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Pathologists' Role in the Evaluation of the Prognostic Implications of Circumferential Resection Margin in Resected Rectal Carcinoma

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Abstract: Colorectal cancer is one of the most common malignancies in Sri Lanka as well as in other parts of the world and has a high incidence of cancer related deaths. Recent advances have been made with regard to the biological understanding of this disease and its treatment. Furthermore, new surgical, chemotherapeutic and radiotherapeutic strategies have been developed over the last decade in view of improving the quality of care. The worldwide introduction of total mesorectal excision (TME) in combination with the increasing use of neoadjuvant therapy has significantly improved the overall outcome. An important prognostic factor in rectal cancer is the status of the circumferential resection margin (CRM). The involvement of this margin has been associated with a poor prognosis. Pathologists play a vital role by providing important information for the clinical management of the patient and for the evaluation of health care as a whole. For the patient it confirms the diagnosis and describes the variables that will affect the prognosis, all of which will be relevant for the future management. For health care evaluation, pathology reports provide information for cancer registration and audit related to diagnostic and surgical procedures. Accurate evaluation of CRM in rectal carcinoma is important to determine the risk of local recurrence, which might subsequently be prevented by additional therapy. An increased risk was seen when the distance to CRM was < 2 mm.

Keywords: Colorectal Cancer, Total Mesorectal Excision, Circumferential Resection Margin

1. Introduction

The incidence and the impact of colorectal malignancy on the burden of cancer is changing in most parts of the world [1]. The dietary habits, environmental factors and life style have been identified as important contributory factors for the increased incidence of colorectal cancer. Higher rates occur in industrialized and high resource countries in contrast to most parts of the Asian and African continents. More than one million new cases are being identified every year throughout the world [2]. In Sri Lanka colorectal cancer is the fourth most common cancer in males, and fifth most common cancer in females [3]. Recent advances in medicine have enabled to understand the biological behavior of colorectal cancer in a more meaningful manner, thus improving the management strategies available for patient care.

Total mesorectal excision (TME) which is now considered as the gold standard for tumours of the middle and the lower rectum was first described in 1982 by Professor Bill Heald at the Basingstoke District Hospital in the United Kingdom [4]. In this procedure the rectum is removed along with the mesorectum up to the levators. This technique ensures the removal of the majority of peri-rectal lymph nodes thus contributing to superior oncological results [5]. Although the total mesorectal excision procedure is strictly applicable in the performance of a low anterior resection for rectal carcinoma, the principles of TME (sharp mesorectal excision) can also be applied during abdominoperineal excision of upper rectal tumours [6]. Anterior resections involving the upper rectum may be completed with mobilization of the rectum to beyond 5 cm of the lower margin of the tumour, and which is often above the level of the levator and is referred to as partial mesorectal excision [7]. With total mesorectal excision there is better clearance of the tumour, thus significantly improving the 5-year survival rate. The circumferential resection margin positivity rate is about 5% or less for low anterior resections with TME. The rate is much

higher for abdominoperineal excision of the rectum. Hence, there is a higher local recurrence rate following abdominoperineal excision of the rectum. Evidence suggests that a circumferential resection margin of 1 mm or less adversely affects cancer-specific survival, local recurrence, and distant metastasis [8].

Histopathological reporting of resection specimens for colorectal cancer should be done by a competent pathologist as it provides important information for the clinical management of the patient [9]. Histopathology report will confirm the diagnosis as well as provide prognostic information for the oncologist. Histopathology reports also provide information for cancer registration and comprehensive data for epidemiological studies. To accomplish all these tasks the information contained within the pathology report must be accurate and complete [10]. Numerous studies have shown that adherence to a minimum data set for reporting colorectal cancer significantly improves the quality of histopathology reports [11].

Objective:

Aim of the study was to review the pathologists' role in the assessment of the circumferential resection margin and determine the prognostic implications of the circumferential resection margin in rectal carcinoma.

2. Methodology

A descriptive cross sectional study done at the Department of Pathology, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka, during the period of June 2016 to December 2018. Study sample included 62 cases of rectal carcinoma in whom a total mesorectal excision or partial TME has been performed. Resected specimens were received in sealed containers having an adequate volume of the fixative (10% formalin). The intact surgical specimen was first inspected externally to locate the tumour and the presence of any perforations which could be going through the tumour. The plane of surgical excision of the mesorectum was carefully evaluated by external examination prior to cutting, and photographs were taken to support the gross examination findings. The circumferential (non-peritonealised) surgical resection margin in the vicinity of the tumour was inked to enable the subsequent identification.

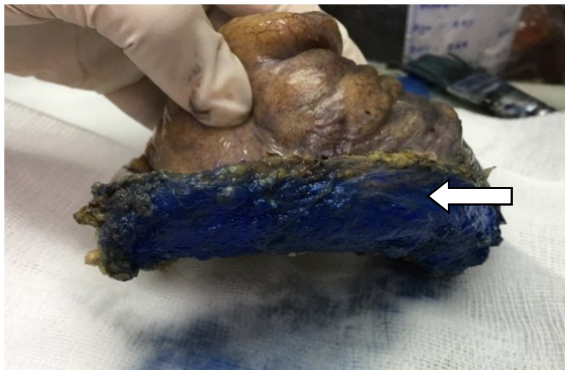

Figure 1. *Non-peritonealised circumferential resection margin which has been inked in blue.*

This margin represents the bare area not covered by a serosal surface. After inking the circumferential margin, the specimen was cut anteriorly apart from a segment extending 20 mm above and below the tumour. Following adequate fixation, the segment of bowel including the tumour and mesentery was transversely sectioned 3-4mm apart to produce sections of the tumour, peri-colic nodes, maximum depth of involvement and the serosal and circumferential margins. Representative histology sections were submitted for processing.

Figure 2. *Transverse sections of the bowel, 3- 4 mm apart.*

Following tissue processing, 3µm thick sections were prepared for staining with the routine hematoxylin and eosin method. Histological diagnoses were reviewed independently by two consultant pathologists. Identification details of the patients were concealed by using a coding system.

3. Results

In the review of the pathologists' role the following macroscopic and microscopic core data items were taken as essential components of the histopathology report format.

Macroscopic core data items

Specimen type

Site of tumour

Maximum tumour diameter

Tumour perforation

Distance to the resection margins (longitudinal & circumferential)

Rectal tumours - Relation to the peritoneal reflection

- Plane of mesorectal excision: mesorectal fascia/ intra mesorectal / muscularis propria
- Mesorectal defects: Yes/ No
- Distance of tumour from the dentate line

Microscopic core data items that were taken in to consideration were the histological tumour type, grade, extent of local invasion, lymphatic invasion, venous invasion, associated pathology, pre-operative therapy, tumour regression, surgical margins, status of lymph nodes, and stage of the tumour.

Table 1. *Macroscopic & microscopic core data items.*

n= 62	Macroscopic core data items	Microscopic core data items
Total mesorectal excision (n=24)	80%	> 98%
Partial mesorectal excision (n=38)	89%	> 98%

The study cohort which included 62 cases had 24 patients with total mesorectal excisions and 38 cases of partial mesorectal excisions. More than 98% of the total sample had the essential microscopic core data items. Essential macroscopic core data items were seen in 80% of the TME specimens and 89% of partial mesorectal excision specimens.

Table 2. *Assessment of the circumferential resection margin.*

Circumferential resection margin	Total mesorectal excision	Partial mesorectal excision
< 2 mm	02	04
2 – 5 mm	02	06
> 5 mm	20	28

n= 62

Distance to the circumferential resection margin was evaluated in 3 categories after considering the normal distribution pattern of the results.

Table 3. *Circumferential margin status in association with tumour stage, grade & recurrence.*

Circumferential margin	Tumour grade	Tumour stage	Recurrence	Statistical significance
< 2 mm	100% -High grade	TNM -III or above Dukes' -C1 or higher	2	Significant ($p< 0.05$)
2 – 5 mm	>90% high grade	TNM -II and III Dukes' – B &C	-	-
> 5 mm	>80% high grade	TNM -I, II, III Dukes' – B &C	-	-

4. Discussion

Pathologists play an important role in the assessment of the circumferential resection margin in TME and partial mesorectal excision specimens. Essential macroscopic core data items were identified in 80% of TME reports and 89% of partial mesorectal excision specimens. Inclusion of microscopic core data items was highly satisfactory and was present in > 98% of cases from each group (table 1). Distance to the circumferential resection margin was analyzed in 3 categories after considering the distribution pattern of the results. The vast majority in both groups had a distance more than 5 mm (table 2). Only two cases out of 24 patients with TME had a minimum clearance of < 2mm from the circumferential margin. In partial mesorectal excision specimens there were four cases with less than 2 mm distance to the circumferential margin.

Rectal carcinoma specimens with < 2 mm distance to the circumferential margin were associated with high grade tumours. TNM and Dukes'stages were III or above and C1 or higher, respectively. (table 3). There were 2 cases of local recurrence in patients with a circumferential margin of < 2 mm. There was a statistically significant association of grade, stage and local recurrence with a CRM distance of < 2 mm.

Scientific publication of Nagtegaal, Iris D et al has discussed similar findings and shown the importance of a 2 mm distance from the circumferential margin [12]. A study done by Healed RJ, Ryall RDH et al, have also shown the prognostic implications of the circumferential resection margin [13]. Garcia–Granero E, Faiz O et al, have discussed in length the macroscopic assessment of mesorectal excision specimens and the important role of the pathologist in compiling the final report [14]. The dataset enables pathologists to grade and stage cancers in an accurate, consistent manner in compliance with international standards and provide prognostic information [15]. We hope to identify the strengths and weaknesses of our system in view of improving the reporting format, to provide a quality service for patient management.

5. Conclusion

The incidence of colorectal cancer is on the increase in developing countries. Pathologists play an important role in the handling of resected specimens of colorectal cancer and providing meaningful information for the clinicians which would have a direct impact on patient management. Total mesorectal excision is a far superior operative procedure which has a longer disease-free interval. TME specimens have to be handled diligently while paying attention to all the important gross abnormalities. The status of the circumferential resection margin should be assessed during the pathological evaluation as its involvement is known to be associated with an adverse outcome. Communication of the pathological findings at the MDT (multidisciplinary meeting) is extremely useful for the surgeon and the oncologist to get a clear idea of the extent of the spread of tumour, status of the resection margins and the presence of nodal involvement. Pathology reports should provide information that is accurate, complete, understandable, timely and transferable. The use of proformas has been found to facilitate these requirements and their use is strongly recommended [16].

CRM involvement is a strong predictor for local

recurrence after surgery. A margin of < 2 mm is associated with a high recurrence risk compared to cases having a clearance of > 2mm (< p 0.05). The prognostic value of CRM involvement could be independent of the TNM classification. Accurate determination of CRM in rectal cancer is important for determination of local recurrence risk, which might subsequently be prevented by additional therapy.

Disclosure of Conflict of Interest

None.

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