

ORIGINAL ARTICLE

## 만성 신부전 환자에서 복막 투석과 혈액 투석에 따른 역류성 식도질환의 비교

송헌정, 김선문, 이유미, 황정아, 문경민, 문창기, 구훈섭, 송경호, 김용석, 이태희, 허규찬, 최용우, 강영우, 황원민, 윤성로

건양대학교 의과대학 내과학교실

### Is There a Difference in the Prevalence of Gastroesophageal Reflux Disease between Peritoneal Dialysis and Hemodialysis Patients?

Hyun Jung Song, Sun Moon Kim, Yu Mi Lee, Jung Ah Hwang, Kyung Min Moon, Chang Gi Moon, Hoon Sup Koo, Kyung Ho Song, Yong Seok Kim, Tae Hee Lee, Kyu Chan Huh, Young Woo Choi, Young Woo Kang, Won Min Hwang and Sung Ro Yun

Department of Internal Medicine, Konyang University College of Medicine, Daejeon, Korea

**Background/Aims:** Gastroesophageal reflux disease (GERD) is a common upper gastrointestinal disorder in patients with chronic kidney disease (CKD). However, little is known about the prevalence of GERD in dialysis patients. The aim of the present study was to investigate the difference in the prevalence of GERD in peritoneal dialysis and hemodialysis patients.

**Methods:** From July 2010 to August 2011, peritoneal dialysis patients (n=30) and hemodialysis patients (n=38) were enrolled. The prevalences of GERD were assessed at a single center with endoscopic findings and interviews using a questionnaire. Also, risk factors of GERD were evaluated.

**Results:** The prevalences of GERD in peritoneal dialysis and hemodialysis patients were 33.3% and 39.5% (p=0.748), respectively. The prevalences of erosive reflux esophagitis (ERD) in peritoneal dialysis and hemodialysis patients were 16.7% and 23.7% (p=0.477), respectively. The prevalences of nonerosive reflux disease (NERD) in peritoneal dialysis and hemodialysis patients were 16.7% and 13.2% (p=0.685), respectively. The prevalences of GERD, ERD and NERD were higher than those of the general population. The risk factor for GERD was age in hemodialysis patients.

**Conclusions:** The prevalence of GERD in dialysis patients was higher than that in the general population. However, there was no significant difference between peritoneal dialysis and hemodialysis patients. (*Korean J Gastroenterol* 2013;62:206-212)

**Key Words:** Gastro-esophageal reflux; Peritoneal dialysis; Renal dialysis; Chronic kidney failure

## INTRODUCTION

Esophagitis, gastritis, duodenitis and gastrointestinal reflux disease (GERD) are common upper gastrointestinal disorders in the chronic kidney disease (CKD).<sup>1-4</sup> However, little is known about the prevalence of GERD in dialysis patients. In a single-center survey, the prevalence of GERD was higher

in hemodialysis patients than that in the general population.<sup>5-10</sup> A previous study reported that the prevalence of GERD was higher in peritoneal dialysis patients than that in hemodialysis patients and in the general population. However, the study included patients who were diagnosed using only clinical symptoms.<sup>11</sup>

The effect of intraperitoneal pressure (IPP) on GERD in per-

Received May 28, 2013. Revised July 22, 2013. Accepted July 22, 2013.

© This is an open access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

교신저자: 김선문, 302-812, 대전시 서구 관저동로 158, 건양대학교병원 내과

Correspondence to: Sun Moon Kim, Department of Internal Medicine, Konyang University Hospital, 158 Gwanjeodong-ro, Seo-gu, Daejeon 302-812, Korea. Tel: +82-42-600-9370, Fax: +82-42-600-9095, E-mail: ismkim@kyuh.ac.kr

Financial support: This work was supported by Konyang University Myunggok Research Fund of 2009. Conflict of interest: None.

itoneal dialysis patients remains controversial. Some previous studies have shown a strong linear correlation between IPP and intraperitoneal fill volume and a significant impact of IPP on the prevalence of GERD in continuous ambulatory peritoneal dialysis, which can be explained by decreased basal tone of the lower esophageal sphincter.<sup>11,12</sup> In contrast, a manometric study showed no effect of dialysate infusion on lower esophageal sphincter pressures due to transient relaxation of lower esophageal sphincter function.<sup>13</sup>

The aim of this study was to determine the differences in the prevalence of erosive reflux esophagitis (ERD) and non-erosive reflux esophagitis (NERD) between CKD patients undergoing peritoneal dialysis and those undergoing hemodialysis.

## SUBJECTS AND METHODS

The study was performed in accordance with the Declaration of Helsinki, and good clinical practice and applicable regulatory requirements. This study was approved by the Konyang University College of Medicine Institutional Review Board (IRB 10-28).

### 1. Study design and patient population

From July 2010 to August 2011, patients with CKD undergoing peritoneal dialysis (peritoneal dialysis patients, n=40) and those undergoing hemodialysis (hemodialysis patients, n=43) for over 1 year were enrolled in this study. Fifteen patients were excluded from the study due to not meeting the inclusion criteria (7 patients) and declining to participate (8 patients). The following patients were excluded from the study: (1) those with a history of abdominal surgery; (2) those treated with a proton pump inhibitor within the past 1 month; and (3) those with eradication of *Helicobacter pylori*. A total of 68 patients were enrolled (peritoneal dialysis patients, n=30, hemodialysis patients, n=38). There were 34 males and 34 females, and the mean age of the patients was 56.3±10.7 years.

### 2. Questionnaire

The prevalences of GERD in peritoneal dialysis and hemodialysis patients were assessed at a single center with endoscopic findings and face-to-face interviews using a validated symptom questionnaire previously used in the general

population.<sup>8</sup> The questionnaire was completed by the patients.

### 3. Esophagogastric examinations

Each patient underwent upper gastrointestinal endoscopic examination, which was performed by a single well-trained gastroenterologist with at least 10 years of endoscopy experience. ERD was classified according to the Los Angeles classification into grades A to D. Minimal changes, such as erythema, increased vascularity, friability and edema,<sup>14</sup> were excluded from ERD.

Patients were diagnosed with NERD if heartburn or acid regurgitation was the most bothersome symptom at a frequency of at least once per week in the absence of ERD.

The CLO<sup>TM</sup> test (ASAN Pharm., Seoul, Korea) for *H. pylori* infection was performed.

### 4. Statistical analysis

Data are presented as mean±SD unless otherwise indicated. The differences of mean value in age, BMI, duration of dialysis were evaluated using Student's t test. Other variables were evaluated using the Pearson chi-square test or Fisher's exact test. The logistic regression test was applied to compare the risk factors for GERD between peritoneal dialysis and hemodialysis patients. The statistical significance level was set at 0.05, and all statistical analyses were performed with PASW Statistics 18.0 (IBM Co., Armonk, NY, USA).

## RESULTS

### 1. Characteristics of the patients at baseline

A total of 68 patients with CKD were divided into 2 groups: those who underwent peritoneal dialysis (n=30) and those who underwent hemodialysis (n=38). Peritoneal dialysis and hemodialysis patients showed similar numbers of females (43% vs. 55%) and age ranges (55.0±11.6 years vs. 57.0±9.9 years).

The most common etiology of CKD was diabetic nephropathy (n=36, 52.9%), followed by hypertensive nephropathy (n=20, 29.4%), glomerulonephritis (n=5, 7.4%), polycystic kidney disease (n=2, 2.9%) and other etiologies (n=6, 8.8%). The mean duration of dialysis was 67.1 (±46.8) months (Table 1).

**Table 1.** Clinical Characteristics

Characteristic	PD (n=30)	HD (n=38)	p-value
Age (yr)	55.0±11.6	57.0±9.9	0.445
Sex (male/female)	17/13	17/21	0.329
BMI (kg/m <sup>2</sup> )	24.6±3.6	24.0±4.1	0.110
Smoking	0 (0)	1 (2.6)	0.383
Alcohol	0 (0)	0 (0)	
Etiology of ESRD			
Diabetic nephropathy	12 (40.0)	23 (60.5)	0.327
Hypertensive nephropathy	11 (36.7)	9 (23.7)	
Glomerulonephritis	4 (13.3)	1 (2.6)	
Polycystic kidney disease	1 (3.3)	1 (2.6)	
Other etiologies	2 (6.7)	1 (2.6)	
Unknown	0	3 (7.9)	
Duration of dialysis (mo)	61.1±42.2	70.5±50.9	0.417
Endoscopic diagnosis			
Erosive reflux esophagitis	5 (16.7)	9 (23.7)	0.477
Hiatal hernia	5 (16.7)	3 (7.9)	0.265
Erosive gastritis	15 (50.0)	18 (47.4)	0.567
Hemorrhagic gastritis	6 (20.0)	8 (21.1)	1.000
Gastric ulcer	3 (10.0)	5 (13.2)	0.688
Gastric polyp	0 (0)	3 (7.9)	0.115
Gastric adenoma	0 (0)	2 (5.3)	0.202
Gastric cancer	0 (0)	0 (0)	
Duodenal ulcer	2 (6.6)	3 (7.9)	0.394

Values are presented as mean±SD, n only, or n (%).

PD, peritoneal dialysis; HD, hemodialysis; ESRD, end stage renal disease.

## 2. Prevalence of GERD

The prevalence of GERD in patients was 36.8%. The prevalences of GERD in peritoneal dialysis and hemodialysis patients were 33.3% and 39.5% ( $p=0.748$ ), respectively (Fig. 1).

### 1) ERD

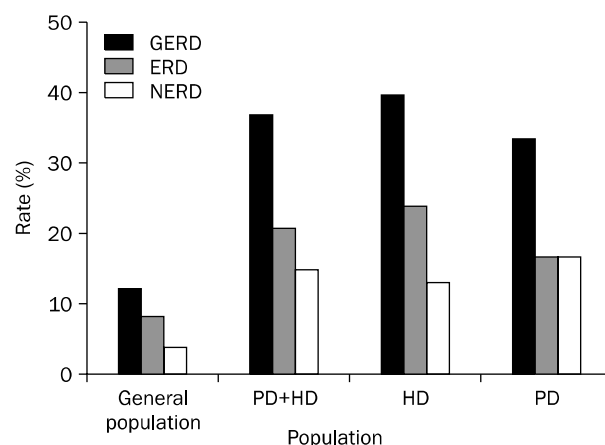
The prevalence of ERD in patients was 20.6% and showed similar values between the two groups, (5/30, 16.7% vs. 9/38, 23.7%;  $p=0.477$ ; Fig. 1).

### 2) NERD

The reported prevalence of NERD was 14.7% and showed similar values between the two groups (5/30, 16.7% vs. 5/38, 13.2%;  $p=0.685$ ; Fig. 1).

## 3. Risk factors for GERD

Peritoneal dialysis and hemodialysis patients were compared in terms of age, BMI and drugs administered. An elderly patient was defined as one at the age of  $\geq 65$  years as with previous studies. In peritoneal dialysis and hemodialysis patients, age was determined to be a significant risk factor (OR, 4.965;  $p=0.027$ ) (Table 2).



**Fig. 1.** Prevalences of gastroesophageal reflux disease (GERD), erosive reflux esophagitis (ERD) and nonerosive reflux disease (NERD).

PD, peritoneal dialysis; HD, hemodialysis.

The general population data from a nationwide multicenter prospective study in Korea abstracted from the article of Kim et al.<sup>8</sup>

In peritoneal dialysis patients, gender and age were not significant risk factors by univariate analysis (Table 3), whereas in hemodialysis patients, age was a significant risk factor (OR, 5.833;  $p=0.030$ ) (Table 4). BMI, as assessed using the Korean normal value of 25 kg/m<sup>2</sup>, was not a significant predictor of GERD in peritoneal dialysis and hemodialysis patients.<sup>15</sup>

Administration of calcium channel blocker, nitrate, and NSAIDs or aspirin was not a significant risk factor for GERD (Tables 3, 4).

The CLO<sup>TM</sup> test for *H. pylori* infection was not a significant risk factor for GERD in peritoneal dialysis and hemodialysis patients (Tables 3, 4).

## DISCUSSION

Many studies have reported upper gastrointestinal disorders in patients with CKD.<sup>16</sup> However, there have been only few studies on the differences in the prevalence of GERD between patients undergoing peritoneal dialysis and those undergoing hemodialysis.

The prevalence of GERD as determined by the Los Angeles classification was 9.8-16.3% in Japanese populations.<sup>17</sup> The prevalence of erosive esophagitis was reported to be 7.91% ( $n=25,536$ ) in the Korean general population according to a 2006 survey using endoscopy.<sup>8</sup> In a 1994 Korean study, an overall prevalence of erosive esophagitis was 2.4%,<sup>18</sup> which

**Table 2.** Factors Associated with Gastroesophageal Reflux Disease in Dialysis Patients by Univariate Analysis

	GERD absent (n)	GERD present (n)	p-value	OR	95% CI
Age (yr)			0.027	4.965	1.20-20.49
≥ 65	8	10			
< 65	35	15			
Sex			0.465	0.637	0.19-2.14
Male	23	15			
Female	20	10			
History of smoking	1	0			
BMI (kg/m <sup>2</sup> )			0.124	2.832	0.75-1.68
≥ 25	14	11			
< 25	29	14			
Calcium channel blocker	23	11	0.093	0.326	0.09-0.20
Nitrate	2	2	0.755	1.435	0.15-13.91
NSAIDs or aspirin	20	15	0.541	1.431	0.45-4.51
Diabetes	23	15	0.994	1.005	0.30-3.42
<i>Helicobacter pylori</i>			0.253	0.500	0.15-1.64
Positive	13	7			
Negative	13	14			

GERD, gastroesophageal reflux disease.

**Table 3.** Factors Associated with Gastroesophageal Reflux Disease in Peritoneal Dialysis Patients by Univariate Analysis

	GERD absent (n)	GERD present (n)	p-value	OR	95% CI
Age (yr)			0.999	1.286	0.24-6.96
≥ 65	5	3			
< 65	15	7			
Sex			0.602	1.055	0.33-6.92
Male	12	5			
Female	8	5			
History of smoking	0	0			
BMI (kg/m <sup>2</sup> )			0.122	4.333	0.85-22.23
≥ 25	7	7			
< 25	13	3			
Calcium channel blocker	12	4	0.442	0.444	0.09-2.09
Nitrate	2	1	0.999	1.000	0.08-12.56
NSAIDs or aspirin	6	4	0.690	1.556	0.32-7.60
Diabetes	9	5	0.796	1.222	0.27-5.59
<i>Helicobacter pylori</i>			0.197	0.238	0.33-1.71
Positive	6	2			
Negative	5	7			

GERD, gastroesophageal reflux disease.

increased to 3.4% in 1996-1997<sup>19</sup> and to 4.4-8.5% in the late 2000s.<sup>20</sup> The prevalence increased over the past 10 years.<sup>5-9,18-20</sup>

Kawaguchi et al.<sup>4</sup> reported that the prevalence of GERD in CKD patients increases probably due to increased gastrin secretion, decreased *H. pylori* prevalence, and interference with gastric emptying.

In our study, the prevalence of GERD was 35.4% (n=24) in all patients, 33.3% (n=10) in peritoneal dialysis patients, and 39.5% (n=14) in hemodialysis patients. These prevalences

are higher than that reported in the general population. Anderson et al.<sup>11</sup> reported that the prevalence of GERD was 44.6% in peritoneal dialysis patients and 19.8% in hemodialysis patients. Peritoneal dialysis patients showed a higher prevalence than hemodialysis patients. Because IPP is increased by peritoneal dialysis, peritoneal dialysis patients tend to suffer from reflux.

In our study, the 20.6% prevalence of ERD is higher than that in the general population.<sup>21</sup> However, the prevalences of GERD were similar between peritoneal dialysis and hemo-

**Table 4.** Factors Associated with Gastroesophageal Reflux Disease in Hemodialysis Patients by Univariate Analysis

	GERD absent (n)	GERD present (n)	p-value	OR	95% CI
Age (yr)			0.030	5.833	1.20-28.37
≥ 65	3	7			
< 65	20	8			
Sex			0.254	2.182	0.57-8.41
Male	11	10			
Female	12	5			
History of smoking	1	0	0.413	1.000	0.08-12.56
BMI (kg/m <sup>2</sup> )			1.000	0.831	0.20-3.54
≥ 25	7	4			
< 25	16	11			
Calcium channel blocker	11	7	0.944	0.955	0.26-3.51
Nitrate	0	1	0.395	1.071	0.94-1.23
NSAIDs or aspirin	14	11	0.501	1.768	0.43-7.30
Diabetes	14	10	0.717	1.286	0.33-5.02
<i>Helicobacter pylori</i>			0.795	0.816	0.18-3.78
Positive	7	5			
Negative	8	7			

GERD, gastroesophageal reflux disease.

dialysis patients (16.6% vs. 23.7%). NERD was also investigated using questionnaires. The total number of NERD patients in peritoneal dialysis and hemodialysis patients was 10 (16.7%) and 5 (13.2%), respectively. There were no significant differences in the prevalence between the 2 groups. However, the prevalence of NERD in CKD was 14.7%, which is higher than that in the general population (4.0%).<sup>8</sup>

Risk factors for GERD have been determined by univariate analysis. The factors known to be associated with reflux have also been studied in dialysis patients. In our study, the prevalence of GERD was lower in men than that in women (26% vs. 42%). This finding was contradictory to those of previous studies which showed male gender as a risk factor.<sup>8,22</sup> GERD is more common in men than in women, and the prevalence of GERD increased with increasing age in Korea.<sup>8</sup> It should be pointed out that, as de Jesús Ventura et al.<sup>23</sup> have documented, the prevalence of GERD is higher in men than in women. Age ≥ 65 years is an independent risk factor for severe esophagitis in other countries.<sup>24</sup> In Korea, being a female aged ≥ 65 years is an independent risk factor for erosive esophagitis.<sup>21</sup> However, clinical symptoms and the prevalence of GERD increase with aging.<sup>25</sup> Fujiwara et al.<sup>26</sup> have reported similar results. In our study, the prevalence of GERD was not affected by aging in peritoneal dialysis patients, while it was related to aging in hemodialysis patients. The risk factors for GERD were as follows: smoking, alcohol consumption, BMI, the prevalence of *H. pylori* infection, and the preva-

lence of diabetes.

BMI exerts no significant effect on GERD. The prevalence of GERD is much lower in Korea than that in Western countries, but the trend of increasing prevalence with increasing BMI has been documented in Korea due to westernized eating habits.<sup>27</sup> Sanchez et al.<sup>28</sup> demonstrated a strong correlation between abdominal pressure and BMI using a bladder catheter to measure abdominal pressure. BMI may explain the reason behind increased abdominal pressure. The results of the aforementioned studies are subjected to at least 2 limitations: patients with higher BMIs become clinically intolerant due to an increase in abdominal pressure and need changes in hemodialysis due to inadequate ultrafiltration.

*H. pylori*-positive status has been found to provide protective effects against erosive esophagitis.<sup>29</sup> This finding suggests that *H. pylori* infection plays a role in the prevention of erosive esophagitis, which is consistent with the results of previous studies. *H. pylori* infection which causes atrophic gastritis by affecting pepsinogen and gastric acid secretion is an important factor for erosive esophagitis.<sup>30</sup> Several studies have demonstrated a negative correlation between GERD and *H. pylori* infection. It is believed that *H. pylori* causes atrophic gastritis and that a relative reduction in gastric acid secretion affects the prevalence of GERD.<sup>22</sup> Some studies have demonstrated that the lower rate of *H. pylori* infection in GERD patients may reflect the role of *H. pylori* infection in reducing the prevalence of GERD.<sup>29,31,32</sup> In addition, erad-

ication of *H. pylori* was not shown to affect the development of reflux esophagitis or GERD symptoms among patients in Korea.<sup>33</sup>

In our study, the relationships between *H. pylori* infection and the prevalence of GERD were not confirmed in peritoneal and hemodialysis patients. However, the limitation of this result is that gastric biopsy and urea breath test were not performed.

In conclusion, there may be no significant difference in the prevalence of GERD in peritoneal dialysis and hemodialysis patients. This was a single-center prospective study of GERD in peritoneal dialysis and hemodialysis patients and has clinically meaning. However, the primary limitation of this study is the small sample size. Further studies using esophageal manometry and 24-hour pH monitoring are warranted.

## REFERENCES

1. Jamidar P, Kendall B. Gastrointestinal disease in patients with chronic renal failure. In: Nissenson AR, Fine RN, Gentile DE, eds. Clinical dialysis. 3rd ed. Norwalk: Appleton and Lange, 1995: 609-611.
2. Bargman JM. Noninfectious complications of peritoneal dialysis. In: Gokal R, Nolph KD, eds. The textbook of peritoneal dialysis. 2nd ed. Dordrecht: Kluwer Academic, 1994:565.
3. Kim MJ, Kwon KH, Lee SW. Gastroesophageal reflux disease in CAPD patients. Adv Perit Dial 1998;14:98-101.
4. Kawaguchi Y, Mine T, Kawana I, et al. Gastroesophageal reflux disease in chronic renal failure patients: evaluation by endoscopic examination. Tokai J Exp Clin Med 2009;34:80-83.
5. Yoo SS, Lee WH, Ha J, et al. The prevalence of esophageal disorders in the subjects examined for health screening. Korean J Gastroenterol 2007;50:306-312.
6. Oh JH, Choi MG, Kim HR, et al. Clinical spectrum of endoscopic reflux esophagitis in routine check-up subjects in Korea. Korean J Neurogastrointest Motil 2006;12:12-18.
7. Na IK, Jung JI, Pard HS. The prevalence and associated factors of reflux esophagitis in routine check-up subjects. J Korean Acad Fam Med 2001;22:1647-1655.
8. Kim N, Lee SW, Cho SI, et al; *H. pylori* and Gerd Study Group of Korean College of Helicobacter and Upper Gastrointestinal Research. The prevalence of and risk factors for erosive oesophagitis and non-erosive reflux disease: a nationwide multicentre prospective study in Korea. Aliment Pharmacol Ther 2008;27:173-185.
9. Cho YK, Kim GH, Kim JH, Jung HY, Lee JS, Kim NY; Korean Society of Neurogastroenterology and Motility. Diagnosis of gastroesophageal reflux disease: a systematic review. Korean J Gastroenterol 2010;55:279-295.
10. Hammer J, Oesterreicher C, Hammer K, Koch U, Traindl O, Kovarik J. Chronic gastrointestinal symptoms in hemodialysis patients. Wien Klin Wochenschr 1998;110:287-291.
11. Anderson JE, Yim KB, Crowell MD. Prevalence of gastroesophageal reflux disease in peritoneal dialysis and hemodialysis patients. Adv Perit Dial 1999;15:75-78.
12. Twardowski ZJ, Khanna R, Nolph KD, et al. Intraabdominal pressures during natural activities in patients treated with continuous ambulatory peritoneal dialysis. Nephron 1986;44: 129-135.
13. Hylander BI, Dalton CB, Castell DO, Burkart J, Rossner S. Effect of intraperitoneal fluid volume changes on esophageal pressures: studies in patients on continuous ambulatory peritoneal dialysis. Am J Kidney Dis 1991;17:307-310.
14. Lundell LR, Dent J, Bennett JR, et al. Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. Gut 1999;45:172-180.
15. Kim DM, Ahn CW, Nam SY. Prevalence of obesity in Korea. Obes Rev 2005;6:117-121.
16. Van Vlem B, Schoonjans R, Vanholder R, Vandamme W, De Vos M, Lameire N. Dyspepsia and gastric emptying in chronic renal failure patients. Clin Nephrol 2001;56:302-307.
17. Rosaida MS, Goh KL. Gastro-oesophageal reflux disease, reflux oesophagitis and non-erosive reflux disease in a multiracial Asian population: a prospective, endoscopy based study. Eur J Gastroenterol Hepatol 2004;16:495-501.
18. Yi SY, Lee SK, Kim MH, Han DS, Kim JW, Min YI. Epidemiologic study of reflux esophagitis in general health screening people. Korean J Med 1994;46:514-520.
19. Lee SJ, Song CW, Jeon YT, et al. Prevalence of endoscopic reflux esophagitis among Koreans. J Gastroenterol Hepatol 2001; 16:373-376.
20. Jung SA, Jung HY, Kim KR, Min YI. The prevalence of reflux esophagitis of Korean adults for 10 years of 1990's. Korean J Gastrointest Motil 2001;7:161-167.
21. Hwang JK, Kim JH, Hong SG, et al. A prospective multicenter study on the prevalence and symptoms of erosive reflux esophagitis in secondary and tertiary hospitals in Korea. Korean J Gastroenterol 2009;53:283-291.
22. Kim BC, Yoon YH, Jyung HS, et al. Clinical characteristics of gastroesophageal reflux diseases and association with *Helicobacter pylori* infection. Korean J Gastroenterol 2006;47:363-369.
23. de Jesús Ventura M, Amato D, Correa-Rotter R, Paniagua R. Relationship between fill volume, intraperitoneal pressure, body size, and subjective discomfort perception in CAPD patients. Mexican Nephrology Collaborative Study Group. Perit Dial Int 2000;20:188-193.
24. Pilotto A, Franceschi M, Leandro G, et al. Clinical features of reflux esophagitis in older people: a study of 840 consecutive patients. J Am Geriatr Soc 2006;54:1537-1542.
25. Cho YS, Choi MG, Jeong JJ, et al. Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Asan-si, Korea. Am J Gastroenterol 2005;100:747-753.
26. Fujiwara Y, Higuchi K, Watanabe Y, et al. Prevalence of gastroesophageal reflux disease and gastroesophageal reflux disease symptoms in Japan. J Gastroenterol Hepatol 2005;20:26-29.
27. Kwon JH, Chung IS, Son HS, et al. The relationship of gastrin, pep-

- sinogen, and *Helicobacter pylori* in erosive reflux esophagitis. Korean J Gastroenterol 2008;51:159-166.
28. Sanchez NC, Tenofsky PL, Dort JM, Shen LY, Helmer SD, Smith RS. What is normal intra-abdominal pressure? Am Surg 2001;67:243-248.
29. el-Serag HB, Sonnenberg A. Opposing time trends of peptic ulcer and reflux disease. Gut 1998;43:327-333.
30. Asaka M, Sugiyama T, Nobuta A, Kato M, Takeda H, Graham DY. Atrophic gastritis and intestinal metaplasia in Japan: results of a large multicenter study. Helicobacter 2001;6:294-299.
31. Gao BX, Duan LP, Wang K, Xia ZW, Lin SR. The roles of *Helicobacter pylori* and pattern of gastritis in the pathogenesis of reflux esophagitis. Zhonghua Yi Xue Za Zhi 2006;86:2674-2678.
32. Masjedizadeh R, Hajiani E, Moezardalan K, et al. *H. pylori* infection and reflux oesophagitis: a case-control study. World J Gastroenterol 2006;12:5658-5662.
33. Kim N, Lee SW, Kim JI, et al; *H. pylori* and GERD Study Group of Korean College of Helicobacter and Upper Gastrointestinal Research. Effect of *Helicobacter pylori* eradication on the development of reflux esophagitis and gastroesophageal reflux symptoms: a nationwide multi-center prospective study. Gut Liver 2011;5:437-446.