J Gastrointest Surg (2009) 13:2252–2259
DOI 10.1007/s11605-009-0986-4

ORIGINAL ARTICLE

Right Colonic Perforation in an Asian Population: Predictors of Morbidity and Mortality

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Received: 1 June 2009 / Accepted: 4 August 2009 / Published online: 26 August 2009

Abstract
Introduction Perforation of the colon is associated with significant morbidity and mortality. Pathologies arising from the right colon differ greatly between Asians and the Western population. The aims of our study were to evaluate the implications of perforated right colon in an Asian population and to identify factors that could predict the perioperative outcome.
Methods A retrospective review of all patients who underwent operative intervention for peritonitis from right colonic perforation from July 2003 to April 2008 was performed. Patients were identified from the hospital's diagnostic index and operating records. The severity of abdominal sepsis for all patients was graded using the Mannheim peritonitis index (MPI). All the complications were graded according to the classification proposed by Clavian and colleagues.
Results Fifty-one patients with a median age of 60 years (range, 22–93 years) formed the study group. Diverticulitis (47.1%) and malignancy (37.3%) accounted for the majority of the pathologies. Right hemicolectomy without diverting stoma (n=34, 66.7%) was performed most commonly. Of our patients, 74.5% had perioperative morbidity with 19 (37.3%) patients having grade III or worse complications. In our series, five (9.8%) patients died. On univariate analysis, American Society of Anesthesiologists (ASA) score ≥3, ≥2 premorbid conditions, raised MPI, raised creatinine, and stoma creation were related to more severe complications (grade III/IV). The following variables were correlated with in-hospital mortality: ASA score ≥3, raised MPI, hematocrit <33%, raised creatinine, malignant perforation, and stoma creation. On multivariate analysis, a higher ASA score ≥3 was predictive of significant morbidity, while both malignant perforation and stoma creation were associated with mortality.
Conclusion Diverticulitis is the commonest cause of right colonic perforation in Asians. Patients with higher ASA score and malignant perforation are at risk of higher morbidity and mortality. Resection with primary anastomosis is safe and patients who require stomas are more likely to do worse.

Keywords Perforation · Right colon · Outcome · Surgery

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Introduction

Perforation of the colon is a serious abdominal emergency. The commonest causes include malignancy and diverticulitis.[1,2] The operative mortality and morbidity in these patients remain significant despite advances in surgical techniques and perioperative care.[1,2]

Most of the published literature on the consequences of perforation of the colon has focused on the left colon due to the high incidence of diverticulitis and malignancy in the descending and sigmoid colon in the Western population.[3] However, numerous studies have shown that pathologies in

Table 1 The MPI

Risk factor score	Score
Age >50 years old	5
Female sex	5
Organ failure	7
Malignancy	4
Preoperative duration of peritonitis	4
Origin of sepsis not colonic	4
Diffuse generalized peritonitis	6
Exudate	
Clear	0
Cloudy, purulent	6
Fecal	12

Kidney failure=creatinine level>177 μmol/L or urea level> 167 mmol/L or oliguria<20 ml/h; pulmonary insufficiency=PO_2< 50 mmHg or PCO_2>50 mmHg; intestinal obstruction/paralysis>24 h or complete mechanical ileus, hypodynamic or hyperdynamic shock

the right colon differ significantly between Asians and the Western population.[4,5]

Colonic diverticulosis in Asians is more commonly confined in the right and in young adults.[5] This preponderance has been postulated to be genetically linked. This is in stark contrast to the Western population where diverticular disease is deemed an acquired disease affecting mostly the sigmoid and descending colon, with less common involvement of the cecum and ascending colon.[6]

Furthermore, the incidence of right-sided colon cancer was shown to be markedly lower in Asians compared to Whites and African Americans.[7] This phenomenon has also been attributed to genetic risk factors or other uncharacterized carcinogens.

In addition, while the appropriate surgical technique (Hartmann's procedure versus primary resection with/without diverting stoma) in handling left-sided colonic perforation is not firmly established despite extensive discussion,[3] the literature reviewing the need for a stoma in right-sided colonic perforation is lacking.

Thus, in view of the numerous unresolved issues surrounding perforation of the right colon, the primary aim of this study was to review the treatment and early outcome of patients who underwent emergency surgery for right colonic perforation. In addition, factors that might predict morbidity and mortality were also evaluated.

Methods

Study Population

Tan Tock Seng Hospital is a 1,300-bed hospital, the second largest in Singapore, and provides secondary and tertiary medical care for about 1.5 million people. A retrospective review of all patients who underwent operative intervention for peritonitis from right colonic perforation from July 2003 to April 2008 was performed. Patients were identified from the hospital's diagnostic index and operating records. Right-sided pathologies were regarded if it was located from the cecum till the transverse colon. Patients who suffered perforated colonic injuries from abdominal trauma were excluded.

The data collected included age, gender, American Society of Anesthesiologists (ASA) score, comorbid conditions, presenting signs and symptoms, and clinical parameters. Laboratory values, including full blood count and renal panel, were also recorded. In addition, duration from symptoms to surgery, duration from admission to surgery, operative findings and interventions, length of surgery, perioperative complications, mortality, and length of hospital stay were also documented.

The severity of abdominal sepsis for all patients was graded using the Mannheim peritonitis index (MPI; Table 1) with a score of >26 being defined as severe.[8] Classification of diverticulitis was assessed using Hinchey's classification,[9] and all colorectal cancers were staged according to the guidelines of the American Joint Committee of Cancer.[10] The grades of complications (GOC) were in concordance with the classification proposed by Clavian and colleagues (Table 2).[11–13]

Statistical analysis was performed using both univariate and multivariate analyses. The variables were analyzed to the various outcomes using Fisher's exact test, and their odds ratio and 95% confidence interval were also reported. For the multivariate analysis, the logistic regression model was applied. All analyses were performed using the SPSS 13.0 statistical package (Chicago, IL, USA) and all p values

Table 2 Classification of surgical complications

Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic, or radiological intervention
Grade IV	Life-threatening complication(s) requiring intensive care unit management (including organ dysfunction)
Grade V	Death of a patient

reported are two-sided, and p values of <0.05 were considered statistically significant.

Results

During the study period, 51 patients underwent surgery for perforation of the right colon. The median age of the study group was 60 years (range, 22–93 years). There were more females (n=28, 54.9%) in the study group and the majority of patients had an ASA score of 2 or 3 (n=39, 76.5%). Hypertension (n=22, 43.1%) was the commonest comorbid condition, with 23.5% having at least two comorbid conditions. There were four (7.8%) patients who were immunosuppressed from either chronic corticosteroid consumption (n=3) or human immunodeficiency virus (HIV) infection.

A total of 30 (58.8%) patients underwent preoperative computed tomographic (CT) scans before surgery, while the remaining 21 (41.2%) were operated after clinical assessment and may be assisted by the associated chest and/or abdominal X-rays. Table 3 illustrates the various characteristics of this study group.

Table 3 Characteristics of the 51 patients who underwent surgery for right colonic perforation

	n (%)
Median age, range (years)	60 (22–93)
≤60	26 (51.0)
>60	25 (49.0)
Gender	
Male	23 (45.1)
Female	28 (54.9)
ASA status	
1	8 (15.7)
2	18 (35.3)
3	21 (41.2)
4	4 (7.8)
Premorbid condition	
Hypertension	22 (43.1)
Diabetes mellitus	6 (11.8)
Hyperlipidemia	8 (15.7)
Ischemic heart disease	4 (7.8)
History of cerebrovascular accident	5 (9.8)
Number of premorbid condition	
0–1	39 (76.5)
2–5	12 (23.5)
Immunosuppression	
No	47 (92.2)
Yes	4 (7.8)
One patient who is HIV positive	
One patient with systemic lupus erythematosus and two patients with rheumatoid arthritis on corticosteroids	
Preoperative CT scan	
Performed	30 (58.8)
Not performed	21 (41.2)

Operative Findings

As shown in Table 4, diverticulitis accounted for majority of the perforations in 24 (47.1%) patients, with malignancy in another 19 (37.3%). Ten of these patients had perforation at the tumor site, while the other nine had perforation of the right colon due to a distal obstructing tumor. Some of the other causes included ischemic colitis (n=3, 5.9%), severe appendicitis causing cecal perforation (n=4, 7.8%) and tuberculosis (n=1, 2.0%).

The commonest site of perforation was at the cecum (n=30, 58.8%), followed by the ascending colon (11, 21.6%; Table 4). The median MPI score was 15 (0–37), with 10 (19.6%) patients having a score of >26. There were a total of 36 (70.6%) colonic anastomoses for which 32 (88.9%) were stapled, with the remaining four (11.1%) handsewn. Right hemicolectomy without diverting stoma (n=34, 66.7%) was performed most commonly while ileocolic resection with stoma was created in 14 (27.5%) patients. Of these 14 patients, only one had perforated diverticulitis, while the rest had either malignant perforation (n=8) or ischemic colitis (n=3). The time from symptoms or admission to surgery and the median duration of surgery were also described in Table 4.

Outcome

Significant proportion (74.5%) of our patients had associated perioperative morbidity, with 19 (37.3%) of them having GOC III or worse complications (Table 4). The majority of these arose from respiratory and wound complications. Five (9.8%) patients died in our series. There was no patient with postoperative anastomotic leak, but there was one patient with ischemic stoma that necessitated revision. The median length of stay was 8 days (range, 3–141 days).

Analysis—Complications

Worse complications (GOC III or IV) occurred more commonly in patients who had a higher ASA score (3–4), ≥2 premorbid conditions, MPI >26, raised preoperative creatinine levels, and in patients who had stoma created. Factors such as age, gender, site, and pathology of perforation were not shown to be significant. Duration from symptoms or admission to surgery and the median

Table 4 Surgical observations and procedures of the study group

	n (%)
Site of perforation	
Cecum	30 (58.8)
Ascending colon	11 (21.6)
Hepatic flexure and transverse colon	10 (19.6)
Cause of perforation	
Diverticulitis	24 (47.1)
Hinchey II	15
Hinchey III	8
Hinchey IV	1
Malignancy	19 (37.3)
Perforation at tumor	10
Perforation proximal to tumor	9
Stage II	5
Stage III	6
Stage IV	8
Severe appendicitis causing cecal perforation	4 (7.8)
Ischemic colitis	3 (5.9)
Tuberculosis	1 (2.0)
Median MPI	15 (0–37)
≤26	41 (80.4)
>26	10 (19.6)
Nature of anastomosis	
Handsewn	4 (7.8)
Stapled	32 (62.7)
No anastomosis (no stoma)	1 (2.0)
No anastomosis (stoma created)	14 (27.5)
Surgery performed	
Right hemicolectomy without stoma	34 (66.7)
Right hemicolectomy with stoma	10 (19.6)
Total colectomy with end ileostomy	4 (7.8)
Total colectomy with ileorectal anastomosis	2 (3.9)
Appendectomy and primary closure of perforation	1 (2.0)
Time from symptoms to surgery	
Within 48 h	28 (54.9)
After 48 h	23 (45.1)
Time from admission to surgery (h)	
<24	33 (64.7)
≥24	18 (35.3)
Median duration of surgery (min)	125 (60–315)
≤120	24 (47.1)
>120	27 (52.9)
GOC	
No complications	13 (25.5)
Grade I	7 (13.7)
Grade II	12 (23.5)
Grade III	6 (11.8)
Grade IV	8 (15.7)
Death or grade V	5 (9.8)
Median length of stay (days)	8 (3–141)

duration of surgery were also not related. ASA score was the only independent variable related to significant morbidity (GOC III or IV) after multivariate analysis (Table 5).

Analysis—Mortality

Mortality from perforated right colon was more likely in patients who had a higher ASA score (3–4), higher MPI, lower hematocrit (<33.0%), and raised preoperative urea and creatinine levels. Malignant perforation and creation of stoma were the only independent variables associated with higher mortality after multivariate analysis (Table 6).

Comparison—Malignancy Versus Diverticulitis

Patients with malignant perforation were older and had a higher ASA score compared to those with perforated diverticulitis. Lower white blood cell and hematocrit were also associated with malignant perforation. Factors such as MPI, site of perforation, and the grading of complications were not associated. Lower hematocrit was the only independent variable predictive for malignancy after multivariate analysis. However, patients with malignant perforation were more likely to have stoma created and perish from their conditions (Table 7).

Comparison—Stoma Versus No Stoma

Creation of stoma was more likely in patients with higher ASA scores and raised creatinine level. Both higher MPI and low hematocrit were the only independent variables associated with stoma creation. Patients with stoma also fared worse than those without (Table 8).

Discussion

Even though our series showed that diverticulitis and malignancy are responsible for majority of right colonic perforation, the distribution is vastly different compared to the West. Malignant perforation accounted for the majority of right colonic perforation in the West, while diverticulitis is the main pathology in our series.[2,14] This has been attributed to the genetic differences between Asians and the Western population.[5–7]

In the acute setting, differentiation between malignant and diverticular-related perforation is difficult and may only be evident after resection. Some of the differences between the two groups included advanced age and higher ASA score in malignant perforation. This is not surprising as cancer patients are typically older and associated with more premorbid conditions, while right-sided diverticular disease are more common in younger Asians. Another important

Table 5 Analysis of patients who developed serious versus minor or no complication

Characteristics	GOC 0–II (n=32), n (%)	GOC III–IV (n=14), n (%)	OR (95%CI)	p value
>60 years old	14 (43.8)	8 (57.1)	1.71 (0.48–6.09)	>0.05
ASA score 3–4	8 (25.0)	12 (85.7)	18.00 (3.30–98.27)[a]	<0.001[a]
≥2 premorbid conditions	4 (12.5)	7 (50.0)	7.00 (1.59–30.80)	0.010
MPI >26	1 (3.13)	6 (42.9)	23.25 (2.44–221.73)	0.002
WBC >10.0×10^9/L	24 (75.0)	10 (71.4)	0.83 (0.20–3.41)	>0.05
Hematocrit <33.0%	7 (21.9)	6 (42.9)	2.68 (0.69–10.31)	>0.05
Serum creatinine >110 μmol/L	1 (3.1)	4 (28.6)	12.4 (1.24–124.22)	0.025
Perforated diverticulitis	18 (56.3)	6 (42.9)	0.58 (0.16–2.07)	>0.05
Malignant perforation	9 (28.1)	5 (35.7)	1.42 (0.37–5.41)	>0.05
Creation of stoma	3 (9.4)	6 (42.9)	7.25 (1.47–35.71)	0.015

[a] Statistically significant on multivariate analysis

clue that our series highlighted was that lower hematocrit of <33.0% was more suggestive of malignant perforation.

Hinchey classification has often been used to predict operative intervention and the associated morbidity and mortality.[9,15] In our series, patients with Hinchey III and IV (four out of nine patients) had more severe complications than patients with Hinchey II (two out of 15 patients). While the ideal surgical procedure for perforated left colonic diverticulitis remains controversial, our series showed that right hemicolectomy with primary anastomosis (23 out of 24 patients, 95.8%) for perforated right colonic diverticulitis was associated with good outcome and minimal complications.[16,17]

Perforation in colorectal cancers occurs due to either direct perforation from tumor necrosis or proximally to an obstructing tumor from a resultant closed-loop syndrome. Recent data has suggested that factors such as perforation proximal to the cancer and number of metastatic lymph nodes were associated with higher perioperative morbidity and mortality.[18–20] In our series, though there were no differences seen in the perioperative outcome between patients who had proximal or tumor site perforation, this could be because of our small numbers.

Mortality rate from perforated colorectal cancers has been reported to be over 40%.[20,21] In our series, the mortality rate was 26.3%. Similar to other studies, the majority of our malignant perforations were either stage 3 or stage 4. Furthermore, malignant perforation has been shown to be associated with an increased risk of local recurrence and carcinomatosis peritonei.[22,23] In these patients, apart from managing the peritoneal contamination and the resultant septicemia, complete oncologic surgery should be attempted to offer the best long-term outcome, but only if the patient's condition allows.

ASA score has been used for decades and is highly predictive of morbidity and mortality in surgical patients.[24–26] In our series, a higher ASA score was the only independent variable predicting severe complications. However, ASA score has been criticized for its failure to include the impact of numerous comorbidities and age. Though our patients with two or more comorbid conditions were associated with worse complications, an increased age

Table 6 Comparison of patients who died and the rest

Characteristics	Alive (n=46), n (%)	Death (n=5), n (%)	OR (95%CI)	p value
>60 years old	22 (47.8)	3 (60.0)	1.64 (0.25–10.73)	>0.05
ASA score 3–4	20 (43.4)	5 (100.0)	NA	0.023
≥2 premorbid conditions	11 (23.9)	1 (20.0)	0.80 (0.08–7.88)	>0.05
MPI >26	7 (15.2)	3 (60.0)	8.36 (1.18–59.43)	0.046
WBC >10.0×10^9/L	34 (73.9)	1 (20.0)	0.09 (0.01–0.87)	0.029
Hematocrit <33.0%	13 (28.3)	4 (80.0)	10.20 (1.04–100.00)	0.037
Serum creatinine >110 μmol/L	5 (10.9)	3 (60.0)	12.30 (1.64–92.33)	0.023
Malignant perforation	14 (30.4)	5 (100.0)	NA	0.005[a]
Creation of stoma	9 (19.6)	5 (100.0)	NA	0.001[a]

[a] Statistically significant on multivariate analysis

Table 7 Comparison of patients with diverticulitis against malignancy

Characteristics	Diverticulitis (n=24), n (%)	Malignancy (n=19), n (%)	OR (95%CI)	p value
>60 years old	8 (33.3)	14 (73.7)	5.6 (1.48–21.13)	0.014
ASA score 3–4	6 (25.0)	15 (78.9)	11.25 (2.67–47.43)	0.001
≥2 premorbid condition	5 (20.8)	6 (31.6)	1.75 (0.44–6.98)	>0.05
MPI >26	3 (12.5)	5 (26.3)	2.50 (0.51–12.18)	>0.05
WBC >10.0×10^9/L	20 (83.3)	9 (47.4)	0.18 (0.04–0.73)	0.021
Hematocrit <33.0%	1 (4.2)	10 (52.6)	25.64 (2.84–250.00)	<0.001[a]
Serum creatinine >110 μmol/L	2 (8.3)	5 (26.3)	3.93 (0.67–23.10)	>0.05
Creation of stoma	1 (4.2)	8 (42.1)	16.67 (1.86–142.86)	0.006
Death	0 (0.0)	5 (26.3)	NA	0.012

[a] Statistically significant on multivariate analysis

did not have a similar relationship. It has been shown in many studies that chronological age is not an independent predictor, but it is logical to deduce that patients who are older are more likely to have more comorbid conditions and a higher ASA score.[27,28]

The severity of peritonitis, and not the surgical procedure or the underlying diagnoses, has also been shown to be directly accountable for the surgical outcome;[2,29–30] however, these data were predominantly based on left colonic pathologies in the Western population.[29] In our series, MPI was used as it is easy to apply, can be used for all diagnoses, and is able to prognosticate the patients according to the severity of the peritonitis.[2,8,29,30] To our knowledge, MPI has never been used for right-sided colonic perforation in an Asian population. Our series concurred with the others that a higher MPI is associated with stoma creation, severe complications, and death.[2,8,29,30] Some of its criticisms included the difficulty in determining the exact timing from perforation to operation and the neglect of patients' hemodynamic and physiological derangement.[31] Nonetheless, even though our series supported the usage of MPI in patients with colonic perforation, a prospective study would be required to further validate its usefulness in Asians.

Though emergency resection for right-sided colonic pathologies has been shown to be technically easier, it still carries an overall morbidity of up to 44%.[32,33] The method of anastomosis, be it handsewn or stapled, has not been shown to be significantly related to the development of an anastomotic leak or other complications in emergency right hemicolectomy.[33–35] This is supported in our series as there was no patient with primary anastomosis from either method that had any anastomotic complications. In addition, right colectomy is associated with a lower rate of anastomotic leakage compared to colocolic or colorectal anastomosis, especially in the presence of an unprepared colon.[36–38]

In our series, stoma was created more often in patients with more severe peritoneal contamination. Patients who required stoma also had worse perioperative outcome. This is not surprising, as diverting stoma has always been advocated in patients who are hemodynamically unstable or in those who are suspected to fare worse.[3,16] However, as

Table 8 Comparison of patients who had stoma created against those who did not

Characteristics	No stoma (n=37), n (%)	Stoma created (n=14), n (%)	OR (95%CI)	p value
>60 years old	18 (48.6)	7 (50.0)	1.06 (0.31–3.61)	>0.05
ASA score 3–4	12 (32.4)	13 (92.9)	27.08 (3.16–231.87)	<0.001
≥2 premorbid conditions	8 (21.6)	4 (28.6)	1.45 (0.36–5.87)	>0.05
MPI >26	2 (5.4)	8 (57.1)	23.33 (3.95–137.68)	<0.001[a]
WBC >10.0×10^9/L	28 (75.6)	7 (50.0)	0.32 (0.09–1.17)	>0.05
Hematocrit <33.0%	7 (18.9)	10 (71.4)	10.75 (2.58–43.48)	0.001[a]
Serum creatinine >110 μmol/L	3 (8.1)	5 (35.7)	6.30 (1.26–31.47)	0.028
Noncecal perforation	14 (37.8)	7 (50.0)	1.64 (0.48–5.68)	>0.05
Malignant perforation	11 (29.7)	8 (57.1)	3.15 (0.88–11.24)	>0.05
GOC 3–4	8 (21.6)	6 out of 9 (66.7)	7.25 (1.48–35.61)	0.015
Mortality	0 (0.0)	5 (35.7)	NA	0.001

[a] Statistically significant on multivariate analysis

the morbidity rate from the complications of a diverting stoma is not negligible,[32,39,40] the authors opined that the optimal choice of surgical intervention should remain at the discretion of the primary surgeon with paramount considerations given to the general condition of the patient and degree of contamination.

As with most studies, there were several limitations in the present study. This series of patients was enrolled from a single institution and any retrospective study has inherent flaws. Even though our study is the largest series in the literature analyzing the consequences of right colonic perforation in an Asian population, the sample size is still very small with only 51 patients. This may mask several other important factors that could be accountable for the outcomes measured. More importantly, there were no standard guidelines or protocol in our institution governing the indications of surgery and the ideal operative techniques to adopt in right colonic perforation with special considerations given to the degree of peritoneal contamination and the patient's general condition. In addition, patients that were managed conservatively for right colonic perforations were not included in our series as our focus was to uncover factors that could predict perioperative outcome.

Although these limitations are significant, this study remains important in highlighting the various issues pertinent in right colonic perforation that are considerably different and rarely seen in the Western population. Our study also identified various factors that could be predictive of a worse perioperative outcome after surgical resection for right colonic perforation.

Conclusions

Diverticulitis is the commonest cause of right colonic perforation in Asians. Anemia is predictive of a malignant perforation in these patients. Patients with higher ASA score and malignant perforation are at risk of higher morbidity and mortality. Resection with primary anastomosis is safe in the majority, and patients who require stomas are more likely to do worse.

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