Early Complications and Morbidity of Radical Cystectomy

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1. Introduction

Radical cystectomy (RC) is the standard treatment for patients with muscle-invasive bladder cancer, and it is also a valid option for selected patients with high-grade non-muscle-invasive bladder cancer, either as a primary treatment modality or for recurrent or refractory tumours after bladder-conserving regimens [1]. Radical cystectomy entails simultaneous surgery on the urinary tract, intestines, and lymph nodes; hence, complications frequently occur after this extensive procedure. According to the literature, the incidence of such secondary conditions varies widely (from 19% to 64%) [2,3], which is probably largely due to disparate definitions of morbidity and to case mix rather than to actual differences. Still, it is essential to consider the whole spectrum of complications, including minor problems as well as perioperative mortality, when planning patient treatment, when evaluating new treatments or surgical techniques, and, most important, when counselling individual patients.

There is a real lack of standardised reporting of complications after RC; thus, it is almost impossible to compare different series of RC cases. Today, the most common complications are gastrointestinal problems followed by infectious events.

2. Mortality

There is considerable variability in the mortality rates reported in the modern urologic literature, with figures ranging from 0.8% [4] to 8.3% [5]. There is also variation in the way that different investigators define perioperative
mortality. It was previously common to use 30-d mortality or in-hospital mortality; however, improvements in postoperative care have further postponed surgery-related deaths, and today, 90-d mortality rates are usually reported. Approximately one-third of postoperative mortality occurs within 30 d, and one-third occurs between 30 d and 60 d. Reporting 90-d mortality adds almost as many deaths as the other two periods combined. An example of the better accuracy of using 90-d mortality is a population-based study that has shown 30-, 60-, and 90-d mortality at 1.1%, 2.4%, and 3.9%, respectively [6].

Numerous studies in the literature suggest a correlation between postoperative mortality after RC and hospital and surgeon volume. Different cut-offs have been used for surgeon volume. One group investigated postoperative mortality in the elderly and noted a very low threshold of >2.75 cystectomies per year and per unit [7], although surgeon volume in this series was also found to have a consistent impact on the mortality. Furthermore, a comparison of all hospitals in Texas in the United States revealed significantly lower mortality rates in the facilities where >10 cystectomies were performed each year [8]. Even with higher numbers of RCs, there still seems to be a relationship between hospital volume and postoperative mortality. To evaluate the impact of procedure volume, Barbieri et al [9] conducted a study using data obtained from the University HealthSystem Consortium Clinical Database, which comprises >6000 cystectomies performed at academic centres. The results revealed lower in-hospital mortality rates at centres that annually performed >50 cystectomies compared with those that handled 26–50 such cases each year (0.54% and 1.42%, respectively; p = 0.007). Barbieri and colleagues, however, did not use multivariable analysis to adjust for patient- and tumour-related variables.

Besides procedure volume, other hospital-related factors that have been suggested to affect mortality include the above-mentioned surgeon volume [7,10] as well as the ratio of registered nurses to patients [8]; however, centre volume probably has a greater impact on mortality than does surgeon volume [7]. Moreover, Gilbert et al [11] proposed that nonindex case volume modifies the effect of hospital volume on mortality after RC, and those researchers observed that postoperative hospital-volume–dependent mortality after RC was also influenced by the volume of other urologic oncologic procedures performed in the same unit.

Mortality after RC is also affected by patient-related factors such as patient age, tumour stage, and histologic subtype, which were recently found to independently predict 90-d mortality in a large dataset (n = 5510) [6]. Furthermore, an analysis using the Adult Comorbidity Evaluation–27 instrument has demonstrated that increased comorbidity is independently associated with an elevated risk of 90-d mortality [12]. Investigators using the modified Charlson score found no such association between increased comorbidity and mortality after RC [8]. The American Society of Anaesthesiologists (ASA) score is perhaps the most frequently used clinical measure of preoperative comorbidity, and it has also been reported to be associated with an increased risk of post-RC mortality [13].

3. Reporting of complications

Standardised methods for reporting data on surgical complications or morbidity after RC are urgently needed [14]. Until recently, complications were frequently classified as being minor or major based on different definitions, which made comparison of series impossible. The rate of such secondary problems or conditions after RC is also affected by the length of follow-up because many complications are time dependent [15]. Hollenbeck et al [16] studied data on 2538 cases obtained from the National Quality Improvement Program, which is a prospective quality management initiative of 123 US Department of Veterans Affairs medical centres, and the results of that evaluation showed that 30.5% of the patients had at least one complication at 30-d follow-up after RC.

The Clavien system for classifying surgical complications was originally developed in the 1990s for use in organ transplant surgery [17], and it was modified in 2004 [18]. Now, it probably represents the coming standard for both complications reporting and quality assessment. This system can be applied to all kinds of surgery in all parts of the world, and it has also been used in RC series [3,19].

4. Short-term complications

On average, a patient loses 560 ml [20] to 3000 ml [21] of blood during RC, indicating that this type of surgery often leads to considerable loss of blood and, consequently, to transfusions. Blood transfusions are associated with major complications [13] and with high total hospital costs for RC [22]. It is plausible that the technical development of radical prostatectomy (ie, a better technique for dorsal venous plexus ligation) has been responsible for the decreased transfusion rates seen over time in some cystectomy series [4]. It has also been suggested that adding epidural anaesthesia to general anaesthesia might decrease the need for perioperative transfusion [23]. In any case, it is likely that other factors are also important, for instance, intraoperative fluid restriction and meticulous performance and haemostasis at surgery. Furthermore, it has been proposed that new technical apparatus such as the bipolar device (LigaSure) [24] and the harmonic scalpel can be useful. The results of a small single-centre randomised trial [25] have suggested that a stapling apparatus can decrease blood loss and lower the need for transfusions.

Feared complications immediately after RC include intestinal anastomotic leak and urinary extravasation caused by anastomotic or reservoir leakage. In a prospective randomised study [26], perioperative stenting was found to decrease urinary leakage. Even in the absence of available evidence, it seems wise to recommend that drains be left in place until anastomotic integrity is established in the intestinal and urinary tracts. Due to the relatively low extravasation rate associated with RC, it is probably not
necessary to perform routine postoperative urography or stentograms in patients with a normal postoperative course [27,28]. Gastrointestinal events probably represent the most common type of complication during the period after RC. Postoperative intestinal anastomotic leakage has been described in 3% of patients [5], but due to lack of corroboration in the urologic literature, no firm recommendation can be made as to how this complication can be avoided (eg, by use of anastomotic techniques).

Compared to urinary or intestinal leakage, intestinal obstruction is more common as a complication of RC, and it was found to affect 23% of patients in a recent cystectomy series [3]. Additionally, 18% postoperative ileus was observed in an assessment of a small single-centre series in which patients were treated with a multimodal approach that included epidural analgesia, early enteral nutrition via jejunal nutrition cannula, early nasogastric tube removal, and abandoning bowel preparation and fasting before surgery [29]. Notably, gum chewing was found to decrease time to bowel movements after RC in a nonrandomised comparative study [30].

Infectious events are the second most common complications of RC, constituting 25% of all early complications within 90 d of the surgery, according to a recent investigation [3]. Furthermore, a nonrandomised prospective study [31] has shown that early nasogastric tube (NGT) removal combined with metoclopramide can decrease atelectasis after RC. Indeed, early NGT withdrawal seems advisable not only because it can combat atelectasis, which is a precursor of pneumonia, but particularly because it might also enhance postoperative bowel recovery [29]. Adequate perioperative antimicrobial prophylaxis to prevent postoperative infectious complications is standard practice in the care of surgery patients, but information is lacking with regard to the optimal schedule in conjunction with RC.

Nevertheless, despite the use of prophylactic treatment in modern surgery, postoperative deep vein thrombosis and pulmonary embolism contribute significantly to the morbidity and complication rates after RC, representing 8% of all complications [3]. Prolonged thromboprophylaxis for up to 4 wk after major abdominopelvic cancer surgery is generally recommended, and even if low-dose unfractionated heparin is more cost effective [32], most patients today receive low-molecular-weight heparin. Such treatment might be enhanced by the use of graduated compression stockings, although as of yet there is no clear evidence supporting that approach in RC patients.

Wound-related complications, primarily dehiscence in the early postoperative period, constitute 15% of all early complications of RC [3]. However, when using a midline incision, several factors might affect the incidence of wound separation, including surgical technical issues. One such factor is a suture-to-wound length ratio ≥4, which was shown in a prospective clinical trial [33] to cause dehiscence in only 0.7% cases, a lower level than those seen in most RC series. In the mentioned study, it was also noted that development of hernias was more extensive in patients with a suture-to-wound ratio < 4 than in those with a ratio ≥4 (24% vs 9%). In contrast, a recent meta-analysis of 23 randomised studies comparing the interrupted and continuous methods of laparotomy wound closure demonstrated that the interrupted technique was associated with significantly less dehiscence (odds ratio: 0.58), whereas there was no difference with regard to hernia risk [34].

Awareness has grown regarding the importance of proper lymph node dissection in conjunction with RC [35], and this awareness has led to increasing use of a more extended dissection template. Specialised high-volume centres have claimed that the more comprehensive dissection strategy is not associated with a rise in morbidity [36]; however, there have been no prospective studies of the incidence of lymphocele after RC with limited versus extended lymphadenectomy [37,38], and it has not been confirmed whether the incidence of lymphoceles is the same in all types of surgical units [39]. In a recent series, for example, 8.1% of lymphoceles requiring treatment were found in patients who underwent extended dissection up to the aortic bifurcation [4]. Decreasing the incidence of lymphoceles will probably require a meticulous surgical technique that includes proper identification and ligation or clipping of lymphatic vessels. Decreased lymphorrhoea has also been observed after subcutaneous heparin was administered in the upper arm instead of in the lower half of the body after lymphadenectomy [40].

**5. Morbidity due to radical cystectomy**

It is well known that oncologic surgery in the pelvis is associated with sexual dysfunction in both men and women. Erectile impairment in males after RC is more extensively described in the literature than female sexual dysfunction [41–43]. The functional length of the vagina is probably less important, although an intraoperative length of >12 cm measured during surgery has been proposed [44]. Retubularisation of the vagina should be done in a longitudinal fashion when possible, although that can cause dyspareunia if it results in lumen narrowing; hence, closing the vagina transversely might be more appropriate, as suggested by some authors [44].

Only half of female patients have successful sexual intercourse after RC; related issues can be ascribed to reduced vaginal lubrication caused by damage to autonomic nerves originating from the hypogastric plexus, inability to have orgasms, decreased sexual desire, and dyspareunia [42,43]. Thus far, only one small study has compared nerve-sparing and non–nerve-sparing cystectomy in females [45], and the findings indicated that sexual disturbances were more pronounced after the non–nerve-sparing surgery. Several publications have described improved functional results in males who underwent nerve-sparing RC or RC including the intention to preserve the prostatic capsule and seminal vesicles, although poorer oncologic outcome has been reported for the latter strategy [46].

Rectal dysfunction after anterior exenteration is probably not uncommon, and distress from bowel symptoms was reported in 40% of cases in a multicentre investigation after RC and ileal conduit diversion [47]. Faecal urgency and faecal leakage have also been observed after RC, although...
the mechanism giving rise to those symptoms is not clear because no prospective studies have evaluated rectal function after such surgery.

6. Predicting complications after radical cystectomy

Patient selection is a crucial aspect of any surgery that is as extensive as RC because it can help prevent complications and morbidity or at least keep them to a minimum. The patient’s gender is obviously not a basis for selection; however, due to the necessity of dissecting the anterior vaginal wall in RC, greater blood loss and increased need for transfusions and intensive care were reported for females in a retrospective comparative study [48]. Furthermore, a multivariate analysis has indicated increased overall complication rates in females compared with males [3]. Increasing age has also been associated with higher complication rates in some series [13,49,50].

Use of the ASA score in preoperative assessment of comorbidities is often done as routine clinical practice. A newer and more detailed perioperative risk assessment has also been proposed that uses the Surgical Apgar Outcome Score in conjunction with RC [51]. In one investigation [13], an ASA score of 3 and 4 was associated with increased risk of early major complications, and the same scores were correlated with any type of complication in a recent large study entailing multivariable analysis [3]. In the latter investigation, it was also noted that prior abdominal or pelvic surgery was associated with major complications, and the type of urinary diversion (continent vs conduit) increased the risk of any complication after surgery. In another study [52], it was found that the risk of complications that require invasive intervention (ie, drainage of symptomatic fluid collections) was higher in patients who had previously undergone pelvic radiation than in nonirradiated patients.

Radical prostatectomy or previous irradiation for localised prostate cancer have also been described as risk factors for complications after RC [53]. Several reports have been published regarding body mass index (BMI) as a risk factor for complications after RC; one has indicated that an elevated BMI entails a greater risk [54], whereas others do not describe any such association [55,56]. Increased BMI, however, is the only preoperative variable that has been found to predict increased blood loss [55], which in itself is related to early major complications after RC [3].

In general, it is impossible to estimate the precise risk of complications for individual patients, and different urologists may have different thresholds for withholding a patient from RC. Curative-intent treatment, for example, is given to fewer patients in low-volume units than in high-volume hospitals (37% vs 26%) [57], possibly due to disparate estimates of risk factors for complications after RC.

7. Robotic and laparoscopic radical cystectomy

Robot-assisted laparoscopic RC has emerged as a minimally invasive treatment modality and has led to significant improvements in intraoperative blood loss and length of hospital stay [58]. The cited authors performed a prospective study to compare open and robotic RC, and they observed that the overall complication rate was greater after the open procedure, although the difference was not statistically significant (62% vs 48%, p = 0.07).

8. Conclusions

RC is associated with rates of complications and morbidity that are much higher than those previously indicated when using strict reporting criteria. All hospitals that perform RCs must prospectively register and report postoperative complications so that they can assess their own results and thereby facilitate counselling of patients and planning of individual treatments. When introducing new therapies such as robot-assisted laparoscopic RC, it is of the utmost importance to use standardised methodology for assessment and reporting of complications.

Conflicts of interest

The author has nothing to disclose.

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References


