Asymptomatic diverticulosis identified by computed tomography is not a risk factor for enteric peritonitis

Susumu Toda, Yasuhiko Ito, Masashi Mizuno, Yasuhiro Suzuki, Isao Ito, Hideki Hiramatsu, Takenori Ozaki, Naotake Tsuboi, Waichi Sato, Shoichi Maruyama, Enyu Imai and Seiichi Matsuo

Department of Nephrology and Renal Replacement Therapy, Nagoya University Graduate School of Medicine, Nagoya, Japan

Correspondence and offprint requests to: Yasuhiko Ito; E-mail: yasuito@med.nagoya-u.ac.jp

Abstract

Background. Colonic diverticulitis is an important cause of polymicrobial peritonitis, which requires surgical treatment and cessation of peritoneal dialysis (PD). The aim of this study was to examine whether plain abdominal computed tomography (CT) is useful for evaluating colonic diverticulosis in chronic kidney disease (CKD) patients and to explore whether colonic diverticulosis is a risk factor for enteric peritonitis.
Methods. The subjects consisted of 137 consecutive CKD patients (Stage 4 or 5) who were candidates for PD from February 2005 to November 2009. Abdominal CT without contrast media was performed in all PD candidates.
Results. Diverticula of the colon were detected by plain CT in 57 cases (41.6%). The number of diverticula tended to increase with age. The most common site of involvement of diverticulosis was the ascending colon. In patients treated with PD, the incidence of peritonitis was higher in patients with diverticulosis than in those without diverticulosis (P = 0.004). However, only one episode of enteric peritonitis was observed among patients with diverticulosis. The presence of diverticulosis did not affect cumulative or technical survival. PD was not selected in four cases due to a high frequency of diverticula with episodes of abdominal pain. Two cases developed severe diverticulitis with peritonitis and underwent resection of the colon.
Conclusions. Our study suggests that plain CT examination is useful for detecting diverticulosis in CKD patients. Silent diverticulosis is not a risk factor for enteric diverticulosis-related peritonitis. PD may be contraindicated in cases having frequent diverticulosis with episodes of lower abdominal pain.

Keywords: CT scan; diverticulitis; diverticulosis; ESRD patients; PD peritonitis

Introduction

Peritonitis is a common complication of peritoneal dialysis (PD) and is associated with hospitalization, catheter loss, technical failure and increased mortality [1]. Recent studies have indicated that peritonitis remains a major cause of patients discontinuing PD and switching to hemodialysis [2, 3]. In cases of peritonitis by multiple enteric organisms, there is a possibility of intra-abdominal pathology. Colonic diverticulitis is an important cause of polymicrobial peritonitis, which often requires surgical treatment and cessation of PD.

Diverticulosis is defined as the presence of diverticula, sac-like protrusions of the colon wall, and diverticulitis refers to inflammation of diverticula [4]. Previous studies have suggested that frequent episodes of diverticulitis are a contraindication for PD, and the presence of diverticulosis in non-sigmoid colon is a risk factor for peritonitis in PD [5–7]. Further studies have suggested that colonic diverticulosis does not affect the outcome of enteric peritonitis; however, the incidence of peritonitis is higher in patients with diverticulosis [8]. In a recent report by the European Renal Best Practice Advisory Board, diverticulosis is not considered to be a contraindication for PD [9].

Colonic diverticular disease is rare in developing countries but is common in Western and industrialized societies. The prevalence is reported to increase with age, ranging from ~5% in adults <40 years of age to 65% among those ≥80 years of age [10, 11]. However, little is known about the prevalence of colonic diverticulosis in patients with end-stage renal disease (ESRD). In addition, methods to investigate diverticular diseases in ESRD patients have not been established, and there are no clear recommendations on which diverticular disease states are unsuitable for PD. Computed tomography (CT) is reported to be useful for evaluating diverticular diseases, including diverticulitis [4, 12–14]. It may be important to identify subgroups that are at greater risk of developing diverticulitis with peritonitis.

The aim of this study was to examine whether plain abdominal CT is useful for evaluating colonic diverticulosis and to investigate the types of colonic diverticulosis that are risk factors for the development of peritonitis. This is the first report to suggest that evaluation by CT is useful for investigating colonic diverticular diseases in chronic kidney disease (CKD) patients.

Materials and methods

Study design and patients

When CKD develops to Stage 4 or 5, nephrologists provide clinical advice and information on renal replacement therapy (RRT) modalities for patients and their families. Patients selecting PD are examined by routine abdominal CT without enhancement by contrast media. Between February 2005 and November 2009, 137 consecutive CKD Stages 4 and 5 patients, who considered undergoing PD at Nagoya University Hospital (Nagoya, Japan), were enrolled. There were 98 men and 39 women. All patients were Japanese aged >18 years, and the mean age of all patients was 57.5 ± 13.7 (range: 24–89) years. Diabetic nephropathy accounted for 42.3% of the primary causes of ESRD. Serum creatinine and blood urea nitrogen levels were measured enzymatically with an automated analyzer (JCA-BM6050; JEOL, Tokyo, Japan). Estimated glomerular filtration rate was calculated as described previously [15]. Past history of abdominal pain was ascertained by the attending physician. Demographic and clinical data were collected by reviewing medical records.

Abdominal CT

All examinations were performed using a CT scanner (Toshiba Aquilion TSX-101A; Toshiba, Otahara, Japan). Slices (7 mm) were taken at 7-mm intervals from the diaphragm to the pelvis. No intravenous contrast agent was administered in any cases. The resulting scans were evaluated for location of diverticula and their numbers were analyzed and calculated by three physicians familiar with the CT findings. The total number of diverticula in 90% of the total cases was the same on analysis by the three physicians, and in cases with different numbers, the three physicians and radiologists discussed the differences and decided on the final number of diverticula.

Peritonitis

Peritonitis was diagnosed when abdominal pain and/or cloudy fluid occurred with or without fever and when peritoneal fluid white blood cell count was >100/mm^3, with >50% polymorphonucleocytes [1]. Episodes with peritoneal eosinophilia but negative bacterial culture were excluded. Microbiological examination was performed according to *International Peritoneal Dialysis Guidelines* [1]. Enteral origin was defined as cases where one species of Enterobacteriaceae (including *Escherichia coli*, *Klebsiella* spp. and *Proteus* spp.), *Clostridium*, *Bacteroides*, *Enterococcus* and *Fusobacterium* was found in the dialysate. Cases with non-typable Gram-negative rods were classified as being of non-enteral origin [6]. The center's peritonitis rate is calculated using the following formula: total treatment duration (months)/number of peritonitis episodes. The average individual peritonitis occurrence rate was compared between the patients with diverticulosis and those without diverticulosis.

Statistical analysis

Statistical analysis was performed using SAS 6.10 (SAS Institute) software. Continuous variables were assessed as mean values ± SD or as incidences (%). Comparisons between two groups were performed using Student's *t*-test or Mann–Whitney *U*-test, and chi-squared test was used for categorical variables. Cumulative survival rates in each group were assessed by the Kaplan–Meier method, and the differences in survival rate between the groups were evaluated by log-rank test. Differences were considered to be statistically significant at $P < 0.05$.

Results

Analysis of all enrolled CKD Stage 4 and 5 patients

Frequency. Diverticula were detected in 57 (41.6%) of 137 patients by CT scan without contrast media (Table 1 and Figure 1). There were no differences in age, sex or cause of renal failure in diabetic nephropathy between patients with and without diverticulosis. Only three cases of autosomal-dominant polycystic kidney disease were included in this study. Eighty cases (58.4% of all cases) had no diverticula, and the number of diverticula ranged from 1 to 3 in 32 patients (23.4%). Nine cases (6.6% of total cases) had >20 diverticula, while the remaining 6.6% of total cases had 10–19 diverticula (Figure 2A).

Table 1. Comparison between ESRD patients with and without diverticulosis evaluated by abdominal CT^a

	With diverticulosis	Without diverticulosis	P
n (%)	57 (41.6%)	80 (58.4%)	
Male (%)	41 (71.9%)	57 (71.3%)	0.926
Age (years)	57.9 ± 12.1	57.2 ± 14.7	0.764
Diabetic nephropathy	28 (49.1%)	34 (42.5%)	0.793
ADPKD (%)	2 (3.5%)	1 (1.25%)	0.589
Creatinine (mg/dL)	6.2 ± 2.3	5.2 ± 2.4	0.024
eGFR (mL/min)	9.4 ± 5.2	11.7 ± 7.6	0.050

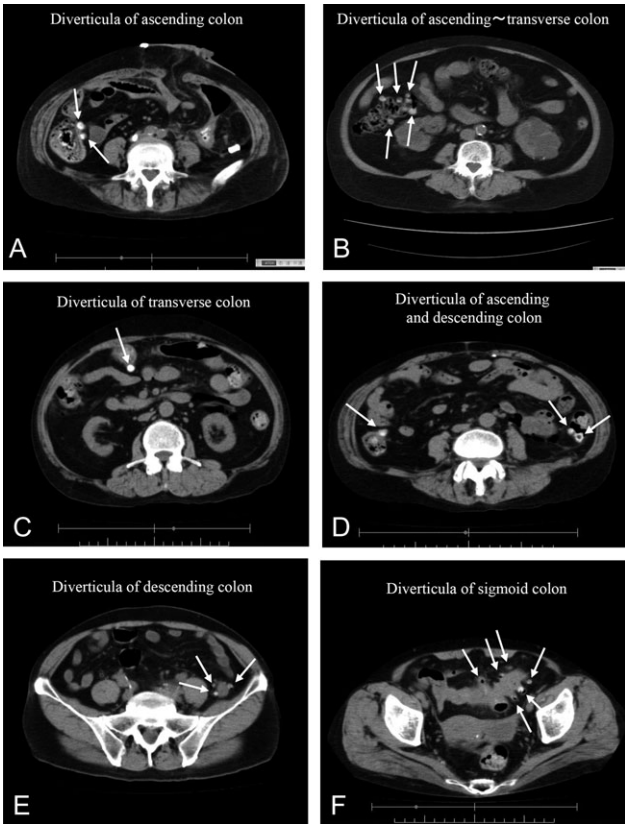^{a}ADPKD, autosomal-dominant polycystic kidney disease.

Fig. 1. Diverticula detected by CT without contrast media in patients with CKD Stage 4 or 5. (**A**) Diverticula of ascending colon. (**B**) Diverticula of ascending–transverse colon. (**C**) Diverticulum of transverse colon. (**D**) Diverticula of ascending and descending colon. (**E**) Diverticula of descending colon. (**F**) Diverticula of sigmoid colon.

Relationship with age and sex. Diverticula were not detected in patients <29 years. Frequency of diverticulosis-positive patients was similar among those aged >30 years (Figure 2B). In contrast, the number of diverticula tended to increase with age (Figure 2C). The incidence of diverticula did not differ between males and females (Table 1).

Distribution of diverticula. The most common site of involvement of diverticulosis was the ascending colon (70.1%), and diverticulosis was not detected in the rectum (Figure 2D). The highest average number of diverticula
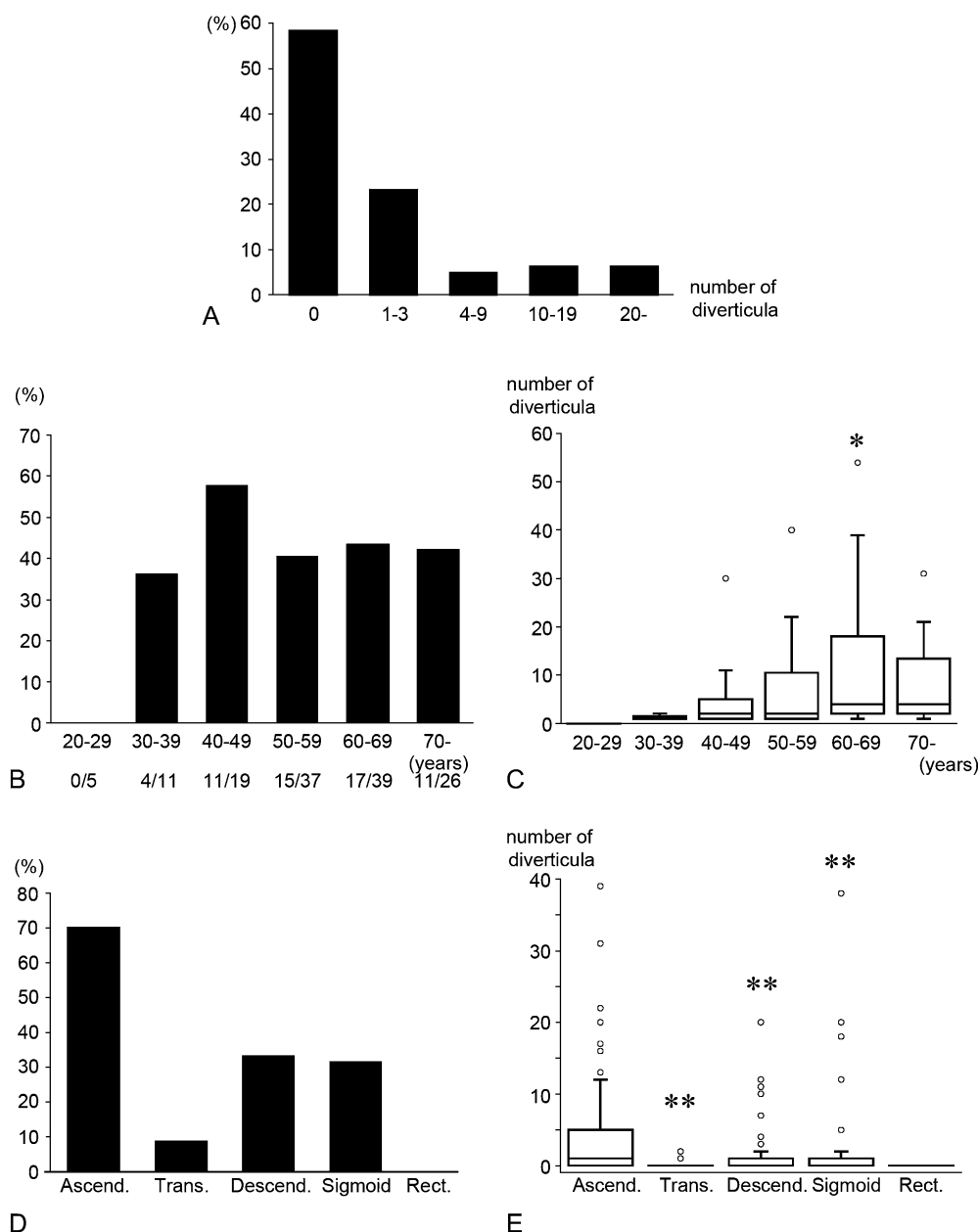
Fig. 2. Prevalence of diverticula in patients with CKD Stage 4 or 5. (**A**) Prevalence of diverticulosis based on number of diverticula. Eighty cases (58.4% of all cases) had no diverticula. Number of diverticula was 1–3, 4–9, 10–19 and >20 in 23.4, 5.0, 6.6 and 6.6% of patients, respectively. (**B**) Occurrence of diverticula in different age groups. Frequency of diverticulosis-positive patients was similar at ages >30 years. (**C**) Number of diverticula in different age groups. The number of diverticula tended to increase with age. The number of diverticula at age 60–69 years is significantly higher than that at age 30–39 years. *$P < 0.05$. (**D**) Occurrence of diverticula in different colonic segments. The most common site of involvement of diverticulosis was the ascending colon (70.1%) and diverticulosis was not detected in the rectum. (**E**) Number of diverticula in different colonic segments. The highest average number of diverticula was 4.66 in the ascending colon. The number of diverticula in ascending colon is significantly higher than in the transverse, descending and sigmoid colon. **$P < 0.001$. Ascend., ascending colon; Trans., transverse colon; Descend., descending colon; Sigmoid., sigmoid colon.

was 4.66 in the ascending colon (Figure 2E). There was a high prevalence of diverticulosis (>10 diverticula) in the ascending and sigmoid colon (Supplementary Figure 1A). The age-related distribution figure demonstrated that the ascending colon is a common site in patients aged >50 years. In contrast, the sigmoid colon is a more frequent site in younger patients (40% at 30–39 years and 30% at 40–49 years) when compared to the ascending colon (Supplementary Figure 1B).

Analysis of patients treated by PD

Of the 137 CKD patients, 61 started PD as RRT. The mean duration of treatment with PD was 33.8 ± 18.9 months (range, 1–67 months). Twenty-five patients (40.9%) were treated by automated PD (APD) and 36 patients (59.1%) were treated with continuous ambulatory PD. There were no differences between the diverticulosis-positive and -negative groups with regard to the usage of APD (Table 2).

Duration of PD was significantly higher in the patients with diverticulosis. During the follow-up period, 15 and 8 episodes of peritonitis were recorded in patients with and without diverticulosis, respectively (Table 3). The center's peritonitis rate was one episode for every 80.0 months (0.128 ± 0.021 episode/patient-month) with diverticulosis and every 106.5 months (0.008 ± 0.023 episode/patient-month) without diverticulosis, respectively. The individual occurrence rate of peritonitis was higher in patients with diverticulosis than in those without diverticulosis ($P = 0.004$, Table 2). However, only one episode of peritonitis due to enteric organisms was recorded in the patients with diverticulosis (Table 2). Enteric peritonitis in this case was induced by perforation with a bamboo stick fragment inadvertently eaten by the patient, and there were no macroscopic findings of diverticulitis during surgery. The number of technical failures was five and three in the patients with and without diverticulosis, respectively. In addition, the number of deaths was two and one in the patients with and without diverticulosis, respectively. The cumulative survival and technical failure survival rate did not differ between the diverticulosis-positive and -negative groups (Figure 3). Nephrologists carefully ascertained the history of abdominal pain and found that 4 of 137 CKD patients (2.9%) had episodes of abdominal pain localized in the left lower quadrant. All four cases had >20 diverticula (Table 4). In addition, two of these four cases had severe diverticulitis and under-went resection of the colon before initiation of dialysis therapy (Table 4, Supplementary Figure 2A and B, Cases 1 and 2). In contrast, 32 patients with diverticulosis without episodes of abdominal pain were successfully treated by PD with no occurrence of peritonitis by diverticulitis for $>38.8 \pm 19.2$ months.

Discussion

Our study indicates that the total incidence of diverticular diseases in Japanese ESRD patients is 41%, which is similar to those previously reported in European countries [6]. Although the cause of colonic diverticular diseases has not yet been conclusively established, epidemiological studies have suggested the effects of low dietary fiber, colonic pressure and motility changes [10, 12]. There are geographic variations between Asian and Western countries, both in the prevalence and pattern of diverticulosis [4, 10]. Diverticulosis is much less common in Asian patients and is more likely to be found in the proximal colon when compared to their Western counterparts, in whom the sigmoid colon is the most commonly affected segment [16].

A review of 13 947 barium enema examinations performed over a 15-year period in Japanese without CKD revealed a

Table 2. Comparison between patients with and without diverticulosis treated by peritoneal dialysis[a]

	With diverticulosis ($n = 31$)	Without diverticulosis ($n = 30$)	P
Male (%)	23 (74.2%)	21 (70%)	0.715
Age (years)	56.2 ± 12.0	57.0 ± 14.6	0.822
APD (%)	14 (45.2%)	11 (36.7%)	0.500
Diabetic nephropathy	23 (74.2%)	21 (70%)	0.715
ADPKD	0 (0%)	0 (0%)	
Duration on PD (months)	38.8 ± 19.2	28.6 ± 17.3	0.044
Individual peritonitis rate (episode/patient-month)	0.128 ± 0.021	0.008 ± 0.023	0.004
Enteric peritonitis rate (/total treatment months)	1 episode/total 1200 months	0 episodes/total 852 months	

[a]ADPKD, autosomal-dominant polycystic kidney disease.

Table 3. Causative organisms of peritonitis

| Causative organism	With diverticulosis ($n = 15$)	Without diverticulosis ($n = 8$)
Coagulase-negative Staphylococcus	4	4
Staphylococcus aureus	1	1
Streptococcus alpha	1	0
Streptococcus salivarius	2	0
Streptococcus sanguinis	1	0
Streptococcus species	1	1
Pasteurella multocida	1	0
Non-fermenting Gram-negative rods	0	1
Fusobacterium nucleatum	1	0
Fungi	0	0
Culture negative	3	1
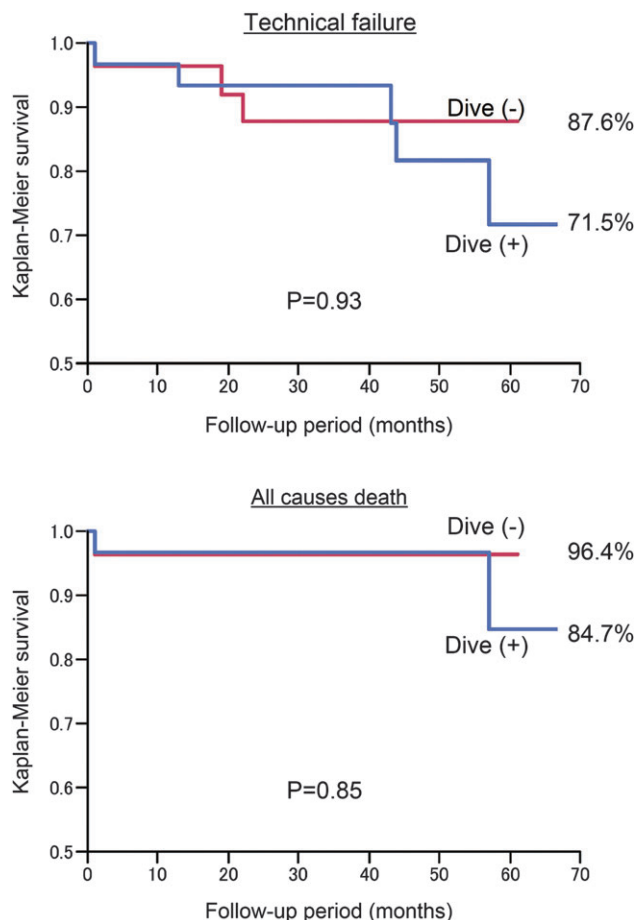
Fig. 3. Cumulative survival and technical failure survival rate did not differ between the diverticulosis-positive [Dive (+)] and -negative groups [Dive (−)]. Dive, diverticulosis.

Table 4. Cases not treated by PD[a]

Case	Age (years)	Sex (M:F)	Renal disease	Distribution of diverticulosis	Number of diverticula	Treatment
1	63	F	IgA N	A(20), T(2) D(20), S(12)	54	Operation because of peritonitis/HD
2	49	M	IgA N	A(0), T(0), D(12), S(18)	30	Emergency operation for peritonitis/HD
3	70	F	ADPKD	A(1), T(0) D(0), S(20)	21	HD
4	76	M	Diabetic N	A(8), T(0) D(1), S(38)	39	HD

[a]A, ascending colon; T, transverse colon; D, descending colon; S, sigmoid colon; HD, hemodialysis.

steady increase in the incidence of diverticulosis, particularly in the right colon [17]. In contrast, left-sided diverticula did not increase in frequency over time [17]. The frequency of diverticulosis was higher in our study (41.6%) when compared with previous data on Japanese without CKD, as reported by Miura (24.5%) and Sugihara (13.3%) in 2000 and 1984, respectively [17, 18]. Consistent with these previous reports, the number of diverticula increased with age and the incidence was higher in the ascending colon at all ages [16, 17]. Interestingly, however, the prevalence was higher in the sigmoid colon at ages <50 years, which may be due to recent changes in Japanese dietary habits.

Diverticulitis is commonly accompanied by microscopic perforation [12], which may be self-limiting and seal off rapidly and spontaneously [12, 19]. However, small leaks from microscopic perforations, which are bathed constantly by dialysate, may not be sealed promptly, leading to polymicrobial peritonitis in PD patients [7, 19]. CT examination is now recommended as an initial radiological examination for diverticulitis [4, 12–14]. Diverticulitis is classified into six stages based on CT findings, from the presence of diverticular disease in the sinus tract to fistula formation in adjacent organs by diverticulitis [13]. CT scans are reported to have high sensitivity (93–97%) and specificity approaching 100% for diagnosis [20, 21]. We found that the prevalence of colonic diverticulosis was similar to that reported previously in PD patients and was higher than previous reports in a Japanese cohort without ESRD. Although comparisons between CT findings and barium enema or endoscopic studies were not performed in our analysis, these findings may allow usage of this method to identify the presence of diverticulosis in ESRD patients.

The occurrence of peritonitis is higher in patients with diverticulosis, but most of the organisms were not enteric bacteria, suggesting that silent diverticular disease is not a risk factor for enteric peritonitis. We did not select PD as RRT in four cases due to the high frequency of diverticula and history of lower abdominal pain. In addition, two cases of diverticulitis were successfully diagnosed based on a history of abdominal pain, physical examination and CT scan (Table 4, Supplementary Figure 2A and B). Thirty-two patients with diverticulosis without episodes of abdominal pain were treated by PD with no occurrence of peritonitis by diverticulitis for >38.8 ± 19.2 months. A high frequency of diverticulosis with episodes of abdominal pain may therefore be a contraindication for PD.

A major limitation of this study is that the follow-up period was relatively short. Future studies are necessary in order to confirm these findings on long-term follow-up in a larger patient cohort. In addition, the present cohort had a low peritonitis rate, and it is unclear whether these results can be applied to other populations with higher baseline peritonitis rates. Finally, while cumulative patient survival and technical survival rates did not differ between the diverticulosis-positive and -negative groups, the small patient numbers suggest that this study was likely underpowered to draw firm conclusions with regard to these outcomes.

In summary, CT examination without contrast media appears to be useful for detecting diverticulosis. Diverticulosis is common in ESRD patients, and recognition of diverticular diseases may be helpful for treating constipation and differential diagnosis of peritonitis. Higher numbers of diverticula with episodes of abdominal pain may also be an important contraindication for PD. Future studies are necessary in order to determine whether high frequencies of diverticulosis detected by CT examination with episodes of abdominal pain are predictive of peritonitis.

Supplementary data

Supplementary Figures 1A and B, and 2A and B are available online at http://ndt.oxfordjournals.org.

References

1. Li PK, Szeto CC, Piraino B *et al.* Peritoneal dialysis-related infections recommendations: 2010 update. *Perit Dial Int* 2010; 30: 393–423
2. Mactier R. Peritonitis is still the achilles' heel of peritoneal dialysis. *Perit Dial Int* 2009; 29: 262–266
3. Davenport A. Peritonitis remains the major clinical complication of peritoneal dialysis: the London, UK, peritonitis audit 2002–2003. *Perit Dial Int* 2009; 29: 297–302
4. Labs JD, Sarr MG, Fishman EK *et al.* Complications of acute diverticulitis of the colon: improved early diagnosis with computerized tomography. *Am J Surg* 1998; 155: 331–336
5. National Kidney Foundation. NKF-K/DOQI clinical practice guidelines for peritoneal dialysis adequacy: update 2000. *Am J Kidney Dis* 2001; 37: S65–S136
6. Tranæus A, Heimbürger O, Granqvist S. Diverticular disease of the colon: a risk factor for peritonitis in continuous peritoneal dialysis. *Nephrol Dial Transplant* 1990; 5: 141–147

7. Wu G, Khanna R, Vas S *et al.* Is extensive diverticulosis of the colon a contraindication to CAPD? *Perit Dial Int* 1983; 3: 180–183

8. Yip T, Tse KC, Lam MF *et al.* Colonic diverticulosis as a risk factor for peritonitis in Chinese peritoneal dialysis patients. *Perit Dial Int* 2010; 30: 187–191

9. Covic A, Bammens B, Lobbedez T *et al.* Educating end-stage renal disease patients on dialysis modality selection: clinical advice from the European Renal Best Practice (ERBP) advisory board. *Nephrol Dial Transplant* 2010; 25: 1757–1759

10. Heise CP. Epidemiology and pathogenesis of diverticular disease. *J Gastrointest Surg* 2008; 12: 1309–1311

11. Comparato G, Pilotto A, Franzè A *et al.* Diverticular disease in the elderly. *Dig Dis* 2007; 25: 151–159

12. Jacobs DO. Clinical practice. Diverticulitis. *N Engl J Med* 2007; 357: 2057–2066

13. Lawrimore T, Rhea JT. Computed tomography evaluation of diverticulitis. *J Intensive Care Med* 2004; 19: 194–204

14. Hachigian MP, Honickman S, Eisenstat TE *et al.* Computed tomography in the initial management of acute left-sided diverticulitis. *Dis Colon Rectum* 1992; 35: 1123–1129

15. Matsuo S, Imai E, Horio M *et al.* Revised equations for estimated GFR from serum creatinine in Japan. *Am J Kidney Dis* 2009; 53: 982–992

16. Sheth AA, Longo W, Floch MH. Diverticular disease and diverticulitis. *Am J Gastroenterol* 2008; 103: 1550–1556

17. Miura S, Kodaira S, Shatari T *et al.* Recent trends in diverticulosis of the right colon in Japan: retrospective review in a regional hospital. *Dis Colon Rectum* 2000; 43: 1383–1389

18. Sugihara K, Muto T, Morioka Y *et al.* Diverticular disease of colon in Japan. A review of 615 cases. *Dis Colon Rectum* 1984; 27: 531–537

19. Moffat FL, Deitel M, Thompson DA. Abdominal surgery in patients undergoing long-term peritoneal dialysis. *Surgery* 1982; 92: 598–604

20. Cho KC, Morehouse HT, Alterman DD *et al.* Sigmoid diverticulitis: diagnostic role of CT—comparison with barium enema studies. *Radiology* 1990; 176: 111–115

21. Ambrosetti P, Grossholz M, Becker C *et al.* Computed tomography in acute left colonic diverticulitis. *Br J Surg* 1997; 84: 532–534