

Total Mesorectal Excision (TME) – Twenty Years On

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Abstract

Introduction: The results of total mesorectal excision (TME) for rectal cancer were first reported 20 years ago. The superior outcome in the original two papers was attributed to the complete excision of the mesorectum, preference for anterior resection over abdominoperineal resection, application of cytotoxic solutions to eradicate exfoliated tumour cells and specialisation in rectal cancer surgery. A review was conducted to examine the evidence from the literature accumulated over the past 20 years in support of this thesis. **Methods:** A Medline search of all studies was carried out pertaining to the issues of mesorectal metastases, anterior resection versus abdominoperineal resection, exfoliated tumour cells in rectal cancer and specialisation in rectal cancer surgery. **Results:** Mesorectal metastases can be found up to 5 cm from the apparent distal edge of a rectal cancer. They occur in pT3 and pT4 tumours. Their presence indicates a poorer prognosis. There is evidence that TME improves outcomes in mid-and low-rectal cancers but its role in upper rectal and rectosigmoid cancers is controversial. It has been difficult to demonstrate the superiority of anterior resection over abdominoperineal resection as comparative studies report similar outcomes. Exfoliated tumour cells have been demonstrated to contribute to anastomotic recurrence and this probability may be reduced by the use of cytotoxic agents to irrigate the rectal stump. Multiple studies have shown that specialisation in rectal cancer surgery result in lower postoperative morbidity and mortality, local and distant recurrence rates and higher rates of sphincter saving resections. **Conclusion:** The majority of tenets espoused in the original papers on TME have found support in follow-up studies since their publication.

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Key words: Rectal cancer surgery, Recurrence, Surgeon, Total mesorectal excision, Tumour implantation

Introduction

In 1982, Heald et al¹ at the Basingstoke District General Hospital introduced the concept of total mesorectal excision (TME) as a means of performing optimal tumour clearance for patients with rectal cancer. Five cases were described where minute foci of adenocarcinoma was demonstrated in the mesorectum several centimetres distal to the apparent distal edge of the tumour. It was reported that total excision of the mesorectum carried out in more than 50 curative anterior resections resulted in no pelvic or staple line recurrence. This dramatic result was published against a background local recurrence rate of up to as high as 32% following rectal cancer at that time.² TME, as described by Heald, involves separate high ligation of the inferior mesenteric vessels, followed by a painstaking downward development of the avascular plane between the rectum and mesorectum on one side, and the sacrum and autonomic nerve plexuses on the other. Sharp dissection is carried out under direct vision and extended to the levators. A right angle clamp is placed below the tumour and the distal rectal stump irrigated. Anastomosis, if performed, is achieved by

stapling. In 1986, Heald and Ryall³ followed up with a paper reporting the oncological results of TME in a 7½-year consecutive series. The cumulative probability of local recurrence at 5 years was 3.7% and that of survival was 87% amongst those who underwent curative resection for rectal cancer. In the discussion section of that paper, the following reasons were advanced as contributing factors to the remarkably low recurrence rates in their series:

- 1) that the mesorectum harboured microscopic and that this was removed in toto in their patients in the process of performing TME;
- 2) that the then standard operation for rectal cancer – abdominoperineal excision – led to poorer results as compared to anterior resection which predominated in their series;
- 3) that special measures were taken to prevent recurrence due to exfoliated tumour cells; and
- 4) that improvements in surgical techniques and specialisation in rectal cancer surgery may substantially improve results.

This article reviews Heald's hypotheses for TME's

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success in light of the evidence that has accumulated over the past 20 years since his original paper. The review also focuses on the application of this knowledge in the current practice of rectal cancer surgery.

Methods

An electronic search of the Medline and PubMed databases was conducted using the following keywords: “total mesorectal excision”, “mesorectum”, “exfoliated tumour cells”, “abdominoperineal resection”, “low anterior resection”, “rectal cancer” and “surgeon”. The terms were mapped to Medline Subject Headings (MESH) terms as well as search for text items. The titles and abstracts of retrieved for assessment and relevant articles were acquired. The references cited in retrieved articles and review articles were crosschecked manually to locate other relevant papers. Papers included in this review were considered pertinent to issues of mesorectal metastases, abdominoperineal resection versus anterior resection, tumour implantation and surgeon-related outcomes in rectal cancer surgery.

Metastases Within the Mesorectum

Heald¹ originally observed that minute foci of adenocarcinoma could be demonstrated in the mesorectum several centimetres distal to the lower edge of a rectal cancer and that these deposits were not necessarily related to lymphatic spread. He posited that failure to totally excise the mesorectum lead to pelvic recurrence as a result of the residual microscopic disease left in situ. The presence of discontinuous spread of rectal cancer within the mesorectum has been confirmed in several studies⁴⁻⁷ and occurs only with tumour depths of pT3 or pT4.^{4,6} The extent of tumour spread was up to 5 cm distal to the lower margin of the rectal cancer in two studies,^{1,5} 3 cm in two other studies^{4,7} and 4 cm in one study.⁶ A 5-cm distal resection margin of the mesorectum would appear to be well supported. This is not an issue in mid- and low-rectal cancers. However, the use of TME in upper rectal and rectosigmoid cancers is controversial. The pathological evidence suggests that TME is unnecessary for tumours at this location. Two clinical studies on the outcomes of the treatment of upper rectal and rectosigmoid cancers treated with wide excision of the mesorectum have demonstrated that the risk of local recurrence is not increased when compared to mid- and low-rectal cancers treated with TME.^{8,9}

When analysed with regards to prognosis, tumour deposits within the mesorectum, whether in the form of lymph node deposits or isolated foci of adenocarcinoma, result in a poorer outcome of patients in terms of overall survival.^{10,11} Heald's original hypothesis that failure to remove the mesorectum completely for mid- and low-rectal cancers results in higher rates of local recurrence and an overall decrease in survival would appear to be well supported by

available evidence.

Anterior Resection versus Abdominoperineal Resection

Heald and Ryall³ alleged the widespread assumption of the day that abdominoperineal resection (APR), which was considered a more “radical” procedure, led to better results. They proposed that anterior resection (AR) should be preferred as long as there was an adequate distal mural clearance of 2 cm and that the mesorectum was completely excised.¹² They argued that manual extraction, lack of dissection under vision, lack of precise definable planes, tearing across the edge of the tumour and leaving soft tissue residue contributed to the higher rates of local recurrence among patients undergoing APR.

There have been no randomised trials comparing AR to APR. Comparable rates of local recurrence and overall survival have been reported when low AR has been matched against APR in non-randomised studies.¹³⁻¹⁷ However, one of Heald's observations that recurrence rates might be increased by inadvertent perforation of the tumour during APR has gained support from a paper by Porter et al.¹⁸ It was reported in this retrospective study that local recurrence was significantly higher in the group that experienced inadvertent perforation during APR compared the group that did not (54% vs 17%, $P < 0.001$). Overall, survival was similarly significantly decreased (29% vs 59%, $P = 0.003$).

One major advantage that AR would appear to have over APR is a better quality of life due avoidance of a permanent colostomy. Again, this has been difficult to prove. Grumann et al¹⁹ performed a quality-of-life study for patients undergoing AR and APR. A multivariate analysis of variance and subsequent post hoc comparisons revealed that patients undergoing APR had consistently better quality-of-life scores than those undergoing AR. Patients undergoing low AR had more gastrointestinal and defaecation-related symptoms resulting in poorer scores.

Nevertheless, AR has superseded APR for mid-rectal and selected distal rectal cancers. Sphincter complex invasion remains an absolute contraindication, whereas pelvic fixation and tumours located less than 2 cm from the proximal margin of the anorectal junction are relative contraindications to performing AR.²⁰

The Significance of Exfoliated Tumour Cells

It has long been known the exfoliated colonic cancer cells are viable and may be the cause of suture line recurrence following large bowel cancer surgery due to implantation.²¹⁻²³ Viable malignant cells scattered onto the raw areas of the freshly dissected pelvis are probably more dangerous than those scattered onto intact peritoneum.²⁴ Gertsch et al²⁵ have been able to demonstrate malignant

cells from the washings of doughnuts' following circular stapling. These viable tumour cells shed intraluminally are capable of growth under favourable circumstances.^{26,27} Umpleby and Williamson²⁸ promoted the routine use of cytotoxic agents to clean the bowel ends to prevent anastomotic recurrence due to implantation. Heald maintained that irrigation of the rectal stump is important if suture line recurrence is to be avoided.³ Agents used for irrigation include chlorhexidine, cetrimide, povidone-iodine, water and mercuric perchloride. Several non-randomised studies have found a significant reduction of the recurrence rate after intraoperative installation of cytotoxic agents, as compared with "historical" patients series.²⁹ A randomised controlled trial has demonstrated that the use of rectal irrigation eliminates exfoliated malignant cells in the rectum in the vicinity of the anastomosis.³⁰ More recently, there has been a proposal to perform whole colon irrigation with cytotoxic solution either preoperatively³¹ or intraoperatively³² to address the problem of exfoliated malignant cells in the proximal bowel. This process may also act as a substitute for mechanical bowel preparation.

Specialisation in Rectal Cancer Surgery

Heald³ attributed part of the reason for his unusually low local recurrence rate following rectal cancer surgery to specialisation. Since then, there have been multiple studies published in support of this contention. Recent research into outcomes of treatment has identified significant surgeon and institutional variability³³ and that these are independent prognostic indicators for rectal cancer.^{33,34} Specialty training in colorectal surgery is associated with a lower rate of APR and a higher proportion of sphincter-saving resections,^{35,36} a more extensive resection,³⁷ lower postoperative morbidity and mortality,^{35,37} a lower local recurrence rate and an increase in overall survival^{18,34-36,38,39} following rectal cancer surgery.

Better oncological results following rectal cancer surgery performed by colorectal surgeons have been observed in several studies. Porter et al¹⁸ reported that the hazard ratio (HR) for local recurrence was 2.5 ($P = 0.001$) when surgery was performed by non-colorectal trained surgeons compared to colorectal trained surgeons. Decreased disease-free survival was associated with non-colorectal trained surgeon (NR = 1.5, $P = 0.03$). Similarly, Penninckx³⁵ reported a relative risk of local recurrence of 0.3–0.8 and a disease free survival of 0.7–0.8 when rectal cancer surgery was performed by sub-specialised surgeons compared to general surgeons. A better outcome after treatment for rectal cancer has been shown to be associated with high volume surgeons^{18,40,41} as well as high volume institutions.^{40,42} Another variable that might explain the better outcome of rectal cancer surgery when performed by

specialised surgeons includes the ability to achieve a higher rate of tumour-free distal and lateral margins⁴³ as well as TME.⁴¹

The results of TME have proven to be reproducible. The Norwegian Rectal Cancer Project⁴⁴ and surgical workshops in Stockholm⁴² both trained surgeons in the use of TME for rectal cancer. Local recurrence rates following rectal cancer in both countries declined from 12% to 6% in Norway and from 10% to 4% in Stockholm.

Conclusion

Most of Heald's^{1,3} original observations regarding the reasons for low local recurrence rate and increased overall disease-free survival following TME have been vindicated. The mesorectum is a repository of discontinuous metastatic tumour deposits that may extend for a variable distance. Total excision of the mesorectum ensures the complete clearance of these deposits for mid-and low-rectal cancer. It has been more difficult to establish if TME benefits patient with upper-rectal and rectosigmoid cancers. It has also been difficult to establish that anterior resection is superior to abdominoperineal resection especially if TME is performed in both operations. Attention to prevention of tumour implantation by the use of cytotoxic agents for irrigation is well supported and reduces the risk of anastomotic recurrence.

Finally, the promulgation of TME has been one of the main drivers of the development of colorectal surgery as a subspecialty. Synergistically, this has led to better outcomes for patients with rectal cancer with improvement in surgical techniques.

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