for Vancomycin or Fluoroquinolones) and that the duration of prophylaxis be less than 24 hours [28]. The use of extended prophylaxis in pelvic tumors has limited literature, however, as mentioned earlier, its use is not uncommon. We recommend the use of prophylaxis for 24 hours, as extended use may also hinder and delay the early diagnosis of other complications such as fistulas, which may have their initial symptoms suppressed by antibiotics.In addition to pelvic abscesses, the accumulation of inflammatory fluid with eventual bacterial translocation, perineal wound dehiscence, or even complex intestinal and urological fistulas can lead to a sequela known as “empty pelvis syndrome” [24]. Such complications should be anticipated during exenteration surgeries and can be prevented or mitigated by the creation of muscle flaps, placement of silicone prostheses, or even by inserting the greater omentum sutured over the pelvis [29].

9. Prevention and Treatment of Ileus

The decision regarding the initiation of an oral diet in patients undergoing pelvic exenteration begins with considering whether a nasogastric tube was placed during surgery. Although in previous decades its use was advocated to reduce abdominal distension and vomiting from major abdominal surgeries due to postoperative ileus, several studies have failed to demonstrate such a benefit [30]. A Cochrane meta-analysis with over 5000 patients confirmed an earlier return of bowel function and fewer pulmonary complications in patients who did not use prophylactic nasogastric tubes [31]. Therefore, prophylactically placed nasogastric tubes should be removed as soon as possible.The prevention of postoperative ileus is another relevant factor for reestablishing the diet of patients. According to the Enhanced Recovery After Surgery (ERAS) protocol [30], the essential elements for reducing ileus are: (a) limiting the administration of opioids through the application of multimodal analgesia techniques (including the use of mid-thoracic epidurals and peripheral nerve blocks), (b) using minimally invasive surgery, (c) eliminating the routine placement of a nasogastric tube, and (d) maintaining fluid balance, including goal-directed fluid therapy, to limit the duration of postoperative ileus. All these items have been discussed, except for the use of minimally invasive surgery, and unfortunately, there is not enough literature for a conclusion regarding its use in this surgery.For the treatment of ileus, chewing gum was initially considered an option with good initial but limited results in low-quality studies [30]. A randomized study [32] showed that the addition of chewing gum to an ERAS postoperative care protocol after elective abdominal surgery did not reduce the length of hospital stay, time to bowel recovery, or rate of postoperative complications.Regarding the pharmacological treatment of ileus, a prospective controlled study [33] observed indices of postoperative ileus with the oral administration of bisacodyl in patients undergoing colorectal surgery. There was a 1-day difference in time to defecation in favor of the bisacodyl group (3.0 versus 4.0 days, $P = 0.001$), while no significant difference in time to first flatus or tolerance to solid food was observed. There was no significant difference in secondary outcomes.

10. Diet

One of the most important advances in the postoperative management of major surgeries has been the understanding of the need to promptly re-establish the patient's diet. The acceptance that even patients with colorectal anastomosis can safely resume a diet 4 hours after surgery with a high rate of acceptance [34,35] was crucial in moving away from old parameters such as the resolution of ileus. Evidently, it is unrealistic to expect patients to achieve the desired level of caloric intake in the first few days.

Therefore, it is important to emphasize the need to guide patients that diet intake should follow their tolerance, and forced feeding is not recommended.

The European Society for Clinical Nutrition and Metabolism (ESPEN) estimated that postoperative protein and energy requirements to maintain postoperative muscle mass are 1.5 g/kg/day and 25-30 kcal/kg/day, respectively [36]. This translates to approximately 2000 kcal for a 70 kg adult. Studies in colorectal surgery patients show that patients' intake in the first days should be around 1300 kcal [37]. To reach the desired level of protein and caloric intake, oral supplements should be used [36-38].It is important to consider that patients undergoing pelvic exenteration are often malnourished. The ESPEN guideline suggests that perioperative immunonutritionor at least postoperative immunonutrition (arginine, omega-3 fatty acids, and ribonucleotides)should be administered to malnourished patients undergoing major cancer surgeries [36]. However, these results also seem to extend to non-malnourished patients, as two randomized clinical trials [39,40], which included non-malnourished patients, showed a reduction in infectious complications with the use of immunonutrition compared to standard oral nutritional supplements.Several studies have compared Total Parenteral Nutrition (TPN) with regular oral intake, and there is evidence that early oral intake of a regular diet after surgery is feasible. A randomized clinical trial [41] published in 2013 with patients undergoing radical cystectomy compared TPN with regular oral intake during the first five days after surgery. Patients who received TPN had a higher rate of postoperative complications (69% versus 49%, p=0.013), including infection (32% versus 11%, p=0.001), with no significant difference in gastrointestinal recovery time and length of hospital stay. Therefore, we prefer to attempt to re-establish the diet orally, leaving the parenteral route as a form of supplementation if the oral route is insufficient.Ileostomies add complexity to the nutritional care of these patients. Nutritional complications of ileostomies include fluid (dehydration) and electrolyte imbalances (mainly hyponatremia), renal dysfunction due to plasma volume depletion, and reduced energy absorption due to the role of the large intestine in energy assimilation [42]. Therefore, strict monitoring of ileostomy output is necessary, and tests to assess fluid and electrolyte disturbances should be routinely performed in these patients to allow for early correction.

11. Rehabilitation and Deep Venous Thrombosis Pro

Early mobilization should be encouraged from the first postoperative day. As soon as patients are clinically stable, without dyspnea or hypotension, they should be encouraged to sit up and then to ambulate, and this should be done with assistance. The impact of early mobilization in critically ill patients was demonstrated in a multicenter randomized clinical trial [43] that evaluated goal-directed mobilization versus usual care in intensive care unit patients. The intervention arm included basic maneuvers such as sitting and standing or stepping in place at the bedside. Early mobilization improved patient mobility throughout the ICU stay, reduced ICU length of stay, and improved patients' functional mobility at hospital discharge.The prevention of DVT is a fundamental part of the rehabilitation process, as this is one of the most frequent complications after patient discharge. Patients in the postoperative period of pelvic exenteration have a risk of up to 4.8% for developing venous thromboembolism [44]. It is recommended that patients undergoing pelvic exenteration use extended prophylaxis for deep vein thrombosis for up to 4 weeks [45].Another crucial part of these patients' rehabilitation is teaching them to manage catheters and stomas. Studies demonstrate the need for assistance and support to be offered to patients by nurses, and the importance of encouraging patients to be involved in stoma care from the beginning, which will contribute to effective and independent self-management [46]. Preoperative and postoperative stoma education in an enhanced recovery program is associated with a significantly shorter hospital stay [47].

12. Conclusion

Pelvic exenteration is a procedure that requires intensive and complex postoperative care, along with a proactive approach from the medical team to optimize surgical outcomes. More studies with this specific group of patients are needed to provide a better understanding of their needs.

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