PJSS Vol. 67, No. 1, January-March, 2012

PJSS PHILIPPINE JOURNAL OF SURGICAL SPECIALTIES

Peri - Operative Outcomes of Abdominotransanal Resection with Total Mesorectal Excision and Coloanal Anastomosis for Primary Distal Rectal Adenocarcinoma

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Background: This study aimed to provide a local report on the peri-operative outcomes as well as the factors that contribute to the development of complications on patients with primary distal rectal cancer who underwent abdominotransanal resection (ATAR) with total mesorectal excision (TME) and transanal handsewn coloanal anastomosis (CAA).

Methods: This retrospective study was conducted by the Division of Colorectal Surgery of the Philippine General Hospital which evaluated 79 adult patients who underwent ATAR with TME and CAA due to primary distal rectal adenocarcinoma from January 1, 2008 to December 31, 2010. The variables such as age, gender, co-morbidities, pre-operative serum albumin level, smoking history, utilization of neoadjuvant therapy, distance of tumor from anal verge, surgical approach, quality of surgical specimen, circumferential resection margin, pathologic stage, length of postoperative hospital stay, type of anesthesia, morbidity and mortality were recorded and analyzed.

Results: Of the 79 patients, 19 patients (24.05%) had reported CAA dehiscence, 3 patients (3.8%) necessitated a relaparotomy with drainage of generalized intra-abdominal abscess, 6 (7.59%) patients underwent transanal drainage of pelvic abscess and 10 (12.66%) patients who presented with pelvic abscess on computed tomography scan (3), purulent discharge with minor coloanal anastomotic disruption (3) and fistula (4) were managed non-operatively. Diabetes mellitus (P=0.043) and history of smoking (P=0.037) were found to be statistically significant factors associated with increased incidence of CAA dehiscence.

Conclusion: Diabetes mellitus and history of smoking lead to statistically significant increase in the development of anastomotic dehiscence following ATAR with TME and CAA for primary distal rectal cancer.

Key words: abdominotransanal resection, low anterior resection, coloanal anastomosis, rectal cancer

The management of primary distal rectal adenocarcinoma presents a considerable challenge to the surgeon in his attempt to preserve anal sphincter function while achieving adequate oncologic clearance.[1,2] Traditionally, distal rectal cancers within 6cm from the anal verge (FAV) have been treated with an abdominoperineal resection (APR) which involves the en bloc removal of the entire rectum, surrounding lymph nodes, anal sphincters and anus resulting in a permanent end colostomy.[3-8] The employment of ATAR with TME and transanal handsewn CAA, a sphincter–sparing technique, within the context of a multimodality approach, allows most patients with primary distal rectal cancer to avoid an APR.[2,9] Although sphincter–sparing operations are initially associated with defecatory problems, APRs are associated with a high rate of postoperative urinary incontinence and sexual dysfunction due to pelvic floor and autonomic nerve damage aside from body image deterioration and greater psychosocial disturbances.[1,10-12]

As with most major surgical procedures, sphincter–saving operations have their own inherent morbidities. These complications adversely prolong the course of convalescence, resulting to increased duration of hospital stay of patients and higher cost of treatment. These may even lead to an increase in local recurrence and mortality rates. These may also cause delays in the delivery of adjuvant therapy.

The aim of this study was to provide a local report on the peri–operative outcomes of adult patients with primary distal rectal cancer who underwent ATAR with TME and CAA. We further report on the factors that contribute to the development of anastomotic complications and provide recommendations to lessen morbidity and improve the overall outcome of sphincter–sparing operations for the treatment of primary distal rectal cancer.

Methods

This is a retrospective study conducted by the PGH Division of Colorectal Surgery that described the outcomes of ATAR with TME and CAA for the treatment of primary distal rectal cancer. The study population consisted of adult patients with primary distal rectal adenocarcinoma who underwent ATAR with TME and CAA at the PGH from January 1, 2008 to December 31, 2010. The patients were presented at the biweekly multidisciplinary conference of the PGH Colorectal Cancer and Polyp Study Group which was composed of representatives from the Division of Colorectal Surgery, Section of Medical Oncology, Section of Radiation Oncology, Section of Gastroenterology, Department of Pathology, Division of Hepatobiliary and Pancreatic Surgery, and Section of Supportive, Palliative and Hospice Care.

After undergoing pre–operative staging, a consensus was made by the Study Group on whether neoadjuvant therapy was warranted. Patients who underwent long course chemoradiation therapy (LCCRT) were subjected to cobalt radiation with a dose of 50Gy over a 28–day period with concurrent doses of 5–fluorouracil (400 mg/m^2/day) on the first 5 days and the last 5 days of radiation as continuous infusion. Patients then underwent resection of the primary tumor 6 to 10 weeks from the last day of neoadjuvant treatment. Those who underwent short course radiation therapy (SCRT), on the other hand, received a total of 54Gy divided over a 5–day period. The surgical operation was then scheduled 7 to 10 days after the last day of radiation.

The decision on whether the patient with primary distal rectal adenocarcinoma was to undergo a sphincter–sparing operation or an APR was also made by the Study Group. At present, the absolute indications to performing an APR are limited to involvement of the levator muscles, external anal sphincters or perianal skin.[1,2]

Exclusion criteria included patients less than 18 years of age, tumors located above 6cm FAV, patients undergoing synchronous resection for stage IV disease, operation performed for an indication other than primary rectal adenocarcinoma (i.e. squamous cell carcinoma, malignant melanoma, gastrointestinal stromal tumor, or recurrent disease), intra–abdominal anastomosis whether stapled or handsewn, and delayed CAA technique.

All ATARs with TME and CAA were performed either by a colorectal surgery consultant who is a Fellow of the Philippine Society of Colon and Rectal Surgeons (PSCRS) or a colorectal surgery fellow–in–training under the direct supervision of a consultant. Mechanical bowel preparation, prophylactic antibiotics, enterostomal therapist referral for pre–operative stoma siting and counseling and cardiopulmonary assessment as deemed necessary were observed.

The surgical technique of ATAR with TME and CAA involves two phases. The abdominal phase is carried out either via a midline laparotomy or a laparoscopic approach with the patient in a lithotomy position. The technique requires high ligation of the inferior mesenteric artery and complete mobilization of the left colon along its lateral and retroperitoneal attachments. The splenic flexure is routinely taken down to provide an adequate length of bowel and allow for a tension–free anastomosis. To further ensure adequate bowel length, the inferior mesenteric vein is ligated at the inferior edge of the pancreas. The principles of TME with autonomic nerve preservation were strictly followed during the rectal dissection, except in cases where the nerve trunks were found to be grossly involved by tumor. Either a transanal mucosectomy or an intersphincteric resection was performed during the perineal phase utilizing a Lone Star retractor (Cooper Surgical Company, Connecticut, U.S.A.) for improved exposure. Once the specimen was resected, the end of the colon was passed down through the levator hiatus and a straight end–to–end CAA was performed (Figure 1). The anastomosis is handsewn using 3-0 braided,

absorbable sutures. A proximal diverting stoma was routinely placed in all patients. A loop ileostomy was created for those without prior proximal diversion. For those who underwent colonic diversion prior to neoadjuvant treatment, the transverse loop colostomy was maintained, unless this had to be taken down and anastomosed to allow for more bowel length. In which case, a loop ileostomy was done.

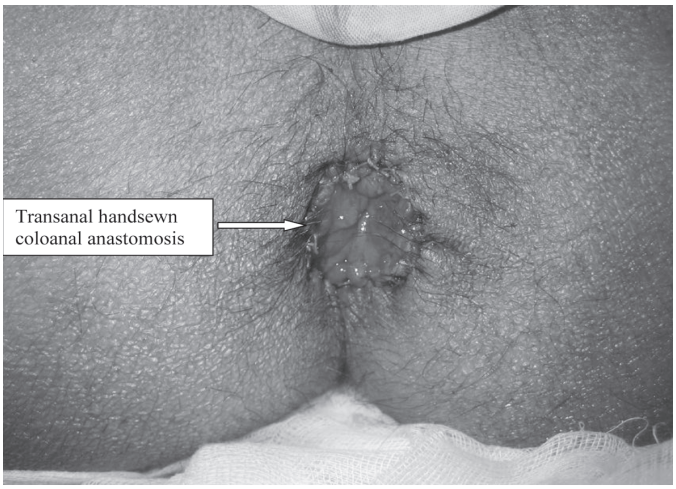

Figure 1. Transanal handsewn end-to-end coloanal anastomosis on a patient with primary distal rectal cancer who underwent ATAR with TME and CAA, PGH, January 1, 2008 - December 31, 2010.

The variables gathered were age, gender, presenting signs and symptoms, associated pre–operative medical co–morbidities, pre–operative serum albumin (g/L), history of smoking, the distance of tumor FAV in centimeters as confirmed by rigid proctoscopy, the utilization of neoadjuvant therapy, level of surgeon performing the procedure, operative approach whether open or laparoscopic. TNM classification following the American Joint Committee on Cancer Staging Manual 7th edition[13] based on the peri–operative imaging, intra–operative findings and the final histopathology report; intra–operative findings indicative of systemic disease such as cytology positive ascites or carcinomatosis, histologic status of proximal, distal and circumferential resection margins (CRM); type of anesthesia, length of postoperative hospital stay, morbidity within 30 days from the time of operation that contributed to prolonged hospital stay, re–admission, or additional procedures; and mortality rate within 30 days postoperatively were recorded and analyzed.

The Integrated Surgical Information System (ISIS), the computerized patient registry of the PGH Department of Surgery, was used to trace patients who were admitted and underwent ATAR with TME and CAA for primary distal rectal cancer from January 1, 2008 to December 31, 2010. Data gathered from ISIS were complemented by the data obtained from the patients' hospital records, official histopathologic results and records of the proceedings of the Multidisciplinary Conferences. All patients whose data were incomplete were excluded in the study. Information pertaining to patients' demographic data, clinical profiles and operative outcome variables within 30 days postoperatively was gathered using a standard data collection form.

The information from the data collection form was encoded on Microsoft Office Excel version 2007 and exported to SPSS version 16 for Microsoft Windows 7 for data analysis. Chi square test was used for statistical analysis and the level of significance was set at α=0.05.

Results

Among the 98 patients with primary distal rectal cancer who underwent sphincter–sparing surgery, 79 patients who underwent ATAR with TME and CAA satisfied the inclusion criteria. There were 43 males (54.43%) and 36 females (45.57%) (male to female ratio of 1.19:1) with a mean age of 52 years (range 29 to 77 years). The most common presenting symptoms were hematochezia (56.96%) and changes in bowel habits (21.52%). Hypertension (24.05%) and diabetes mellitus (17.72%) were the most commonly associated co–morbidities. A history of smoking was reported in 21 patients (26.58%). Malnutrition based on low level of serum albumin (<35 g/L) was noted in 37.98 percent (30/79 patients) of the study population. The mean distance of tumor FAV is 4.51cm (range: 2cm to 6cm). Eighty–one percent of patients received neoadjuvant treatment prior to surgery (LCCRT = 46; SCRT = 18). One patient who had

potentially resectable liver metastasis on pre–operative evaluation was given systemic chemotherapy prior to sphincter–saving operation. Majority of the patients were performed by the subspecialty fellow–in–training of colorectal surgery (68.35 %). (Table 1)

Table 1. Epidemiologic and clinical profile of patients with primary distal rectal cancer who underwent ATAR with TME and CAA, PGH, January 1, 2008 - December 31, 2010.

Epidemiologic and Clinical Profile	Number	Percent
Age		
Mean ± standard deviation	52.08 ± 11.94	
> 50 years	43	54.43%
≤ 50 years	36	45.57%
Gender		
Male	43	54.43%
Female	36	45.57%
Main Presenting Sign and Symptom		
Hematochezia	45	56.96%
Change in bowel habits	17	21.52%
Intestinal obstruction	12	15.19%
Tenesmus or pelvic pain	5	6.33%
Associated Co-morbidity		
Hypertension	19	24.05%
Diabetes mellitus	14	17.72%
None	46	58.23%
History of Smoking		
Smokers	21	26.58%
Non-smokers	58	73.42%
Serum Albumin Level		
Mean ± standard deviation	34.8 ± 4.64	
≥ 35 g/L	49	62.02%
< 35 g/L	30	37.98%
Distance of Tumor FAV		
Mean ± standard deviation	4.51 ± 1.09	
2 cm FAV	3	3.79%
3 cm FAV	10	12.66%
4 cm FAV	27	34.18%
5 cm FAV	22	27.85%
6 cm FAV	17	21.52%
Neoadjuvant Therapy		
LCCRT	46	58.22%
SCRT	18	22.79%
Chemotherapy	1	1.27%
None	14	17.72%
Surgeon		
Consultant	25	31.65%
Fellow-In-Training	54	68.35%

All patients were operated on an elective basis. The abdominal phase in 70 patients were performed through an open approach (88.61%) while 9 patients were completed laparoscopically (11.39%). None of those approached through minimally - invasive means were converted to open surgery. A transanal, straight end–to–end, handsewn CAA was performed in all patients. Most (59.49%) were operated under a combined general–epidural anesthesia. The mean length of hospital stay after surgery was 7.52 days (range: 3 to 23 days). But with the occurrence of morbidity mostly requiring readmission, the mean length of hospital stay increased to 11.39 days (range: 6 to 23 days). This included the patient's length of stay on re–admission. (Table 2)

Table 2. Peri-operative profile of patients with primary distal rectal cancer who underwent ATAR with TME and CAA, PGH, January 1, 2008 - December 31, 2010.

Peri-Operative Profile	Number	Percent
Operative Approach		
Open	70	88.61%
Laparoscopic	9	11.39%
Type of Anesthesia		
Combined General - Epidural	47	59.49%
Regional	32	40.51%
Mean Length of Postoperative Hospital Stay (Days)		
Mean ± standard deviation	7.52 ± 3.71	
With morbidity (including readmission)	11.39	N/A
Without morbidity	6.37	

Sixty–four patients received neoadjuvant therapy (81.01%). Among the 46 patients who had LCCRT, 23.91 percent had a complete pathologic response based on the final histopathology report. The majority of pTNM staging on patients who had prior LCCRT were ypT0 (26.09%) and ypN0 (76.09%). However, there were 3 patients who received LCCRT but were noted to have liver metastasis intra–operatively, which may relate to inadequate pre–operative evaluation. Based on the final

pTNM classification of all patients who underwent ATAR with TME and CAA, most were pT2 (27.85%), pN0 (69.62%) and M0 (93.67%). Five patients (6.33%) had a positive CRM involvement. (Table 3)

The most common complications within 30 days following surgery were related to the transanal handsewn CAA which occurred in 19 patients (24.05%). The other reported complications were 6 superficial (7.59%) and one deep (1.27%) surgical site infection of the midline laparotomy incision all of which were successfully treated with adequate drainage. Five patients (6.33%) were readmitted due to partial gut obstruction from early postoperative adhesions, with all resolving with conservative management. One patient (1.27%) developed a low output enterocutaneous fistula, likely from an iatrogenic injury. The fistula was managed conservatively until spontaneous closure with the aid of modified vacuum assisted closure (VAC).[14] One patient (1.27%) was noted to have been readmitted for a cerebrovascular disease. Four patients (5.06%) were readmitted due to dehydration and/or electrolyte abnormalities from the high effluent volume of their protecting loop ileostomies (Table 4).

Table 5 shows the complications related to the transanal handsewn CAA. Three patients (3.8%) necessitated a relaparotomy with drainage of intra–abdominal abscess after an associated circumferential or near–circumferential CAA disruption with accompanying neorectal retraction. Six patients (7.59%) were readmitted within 2 weeks postoperatively and

Table 4. Morbidities observed in patients with primary distal rectal cancer who underwent ATAR with TME and CAA, PGH, January 1, 2008 – December 31, 2010.

Morbidity	Number	Percent
CAA complications	19	24.05%
Surgical site infections	7	8.86%
Small bowel obstruction secondary to early postoperative adhesions	5	6.33%
Dehydration and electrolyte abnormalities	4	5.06%
Enterocutaneous fistula	1	1.26%
Cerebrovascular disease	1	1.26%
TOTAL	37	46.83%

Table 3. TNM staging of patients with primary distal rectal cancer who underwent ATAR with TME and CAA, PGH, January 1, 2008 – December 31, 2010.

TNM Staging	Number	Percent
ypT Classification After LCCRT (n = 46)		
ypT0	12	26.09%
ypT1	2	4.35%
ypT2	11	23.91%
ypT3	11	23.91%
ypT4	10	21.74%
pT Classification After SCRT (n = 18)		
pT0	2	11.11%
pT1	3	16.67%
pT2	6	33.33%
pT3	4	22.22%
pT4	3	16.67%
pT Classification (No Neoadjuvant Therapy) (n = 15)		
pT1	2	13.33%
pT2	5	33.33%
pT3	4	26.67%
pT4	4	26.67%
pT Classification Overall (n = 79)		
pT0	14	17.72%
pT1	7	8.86%
pT2	22	27.85%
pT3	19	24.05%
pT4	17	21.52%
ypN Classification After LCCRT (n = 46)		
pN negative	35	76.09%
pN positive	11	23.91%
pN Classification Overall (n = 79)		
pN negative	55	69.62%
pN positive	24	30.38%
M Classification (n = 79)		
M0	74	93.67%
M1	5	6.33%
Pathologic Stage After LCCRT (n = 46)		
0	11	23.91%
I	10	21.74%
II	14	30.44%
III	8	17.39%
IV	3	6.52%
Pathologic Stage Overall (n = 79)		
0	13	16.46%
I	23	29.11%
II	20	25.32%
III	18	22.78%
IV	5	6.33%
CRM (n = 79)		
Negative	74	93.67%
Positive	5	6.33%

underwent examination under anesthesia (EUA) due to an almost 50 percent disruption of the CAA with pelvic abscesses concomitantly drained through the perineal wound. Among the 10 patients (12.66%) who were deemed to have minor CAA disruption, 3 patients (3.8%) were noted to have pelvic abscess based on abdominopelvic CT scan with triple contrast which were managed non–operatively. Four patients (5.06%) on the other hand, were noted to have fistula during out–patient follow–up. Among the patients who developed a fistula, one male patient developed a neorectovesical fistula which resulted in multiple readmissions due to recurrent urinary tract infection; while 3 female patients had neorectovaginal fistula. Another 3 patients reported of apparent purulent discharge but were not found to have any abscess formation clinically and radiographically.

On simple regression analysis, diabetes mellitus was a significant factor in the development of CAA complications (P = 0.005). In addition, history of smoking (P = 0.079) and circumferential resection margin positivity (P = 0.052), were clinically significant factors that may increase the incidence of CAA morbidities (Table 6). On stratified analysis, the presence of diabetes mellitus (P = 0.008) and history of smoking (P = 0.037) were both associated with significant increase in the development of CAA dehiscence that will require surgical intervention (Table 7).

Table 5. Anastomotic complications on patients with primary distal rectal cancer who underwent ATAR with TME and CAA, PGH, January 1, 2008 – December 31, 2010.

CAA Complications	Number	Percent
Managed with relaparotomy	3	3.80%
Managed with EUA, transanal drainage of abscess	6	7.59%
Pelvic abscess, managed non - operatively	3	3.80%
Fistula	4	5.06%
Minor CAA disruption with reported purulent discharge, managed conservatively	3	3.80%
TOTAL	19	24.05%

The only reported mortality was on a 51 year–old patient with co–existing hypertension and chronic obstructive pulmonary disease who died on the twelfth day postoperatively due to the development of acute respiratory distress syndrome secondary to healthcare–associated pneumonia (1.27%).

Discussion

The adoption of a multidisciplinary team approach to rectal cancer management, as well as the widespread application of neoadjuvant chemoradiation therapy, a deeper understanding of the concepts of TME, autonomic nerve preservation and CRM; improved stapling devices for bowel anastomosis, the cylindrical technique in APR, and anal sphincter–sparing surgery have all contributed in revolutionizing the management of rectal cancer over the last decade. Surgery remains to be the mainstay of curative therapy for rectal cancers.[2,8,9,15] Different surgical approaches have been used depending on the distance of the rectal tumor from the anal verge. For distal rectal adenocarcinoma, ATAR with TME and transanal handsewn CAA, a sphincter–sparing surgical procedure, is advocated. An APR is indicated in those with local involvement of the anal sphincters, levator muscles, or perianal skin.[1,2,16]

The goal of ATAR with TME and CAA is to preserve the anal sphincters and restore bowel continuity after total removal of the rectum, while ensuring adequate oncologic clearance.[2,3,17] The oncologic outcomes of sphincter–sparing techniques have been reported to be similar to the more radical and disfiguring APR.[1,2,6,9,18,19] Studies have shown that despite a more conservative surgery in patients with a tumor close to the anal canal, local control and survival are not compromised.[2,3,8,10,20-23] Likewise, there was no significant difference in the reported morbidity rates between APR and sphincter–sparing surgery.[2,18,20]

The peri–operative surgical morbidity rate associated with ATAR with TME and CAA ranged from 22 to 35 percent as reported by several studies. These consisted of anastomotic dehiscence, pelvic abscess, anastomotic fistula, anastomotic stricture, bleeding, and small bowel obstruction.[2,3,19,24-27] The morbidity rate associated with CAA was reported to be at 24.05 percent. Other reported

Table 6. Risk factors for anastomotic complications in patients with primary distal rectal adenocarcinoma who underwent ATAR with TME and CAA, PGH, January 1, 2008 – December 31, 2010.

Demographic Profile, Clinical Factors and Operative Outcomes	Incidence of CAA Complications		P value
	Positive	Percent	
Median Age			0.216
> 50 years	8	18.61%	
≤ 50 years	11	30.56%	
Gender			0.478
Male	9	20.93%	
Female	10	27.78%	
Associated Co-Morbidities			0.005
Diabetes mellitus	8	57.14%	
Hypertension	2	10.53%	
None	9	19.57%	
Serum Albumin Level			0.510
≥ 35 g/L	13	26.53%	
34 g/L and below	6	20.00%	
History of Smoking			0.079
Smoker	8	38.09%	
Non-smoker	11	18.97%	
Distance of Tumor FAV			0.427
5 cm and above	11	28.21%	
4 cm and below	8	20.00%	
Neoadjuvant Therapy			0.463
LCCRT	13	28.26%	
SCRT	2	11.11%	
Chemotherapy	0	0%	
None	4	28.57%	
Surgeon			0.567
Consultant	5	20.00%	
Fellow-in-Training	14	25.93%	
Operative Approach			
Open	16	22.86%	0.489
Laparoscopic	3	33.33%	
ypT Classification After LCCRT			0.473
ypT0, ypT1, and ypT2	8	32.00%	
ypT3 and ypT4	5	23.81%	
pT Classification Overall			0.728
pT0, pT1, and pT2	11	34.38%	
pT3 and pT4	8	22.22%	
pN Classification			0.061
pN positive	2	8.33%	
pN negative	17	30.91%	
M Classification			0.827
M0	18	24.32%	
M1	1	20.0%	
Pathologic Stage After LCCRT			0.178
Stage 0, I and II	11	31.43%	
Stage III and IV	2	18.18%	
Pathologic Stage Overall			0.061
Stage 0, I and II	17	30.91%	
Stage III and IV	2	8.33%	
CRM			0.052
Positive	3	60.0%	
Negative	16	21.62%	
Type of Anesthesia			0.709
Combined general - epidural	12	25.53%	
Regional	7	21.88%	

Table 7. Stratified analysis on risk factors for specific anastomotic complications in patients with primary distal rectal adenocarcinoma who underwent ATAR with TME and CAA, PGH, January 1, 2008 to December 31, 2010.

Demographic Profile, Clinical Factors, and Operative Outcomes	Surgical Count (%)	Pelvic Count (%)	Fistula Count (%)	Non-surgical Count (%)	P value
Median Age					0.294
> 50 years	3 (6.98%)	2 (4.65%)	1 (2.33%)	2 (4.65%)	
≤ 50 years	6 (16.67%)	1 (2.78%)	3 (8.33%)	1 (2.78%)	
Gender					0.879
Male	5 (11.63%)	2 (4.65%)	1 (2.33%)	1 (2.33%)	
Female	4 (11.11%)	1 (2.78%)	3 (8.33%)	2 (5.56%)	
Associated Co-Morbidities					0.008
Diabetes mellitus	5 (35.71%)	1 (7.14%)	2 (14.29%)	0	
Hypertension	1 (5.26%)	0	0	1 (5.26%)	
None	3 (6.52%)	2 (4.35%)	2 (4.35%)	2 (4.35%)	
Serum Albumin Level					0.909
≥ 35 g/L	6 (12.25%)	2 (4.08%)	3 (6.12%)	2 (4.08%)	
34 g/L and below	3 (10.0%)	1 (3.33%)	1 (3.33%)	1 (3.33%)	
History of Smoking					0.037
Smoker	6 (28.57%)	0	1 (4.76%)	1 (4.76%)	
Non-smoker	3 (5.17%)	3 (5.17%)	3 (5.17%)	2 (3.45%)	
Distance of Tumor FAV					0.820
4 cm and above	8 (12.12%)	2 (3.03%)	4 (6.06%)	2 (3.03%)	
3 cm and below	1 (7.69%)	1 (7.69%)	0	1 (7.69%)	
Neoadjuvant Therapy					0.539
LCCRT	7 (15.22%)	2 (4.35%)	3 (6.52)	1 (2.17%)	
SCRT	0	0	0	2 (11.11%)	
Chemotherapy	0	0	0	0	
None	2 (14.29%)	1 (7.14%)	1 (7.14%)	0	
Surgeon					0.724
Consultant	2 (8.0%)	1 (4.0%)	2 (4.0%)	0	
Fellow-in-Training	7 (12.96%)	2 (3.70%)	2 (5.56%)	3 (5.56%)	
Operative Approach					0.205
Open	6 (8.57%)	3 (4.29%)	4 (5.71%)	3 (4.29%)	
Laparoscopic	3 (33.33%)	0	0	0	
ypT Classification After LCCRT					0.627
ypT0, ypT1, and ypT2	4 (16.0%)	2 (8.0%)	2 (8.0%)	0	
ypT3 and ypT4	3 (14.29%)	0	1 (4.76%)	1 (4.76%)	
pT Classification Overall					0.940
pT0, pT1, and pT2	5 (11.63%)	2 (4.65%)	3 (6.98%)	1 (2.33%)	
pT3 and pT4	4 (11.11%)	1 (2.78%)	1 (2.78%)	2 (5.56%)	
pN Classification					0.418
pN positive	1 (4.17%)	1 (4.17%)	0	0	
pN negative	8 (14.55%)	2 (3.64%)	4 (7.27%)	3 (5.46%)	
M Classification					0.302
M0	9 (12.16%)	2 (2.70%)	4 (5.41%)	3 (4.05%)	
M1	0	1 (20.0%)	0	0	
Pathologic Stage After LCCRT					0.583
Stage 0, I and II	5 (14.29%)	2 (5.71%)	3 (8.57%)	1 (2.86%)	
Stage III and IV	2 (18.18%)	0	0	0	
Pathologic Stage Overall					0.418
Stage 0, I and II	8 (14.29%)	2 (3.57%)	4 (7.14%)	3 (5.36%)	
Stage III and IV	1 (4.35%)	1 (4.35%)	0	0	
CRM					0.154
Positive	2 (40.0%)	0	1 (20.0%)	0	
Negative	7 (9.46%)	3 (4.05%)	3 (4.05%)	3 (4.05%)	
Type of Anesthesia					0.724
Combined general - epidural	6 (12.77%)	2 (4.26%)	3 (6.38%)	1 (2.13%)	
Regional	3 (9.38%)	1 (3.13%)	1 (3.13%)	2 (6.25%)	

Labels: Surgical = Managed with relaparotomy or EUA transanal drainage of abscess
Pelvic = Pelvic abscess, managed non - operatively
Fistula = Fistula
Non-surgical = Minor CAA disruption with reported purulent discharge, managed conservatively

morbidities were surgical site infections (8.86%), early partial gut obstruction due to postoperative adhesions (6.33%), electrolyte imbalances due to high effluent volume of protecting loop ileostomy (5.06%), enterocutaneous fistula (1.27%) and cerebrovascular disease (1.27%).

A very low anastomosis is associated with higher rates of dehiscence.[4,26-31] Several series reported clinically evident anastomotic leakage following CAA ranging from 5 to 24 percent.[2,25,32,33] The CAA dehiscence was 24 percent. Among these, 9 (47.37%) required surgical intervention — either a re–laparotomy (3) or a transanal drainage of abscess (6). Four patients developed a fistula postoperatively (1 male with neorectovesical fistula and 3 with neorectovaginal fistulas). While 6 patients developed draining pelvic abscess or minor CAA disruptions that were successfully treated non–operatively.

This study demonstrated that diabetes mellitus and history of smoking were both significant factors in the development of CAA dehiscence. Both factors may cause impaired microcirculation that contributes to ischemia. Kasperk, et al. in a study of risk factors for anastomotic leakage involving 98 patients who underwent very low CAA, reported 18 patients (18.37%) developed a dehiscence; and smoking was the only independent risk investigated. The other variables were experience of the surgeon, stage of the tumor, creation of diverting stoma, use of radiation therapy, or the need for blood transfusions.[31]

Attaining negative CRM is very important in reducing local recurrence. In very low rectal cancers, however, negative radial margins is usually more challenging as the mesorectum is thin or absent at this level. Six percent of patients, all of whom were locally advanced tumors, had CRM involvement. This was found to be a clinically significant factor (P = 0.052) in the development of CAA dehiscence in this study. The CRM positivity rate is comparable to studies conducted by the group of Weiser and Rullier, reporting 7 to 11 percent involvement among locally advanced rectal adenocarcinoma who underwent surgical resection.[2,3] These patients oncologically would do better with an APR if we were able to predict pre-operatively that they were likely to end up with a positive CRM. However, due to financial limitations on most of our patients, pelvic CT scan or MRI to assess tumor response after neoadjuvant treatment was not routinely performed.

The narrower male pelvis probably influences low rectal anastomosis as it makes dissection and anastomosis more challenging during low anterior resection. Rudinskaite and colleagues reported that male sex is an independent risk factor in the development of anastomotic leakage for CAA (P = 0.002) while the other factors such as ASA grade, technique of anastomosis, the stage of the tumor, the height of the tumor, and diverting stoma were all non-contributory.[28] However, this study reported the gender to be non-contributory to the development of CAA dehiscence.

Nutritional state is an important factor contributing to dehiscence following intestinal anastomosis but our study correlating low serum albumin levels with risk of CAA leakage was not significant probably because all our patients had pre–operative nutritional assessment as well as nutritional support to reverse any catabolic state when detected prior to their elective sphincter–saving operations.

Neoadjuvant therapy is the standard of care for rectal cancers that are classified as cT3, cT4, or N-positive pre–operatively. It may purportedly improve our ability to perform sphincter–sparing operations as well as reduce local recurrence and improve survival.[2,16,18] Our results demonstrated that neoadjuvant chemoradiation therapy was not associated with increased risk of anastomotic dehiscence following CAA which is similar to several published studies.[5,16,27,34] However, there were 3 patients in our series who received LCCRT but were noted to have liver metastasis intra-operatively which may relate to inadequate preoperative evaluation due to either institutional limitations or patients' financial difficulties.

Four patients (5.06%) who underwent CAA developed fistula from the neorectum to the vagina (n = 3) and urinary bladder (n = 1). Baik, et al. reported 9 percent rate of fistula formation of the neorectum to either the vagina or the perineum while Weiser, et al, reported 5 percent rate of rectovaginal fistula in their series.[2,19]

The reported peri–operative mortality rate of ATAR with TME and CAA is between 2 to 15 percent in most

studies most of which were secondary to anastomotic dehiscence.[18,19,25,27,28,32] The only reported mortality (1.27%) was due to acute respiratory distress syndrome secondary to healthcare – associated pneumonia.

A diverting stoma, whether a loop ileostomy or colostomy, is recommended to reduce the clinical severity and attenuate life–threatening complications following a coloanal anastomotic leakage.[16,21,26,28,29,35] Twelve patients (15.19%) underwent creation of transverse loop colostomy due to intestinal obstruction prior to the initiation of neoadjuvant chemoradiation therapy while the rest of the patients (84.81%) had creation of protecting loop ileostomy during the sphincter–sparing surgery. None of our patients who had anastomotic dehiscence resulted in mortality nor conversion to permanent stoma. Non-closure of diverting stoma or the creation of a permanent stoma following transanal handsewn CAA leakage is associated with diminished quality of life.[2,36]

The downside of sphincter–sparing surgery was the functional outcomes, particularly in terms of bowel frequency and urgency of defecation.[9,10,32] However, the short follow–up period averted the opportunity to evaluate postoperative functional outcomes objectively. Likewise, this study is subject to the partialities and limitations inherent in retrospective analyses.

Conclusion

The investigators demonstrated that diabetes mellitus and history of smoking may significantly increase the risk of CAA dehiscence following ATAR with TME for primary distal rectal adenocarcinoma. Likewise, CRM positivity and node negative specimen on final histopathology were clinically significant factors that may contribute to the development of anastomotic leak.

Recommendations

The PGH Division of Colorectal Surgery is at present undertaking a separate study to validate the functional outcome and quality of life following ATAR with TME and CAA for primary distal rectal cancer. In addition, delayed CAA technique without protecting proximal stoma, which was reported to be associated with lower rates of dehiscence and may be associated with improved quality of life due to the absence of stoma and its stoma–associated complications. It is also currently being evaluated by the Division. Apart from the reported decrease of dehiscence, the technique may also avoid the complications related to stoma care and closure. Finally, it recommends to include other possible risk factors for CAA dehiscence such as obesity, accompanying weight loss, alcoholic use, steroids, American Society of Anesthesiologists' classification, operative time, peri – operative blood transfusion requirements, amount of blood loss and iatrogenic perforation of surgical specimen for data analysis should a prospective study with a larger patient population and long–term follow–up is initiated to further validate our results. A multi – institutional collaboration may provide results with greater statistical power.

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