Available online at www.sciencedirect.com
ScienceDirect
Journal of the Chinese Medical Association 74 (2011) 69–74
www.jcma-online.com

Original Article

Clinical experience in 89 consecutive cases of chronic radiation enterocolitis

Ming-Cheng Chen [a], Feng-Fan Chiang [a], Ta-Wen Hsu [a,b], Joe-Bin Chen [a], Te-Hsin Chao [a], Hsiu-Feng Ma [a], Hwei-Ming Wang [a,*]

[a] *Division of Colorectal Surgery, Department of Surgery, Taichung Veterans General Hospital, Taichung, Taiwan, ROC*
[b] *Division of General Surgery, Department of Surgery, Buddhist Dalin Tzu Chi General Hospital, Chiayi County, Taiwan, ROC*

Received January 20, 2010; accepted July 25, 2010

Abstract

Background: Pelvic irradiation has been a popular therapy modality for cervical cancer for many years, and its usage in rectal cancer and prostate cancer cases is on the rise. However, it is associated with significant side effects. In this study, we compared the different characteristics of surgical and nonsurgical patients who were treated for radiation enterocolitis, the treatment results, posttreatment quality of life (QOL), nutrition status, and predisposing factors for surgery.

Methods: From 1985 to 2009, the records of a total of 89 patients with chronic radiation enterocolitis in our hospital were retrospectively reviewed for demographic data, operative data and long-term treatment results. Posttreatment QOL and nutrition status were also recorded. Univariate and multivariate analyses were performed to identify the independent predicting factors associated with surgical intervention. Characteristics of surgical and nonsurgical patients were compared.

Results: Radiotherapy before 1995, concomitant radiation uropathy and smoking were independent predictive factors for surgery. Surgical and nonsurgical cases had similar Kaplan–Meier curves. Although the recurrence rate of radiation enterocolitis was much higher for the surgical group ($p = 0.031$), both groups had similar QOL score (median: 8 *vs*.7; $p = 0.709$), serum albumin level (3.29 g/dL *vs*. 3.16 g/dL; $p = 0.095$), and body mass index (20.19 *vs*. 19.86; $p = 0.603$).

Conclusions: We confirmed that as compared with recently developed innovative techniques, early primitive radiotherapy techniques were associated with more severe radiotherapy complications that required surgery. Smoking may enhance patients' vulnerability to severe radiation injury. Surgery for radiation-induced intestinal obstruction, intestinal fistula and perforation is warranted because QOL, serum albumin level and body mass index were similar between the surgical and nonsurgical groups.

Keywords: Predictive factor; Radiation colitis; Radiation enterocolitis; Radiation injury; Risk factor; Surgery

1. Introduction

Radiotherapy for locally advanced gynecological, rectal and prostate malignancies is on the rise, with proven efficacy. However, it is associated with significant side effects. Radiation enterocolitis, especially chronic radiation enterocolitis, is the most dreaded side effect of radiotherapy. Unlike acute radiation enterocolitis, which is a transient and self-limited disease,[1,2] chronic radiation enterocolitis usually manifests with an irreversible and progressive disease pattern with variable gastrointestinal manifestations.[3,4] The latency period from radiotherapy to onset of radiation enterocolitis is also variable, ranging from 3 months to 30 years.[5] The prognosis for chronic radiation enterocolitis is unpredictable. Some patients enjoy sustained remission under proper medical treatment, although others experience progression of radiation enterocolitis to such an extent that surgery is required.[6] Recurrence after treatment is common.[7] Iraha et al. identified three risk factors for surgery: smoking, diabetes mellitus and abdomino-pelvic surgery.[8] In the literature, about 20–40% of patients with these risk factors died of radiation injury.[6,9,10] Fortunately, many radiation techniques, such as three-dimensional conformal radiotherapy, greatly

* Corresponding author. Dr. Hwei-Ming Wang, Division of Colorectal Surgery, Department of Surgery, Taichung Veterans General Hospital, 160, Section 3, Chung-Kang Rd., Taichung 407, Taiwan, ROC.
E-mail address: henry_chen@vghtc.gov.tw (H.-M. Wang).

1726-4901/$ - see front matter
doi:10.1016/j.jcma.2011.01.014

enhance the efficacy of radiotherapy and reduce its side effects. Novel therapeutic modalities, such as hyperbaric oxygen therapy (HBOT),[11,12] formalin instillation and prostaglandin E1(PGE1) infusion,[13,14] were developed to treat radiation enterocolitis after 2000. As such, the disease patterns and outcomes of patients may have been altered by advances in technology. In this study, we retrospectively analyzed singlecenter cases of chronic radiation enterocolitis in the past 25 years to establish a Taiwanese database of patients characteristics, disease patterns and treatment results. In addition, we identified predictive factors associated with development of surgical conditions. The quality of life (QOL) and nutrition status of patients after surgical and nonsurgical treatment were also compared.

2. Methods

2.1. Patients

Taichung Veterans General Hospital (TCVGH) is a tertiary referral center in central Taiwan. Cases in areas including Nantou, Chiayi, Yunlin, Miaoli and Changhwa were included.

From 1985 to 2009, all patients who were treated for radiation enterocolitis in our radiation oncology department, surgical department, medical department, gynecology department and hyperbaric oxygen therapy unit (launched in June 2003) were retrospectively evaluated for eligibility. To be included in the study, the patient was required to meet at least one of the following criteria: (1) pathologist diagnosis of radiation enterocolitis according to surgical specimen, (2) pathologist diagnosis of radiation enterocolitis according to specimen obtained from colonoscopy biopsy, or (3) no biopsy was obtained, but the colonoscopy features were compatible with radiation colitis or the onset of symptoms had a clear chronological relationship to that of radiotherapy. To exclude cases of acute radiation enterocolitis, the latency period had to be longer than 10 months.[5,15] A retrospective review of medical records was performed for demographic data, details of operation, manifestation of radiation enterocolitis, treatment course and comorbidities. The latency period of radiation enterocolitis was recorded as the period from termination of radiotherapy to the time when the disease was diagnosed. The cancer status (no evidence of disease or uncured), radiation dosage and previous abdomino-pelvic surgery were also recorded.

2.2. Follow-up

The long-term outcomes were evaluated carefully. Survival status and disease status of radiation enterocolitis were evaluated by reviewing the medical database reinforced by telephone follow-up to all the patients who received no regular postoperative outpatient department examinations for more than 3 months.

2.3. Surgical and nonsurgical cases

All the cases were assigned into either nonsurgical group or surgical group according to whether or not surgical intervention was performed. The characteristics of nonsurgical and surgical patients including demographics, radiation dosage, presenting symptoms, latency period, cancer status, remission and recurrence of symptomatic radiation enterocolitis, and presence of concomitant radiation uropathy were recorded and compared. The parameters of posttreatment nutrition status, such as serum albumin level and body mass index, were recorded retrospectively at about 1 year after treatment for both groups of patients. For surgical patients, surgical mortality and surgical complications which have long-lasting effect on life quality (short bowel syndrome, enterocutaneous fistula, ventral hernia, pulmonary insufficiency which required long-time mechanical ventilation) were recorded.

2.4. Predicting factors for surgery

Predicting factors associated with surgery for radiation enterocolitis were evaluated. Following the series of Iraha et al,[8] we analyzed history of diabetes mellitus, smoking and abdomino-pelvic surgery as possible predisposing factors. Because HBOT was believed to enable conversion of possible surgical cases into nonsurgical cases, we analyzed "treatment before the HBOT era" as a predisposing factor. Early primitive radiotherapy was also analyzed as a possible predisposing factor. Furthermore, all factors that were found to be associated with surgery in the cross-group comparison were subjected to univariate and multivariate analyses.

2.5. QOL evaluation

In June 2010, each patient who survived at that time point was evaluated for life quality. We adapted the QOL scoring system for abdominal surgery from the *Journal of the American College of Surgeons* (supplemental Table 1).[25] The scoring system uses a 12-point scale, with 12 indicating the best QOL status and 0 indicating the worst QOL.

2.6. Statistical analysis

All statistical analyses were performed using SPSS 16.0 for Windows (SPSS Inc., Chicago, IL, USA). Fisher's exact test was used to compare categorical variables, although continuous variables were compared with the Mann–Whitney *U* test. Overall survival rates were estimated by the Kaplan–Meier method. Survival curves were statistically compared using the log-rank test. Variables with $p < 0.1$ in univariate analysis were subjected to multivariate Cox regression modeling using backward stepwise variable selection. A two-tailed p value of <0.05 was considered statistically significant for all tests.

3. Results

3.1. Comparison between surgical and nonsurgical patients

A total of 89 patients who were diagnosed as radiation enterocolitis between 1985 and 2009 in TCVGH were enrolled in

Table 1
Characterization of surgical and nonsurgical patients

	Surgical ($n = 35$)	Nonsurgical ($n = 54$)	p
Age, yr	65.09 ± 10.11	61.61 ± 15.08	*0.011[d]
Female, %	27 (77.14)	33 (66.11)	0.083[a]
Median radiation dosage, cGy	5,120 ± 2,908	5,075 ± 3,262	0.152[d]
Median latency period, mo	17.08 ± 98.45	8.59 ± 76.59	*0.037[d]
Gynecological malignancy	26 (74.29)	22 (40.74)	*0.002[a]
Manifestation number			*<0.0001[a]
Obstruction	13 (37.14)	1 (1.85)	
Fistula	10 (28.57)	0	
Bleeding	7 (20.00)	36 (66.67)	
Perforation	5 (14.28)	0	
Enterocolitis	0	17 (31.48)	
Uncured cancer (%)	25.70	59.20	*0.002[b]
Presence of radiation uropathy	19 (54.28)	7 (12.96)	*<0.0001[b]
Survive	20 (57.14)	*25* (46.29)	0.434[b]
Symptom free	22 (66.85)	47 (87.03)	*0.016[b]
Abdomino-pelvic operation	23 (65.71)	25 (46.29)	0.085[b]
Biopsy-proved radiation enterocolitis	27 (77.14)	36 (66.67)	0.354[b]
Treatment before the era of HBOT	15 (42.85)	9 (16.67)	*0.014[b]
Older age > 65 yr	21 (60.00)	23 (42.59)	0.132[a]
Smoking	4 (12.90)	9 (16.66)	0.555[c]
Diabetes mellitus	4 (11.42)	18 (14.81)	0.65[c]
Uremia	1 (2.86)	2 (3.7)	0.829[c]
Received HBO therapy	2 (5.71)	4 (7.40)	0.644[c]
Radiation related death	10 (28.5)	7 (12.96)	0.553[b]

[a] Yate's correction of contingency.
[b] Fisher's exact test.
[c] Peason's chi-square test.
[d] Mann–Whitney U test.
Data are presented as mean ± standard or n (%).
HBO = hyperbaric oxygen; HBOT = hyperbaric oxygen therapy; SD = standard deviation.

this study. Among them, 35 patients later underwent surgery for radiation enterocolitis, although 54 patients had medical treatment only. As compared with nonsurgical patients, surgical patients were significantly older in age ($p = 0.011$), had a longer latency period ($p = 0.037$), and were associated with a higher percentage of gynecological malignancies ($p = 0.002$). Surgical cases manifested more frequently with symptoms of obstruction and fistula, although nonsurgical cases manifested mainly with bleeding and chronic diarrhea ($p < 0.0001$). Surgical cases were more likely to have concomitant radiation uropathy ($p < 0.0001$), although nonsurgical cases were more likely to have uncured cancer ($p = 0.002$). Compared with nonsurgical cases, a higher percentage of surgical cases were diagnosed and treated before the era of HBOT ($p = 0.014$) (Table 1).

The length of the latency period was associated with the presenting symptom ($p < 0.0001$) (Table 2). In cases presenting with obstruction or fistula, the mean latency period was 95.15 months, which was significantly longer than that for cases with perforation or hemorrhage (39.95 months) ($p = 0.019$). The cases presenting with chronic diarrhea had the shortest mean latency period (12.10 months, $p = 0.04$) (Table 2).

Table 2
Differences in latency period of symptoms

Symptom	Mean latency in months (SD)	p
1. Obstruction & fistula	95.15 (109.88)	<0.0001[a]
2. Perforation & bleeding	39.95 (79.00)	0.019[b]
3. Chronic diarrhea	12.10 (33.24)	0.04[c]

[a] Kruskal–Wallis test
[b] Mann–Whitney U test, 1 and 2
[c] Mann–Whitney U test, 2 and 3.
SD = standard deviation.

In univariate analysis (Table 3), older age > 65 years ($p = 0.04$), radiotherapy before 1995 ($p = 0.029$), diagnosed as having radiation enterocolitis before the era of HBOT ($p = 0.009$), symptom of obstruction or fistula ($p = 0.026$) and history of smoking ($p = 0.025$) were significantly associated with surgical intervention for radiation enterocolitis (Table 4). Radiotherapy before 1985 ($p = 0.099$) and concomitant radiation uropathy ($p = 0.053$) tended to be associated with operation but without statistical significance.

In multivariate analysis (Table 4), radiotherapy before 1995 ($p = 0.022$), symptom of obstruction or fistula ($p < 0.0001$), history of smoking ($p = 0.015$) and concomitant radiation uropathy ($p = 0.026$) were identified as independent risk factors associated with surgical intervention in patients with chronic radiation enterocolitis.

3.2. QOL, nutrition status and operative complications after treatment

The median QOL score for the surgical group was 8, as compared with 7 for the nonsurgical group ($p = 0.709$). One year after treatment, the mean serum albumin level was 3.29 g/dL for the surgical group and 3.16 g/dL for the nonsurgical group ($p = 0.095$). The mean body weight mass index after treatment was 20.09 for the surgical group and 19.86 for the nonsurgical group ($p = 0.603$). The complication rate for surgery was 22.9%, and the surgical mortality rate was 5.7% (Table 5).

Table 3
Univariate analysis of factors associated with operation for enterocolitis

Risk factors	p
Older age > 65 yr	0.04**
Radiotherapy before 1985	0.099*
Radiotherapy before 1995	0.029**
Treatment before the era of HBOT	0.009**
Symptom of obstruction or fistula	0.026**
Uncured cancer	0.473
Gynecological malignancy	0.96
Diabetes mellitus	0.721
Smoking	0.025**
Abdomino-pelvic operation	0.136
Uremia	0.696
Radiation uropathy	0.053*
Latency > 5 yr	0.424
Radiation dose > 7,000 cGy	0.588
Radiation dose > 9,000 cGy	0.872

HBOT = hyperbaric oxygen therapy.
*$p < 0.1$ = **$p < 0.05$ by log-rank test.

Table 4
Multivariate analysis of factors associated with surgery for radiation enterocolitis

Risk factors	Hazard ratio (95%CI)	Standard error	*p*
Radiotherapy before 1995	2.898 (1.162–7.246)	0.466	0.022[a]
Symptom of obstruction or fistula	3.412 (1.763–6.622)	0.337	<0.0001[a]
Smoking	4.379 (1.339–14.324)	0.605	0.015[a]
Concomitant radiation uropathy	2.332 (1.104–4.926)	0.381	0.026[a]

[a] Backward stepwise (Wald).

After a median follow-up period of 20.86 months, the 5-year survival rate was 54% for surgical cases and 38% for nonsurgical cases ($p = 0.072$) (Fig. 1). Because there were a significantly higher percentage of patients with uncured cancer in the nonsurgical group, we analyzed survival curves stratified by cancer status to avoid the confounding effect of cancer status. There was no difference in the survival curves for the two no evidence of disease cases ($p = 0.930$) (Fig. 2A) and the uncured cancer cases ($p = 0.213$) (Fig. 2B).

3.3. Surgical patients had significantly more recurrences of radiation enterocolitis

The 5-year and 10-year recurrence rates for the nonsurgical group were both 18%, suggesting that the recurrence rate remained steady after 5 years and thereafter for the nonsurgical group. In contrast, the recurrence rate for surgical patients rose continually through the 5th to the 10th posttreatment years, being 28% at the 5th year and 52% at the 10th year. The recurrence rate was significantly higher for surgical patients ($p = 0.031$) (Fig. 3).

4. Discussion

Chronic radiation enterocolitis, a dreaded complication of radiotherapy with a considerable mortality rate, is currently receiving more attention because of increasing usage of radiotherapy in pelvic malignancies.[26,27] To our knowledge, this is the largest series of chronic radiation enterocolitis cases in Taiwan which analyzes different characteristics of surgical and nonsurgical cases, treatment results, posttreatment QOL and risk factors predisposing to surgical intervention.

Table 5
Life quality, gastro-intestinal function and operative complications after treatment

	Surgical group ($n = 35$)	Nonsurgical group ($n = 54$)	*p*
Surgical complication	8 (22.9)	0	0.003[b]
Surgical mortality	2 (5.7)	0	0.076[b]
Median quality of life score	8 ± 0.243	7 ± 0.298	0.709[a]
Serum albumin (g/dL)	3.29	3.16	0.095[a]
Body mass index	20.09	19.86	0.603[a]

[a] Mann–Whitney *U* test
[b] Pearson's chi-square test.
Data are presented as *n* (%) or median ± standard deviation.

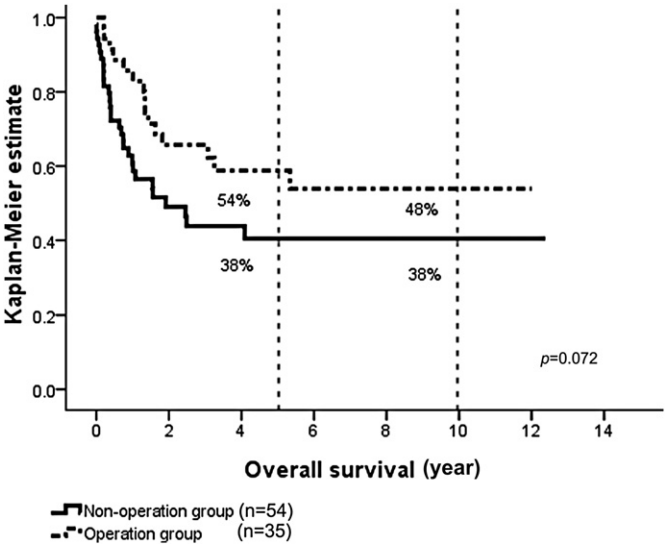

Fig. 1. Overall survival of surgical and nonsurgical patients following treatment.

The likelihood of developing radiation enterocolitis after radiotherapy is dosage-dependent. A radiation dosage of 4,000—4,500 cGy is thought to be the triggering factor.[16] However, the severity of radiation enterocolitis does not seem to correlate to radiation dosage.[7,9,10] Higher radiation dosage may not predispose patients to severe radiation enterocolitis and even surgery.[17] Thus, efforts have been made to identify those patients who are at risk of developing severe radiation enterocolitis. In the series of Iraha et al, diabetes mellitus, smoking and previous abdomino-pelvic surgery are identified as risk factors for surgery.[8] In our series, we confirmed smoking as an independent risk factor associated with surgery. Recent human and animal studies suggest that elevated levels of mucosal proinflammatory cytokines such as interleukin 2, interleukin 6 and tumor-necrosis factor α may be responsible for vulnerability to radiation enterocolitis.[20,21] It is likely that smoking has an effect on systemic inflammatory response and hence on elevated proinflammatory cytokines, making patients more vulnerable to severe radiation injury. However, this theory requires further investigation.

By identifying radiotherapy before 1995 as an independent predictor for surgery, we confirmed the long standing belief that early primitive radiotherapy techniques actually brought about more complications that required surgery. A series of innovative radiotherapy techniques developed in the late 1990s and the early 2000s, such as IMRT (intensity-modulated radiation therapy), may have effectively reduced the incidence of severe radiation enterocolitis.

To our knowledge, the association of concomitant radiation uropathy with surgical condition has not yet been discussed elsewhere. The existence of concomitant radiation uropathy

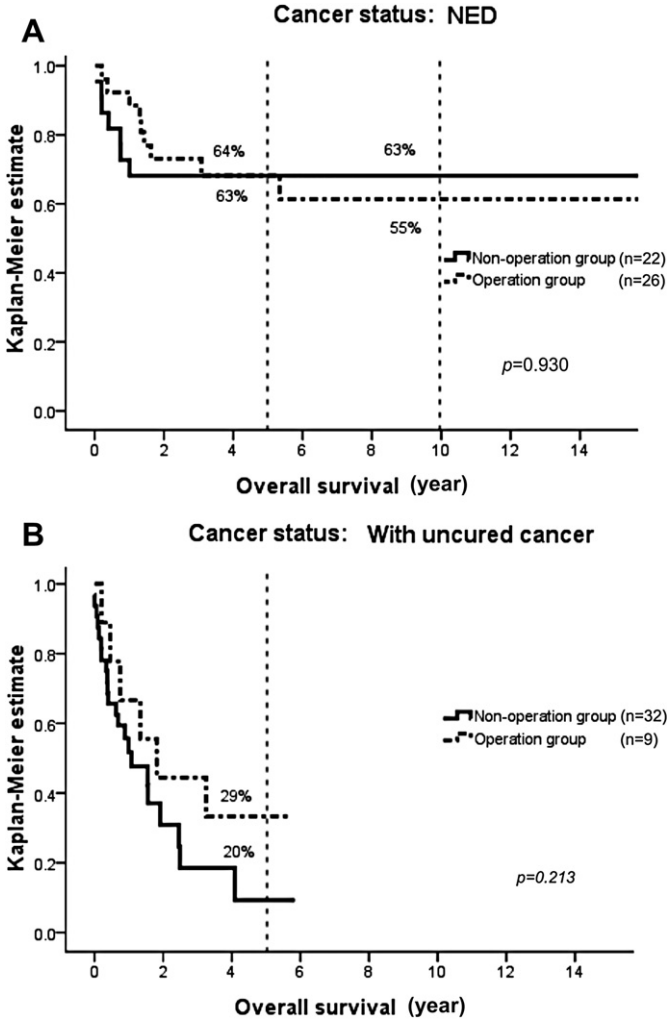

Fig. 2. Overall survival of patients stratified by cancer status, stratified by cancer status. (A) No evidence of disease. (B) With uncured cancer.

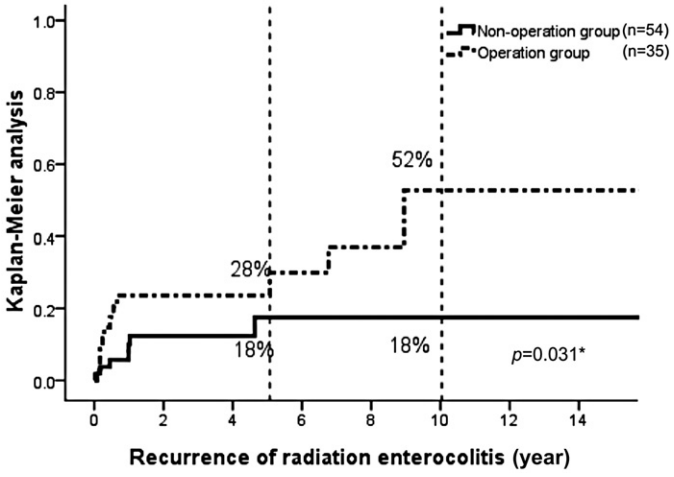

Fig. 3. Recurrence of radiation enterocolitis in surgical and nonsurgical groups.

may indicate extensive disease and vulnerability of patients to radiation injury. In accordance with this possibility, physicians may encounter a severe radiation injury if radiation uropathy develops.

The surgical indication for radiation enterocolitis is changing. There are numerous reports about the success of HBOT in treatment of hemorrhagic proctitis.[11,12] Thus, the number of surgeries for radiation proctitis is expected to decline with the availability of HBOT. Total parenteral nutrition and naso-gastric tube decompression are notoriously ineffective for intestinal obstruction caused by radiation injury.[18,19] Thus, 94% of such patients require surgery because of the disease's progressive and irreversible nature.[7] One report in Taiwan also confirmed this point of view[24]; thus, conservative treatment is no longer recommended. For intestinal fistula, the chance of spontaneous closure is slim because of the poor healing power of irradiated tissue. Patients with radiation related intestinal fistula frequently require resection of fistula containing intestine or a diversion procedure to correct this condition.

Once a surgical condition develops, surgical intervention may be justified because the survival curves of surgical cases and nonsurgical cases are similar despite the fact that surgical cases are usually associated with severe symptoms. Although the recurrence rate for radiation enterocolitis was much higher for the surgical group, the posttreatment gastro-intestinal tract function, nutrition status (serum albumin and body mass index) and QOLscore were similar in both groups despite usually severe symptoms in the surgical group, which further justifies operation in such patient groups. The recurrence rate for the conservative treatment group was very low and, remarkably, there were very few cases of recurrence after 5 years for the conservative treatment group. Radiation proctitis and radiation enterocolitis with chronic diarrhea have a benign nature and are medical diseases which should not be treated surgically. The fact that surgical symptoms of obstruction and fistula are associated with a significantly longer latency period suggests that the irreversible nature of surgical symptoms may require longer incubation time. The pathological findings of surgical specimens from such cases featured stromal fibrosis and vascular ischemia, which were irreversible and required surgical correction.[3–5]

Recent human and animal studies suggest that radiation enterocolitis and inflammatory bowel disease may share the same molecular pathways in pathogenesis.[22,23] As such, the drugs used for inflammatory bowel disease, such as 5-ASA and tumor-necrosis factor α blocker, may be promising agents for treatment of radiation enterocolitis.[23] Every effort should be made to prevent radiation injury. We hope that new therapeutic and protective agents will be developed to further reduce the mortality rate of chronic radiation enterocolitis.

In conclusion, radiation enterocolitis is a progressive disease with an ill-defined nature. We identified smoking, radiotherapy before 1995, and concomitant radiation uropathy as independent risk factors associated with surgical intervention. In this series, the surgical group was associated with a longer latency period than the nonsurgical group. Finally, surgery may be justified once a surgical condition develops because surgical cases have similar survival curves, QOL-scores and nutrition status to those of nonsurgical cases despite severe symptoms.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jcma.2011.01.014.

References

1. O'Brien PC, Hamilton CS, Denham JW, Gourlay R, Franklin CI. Spontaneous improvement in late rectal mucosal changes after radiotherapy for prostate cancer. *Int J Radiat Oncol Biol Phys* 2004;**58**:75−80.
2. Hovdenak N, Fajardo LF, Hauer-Jensen M. Acute radiation proctitis: a sequential pathologic study during pelvic radiotherapy. *Int J Radiat Oncol Biol Phys* 2000;**48**:1111−7.
3. Berthrong M, Fajardo LF. Radiation injury in surgical pathology. *Am J Surg Pathol* 1981;**5**:153−75.
4. Hasleton PS, Carr N, Schofield PF. Vascular changes in radiation bowel disease. *Histopathology* 1985;**9**:517−34.
5. Berthrong M. Pathologic changes secondary to radiation. *World J Surg* 1986;**10**:155−70.
6. Gilinsky NH, Burns DG, Barbezat GO, Levin W, Myers HS, Marks IN. The natural history of radiation-induced proctosigmoiditis: an analysis of 88 patients. *Q J Med* 1983;**52**:40−53.
7. Miller AR, Martenson JA, Nelson H, Schleck CD, Ilstrup DM, Gunderson LL, et al. The incidence and clinical consequences of treatment-related bowel injury. *Int J Radiat Oncol Biol Phys* 1999;**43**:817−25.
8. Iraha S, Ogawa K, Moromizato H. Radiation enterocolitis requiring surgery in patients with gynecological malignancies. *Int J Radiat Oncol Biol Phys* 2007;**68**:1088−93.
9. Wobbes T, Verschueren RC, Lubbers EJ, Jansen W, Paping RH. Surgical aspects of radiation enteritis of the small bowel. *Dis Colon Rectum* 1984;**27**:89−92.
10. Regimbeau JM, Panis Y, Gouzi JL, Fagniez PL. Operative and long-term results after surgery for chronic radiation enteritis. *Am J Surg* 2001;**182**:237−42.
11. Feldmeier JJ, Hampson NB. A systematic review of the literature reporting the application of hyperbaric oxygen prevention and treatment of delayed radiation injuries: an evidence-based approach. *Undersea Hyperb Med* 2002;**29**:4−30.
12. Bem J, Bem S, Singh A. Use of hyperbaric oxygen chamber in the management of radiation-related complications of the anorectal region: report of two cases and review of the literature. *Dis Colon Rectum* 2000;**43**:1435−8.
13. Miura M, Sasagawa I, Kubota Y, Iijima Y, Sawamura T, Nakada T. Effective hyperbaric oxygenation with prostaglandin E1 for radiation cystitis and colitis after pelvic radiotherapy. *Int Urol Nephrol* 1996;**28**:643−7.
14. Pikarsky AJ, Belin B, Efron J, Weiss EG, Nogueras JJ, Wexner SD. Complications following formalin installation in the treatment of radiation-induced proctitis. *Int J Colorectal Dis* 2000;**15**:96−9.
15. Galland RB, Spencer J. Natural history and surgical management of radiation enteritis. *Br J Surg* 1987;**74**:742−7.
16. De Parades V, Bauer P, Marteau P, Chauveinc L, Bouillet T, Atienza P. Nonsurgical treatment of chronic radiation-induced hemorrhagic proctitis. *Presse Med* 2008;**37**:1113−20 [French].
17. Okunieff P, Cornelison T, Mester M, Liu W, Ding I, Chen Y, et al. Mechanism and modification of gastrointestinal soft tissue response to radiation: role of growth factors. *Int J Radiat Oncol Biol Phys* 2005;**62**:273−8.
18. Silvain C, Besson I, Ingrand P, Beau P, Fort E, Matuchansky C, et al. Long-term outcome of severe radiation enteritis treated by total parenteral nutrition. *Dig Dis Sci* 1992;**37**:1065−71.
19. McGough C, Baldwin C, Frost G, Andreyev HJ. Role of nutritional intervention in patients treated with radiotherapy for pelvic malignancy. *Br J Cancer* 2004;**90**:2278−87.
20. Indaram AV, Visvalingam V, Locke M, Bank S. Cytokine production in radiation-induced proctosigmoiditis compared with inflammatory bowel disease. *Am J Gastroenterol* 2000;**95**:1221−5.
21. Skwarchuk MW, Travis EL. Changes in histology and fibrogenic cytokines in irradiated colorectum of two murine strains. *Int J Radiat Oncol Biol Phys* 1998;**42**:169−78.
22. Yeoh AS, Bowen JM, Gibson RJ, Keefe DM. Nuclear factor kappaB (NFkappaB) and cyclooxygenase-2 (Cox-2) expression in the irradiated colorectum is associated with subsequent histopathological changes. *Int J Radiat Oncol Biol Phys* 2005;**63**:1295−303.
23. Keskek M, Gocmen E, Kilic M, Gencturk S, Can B, Cengiz M, et al. Increased expression of cyclooxygenase-2 (COX-2) in radiation-induced small bowel injury in rats. *J Surg Res* 2006;**135**:76−84.
24. Tsai MS, Liang JT. Surgery is justified in patients with bowel obstruction due to radiation therapy. *J Gastrointest Surg* 2006;**10**:575−82.
25. Urbach DR, Harnish JL, McIlroy JH, Streiner DL. A measure of quality of life after abdominal surgery. *J Am Coll Surg* 2004;**3**:S70.
26. Chen WJ, Kuo JY, Chen KK, Lin AT, Chang YH, Chang LS. Primary urothelial carcinoma of the ureter: 11-year experience in Taipei Veterans General hospital. *J Chin Med Assoc* 2005;**68**:522−30.
27. Chen WM, Yang CR, Ou YC, Chen CL, Kao YL, Ho HC, et al. Clinical outcome of patients with stage T1a prostate cancer. *J Chin Med Assoc* 2003;**66**:236−40.