Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Impaired outcome colitis-associated rectal cancer *versus* sporadic cancer

Coen L. Klos, MD, Bashar Safar, MD,[1] *Paul E. Wise, MD, Steven R. Hunt, MD, Matthew G. Mutch, MD, Elisa H. Birnbaum, MD, James W. Fleshman, MD,*[2] *and Sekhar Dharmarajan, MD*[*]

Section of Colon and Rectal Surgery, Department of Surgery, Washington University School of Medicine, St Louis, Missouri

ARTICLE INFO

Article history:
Received 11 December 2015
Received in revised form
14 February 2016
Accepted 2 March 2016
Available online 10 March 2016

Keywords:
Inflammatory bowel disease
Rectal cancer
Proctectomy
Proctocolectomy
Colitis

ABSTRACT

Background: The surgical management of colitis-associated rectal cancer (CARC) is not well defined. This study determines outcomes after surgery for CARC compared with sporadic rectal cancer.

Materials and methods: This is a retrospective cohort study comparing 27 patients with CARC with 54 matched patients with sporadic cancer. Matching criteria included age, gender, neoadjuvant chemoradiation, and American Joint Committee on Cancer stage. Outcome measures were disease-free and overall survival, tumor characteristics, and postoperative morbidity.

Results: Compared to those with sporadic rectal cancer, patients with CARC underwent proctocolectomy more frequently (21 [78%] *versus* 6 [22%] $P < 0.001$) and were more likely to have mucinous tumors (11 [40.7%] *versus* 12 [22.3%] $P = 0.03$). Overall 3-y survival was significantly reduced in CARC patients compared with patients with sporadic rectal cancer. Those with CARC undergoing segmental proctectomy only demonstrated reduced overall and disease-free survival compared to patients with sporadic rectal cancer and to colitis patients undergoing proctocolectomy ($P = 0.002$).

Conclusions: Patients with CARC undergoing proctectomy demonstrate reduced disease-free survival *versus* those undergoing proctocolectomy, and *versus* patients with sporadic rectal cancer undergoing proctectomy. These findings warrant further study and suggest that proctocolectomy should be considered the preferred surgical approach for CARC.

Introduction

Inflammatory bowel disease (IBD) is a well-established risk factor for the subsequent development of colorectal cancer (CRC).[1-3] Those with primary sclerosing cholangitis, a family history of CRC, young onset of IBD, long duration of IBD, and high severity of disease are at particularly increased risk of developing CRC.[4-6] However, improved and targeted screening methods[7] in combination with timely prophylactic surgical resection[8,9] have been shown to reduce the incidence of colitis-associated CRC.[10-12] Despite these preventative measures, however, up to 15% of all IBD-related mortality can be attributed to CRC.[13-15] There is

[*] *Corresponding author*. Section of Colon and Rectal Surgery, Department of Surgery, Washington University School of Medicine, Campus Box 8109, 660 South Euclid Avenue, St Louis, MO 63110. Tel.: +1 314 454 7204; fax: +1 314 454 5249.
E-mail address: dharmarajans@wudosis.wustl.edu (S. Dharmarajan).
[1] Present address: Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD.
[2] Present address: Department of Surgery, Baylor University Medical Center, Dallas, TX.

0022-4804/$ – see front matter
http://dx.doi.org/10.1016/j.jss.2016.03.006

conflicting literature on oncologic outcomes after surgery with curative intent in patients with IBD-associated CRC compared with matched groups of patients with sporadic CRC.[16-19] Previous reports suggest that IBD patients present with CRC at an earlier age and with more advanced disease than those with sporadic CRC.[20,21] The literature is limited, however, with respect to colitis-associated rectal cancer (CARC) specifically, which has unique considerations such as surgical approach and use of neoadjuvant therapy. Although total proctocolectomy is generally the procedure of choice for those with ulcerative colitis (UC) and Crohn's disease, segmental resection is used in select cases for those with Crohn's disease.[19] However, the impact of the type of surgical procedure on the oncologic outcome in patients with CARC is not well defined. Accordingly, the primary aim of this study was to compare oncologic outcomes in patients with CARC to a matched (1:2) group of patients undergoing resection for sporadic rectal cancer. Secondary aims include comparing short-term surgical morbidity, surgical approach, and tumor histopathology.

Methods

Patients

This study was conducted as an institutional review board–approved retrospective review (institutional review board ID# 201402017) performed on a prospectively maintained database of patients undergoing colorectal surgery at Washington University School of Medicine in St Louis. The database was queried for patients with IBD undergoing surgery for rectal cancer between 1993 and 2012. Only patients with both diagnoses (IBD and rectal adenocarcinoma) confirmed on final histopathologic evaluation of the surgical specimen were included. These patients were matched 1:2 to patients undergoing resection of sporadic rectal cancer between 2002 and 2009 by the following criteria: age at surgery (±5 y), gender, neoadjuvant chemoradiation, and American Joint Committee on Cancer stage. Patients with a positive test result for a hereditary CRC syndrome on genetic screening, pathology reports unavailable for review, and those lost to follow-up after hospital discharge were excluded from the study. Patient demographics, comorbidities, detailed operative information, histopathologic tumor features, and follow-up data were obtained by medical record review. If required, survival data were supplemented by querying the US Social Security Death Index. The primary outcomes compared were disease-free and overall survival. Recurrent disease was defined as disease that became apparent after a period of undetectable disease including local recurrence in the same location as the primary tumor, regional recurrence, and distant recurrence in other organs such as liver and lungs. Secondary outcomes studied included tumor characteristics and histology, surgical approach (proctectomy *versus* proctocolectomy), and short-term (30 d) surgical outcome.

Surgical procedures

All surgical procedures were performed by board-certified colon and rectal surgeons at a tertiary referral center. Resections for rectal cancer included segmental proctectomy using standard total mesorectal excision technique by low anterior resection or abdominoperineal resection and extended resection by total proctocolectomy. The decision to perform proctectomy or proctocolectomy in CARC patients was made based on an informed discussion between the surgeon and patient, considering the type (UC *versus* Crohn's), extent and severity of colitis, risk of recurrence of cancer and/or colitis, patient characteristics including age, comorbidities, and continence/sphincter function, and expected results of the type of surgery on quality of life. The severity of 30-d postoperative complications was graded using the accordion severity grading system of surgical complications.[22]

Statistical analysis

Categorical variables are expressed as percentages and compared by Fisher's exact test or chi-square test as deemed appropriate. Continuous variables are presented as the mean ± the standard error of the mean or the median and interquartile range (IQR) per group and are compared using two-tailed Student *t*-test. The Kaplan–Meier method was used to generate 1-, 3-, 5-, and 10-y survival curves, and survival was compared by log-rank test. Survival percentages per measured time point are reported with 95% confidence interval (CI). Significance was set at $P < 0.05$. Calculations were performed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp, Armonk, NY) and GraphPad Prism version 6.03 for Windows (GraphPad Software, La Jolla, CA; www.graphpad.com).

Results

Patient demographics

A total of 36 patients with CARC undergoing surgery were identified from our database, and 27 of 36 (75%) were used for further analysis after applying exclusion criteria. Ten of twenty-seven (37%) patients were diagnosed with UC, and 14 of 27 (52%) were diagnosed with Crohn's disease. In addition, 22 of 27 (81%) had biopsy-confirmed rectal adenocarcinoma before surgery, and the remaining five (9%) underwent surgery for dysplasia in combination with an endoscopically confirmed mass and/or stricture (Table 1). The 27 CARC patients were matched to 54 of 1073 sporadic rectal cancer patients. All matching criteria were met. Median follow-up after surgery for rectal cancer in the CARC group was 2.7 y (IQR 1.3-10.1) and 5.3 y (IQR 4.1-8.0) in the sporadic group.

Overall survival and disease-free survival

Overall survival was not significantly different at 1, 5, and 10 y after surgery, but at 3 y after surgery, CARC patients demonstrated significantly increased mortality when compared with patients with sporadic rectal cancer (Fig. 1A). There was no difference in disease-free survival at 1, 3, 5, and 10 y after surgery between sporadic and CARC patients (Fig. 1B).

Surgical approach, complications, and oncologic outcome

In patients with CARC, significantly more underwent total proctocolectomy as opposed to segmental proctectomy alone