Case Analysis

Aggressive Surgical Treatment is Justified towards Colovesical Fistulae of Benign Diseases and Post-Radiation Injury: A 10-Year Retrospective Review in 60 Patients

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Key Words
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Follow-up study

Background. Colovesical fistula (CVF) is a rare complication of inflammation, located between colon and urinary bladder. Surgical intervention of CVF remained controversial.
Patients and Methods. Over a 10-year period, consecutive 60 patients with CVF underwent surgical intervention in Chang-Gung Memorial Hospital. Their demographic data, clinical features, final diagnoses, treatment and surgical outcomes were analyzed.
Results. The study recruited 28 males and 32 females, with a mean age of 60.5 years. Of them, 87% had urologic symptoms (fecaluria 68% and pneumoturia 40%), while intestinal symptoms were evident in only 15% of patients. The major causes of the disease included diverticular disease (n = 18, 30%), malignancy invasion (n = 16, 27%) and post-radiation injury (n = 14, 23%). Resection with and without anastomosis was performed in 22 and 9 patients, respectively. Diversion was introduced in 27 patients, while local repair was done in 2 patients. During an averaged 66-month follow-up, survival of patients of post-radiation injury and benign etiologies was significantly different from that of malignancy invasion subgroup ($p < 0.001$); on the contrary, the survival difference was insignificant between subgroups of benign etiologies and radiation injury ($p = 0.302$). The mean survival period of benign disease and radiation injury group were 89.0 and 69.6 months, respectively. The 7-year survival rates of the two groups were 59.3% and 53.6%, respectively. The surgical/hospital mortality rates in these two groups were lower (6.7% and 7.1 %) than that of malignancy invasion (25%).
Conclusion. This study showed the limited surgical mortality rate and long-term disease free survival in CVF patients with benign disease and post-radiation injury, so aggressive surgical intervention was recommended.
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Colovesical fistula (CVF) is a rare complication of inflammation, located between colon and urinary bladder. The incidence was less than one in every 3,000 admissions.[1] Its etiologies are mainly related to

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inflammation and neoplasm, usually the diverticular disease, colon cancer, and Crohn's disease. Barium enema, colonoscopy, cystoscopy, contrasted urography, computed tomography (CT) scans and Magnetic resonance imaging (MRI) are commonly applied to the disease preoperatively.[2-9] Resection or diversion of the involved segment of bowel, with or without repair of the bladder defect, can alleviate the symptoms; however, the high morbidity and mortality rates undermined the merit of surgery.[2,3,9] Therefore, conservative management for patients with CVF of benign etiologies was proposed.[9,10] However, nonsurgical treatment predisposes patients to persistent urinary septicemia and deterioration of renal function.[10,11] Furthermore, most previous studies did not provide complete follow-up data of their long-term postoperative results.[2,6-9] This study was conducted in a tertiary referral center in north Taiwan to evaluate long-term postoperative outcomes among consecutive 60 patients with CVF during 10 years.

Patients and Methods

This study recruited patients on surgeries for CVF in the Colorectal Surgical Section of Chung-Gung Memorial Hospital, Linkuo, from August 1997 to August 2007. Sixty-seven patients were identified, and seven of them were excluded due to incomplete follow-up data. All lesions were confirmed through clinical presentation and pathological documentation. The demographic data, clinical features, diagnostic methods, causes of the disease, surgical techniques and outcomes were collected from the computerized database, medical charts as well as telephone interviews. This study was approved by the Institutional Review Board for Human Studies in our institute.

Preoperative evaluation of the patients included cystoscopy, coloscopy, contrasted urology and barium enema, computer tomography (CT) and Magnetic resonance imaging (MRI). The evidence of CVF in cystoscopy and coloscopy included local inflammation with bullous edema of the lining, or visualization of the fistulous opening. The fistulous tract was also identified by contrasted urography, barium enema, CT and MRI.

The operative procedures included repair only, resection with or without re-anastomosis, diverting and defunctional ostomy. The diagnostic tools and the operative methods were dictated by the clinicians. Follow-up data were obtained from medical records and referring physicians. Survival data were updated every 3 months. Patients were then followed up until death (or a minimum of 2 years). Data analysis was closed on March 1, 2011.

Statistical analysis

The survival period was defined from the date of surgery until the date of death; otherwise the patients were censored on the date of the most recent follow-up if they were still alive. Excel 2000 (Microsoft corporation, Redmond, WA) and the Statistical Package for the Social Sciences (release 17.0; SPSS Inc., Chicago, IL, USA) were applied to analyzed the data. The chi-squared X^2 test for trends of Fisher's exact test was used whenever appropriate. Overall survival and differences between groups were estimated through Kaplan-Meier method and the log rank test, respectively. Statistical significance was determined as two-sided $p < 0.05$.

Results

Total 60 patients (28 males and 32 females) were included in this study, with the mean age of 60.5 ± 17.7 years (range: 17-92 years old). The average postoperative follow-up period was 65.8 ± 7.3 months.

Clinical features were categorized of urologic, intestinal, and miscellaneous (Table 1). The average duration of the symptoms was 114.3 ± 177.6 days (range: 1 day-2 years). The majority (87%) of clinical presentation was urologic symptoms and signs, while only 15% was intestinal ones. Fecaluria (68%) and pneumoturia (40%) were the first two frequent symptoms, followed by flank/abdominal pain (40%). Sixteen (27%) patients were diagnosed of urinary tract infection before operation, and ten of them had experienced recurrent courses for more than two months. Multi-microbacterial strains were identified in all of the 16 patients. Of them, Escherichia coli was the

most common pathogen, growing in 90% of all cultures.

The results of diagnostic tools were summarized in Table 2. Computed tomography (CT) scans, low gastrointestinal (LGI) series, and cystography were the three common tools used in our series. Sensitivity (directly visualizing CVF tract) of cystography and LGI in our series was 95% and 88% respectively, while CT scans can localize fistula tract in 68% (18/26) of patients. Cystoscopy detected fistulous orifices as well as bullous edema of mucosa in two of three patients, while fistula openings were disclosed in two of nine patients through colonoscopy.

Diverticular disease (n = 18, 30%) was the leading cause of CVF in our series, followed by malignancy (n = 16, 27%) and radiation injury (n = 14, 23%). The most frequent location of diverticulitis was sigmoid colon (n = 16), followed by rectum (n = 1), and ileocecum (n = 1). Cancerous fistulae of colon cancer originated in sigmoid colon (n = 7), ascending colon (n = 2), descending colon (n = 1), and rectum (n = 1). Of these patients, nine and two were with newly diagnosed and with recurrent colon cancers, respectively. Three patients (two newly diagnosed and one recurrent) were identified of cervical cancer invasion. Fourteen patients had accepted adjuvant radiation for cervical neoplasm, and previous abdominal hysterectomy was documented in all of them. The total radiation doses ranged from 2400 to 6600 cGy and the intervals between completion of radiation and presence of symptoms ranged from 1 to 12 years. Six patients were diagnosed of iatrogenic injuries, including complications of transurethral resection of prostate (TURP) (n = 2) and post-operative adhesion (n = 4). Urolithiasis and trauma were identified in one and three (including two by blunt trauma and one by sharp injury) patients, respectively.

Twenty-two of sixty patients underwent one-stage resection with anastomosis in our series (diverticulitis, n = 10; cancer, n = 5; radiation injury, n = 4; iatrogenic injury, n = 1; soft tissue infection, n = 1; urolithiasis, n = 1). Hartmann operation was carried out

Table 1. Clinical manifestations in 60 patients

	Patient No. (%)
Urologic symptoms/signs	
Any	52 (87%)
Fecaluria/urine turbidity	41 (68%)
Pneumoturia	24 (40%)
Dysuria	19 (32%)
Hematuria	10 (17%)
Urinary tract infection	16 (27%)
Intestinal symptoms/signs	
Any	9 (15%)
Diarrhea	9 (15%)
Tenesmus	2 (3%)
Miscellaneous	
Abdominal/flank pain	24 (40%)
Inflammatory mass	6 (10%)
Fever and septisemia	3 (5%)
Urine per anus	2 (3%)

Table 2. Diagnostic tools in 60 patients

	No. of test positive/test done (%)
Intestinal contrast radiography	
LGI series	18/21 (88%)
Urology contrast radiography	
Cystogram	18/19 (95%)
Retrograde pyelogram	1/1 (100%)
Voiding cystourethrogram	2/2 (100%)
Fistulogram	1/1 (100%)
Intravenous pyelogram	0/5 (0%)
Endoscopy	
Cystoscopy	2/3 (67%)
Coloscopy	2/9 (22%)
Cross-section image	
Computed tomography	17/25 (68%)
Magnetic resonance imaging	1/2 (50%)

Table 3. Etiologies in 60 patients

	Patient No.
Diverticular disease	18
Malignancy	
Colorectal cancer	11
Cervical cancer	3
Ovarian cancer	1
Urechal cancer	1
Radiation injury	14
Miscellaneous	
Iatrogenic injury	
Postoperative adhesion	4
TURP	2
Trauma	3
Necrotizing fasciitis	2
Urolithiasis	1

in 9 patients (diverticulitis, n = 3; cancer, n = 1; radiation injury, n = 1; iatrogenic injury, n = 2; trauma, n = 1; soft tissue infection, n = 1) while twenty-seven patients received permanent diverting colostomy (diverticulitis, n = 5; cancer, n = 10; radiation injury, n = 9; iatrogenic injury, n = 3). Repair via therapeutic colonoscopy and Kraske repair were performed in one patient each, respectively (trauma, n = 2).

Surgical complications, including urinary retention, gastrointestinal (GI) bleeding, and wound infection, were detailed in Table 4. Anastomosis leakage occurred in three patients. Re-operation (n = 2) and CT-guided drainage (n = 1) were performed among these patients. Seven patients had postoperative pulmonary complications, and four of them died of uncontrolled lung infections. Deep venous thrombosis occurred in one patient who did not receive further intervention and was followed up in outpatient clinic without morbidity. Postoperative sepsis occurred in four patients and three of them died 1 to 3 months later.

Throughout the follow-up period, only two patients encountered disease recurrence. One patient with radiation-injury receiving Hartmann's procedure and the other with post-TURP receiving 3-staged operation developed recurrence 14 and 79 months later respectively. These two patients underwent diversion T-loop colostomy and repair, and both had been followed up with disease free for 42 and 61 months respectively.

In survival analysis, patients were categorized according to the nature of the underlying causes, including benign disease (diverticulitis and miscellaneous causes), malignance invasion (advanced colorectal cancers) and post radiation injury subgroups. Survival curves of these 60 patients were shown in Fig. 1. The mean survival of patients with benign disease, cancer, radiation injury were 89.0 ± 9.9, 16.6 ± 4.3, 69.6 ± 12.0 months, respectively. The survival difference was significant either between benign disease and the malignance invasion group ($p < 0.001$), or between malignance invasion and post-radiation injury groups ($p < 0.001$), but was not significant between benign and radiation injury groups ($p = 0.302$). The 3/5/7-year survival rate of benign disease group was 79.5/71.1/59.3%, while those of malignancy and post-radiation injury groups were 9.4/0/0%, and 64.3/53.6/53.6% respectively.

Table 4. Surgical complications in 60 patients

	Patient No.
Urinary retention	1
GI bleeding	2
Anastomosis leakage	3
Chest infection	7
Deep vein thrombosis	1
Wound infection	5
Wound herniation	1
Colostomy fistula	1
Sepsis	4
Any of above	13 (13/60, 21.7%)

Discussion

To our knowledge, this is the largest cases series of Asian population. CVF is a rare complication of inflammation with significant gender discrepancy. The male-to-female ratio was approximately 1 to 1 in our series; however, a ratio of 3 to 1 was derived if presence of corpus uterus was taken into consideration. Previous studies reported male-to-female ratio ranging from 1.5:1 to 2.5:1.[2,3,6,8] These reports thus highlighted the protective effect of corpus uterus on

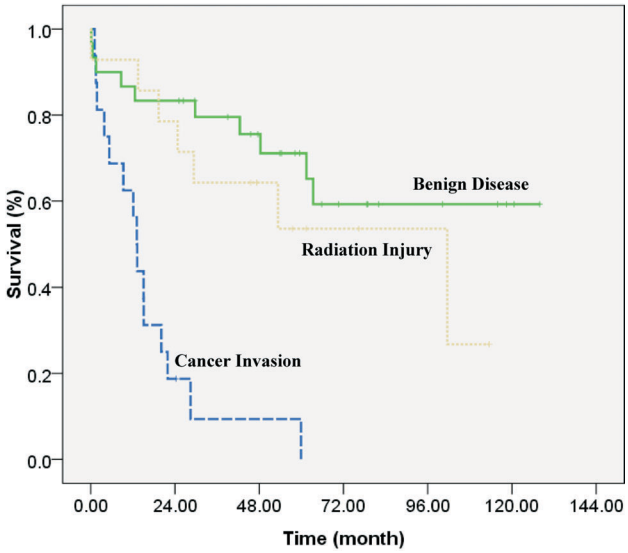

Fig. 1. Overall survivals grouped by etiologies for 60 patients accepting surgical intervention for colovesical fistula.

fistulization of the diseased bowel.

The most common symptoms of CVF are recurrent urinary tract infections, fecaluria and pneumoturia, affecting 40-90% patients with the disease,[2-8,12] which are caused by the higher pressure in the digestive tract pushing stool to the urinary tract through communication between the two tracts. In contrast, passage of urine per anus happened less, involving 6.6-40% of patients.[4,8] In this study, 87% of our patients experienced at least one of the urologic symptoms, while passage of urine per anus was documented in only 3% of our patients. Other diverse gastrointestinal and somatic discomfort, including abdominal and flank pain, with or without iliac fossa tenderness, were reported in 22-71% of patients in previous studies,[2,7,8] and so were in 39% of our patients.

Diverticulitis, malignant disease, and Crohn's disease were most commonly reported etiologies of CVF among Western countries.[2-8,12-16] Due to low incidences of diverticulits and Crohn' disease in Asian population, fewer cases were reported. However, higher incidence of CVF related to pelvis radiation (n = 14, 23%), rare in the Western reports, was disclosed in this study.[8,13,17] The result may be related to our entity of the referral cancer center. Such cases were decreasing due to improvement of the recent radiation technology and technique. Intervals between radiation therapies and appearance of fistulae were7.4 ± 3.6 years in average (range: 1-12 years). Diverticulitis (n = 18, 30%) and malignancy (n = 16, 27%) were two other common causes in this study. Diverticulitis, the most common cause among Western series, constituted 71-75% of cases with CVF.[2,6,18] The other two previous Asian series reported less than 10% CVF were associated with diverticulitis.[7,8] The increased diverticulitis-related fistulae (n = 18, 30%) in our patients were probably related to the increasing diverticular diseases in Taiwan population, which may be influenced by westernized food, metabolic disorders and prolonged lifespan over the recent two decades. Malignancy remained the leading cause of the disease in comparison with our prior 10-year cohort studies.[7] However, the significant decrease in cases (Liu et al. n = 38, 92.7% versus ours n = 16, 27%) implied improved public health and cancer care diminishing such complications in Taiwan.

CT and MRI scans recently became the main stream in identifying the tract lesions with high sensitivity and the underlying causes of CVF, though conventional barium intestinal and urology examination, and cystoscopy were recommended in the past studies.[8,13-16,19,20] The direct anatomic description on cross sections facilitated the preoperative evaluation and planning in a less invasive manner.[2-6,12] Both LGI series and cystogram (18/21 [88%], and 18/19 [95%]) detected tract lesions best in our series, but cannot offer enough information of underlying diseases. In this study, the rate of illustrating fistulous tracts, defined by direct vision of lesions, in CT scans (17/25 [68%]) was inferior to those in LGI series and cystogram. In some studies, indirect evidences suggesting CVF, such as presence of gas in the bladder without urinary instrumentation immediately before scanning, oral contrast medium in the bladder on non-intravenous contrasted scans, and local colonic thickening adjacent to an area of locally thickened bladder, were adopted as positive diagnosis. When including these indirect evidences (23/25 [92%]) in our series, the diagnostic yields of cystogram, LGI series and CT were similar. The sensitivity of cystoscopy and colonoscopy in our series (n = 2/3 [66.7%] and n = 2/9 [22.2%]) was consistent with the other series, with the diagnostic rate of 46.2-89% and 0-54.5%, respectively,[2-6,18] but the small number of our patients limited the power of data.

The query about surgery in benign CVF remained existed. Indeed, the only indication of surgery in patients with benign etiology is the quality of life and relief of distressing symptoms. The main factors challenging the decision of surgery are the related morbidity and the relatively short lifespan. Some authors suggested conservative treatment in patients with benign etiologies,[3,9,10] because the risks of urinary septicemia and renal failure were negligible in untreated cases and most patients with CVF were elderly and medically morbid. Moreover, the limited lifespan in patients with CVF was observed whether they were conservatively or surgically treated. However, the high mortality rate, 75%, of septic complications was observed in patients without surgical intervention by the other authors.[10,11] In a recent study, eighteen patients declining surgery for CVF ended up

seven deaths at the one-year follow-up.[2] Most studies did not demonstrate their long-term postoperative follow-up data. In this study, a mean follow-up period of 65.8 ± 7.3 months was conducted in the 60 patients, revealing an overall 5-year survival rate of 45%, similar to the previous studies (Walker et al. and Solkar et al., 5-year-survival rate 42-56%).[3,5] However, in this study, only subgroups of benign disease and post-radiation injury achieved 5-year survival rates with 71.1% and 53.6%, respectively, as well as the limited surgical mortality rates (6.7% and 7.1%). These data implied the value of surgical intervention in these subgroups of CVF with a limited risk. Those patients with untreated septic fistula may encounter more complicated infection and renal function impairment. Thus, it is appropriate to treat the disease definitely rather than to leave it watchful waiting because a relatively long life span can be expected in patients with benign etiologies and radiation injury.

The morbidity and mortality rate in patients accepting surgeries for CVF were approximately 15-42% and 1.4-12%, and their surgical morbidities were compatible with those in general abdominal surgeries.[2-8] In this series, nine patients required invasive procedures or intensive care, and seven of them were dead. Further analyzing the deceased seven patients, two were in pre-operative critical status, and the remaining five experienced progressed underlying cancer and/or relevant physical illness. All deaths in our series were directly associated either with severe sepsis or uncontrolled lung infection. Our experience suggested that poor physical status and uncontrolled morbidities were directly associated with short postoperative survival.

Conclusion

This study reviewed consecutive 60 patients with CVF undergoing surgical intervention. Although manifestations and investigation of this disease were similar to those of Western studies, the increased cases of radiation-related etiology differed from Western series. Increasing fistulae caused by diverticulitis were observed in Asia. According to experience in this study, longer survival of CVF can be expected in patients with benign disease and post-radiation injury subgroups with limited surgical mortality rate. The surgical intervention for these patients is thus strongly recommended.

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病例分析

積極外科手術治療對良性疾患與放射傷害造成的大腸膀胱廔管是值得推薦的：十年間 60 案例的追蹤分析

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背景　大腸膀胱廔管是一罕見肇因於發炎與腫瘤侵犯的併發症；肇因於此類病人手術介入的偏高罹病/死亡率，手術治療的適應症是被存疑的。

材料與方法　於林口長庚醫院，十年間共 60 案例，其資料、病徵、處置、與預後追蹤接受回溯性分析。

結果　共 28 位男性與 32 位女性，平均年紀 60.5 歲，被納入研究。其中 87% 以泌尿道症狀作表現 (尿液中混糞便 68%、尿液中混腸氣 40%)，而僅有 15% 是以腸胃道症狀作表現。疾病的成因包含憩室炎 (n = 18, 30%)、惡性腫瘤侵犯 (n = 16, 27%)、以及放射治療傷害 (n = 14, 23%)。22 與 9 位患者接受腸道切除併吻合與不併吻合手術，27 位僅接受腸道分流手術，2 位接受局部修補手術。在平均 66 個月的追蹤，良性疾患與放射傷害造成的大腸膀胱廔管患者的存活顯著異於肇因於惡性腫瘤侵犯的患者 ($p < 0.001$)，而良性疾患與放射傷害造成的大腸膀胱廔管患者的存活比較是無到達顯著差異 ($p = 0.302$)。良性疾患與放射傷害造成的大腸膀胱廔管患者的平均存活分別是 89.0 與 69.6 個月；其 7 年的的存活率分別是 59.3% 與 53.6%。其手術/住院的死亡率在前二組，相比於肇因於惡性腫瘤侵犯的病人 (25%)，是比較低的 (分別是 6.7% 與 7.1%)。

結論　本研究顯示低手術併發症與長期存活在良性疾患與放射傷害造成的大腸膀胱廔管是可預期的，其積極手術介入是具正當性的。

關鍵詞　大腸膀胱、腸膀胱廔管、憩室炎、外科手術、追蹤研究。