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## Sphincter preservation for distal rectal cancer - a goal worth achieving at all costs?

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### Abstract

To assess the merits of currently available treatment options in the management of patients with low rectal cancer, a review of the medical literature pertaining to the operative and non-operative management of low rectal cancer was performed, with particular emphasis on sphincter preservation, oncological outcome, functional outcome, morbidity, quality of life, and patient preference. Low anterior resection (AR) is technically feasible in an increasing proportion of patients with low rectal cancer. The cost of sphincter preservation is the risk of morbidity and poor functional outcome in a significant proportion of patients. Transanal and endoscopic surgery are attractive options in selected patients that can provide satisfactory oncological outcomes while avoiding the morbidity and functional sequelae of open total mesorectal excision. In complete responders to neo-adjuvant chemoradiotherapy, a non-operative approach may prove to be an option. Abdominoperineal excision (APE) imposes a permanent stoma and is associated with significant incidence of perineal morbidity but avoids the risk of poor functional outcome following AR. Quality of life following AR and APE is comparable. Given the choice, most patients will choose AR over APE, however patients following APE positively appraise this option. In striving toward sphinc-

ter preservation the challenge is not only to achieve the best possible oncological outcome, but also to ensure that patients with low rectal cancer have realistic and accurate expectations of their treatment choice so that the best possible overall outcome can be obtained by each individual.

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**Key words:** Rectal cancer; Survival; Local recurrence; Morbidity; Anorectal function; Quality of life; Patient preference

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### INTRODUCTION

In the management of patients with rectal cancer, sphincter preservation is a priority and regarded a marker of surgical quality. Technical and technological advances have led to an increase in sphincter preserving surgery and a fall in the rate of abdominoperineal excision (APE)<sup>[1]</sup>. Furthermore, the recognition of the oncological importance of the circumferential, rather than distal resection margin, has allowed an increasingly aggressive surgical approach. The knowledge that a distal margin of 1 cm will safely allow complete tumor removal affords an ever greater proportion of patients the opportunity of sphincter preserving surgery for low rectal cancer<sup>[2]</sup>. In addition, our ever increasing understanding of tumor behaviour gives patients new options in the form of non-operative

treatment (following complete response to neo-adjuvant treatment), or transanal excision in selected circumstances. On the other hand, tumor down-staging following neo-adjuvant chemoradiotherapy has not led to the expected increase in sphincter preserving surgery.

Thus, for patients with low rectal tumors, and for whom APE would formerly have been the only option, a number of sphincter preserving options are now available. However, while it may be technically possible to reconstruct (or avoid radical surgery altogether) an increasing majority of patients with rectal cancer, we should pause to consider the overall merits of this approach and consider the patient's overall outcome (both oncological and functional), while remembering that there remain acceptable non-reconstructive alternatives (APE or low Hartmann's procedure). In doing so, a number of factors must be considered and the 'costs' of sphincter preservation evaluated.

## ONCOLOGICAL OUTCOME IN THE TREATMENT OF RECTAL CANCER

The oncological outcome is of paramount importance whether anterior resection (AR), APE, transanal excision, or a non-operative approach is adopted in the treatment of low rectal cancer.

High rates of circumferential resection margin (CRM) positivity (up to 40%) following APE in some series and consequent high local recurrence rates have led to suggestions that the outcome following APE is inherently worse than that following AR. It does appear that rectal tumors in patients who undergo APE are often more locally advanced, more poorly differentiated, and show a lesser response to neo-adjuvant chemoradiotherapy<sup>[3]</sup>. However, with meticulous surgery and the avoidance of tumor perforation and margin positivity, results following APE can be similar to those after AR<sup>[4]</sup>. Indeed, local recurrence rates in the order of 5% can be achieved following the application of a standardised approach<sup>[5,6]</sup>.

Undoubtedly the technique of APE has drifted from that originally described by Miles<sup>[7]</sup> in which a wide dissection of the rectum was performed to produce a cylindrical specimen. Application of TME principles and evolution in technique have resulted in an APE in which the specimen tapers (Morson's waist) at the level of the pelvic floor with a consequent narrow circumferential resection margin and risk of CRM positivity and tumor perforation. Recourse to originally described principles *via* an extra-levator approach avoids "waisting" of the specimen<sup>[8]</sup> and reduces the rate of CRM involvement<sup>[9]</sup>. Nonetheless, rates of CRM involvement may still lag behind those seen in AR<sup>[10]</sup> and there remains a need to further examine surgical technique in APE and develop a standardised approach with appropriate training if needed.

Inter-sphincteric resection represents the most extreme form of sphincter preserving surgery in which part, or all, of the internal sphincter is resected. This approach may be applied to tumors within 2 cm of the sphincter

complex and is made feasible by the recognition that distal intramural tumor spread beyond 1 cm is uncommon. Thus, inter-sphincteric resection becomes an option for patients with tumors within 2 cm of the sphincter complex, in whom pre-operative continence is intact, and for whom the tumor, at least in its distal part, is confined to the rectal wall. Follow-up suggests that local (6.6%) and distant (8.8%) recurrence rates<sup>[11]</sup> are comparable to those in published series of APE. Patients with locally advanced (T3-T4) tumors may become candidates for inter-sphincteric resection if a favourable down-staging response to neo-adjuvant chemoradiotherapy is demonstrated<sup>[3]</sup>. Those who are not suitable for inter-sphincteric resection and require APE are likely to self-select as they have locally advanced tumors, that are poorly differentiated and show poor response to neo-adjuvant treatment<sup>[3]</sup>.

Laparoscopy is increasingly employed as a less invasive approach in the management of rectal cancer. While the initial results from the UK MRC CLASSIC trial highlighted increased rates of margin positivity following laparoscopic rectal cancer surgery (when compared to conventional, open TME)<sup>[12]</sup>, the long-term oncological outcomes do not appear to be compromised<sup>[13,14]</sup>. This study remains the only randomised controlled trial to assess the role of laparoscopy in rectal cancer, however results from prospective series of laparoscopic resection have also demonstrated similar oncological outcomes to those reported following open TME<sup>[15]</sup>.

Transanal surgery for rectal cancer represents an attractive approach that may allow the morbidity and functional sequelae of total mesorectal excision (TME) to be avoided. Better surgical results with lower margin positivity are achieved following transanal endoscopic microsurgery (TEMS) than conventional transanal (TA) excision (2% *vs* 16%)<sup>[16]</sup>, however outcomes are generally inferior to those following radical resection with a 3-5 fold increased local recurrence risk<sup>[17]</sup>. TEMS appears to be a reasonable option (LR < 5%) in selected patients with favourable pathological features (pT1 Sm1; well or moderately differentiated; < 3 cm diameter; no lymphovascular invasion)<sup>[18]</sup>. For tumors with less favourable features, the oncological result following TEMS is inferior to that seen after TME. Difficulty in reliably predicting the T-stage pre-operatively remains an obstacle to patient selection. Likewise, prediction of N-stage is problematic as up to 18% of T1 tumors will have associated nodal disease. However, in patients with adverse pathological features after TEMS, subsequent conversion to radical surgery does not appear to be associated with significantly increased LR rates<sup>[18]</sup>. In reality, the decision to adopt a transanal approach is frequently based upon the fitness of the patient.

One-fifth to one-quarter of patients following neo-adjuvant chemoradiotherapy will show a complete pathological response. Predicting those likely to respond and those who have had a complete pathological response remains difficult - up to 40% of patients who appear to have had a complete clinical response have residual disease following

resection<sup>[19]</sup>. Conversely, approximately 10% of patients who have an incomplete clinical response will show a complete pathological response<sup>[20]</sup>. Observation alone may be a viable alternative in selected patients who show a complete clinical response to neo-adjuvant therapy<sup>[20]</sup>. Local recurrence has been reported in 11% of those who had a sustained complete clinical response. These patients appear amenable to salvage therapy without adverse oncological outcome in the event of local recurrence<sup>[21]</sup>.

There may also be a role for full thickness transanal excision of tumor in selected patients with T3 tumors who show an excellent response to neo-adjuvant chemoradiotherapy and who are deemed unfit for or refuse TME, or who had a perceived complete response to neo-adjuvant treatment. The limited available data point to local recurrence and survival figures that are comparable to those achieved with radical surgery<sup>[22]</sup>. This approach requires further validation.

Finally, endoscopic submucosal dissection is an evolving technique that may represent an alternative sphincter preserving approach in the management of rectal tumors. This technique has been reported with low complication rates and in patients in whom complete resection is achieved (approximately 70%) recurrence rates at short-term follow-up are low<sup>[23]</sup>. Further studies are required to establish the role of this technique.

## FUNCTIONAL OUTCOME AND QUALITY OF LIFE FOLLOWING SURGERY FOR RECTAL CANCER

### Functional outcome

Frequency, urgency, and soiling (anterior resection syndrome) are common problems after anterior resection that reflect loss of the capacitance and compliance of the rectal reservoir. Approximately 60% of patients experience some degree of incontinence, while one-third experience frequent symptoms of urgency and frequency. Post-operative studies suggest that anorectal dysfunction after low anterior resection is more a factor of reduced compliance and capacity, than diminished sphincter function<sup>[24,25]</sup>. Furthermore, reflexes of the anal sphincter that help to maintain continence are preserved after low anterior resection<sup>[26]</sup>.

Patients undergoing inter-sphincteric resection have the additional insult of reduced internal sphincter function<sup>[24]</sup>. Inter-sphincteric resection is associated with a fall in resting anal canal pressures<sup>[27]</sup> and continence when compared to conventional anastomosis, but not with a worsening of stool frequency (typically averaging 2/24 h<sup>[28]</sup>) and urgency<sup>[29]</sup>. Long-term satisfactory continence rates are achievable in 75% of patients<sup>[11]</sup>. Outcomes, particularly in the first post-operative year, can be improved by performing only a partial or subtotal resection of the internal sphincter and through construction of a colonic J-pouch<sup>[27,30,32]</sup>. Pre-operative radiotherapy significantly worsens the functional outcome following inter-sphincteric resection<sup>[11]</sup>.

Following straight anastomosis progressive dilatation

of the neorectum can allow some improvement in compliance<sup>[33]</sup> and function over time. Colonic reservoirs (J-pouch or coloplasty) may allow early preservation of function by providing a neorectum functionally comparable to the resected rectum. It is technically possible to create a J-pouch in the majority of patients (95%)<sup>[34]</sup>. With optimum pouch size (5 cm)<sup>[35,36]</sup> and level of anastomosis (< 8 cm from the anal verge)<sup>[37]</sup>, there appear to be functional advantages to the creation of a colonic J-pouch. Patients undergoing low anterior resection with J-pouch reconstruction have less stool frequency and urgency when compared to those with a straight anastomosis, however this benefit is not maintained beyond two years<sup>[34]</sup>. Surprisingly, this functional gain may not impact positively on quality of life after surgery<sup>[38]</sup>. Evidence would suggest that there is no significant advantage to coloplasty over straight anastomosis<sup>[38]</sup>. Side-to-end anastomosis using a short side limb may represent an alternative to colonic pouch with the limited available data suggesting comparable functional and surgical outcomes, however further studies are needed<sup>[39-41]</sup>.

The benefits of the colonic pouch may not be attributable to an increased capacity when compared to straight anastomosis, but rather due to the interruption of normal propulsive motility<sup>[42,43]</sup>.

Pre- or post-operative irradiation has a significant negative impact on function following anterior resection. In the Dutch TME study, pre-operative radiotherapy was associated with a significant increase in bowel frequency and incontinence (62% *vs* 38% for surgery alone) and this had a significant negative impact on patient satisfaction and daily activity<sup>[44]</sup>. Incontinence was worst in patients with lower tumors<sup>[44]</sup>. These findings have been replicated in other studies with long-term follow-up showing an approximate doubling of symptoms of faecal incontinence, soiling and bowel frequency when compared to patients treated with surgery alone<sup>[45]</sup>. Anorectal manometry has shown irradiated patients to have significantly lower resting and squeeze pressure, while endoanal ultrasound has shown increased scarring of the anal sphincter when compared to non-irradiated patients<sup>[24,45]</sup>. Short course pre-operative radiotherapy and pre-operative long-course chemoradiotherapy appear to impact similarly on anorectal function<sup>[46]</sup>. The functional outcome following post-operative radiotherapy is worse than following pre-operative treatment with patients experiencing increased frequency of defecation and clustering<sup>[47]</sup>.

While reduced following pre-operative radiotherapy, the functional result in patients undergoing low anterior resection with colo-anal anastomosis appears to better with a colonic J-pouch rather than straight anastomosis or coloplasty at 24 mo follow-up<sup>[48]</sup>.

Despite increased tumor down-staging, pre-operative conventionally fractionated radiotherapy does not appear to confer an advantage with respect to sphincter preservation over short-course radiotherapy<sup>[49]</sup>.

Extended pelvic lymphadenectomy is frequently performed in Japan as an adjunct to TME, and often without neo-adjuvant treatment. This approach does not appear to confer an oncological advantage when compared to

TME alone (with neoadjuvant treatment) and is associated with an increased incidence of urinary and sexual dysfunction<sup>[50-52]</sup>.

### Quality of life

There is an absence of randomised studies comparing outcomes following APE and AR for low rectal tumors (due to presumption that AR is superior). As a result, inferences as to their comparative quality of life outcomes can only be drawn from individual studies. None-the-less, the available data challenges the presumption that a permanent stoma automatically renders an inferior quality of life outcome when compared to that following restorative surgery. A meta-analysis of over 1400 patients from 11 studies showed no difference in general quality of life scores between patients who underwent APE and AR. While APE was associated with better emotional and cognitive function scores and superior future perspectives (patients' understanding of disease stage), vitality and sexual function scored better in patients undergoing AR<sup>[53]</sup>. These findings were consistent with those of an earlier meta-analysis<sup>[54]</sup>, however, their interpretation must be tempered by the poor quality of a number of individual studies, and the limited follow-up duration which fails to allow for the progressive functional improvement patients often experience following AR.

### MORBIDITY

The argument in favour of observation (and/or trans-anal excision) in complete responders to neo-adjuvant treatment is the avoidance of the morbidity and functional loss associated with TME, with or without a temporary or permanent stoma. Anorectal dysfunction, sexual dysfunction, difficulty voiding, and urinary incontinence are seen in up to one-third of patients following TME. Furthermore, these problems are exacerbated by pre-operative radiotherapy. Post-operative morbidity following laparoscopic and open rectal resection appears to be similar<sup>[12]</sup>, while a benefit to the laparoscopic approach with respect to long-term complications such as adhesion small bowel obstruction and incisional hernia remains to be proven<sup>[55]</sup>. Laparoscopic resection appears to impact similarly on bladder function when compared to open TME, but may be associated with a worse outcome with regard to male sexual function<sup>[56]</sup>.

For patients undergoing TME, larger studies have shown overall rates of early morbidity of approximately 40%. This figure increases to almost 50% following pre-operative radiotherapy. Of patients undergoing APE, approximately one-fifth develop perineal wound problems<sup>[57]</sup>. The incidence of perineal wound problems rises to 30% following radiotherapy<sup>[57]</sup> and doubles following extralevator APE (38%)<sup>[10]</sup>. Eleven percent of patients undergoing AR developed clinical anastomotic leaks in the Dutch TME trial. The leak rate was not affected by pre-operative radiotherapy, but was reduced with proximal defunctioning stoma (8% *vs* 16%)<sup>[57]</sup>. The mortality rate for non-irradiated patients was 3.3% in the same study.

Again, from the Dutch study we know that approximately 50% of patients undergoing AR will have a de-functioning stoma. It is worth noting that at long-term follow-up (median 48 mo) 21% of patients in one study who had undergone sphincter preserving surgery still had a stoma<sup>[58]</sup>. Loop ileostomy closure is associated with 17% morbidity, however the majority (80%) of patients can be managed non-operatively<sup>[59]</sup>.

### PATIENT PREFERENCE

The limited available evidence suggests that a majority (65%) of patients with rectal cancer are willing to defer decision making about their surgery to their surgeon<sup>[60]</sup>.

What is not known, unlike for breast cancer, is the role that patients with rectal cancer would like to adopt in decision making, and how their given role influences their satisfaction with decision making and outcomes. We do know however that the relative importance that surgeons place on various outcomes such as permanent stoma and incontinence is often not matched by their patients<sup>[61]</sup>. Surgeons may in particular underestimate their patients' concerns. Furthermore, surgeon's choices may frequently be at odds with their patient's inherent and perhaps unrecognised true preference<sup>[62]</sup>. Patients, for example, express a stronger desire to avoid chemotherapy than to avoid permanent stoma, while doctors express the opposite view.

Multimedia decision aids (incorporating patient values into evidence based data) have been used to assess and quantify the relative importance patients with rectal cancer place on different quality of life outcomes. Patients who have had surgery place greater emphasis on the avoidance of incontinence post-operatively than the avoidance of a permanent stoma<sup>[61]</sup>.

Trade-off techniques are another useful means of gauging patient's true preferences and will often highlight disparity between patients' preferences and those of their physicians<sup>[62]</sup>. Using this technique, the strength of a preference is measured by determining the degree of risk of a particular (poor) outcome that the patient would be willing to accept in order to have the treatment. When patient preferences are assessed using time-trade methods, patients strongly express a desire to avoid a stoma with 65% willing to trade a mean of 34% of their life expectancy to avoid this outcome<sup>[63]</sup>. Furthermore, patients expressed a stronger desire to avoid the option of APE and thus permanent stoma than their treating physicians. Again, in patients who have had surgery for rectal cancer, the majority of those without a stoma would be willing to trade frequent (monthly) episodes of incontinence in order to avoid a permanent stoma<sup>[64]</sup>. APE patients would however hypothetically trade fewer years of remaining life to be without a stoma, than AR patients would to be without incontinence<sup>[65]</sup>.

While patients may often be happy to defer decisions as to the type of surgery to their surgeons, the majority of those patients who do choose, would favour AR over APE<sup>[60]</sup>. More patients who have had AR would choose



that option again, than patients who have had APE (69% vs 46%)<sup>[60]</sup>. Interestingly, at longer term follow-up 80% of patients who had APE indicate that they would choose the same option given the benefit of their experience<sup>[60]</sup>.

## CONCLUSION

Sphincter preservation in rectal cancer - a goal worth achieving at all costs? The answer must be no. While we should strive toward sphincter preserving options, we must recognize the limitations of currently available approaches and accept that sphincter preservation may not be the best overall option for each individual patient.

Oncological outcomes following AR and APE should be equivalent, however there remains room to uniformly improve and standardise approaches and outcomes in APE. If equivalence for oncological outcome is achieved, then functional outcome, quality of life, and ultimately patient preference become of paramount importance in decision making for the treatment of low rectal cancer. Anorectal dysfunction and poor functional outcome are common following AR. The alternative of APE or low Hartmann's procedure imposes a permanent stoma. Quality of life following APE appears to be similar to that following AR. Given the choice, most patients would choose AR over APE. It is doubtful however that patients appreciate fully the functional outcome following AR, and also likely that patients harbour excessively negative misconceptions about life with a permanent stoma. Patients must be informed that function may not be as good as they expect after AR, and also that patients who have undergone APE positively appraise this option at follow-up. The morbidity associated with stoma reversal (following AR), and the significant risk of perineal wound problems following APE must also be considered. Non-radical and even non-operative approaches are increasingly an option in the management of selected patients with low rectal cancer that obviate the morbidity and outcomes following TME. Ultimately we must ensure that patients with low rectal cancer have realistic expectations of their treatment options and that their decisions are truly informed.

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