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• COLORECTAL CANCER •

Dose surgical sub-specialization influence survival in patients with colorectal cancer?

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Abstract

AIM: To perform a review of patients with colorectal cancer to a community hospital and to compare the risk-adjusted survival between patients managed in general surgical units versus a colorectal unit.

METHODS: The study evaluated all patients with colorectal cancer referred to either general surgical units or a colorectal unit from 1/1996 to 6/2001. These results were compared to a historical control group treated within general surgical units at the same hospital from 1/1989 to 12/1994. A Kaplan-Meier survival analysis compared the overall survivals (all-cause mortality) between the groups. A Cox proportional hazards model was used to determine the influence of a number of independent variables on survival. These variables included age, ASA score, disease stage, emergency surgery, adjuvant chemotherapy and/or radiotherapy, disease location, and surgical unit.

RESULTS: There were 974 patients involved in this study. There were no significant differences in the demographic details for the three groups. Patients in the colorectal group were more likely to have rectal cancer and Stage I cancers, and less likely to have Stage II cancers. Patients treated in the colorectal group had a significantly higher overall 5-year survival when compared with the general surgical group and the historical control group (56 % versus 45 % and 40 % respectively, $P<0.01$). Survival regression analysis identified age, ASA score, disease stage, adjuvant chemotherapy, and treatment in a colorectal unit (Hazards ratio: 0.67; 95 % CI: 0.53 to 0.84, $P=0.0005$), as significant independent predictors of survival.

CONCLUSION: The results suggest that there may be a survival advantage for patients with colon and rectal cancers being treated within a specialist colorectal surgical unit.

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INTRODUCTION

The question of who should be performing surgery on patients with colorectal cancer has important implications for both specialist colorectal surgeons and general surgeons. This is because it impacts on not only patient management, but also surgical training and the provision of surgical services in regional areas.

A significant volume of literature has been devoted to try and define if sub-specialization benefits patients with colorectal cancer[1-3]. However, there is currently little convincing evidence that specialist colorectal surgeons can achieve superior results when compared to general surgeons. The Australian NHMRC guidelines for the management of colorectal cancer[4] address only the issue of who should perform elective rectal cancer surgery. It states rather enigmatically that "*such surgery should be performed by surgeons who have undergone a period of special exposure to this form of surgery and who have satisfactory experience in the surgical management of rectal cancer*".

The aim of this study was to determine if there was a risk-adjusted survival advantage for patients with colorectal cancer being treated within a specialist colorectal surgical unit when compared to general surgical units.

MATERIALS AND METHODS

The colorectal service was established at Fremantle Hospital in 1996 with the appointment of a single surgeon who had received accredited training in colorectal surgery. The management of these patients was standardized through the use of treatment pathways, and protocols for the use of adjuvant chemo and/or radiotherapy. All patients referred to the service with a histologically proven colorectal cancer were prospectively entered into a designated colorectal computer database (Filemaker Pro 3.0 and 5.0, Claris) managed by the service. The three general surgical units at the hospital comprised of 10 different general surgeons who were employed by the hospital over the study period. All patients referred to these units with a histologically proven colorectal cancer were prospectively entered into the general surgical database managed through the Department of Surgery. A medical student group crosschecked these database entries with the patients' medical records and pathological records to accurately determine tumour stage, use of adjuvant therapy, and whether the operation was an emergency. These data were validated by the author. The study period was from 1/1/1996 to 1/6/2001. Patients presenting with recurrent colorectal cancers for management were included in the analysis.

The historical control group consisted of a cohort of patients with colorectal cancer who had been managed at Fremantle Hospital from 1/1989 to 12/1994 by a group of 8 general surgeons. This group of 475 patients had previously been part of a retrospective analysis performed in 1996 by the author, and the results published in 1997[5]. In view of the retrospective nature of the data collection, some areas of information were not collected as accurately as in the present prospective trial. In particular, the information required to calculate cancer free survivals was not available. This control group was chosen because it predated the widespread acceptance and use of adjuvant chemotherapy and radiotherapy at Fremantle Hospital. All the endpoints were defined prior to the collection of data.

The surgical procedure was termed curative if there was macroscopic removal of all the tumour and histological assessment showed there to be clear margins. A palliative procedure was where the surgeon had left tumour remaining following surgery, or where no attempt had been made to remove the tumour. Histological assessment of the resected specimen was required to adequately determine this. A positive surgical margin was defined as the presence of tumour within 1 mm of the resection line.

Primary was defined as the first presentation with a colorectal neoplasia, or if a second presentation, where the tumour occurred in a metachronous location. The rectum was defined as commencing in the area where the taenia coli of the sigmoid colon coalesce into a uniform outer longitudinal muscular wall. At colonoscopy, it included the area up to 18 cm from the anal verge. An emergency procedure was where a patient underwent urgent surgery (i.e. within 24 hours of admission) without recourse to the normal pre-operative work up which includes colonoscopy and bowel preparation (including presentations with acute obstruction, perforation, and massive bleeding). The American Society of Anaesthesia score (ASA score) was used as a general measure of patient well-being. The TNM staging system was used in this study. For those patients who received pre-operative radiotherapy to their rectal cancers, and where there had been complete resolution of the primary tumour, the staging was based upon the pre-treatment endoanal ultrasound and CT scan.

In the colorectal group, adjuvant chemotherapy was offered to all patients with Stage III colon cancers and a selected group of Stage II colon cancers if there was evidence of poor prognostic markers (i.e. poorly differentiated, lymphovascular invasion) or if they were of young age (<50 years). Adjuvant preoperative radiotherapy was offered to patients with rectal cancers if the lesion was - (1) less than or equal to 12 cm from the anal verge, (2) fixed in position, (3) mobile lesions if found on endorectal ultrasound to be T3 or T4 in staging, (4) no associated metastatic disease found on abdominal CT scan. The general surgeons did not maintain guidelines for the use of adjuvant chemo/radio therapy. There was minimal use of adjuvant therapy in the historical control group.

The three data sets (a. colorectal group, b. general surgeon group, c. historical group) were then linked to the Mortality Registry of the Health Department of Western Australia. This enabled cross checking of the date of death of patients, and the survival curves were calculated from this information.

Statistical analysis

The mean, standard deviation, and range were used as descriptive statistics. Survival was calculated using the Kaplan-Meier product-limit estimate of survival. The survival time was calculated from the time of initial surgery (or if no surgery was performed, from initial consultation) to either death or 1-12-2002. The survival analysis was an overall analysis and included patients dying - (1) in the 30 day postoperative period, (2) from colorectal cancer, or (3) from unrelated causes (e.g. myocardial infarct). Patients presenting with recurrent cancer were included in the survival analysis. Comparisons of the overall (all-cause mortality) survival data were made between the study groups using the log rank test and the Breslow-Gehan-Wilcoxen test. The latter test was chosen because it could give greater weight to times with more observations in the risk set, and was therefore less sensitive than the log rank test to late events when few subjects remained in the study. The Chi-square test was used in comparisons of nominal data.

A Cox proportional hazards model (Statview 5.0, SAS Institute Inc.) was then applied to identify those factors associated with the improved survival of patients with colorectal cancer. The variables which were evaluated were: (1) patients age, (2) stage of disease, (3) location - colon versus rectum, (4) surgical timing - elective versus emergency, (5) surgical management group - colorectal group and the general surgical group versus the historical control group, (6) use of adjuvant chemotherapy, (7) use of adjuvant radiotherapy (8) ASA score. Those factors identified on univariate analysis as significant predictors of survival were then included in a forward multiple linear regression analysis (Statview 5.0, SAS Institute Inc.). Significance was defined as the probability of a type I error of less than 5 %.

RESULTS

There were 974 patients involved in this study. The basic demographic data for the study groups was detailed in Table 1. The only significant differences noted were that patients in the colorectal group were more likely to have a rectal cancer, and those patients in the colorectal group and general surgical groups were more likely to have an ASA score of 3 or 4 when compared with the controls. The mean follow up time in the colorectal group was shorter than that in the general surgical group. This was because the rate of referrals was increasing in the former and declining in the latter. For example, the general surgical group managed only 11 colorectal cancers during 2000.

Table 1 Basic demographic data for the study groups of patients with colorectal cancer

	Colorectal group	General surgical group	Historical group
Number	362	137	475
Mean age–years	69 (±12)	70 (±11)	69 (±13)
Age range-years	29 to 93	38 to 93	32 to 95
Sex ration M:F	1.3:1	1.4:1	1.4:1
ASA score of 3 or 4	40 %	39 %	22 %
Elective *vs* emergency	319 *vs* 43	112 *vs* 25	394 *vs* 81
procedures	(88% *vs* 12%)	(78% *vs* 18%)	(79% *vs* 17%)
Curative *vs* palliative	264 *vs* 80	101 *vs* 23	366 *vs* 85
pesections	(73 % *vs* 22%)	(74 % *vs* 17%)	(77 % *vs* 18%)
No surgery	18 (5%)	13 (9%)	24 (5%)
Colon cancer	170 (47%)[a]	90 (66%)	314 (66%)
Rectal cancer	192 (53%)[b]	47 (34%)	161 (34%)
Adjuvant chemotherapy	116 (32%)[c]	19 (14%)	17 (4%)
Adjuvant radiotherapy	65 (18%)[d]	9 (7%)	14 (4%)
Mean follow-up-years	2.75 (±1.2)[e]	4.5 (±1.4)	5.1 (±4.5)
Max follow-up-years	6.8	6.9	13.9

[a,b,c,d,e,f]$P<0.05$ *vs* the other two group.

The information for staging for both colon and rectal cancers for the three groups was presented in Table 2. Patients in the colorectal group were significantly more likely to have a stage I cancer, and had significantly fewer stage II cancers, when compared with the other two groups. There was also a significant difference between the two groups in the use of adjuvant chemotherapy for patients who were less than 75 years of age and who had stage III colorectal cancers. For this group of patients, the percentage receiving adjuvant therapy was 89 % in the colorectal group, versus 41 % in the general surgery group, and 5.8 % in the historical group. For patients with stage II colorectal cancer, adjuvant chemotherapy was administered to 11 % of patients in the colorectal group, and no patients in the general surgery or historical groups. No patients with stage I cancer received adjuvant chemotherapy in either group.

Table 2 Staging information for colorectal cancers for the study groups

Stage	Colorectal group number (%)	General surgical group number (%)	Historical group number (%)
Stage I	81 (22 %)[a]	9 (7 %)	57 (12 %)
Stage II	95 (26 %)[b]	53 (39 %)	159 (33 %)
Stage III	91 (25 %)	41 (30 %)	146 (31 %)
Stage IV	91 (25 %)	29 (21 %)	106 (22 %)
Stage unknown	4 (1 %)	4 (3 %)	7 (2 %)

[a,b]$P<0.05$ *vs* the other two group with the Chi-square test.

A comparison of the survival between the study groups found that patients in the colorectal group had a significantly higher overall 5 year survival when compared with the general surgical group and historical groups (56 % versus 45 % and 40 % respectively, $P<0.0001$). The survivals for the various study groups based on the tumour stage were presented in Table 3. Patients in the colorectal group who had either Stage I or Stage III cancers were noted to have significantly higher survivals when compared to the other two groups.

Table 3 A comparison of the overall 5 year survival based on stage for the study groups

Stage	Colorectal group	General surgical group	Historical group
I	90 %[a]	67 %	72 %
II	62 %	57 %	58 %
III	60 %[b]	46 %	34 %
IV (2 year survivals)	22 %	21 %	19 %

[a,b]$P<0.05$ *vs* the other two group.

In the uni-variate analysis, those factors that were found to be significant predictors of overall survival were: age, ASA score, emergency surgery, and stage of disease, adjuvant chemotherapy, adjuvant radiotherapy, and the surgical unit the patients were managed in. These independent variables were then entered into a multiple logistic regression analysis (Table 4) that identified: age, ASA score, stage of disease, the use of adjuvant chemotherapy, and management in the colorectal surgical group as significant independent predictors of survival. The comparisons for the surgical groups were made against the historical control group, with the general surgical group showing no improvement in survival when compared with the controls.

Table 4 Cox survival regression analysis of independent predictors of the overall survival in the 974 patients with colorectal cancer

Independent variables	*P*	Hazard ratio	95% Confidence interval
Age	0.15	1.011	1.002-1.020
ASA score	<0.0001	1.477	1.29-1.69
Adjuvant chemotherapy	0.047	0.634	0.405-0.993
Stage I	<0.0001	0.211	0.107-0.418
Stage II	0.003	0.397	0.214-0.738
Stage III	0.19	0.665	0.358-1.237
Stage IV	0.009	2.27	1.229-4.186
Colorectal surgical unit *vs* control	0.0005	0.667	0.531-0.837

DISCUSSION

The results of this study suggest that there was a survival advantage for patients with colorectal cancer being managed within a specialist colorectal surgical unit at a community based teaching hospital. These improvements in survival appear to be independent of other known predictors of survival that include stage of disease at presentation, emergency procedures, and the use of adjuvant chemotherapy. It remains to be determined as to why these differences exist. Do they simply reflect a higher surgical case load, or are they a result of improved surgical technique, better utilization of adjuvant therapy, or even standardized care through the use of treatment pathways?

There are a number of difficulties in designing a study to determine if there is a survival advantage in patients with colorectal cancer being managed by different groups of surgeons. A review of the surgical literature will show that rarely have clinical trials been conducted which compared the performance of different groups of surgeons. The logistics of trying to randomize patients into such a trial are very difficult. In this study, we have attempted to compare the risk adjusted survival of patients managed in general surgical units with those in a colorectal unit, and have compared these results with a well studied control group to see if there have been any improvements. Evaluating risk-adjusted survival in large cohorts of patients using historical controls is one recognized technique for addressing this issue. Clearly there were significant differences between the groups, with those patients in the colorectal group more likely to have Stage I disease and rectal cancers and with a trend towards fewer emergency procedures. However, the multivariate analysis is designed to account for these differences, and to include those factors that have been identified as independent predictors of survival. The individual surgeon was not included as an independent risk factor in this study because the majority of the general surgeons performed less than 20 cases during the study period. Such a small number makes it difficult to assess an individual surgeon' s performance.

There have been a number of reports in the literature detailing wide variations in outcomes between surgeons managing patients with malignant disease[1-3]. An important aspect to this variation appears to be case loads[6-8]. In both patients with breast cancer[6], oesophageal cancer[7] and rectal cancer[1], surgeons managing higher numbers of patients seem to gain improved results. A comprehensive review of the relationship between volume of surgical procedures and outcome has recently been published[9,10]. This review assessed 88 studies and found that 77 % of the trials demonstrated a positive relationship between volume of work and reduced mortality, with the other 23 % of studies showing no relationship. None of the studies demonstrated a negative relationship.

The question of whether a surgeon who is sub-specialized in colorectal surgery can achieve improved results remains an unresolved issue. Porter *et al.*[1], in their study on factors which influenced survival and local recurrence rates in patients treated for rectal cancer, found that surgeons who were trained in colorectal cancer had significantly improved survivals and reduced local recurrence rates when compared to general surgeons performing less than 21 procedures over the eight year study period. Nonetheless, there results were not significantly better than when compared to general surgeons performing greater than 21 procedures in the study period. Yet again this study focuses on rectal cancer and ignores colonic cancers. It remains to be determined whether these improvements relate to factors such as accuracy of tumour excision, minimizing tissue trauma, reduced incidence of septic

complications (which may influence cancer survival)[11], and even possible to reduced blood loss and transfusion requirements.

In conclusion, there appears to be a survival advantage for patients with colorectal cancer being managed within a specialized colorectal unit. However, it remains to be determined which aspects of the management in such a unit are the most important determinates in this improvement in out-come.

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