

Research Article



Charlson comorbidity index as a predictor of periodontal disease in elderly participants

Jae-Hong Lee ¹, Jung-Kyu Choi ², Seong-Nyum Jeong ¹, Seong-Ho Choi ^{3,*}

¹Department of Periodontology, Daejeon Dental Hospital, Institute of Wonkwang Dental Research, Wonkwang University College of Dentistry, Daejeon, Korea

²Department of Health Insurance Research, Ilsan Hospital, National Health Insurance Service, Goyang, Korea

³Department of Periodontology, Research Institute for Periodontal Regeneration, Yonsei University College of Dentistry, Seoul, Korea



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*Correspondence:

Seong-Ho Choi

Department of Periodontology, Research Institute for Periodontal Regeneration, Yonsei University College of Dentistry, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.

E-mail: shchoi726@yuhs.ac

Tel: +82-2-2228-3189

Fax: +82-2-392-0398

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ORCID iDs

Jae-Hong Lee

<https://orcid.org/0000-0002-2375-0141>

Jung-Kyu Choi

<https://orcid.org/0000-0001-5176-0534>

Seong-Nyum Jeong

<https://orcid.org/0000-0003-4890-989X>

Seong-Ho Choi

<https://orcid.org/0000-0001-6704-6124>

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Author Contributions

Conceptualization: Jae-Hong Lee, Seong-Ho Choi; Data curation: Jae-Hong Lee, Jung-Kyu Choi, Seong-Nyum Jeong, Seong-Ho Choi; Formal analysis: Jae-Hong Lee, Jung-Kyu Choi, Seong-Nyum Jeong; Funding acquisition:

ABSTRACT

Purpose: This study investigated the validity of the Charlson comorbidity index (CCI) as a predictor of periodontal disease (PD) over a 12-year period.

Methods: Nationwide representative samples of 149,785 adults aged ≥ 60 years with PD (International Classification of Disease, 10th revision [ICD-10], K052–K056) were derived from the National Health Insurance Service-Elderly Cohort during 2002–2013. The degree of comorbidity was measured using the CCI (grade 0–6), including 17 diseases weighted on the basis of their association with mortality, and data were analyzed using multivariate Cox proportional-hazards regression in order to investigate the associations of comorbid diseases (CDs) with PD.

Results: The multivariate Cox regression analysis with adjustment for sociodemographic factors (sex, age, household income, insurance status, residence area, and health status) and CDs (acute myocardial infarction, congestive heart failure, peripheral vascular disease, cerebral vascular accident, dementia, pulmonary disease, connective tissue disorders, peptic ulcer, liver disease, diabetes, diabetes complications, paraplegia, renal disease, cancer, metastatic cancer, severe liver disease, and human immunodeficiency virus [HIV]) showed that the CCI in elderly comorbid participants was significantly and positively correlated with the presence of PD (grade 1: hazard ratio [HR], 1.11; $P < 0.001$; grade ≥ 2 : HR, 1.12, $P < 0.001$).

Conclusions: We demonstrated that a higher CCI was a significant predictor of greater risk for PD in the South Korean elderly population.

Keywords: Comorbidity; Periodontal disease; Risk factors

INTRODUCTION

Chronic periodontal disease (PD) is a bacteria-induced chronic inflammatory disease. Although several aspects of this disease remain controversial, it is known to share proinflammatory cytokines and mediators with various lifestyle-related comorbid diseases (CDs), such as cardiovascular disease, pulmonary disease, diabetes mellitus, rheumatoid arthritis, vasculogenic erectile dysfunction, osteoporosis, and cancer [1-5]. These CDs may act as risk factors for PD, and PD can simultaneously be a risk indicator or risk factor for these comorbid conditions [6].

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Many recent studies have found associations between PD and mortality from CDs. LaMonte et al. [7] reported that the presence of severe PD in elderly women increased their risk of total mortality by 12% (hazard ratio [HR], 1.12; 95% confidence interval [CI], 1.05–1.21; $P=0.002$). Sharma et al. [8] further reported that the 10-year all-cause mortality rates of patients with chronic kidney disease were 32% and 41% without and with PD, respectively. Moreover, Saremi et al. [9] reported a 3.2-fold increase (95% CI, 1.1–9.3) in cardiorenal mortality (ischemic heart disease and diabetic nephropathy combined) when patients with PD were followed up for an average of 11 years, indicating that PD may be a major predictor of mortality due to ischemic heart disease and diabetic nephropathy. These findings indicate that PD is very common in elderly patients with CDs and may also be associated with health decline and mortality.

Evaluating systemic diseases in a patient before initiating treatment can be useful for predicting treatment results, such as the re-admission, re-operation, complication, and mortality rates; the validity of these factors has been evaluated in various clinical areas, and new evaluation methods are continuously being developed. Several methods, such as the Charlson comorbidity index (CCI), the Cumulative Illness Rating Scale, the Index of Coexistent Disease, and the Kaplan-Feinstein Scale, have been developed for the comprehensive and systematic assessment of CDs [10]. The CCI is the most widely used tool for estimating the prognosis of patients with CDs [11]. The use of this index with weights that vary (from 1 to 6) according to the severity of different diseases was shown to be effective in predicting the 1-year mortality rate based on the following 19 conditions: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, peptic ulcer disease, mild liver disease, diabetes without end-organ damage, hemiplegia, moderate or severe renal disease, diabetes with end-organ damage, tumor without metastases, leukemia, lymphoma, moderate or severe liver disease, metastatic solid tumor, and acquired immunodeficiency syndrome (AIDS) [11].

Although results from many studies have consistently supported using the CCI as a significant and independent prognostic indicator in various cancers and inflammatory diseases, the prognostic significance of this index has not been validated in PD patients, including elderly PD patients [12,13]. Therefore, the aim of the present study was to determine the validity of the CCI as a predictor of PD in elderly participants using the database of the nationwide population-based National Health Insurance Service-Elderly Cohort (NHIS-EC), which was newly released in 2016.

MATERIALS AND METHODS

Study design and data collection

This study selected 5.1 million elderly people (older than 60 years at the end of December 2002) during 2002 and 2003 as the entire population, from which 10% ($n=558,147$) were sampled by simple stratification by the National Health Insurance Service (NHIS) Big Data Steering Department. This database covered the following parameters: sociodemographic and socioeconomic information, insurance status, health check-up examinations, and records of patients' medical and dental history. These parameters were stratified to cover 12 years (2002–2013) and anonymized to protect individuals' privacy within the cohort study.

This study conformed to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational cohort studies (www.strobe-statement.org) and was approved by the Institutional Review Board of Daejeon Dental Hospital, Wonkwang University (approval No. W1704/001-001).

Definition of sociodemographic factors

The following potential confounding sociodemographic factors of PD were collected from the NHIS-EC database and assessed: sex, age (6 groups: those aged 60–84 years in 5-year intervals, and those aged ≥85 years), household income (5 groups: those with area-based [10 groups] and job-based [10 groups] health insurance were divided into 5 quintiles, with the Medical Aid Program [MAP] included in the first quintile), insurance status (3 groups: classified into the MAP group and NHIS [employees and self-employed] groups), residence area (3 groups: classified into metropolitan [≥10 million], urban [≥1 million], and others), and health status (3 groups: those classified as healthy, and with major and minor disabilities according to the Handicapped Welfare Law). All participants with responses regarding sociodemographic factors with either missing or unknown parameters were excluded from the current analysis.

Assessment of the CCI and PD

Elderly patients diagnosed with PD and CDs corresponding to the CCI prior to 2002 were excluded from the analysis, and the baseline was then established. Among the patients who had been diagnosed with CDs, we assessed the CCI during the follow-up period from 2002 to 2003. The CCI with International Classification of Disease, 10th revision (ICD-10) codes has been verified by Deyo et al. [14] and Sundararajan et al. [15], and we defined CDs using the ICD-10 codes provided by Sundararajan et al. [15]. The CCI assigns a weight of 1–6 points to each CD as follows, with the sum of individual scores serving as a measure of the overall comorbidity of a participant. If the weight was 0, the CDs listed below were not diagnosed (Table 1):

- 1 point was assigned for a history of acute myocardial infarction (including coronary artery bypass graft, percutaneous transluminal coronary angioplasty, and angina pectoris; codes I21, I22, and I252, respectively), congestive heart failure (I50), peripheral vascular disease

Table 1. ICD-10 codes and weights for the CCI scoring system

Condition	Weighting	Codes (ICD-10)
Acute myocardial infarction ^{a)}	1	I21, I22, I252
Congestive heart failure	1	I50
Peripheral vascular disease	1	I71, I739, I790, R02, Z958, Z959
Cerebral vascular accident	1	I60–69, G450–452, G454, G458, G459, G46
Dementia	1	F00–F02, F051
Pulmonary disease	1	J40–J47, J61–J67
Connective tissue disorders	1	M32–M35, M058–M060, M063, M069
Peptic ulcer	1	K25–K28
Liver disease	1	K702, K703, K717, K73, K740, K742–K746
Diabetes	1	E101, E105, E109, E111, E115, E119, E131, E135, E139, E141, E145, E149
Diabetes complications	2	E102–104, E112–114, E132–134, E142–144
Paraplegia	2	G041, G81–G822
Renal disease	2	N01, N03, N052–N056, N072, N18, N19, N25
Cancer	2	C0–C96
Metastatic cancer	3	C77–C80
Severe liver disease	3	K721, K729, K766, K767
HIV	6	B20–B24

ICD-10: International Classification of Disease, 10th revision, CCI: Charlson comorbidity index, HIV: human immunodeficiency virus.

^{a)}Including coronary artery bypass graft, percutaneous transluminal coronary angioplasty, and angina pectoris.

(I71, I739, I790, R02, Z958, and Z959), cerebral vascular accident (I60–I69, G450–G452, G454, G458, G459, and G46), dementia (F00–F02 and F051), pulmonary disease (J40–J47 and J61–J67), connective tissue disorders (M32–M35, M058–M060, M063, and M069), peptic ulcer (K25–K28), liver disease (K702, K703, K717, K73, K740, and K742–K746), and diabetes without end-organ damage (E101, E105, E109, E111, E115, E119, E131, E135, E139, E141, E145, and E149).

- 2 points were assigned for diabetes complications (E102–104, E112–114, E132–134, and E142–144), paraplegia (G041 and G81–G822), renal disease (N01, N03, N052–N056, N072, N18, N19, and N25), and cancer (C0–C96).
- 3 points were assigned for metastatic cancer (C77–C80) and severe liver disease (K721, K729, K766, and K767).
- 6 points were assigned for human immunodeficiency virus [HIV] (B20–B24).

Participants who were diagnosed with PD prior to 2003 were excluded, and we included participants who were newly diagnosed with PD (acute periodontitis [ICD-10, K052], chronic periodontitis [K053], periodontosis [K054], other periodontal disease [K055], and unspecified periodontal disease [K056]) and who received periodontal treatment (including NHIS prescription codes: U1010, subgingival curettage; U1020, excisional new attachment procedure; U1051–1052, simple/complex periodontal flap operation; U1071–1072, bone graft for alveolar bone defects; or U1081–1083, guided tissue regeneration) based on the guidelines of the Centers for Disease Control and American Academy of Periodontology using dental history questionnaires, clinical signs, and an oral examination and radiographic evaluation by a registered general dentist or periodontist who was qualified to perform a dental check-up [16,17]. To increase the validity of the PD diagnoses obtained in this study, we only selected PD participants who had been diagnosed and treated at least twice from 2004 to 2013.

Statistical analysis

We calculated HRs with 95% CIs using multivariate Cox proportional-hazards regression analysis, adjusting for sociodemographic factors (sex, age, household income, insurance status, residence area, and health status) and CDs (acute myocardial infarction, congestive heart failure, peripheral vascular disease, cerebral vascular accident, dementia, pulmonary disease, connective tissue disorders, peptic ulcer, liver disease, diabetes, diabetes complications, paraplegia, renal disease, cancer, metastatic cancer, severe liver disease, and HIV). The cumulative incidence of PD in participants with CDs was estimated using a Kaplan-Meier curve, with differences assessed using the log-rank test. All statistical tests were 2-sided, and a *P* value of <0.05 was considered to indicate statistical significance. Analyses were performed using SAS (version 9.2, SAS Institute, Cary, NC, USA) by the Department of Health Insurance Research, Ilsan Hospital, NHIS.

RESULTS

Results for the CCI and the incidence of PD in participants with CDs

Table 2 presents the data for the incidence of CDs in study subjects with PD. The incidence of CDs in participants with PD was highest for pulmonary disease (*n*=123,556, 82.5%), followed by peptic ulcer (*n*=123,191, 82.2%), liver disease (*n*=105,157, 70.2%), diabetes (*n*=91,047, 60.8%), peripheral vascular disease (*n*=80,058, 53.4%), cerebral vascular accident (*n*=72,245, 48.2%), connective tissue disorders (*n*=45,401, 30.3%), cancer (*n*=44,294, 29.6%), congestive

Table 2. Incidence of comorbid diseases corresponding to the CCI together with periodontal disease in the study subjects

Condition	Weighting	Males (n=65,817) No. (%)	Females (n=83,968) No. (%)	P ^{a)}
Acute myocardial infarction	1	7,768 (11.8)	8,161 (9.7)	<0.001
Congestive heart failure	1	14,793 (22.5)	23,876 (28.4)	<0.001
Peripheral vascular disease	1	31,753 (48.2)	48,305 (57.5)	<0.001
Cerebral vascular accident	1	29,884 (45.4)	42,361 (50.4)	<0.001
Dementia	1	10,930 (16.6)	19,748 (23.5)	<0.001
Pulmonary disease	1	53,354 (81.1)	70,202 (83.6)	<0.001
Connective tissue disorders	1	14,155 (21.5)	31,246 (37.2)	<0.001
Peptic ulcer	1	52,309 (79.5)	70,882 (84.4)	<0.001
Liver disease	1	45,961 (69.8)	59,196 (70.5)	<0.001
Diabetes	1	38,838 (59.0)	52,209 (62.2)	<0.001
Diabetes complications	2	2,172 (3.3)	3,013 (3.6)	<0.001
Paraplegia	2	667 (1.0)	785 (0.9)	<0.001
Renal disease	2	5,292 (8.0)	4,431 (5.3)	<0.001
Cancer	2	25,718 (39.1)	18,576 (22.1)	<0.001
Metastatic cancer	3	3,081 (4.7)	2,864 (3.4)	<0.001
Severe liver disease	3	5,764 (8.8)	3,639 (4.3)	<0.001
HIV	6	67 (0.1)	63 (0.1)	<0.001

CCI: Charlson comorbidity index, HIV: human immunodeficiency virus.

^{a)}All P values from the χ^2 test are significantly statistics ($P<0.05$).

heart failure (n=38,669, 25.8%), dementia (n=30,678, 20.5%), acute myocardial infarction (n=15,929, 10.6%), renal disease (n=9,723, 6.5%), severe liver disease (n=9,403, 6.3%), metastatic cancer (n=5,945, 4.0%), diabetes complications (n=5,185, 3.5%), paraplegia (n=1,452, 1.0%), and HIV (n=130, 0.1%).

Associations of the CCI with incident PD in elderly participants

Figure 1 presents the adjusted Kaplan-Meier curve for elderly comorbid participants with PD and a known CCI. Higher CCIs were associated with a higher incidence of PD in elderly comorbid participants ($P<0.001$). As indicated in Figure 2, the multivariate Cox proportional-hazards regression analysis with adjustment for sociodemographic factors, CCI, and CDs showed that the incidence of PD in elderly comorbid participants had a significant positive relationship with household income, insurance status, the CCI, peripheral vascular disease, cerebral vascular accident, pulmonary disease, connective tissue disorders, peptic ulcer, liver disease, diabetes, and cancer.

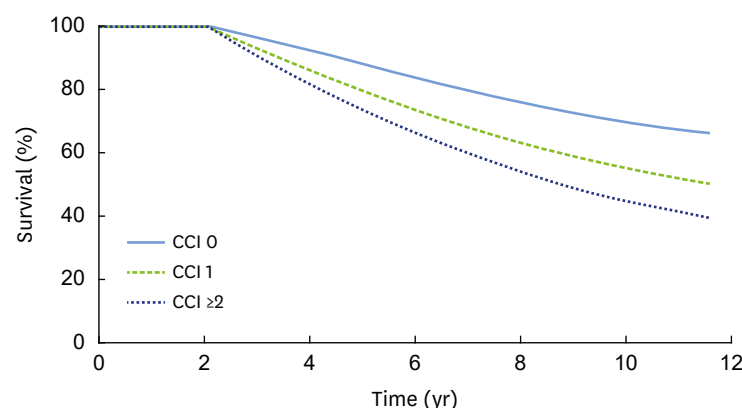


Figure 1. The cumulative incidence of PD in patients with CDs was estimated using the Kaplan-Meier method and compared using the log-rank test. A higher CCI was associated with a higher incidence of PD in elderly participants with comorbidities ($P<0.001$).

PD: periodontal disease, CD: comorbid disease, CCI: Charlson comorbidity index.

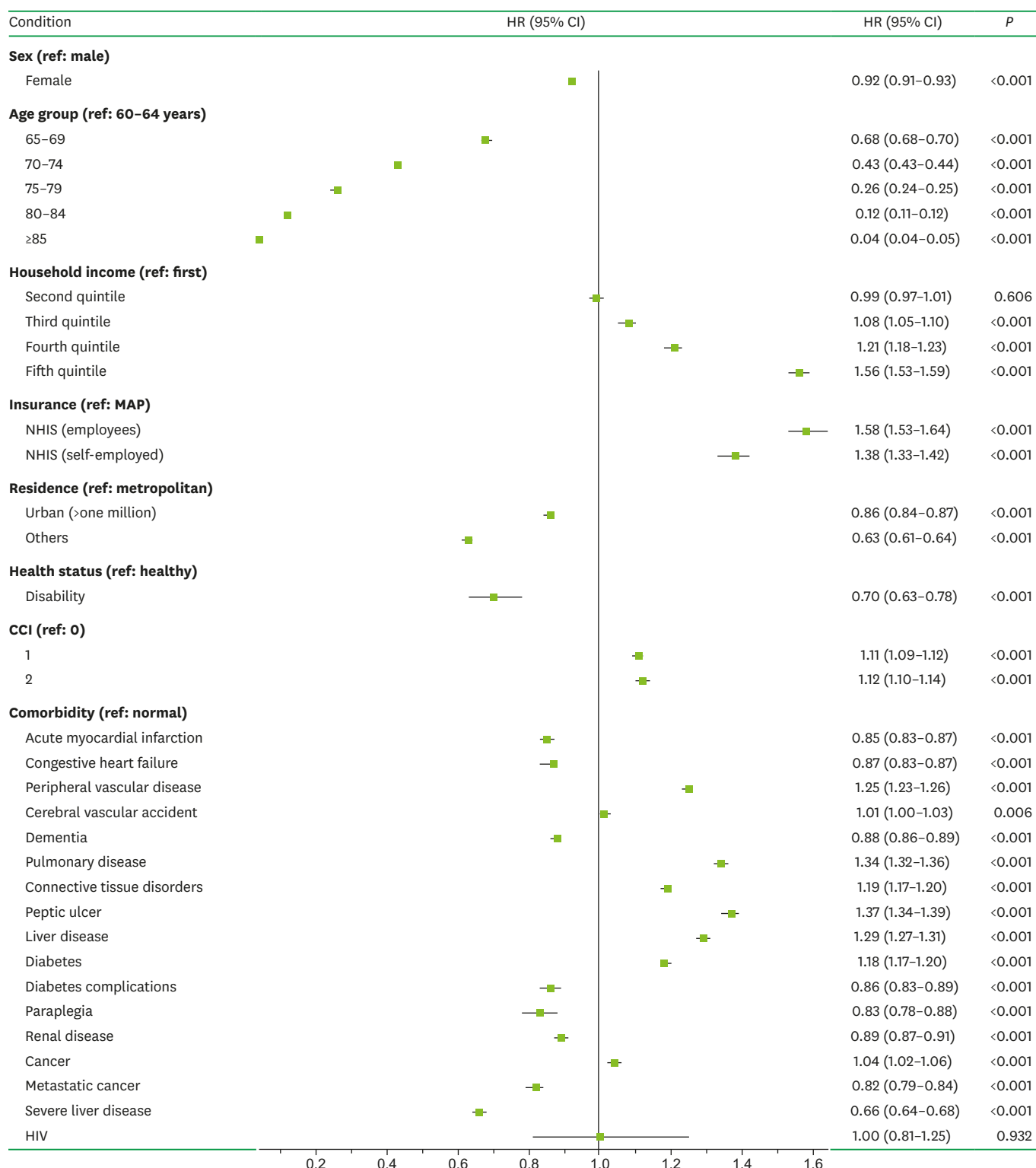


Figure 2. Associations of comorbidities with PD in elderly participants in the multivariate regression analysis. The multivariate Cox proportional-hazards regression analysis adjusted for sex, age, household income, insurance status, residence area, health status, acute myocardial infarction, congestive heart failure, peripheral vascular disease, cerebral vascular accident, dementia, pulmonary disease, connective tissue disorders, peptic ulcer, liver disease, diabetes, diabetes complications, paraplegia, renal disease, cancer, metastatic cancer, severe liver disease, and HIV. Data are HRs with 95% CIs. PD: periodontal disease, HIV: human immunodeficiency virus, HR: hazard ratio, CI: confidence interval, MAP: Medical Aid Program, NHIS: National Health Insurance Service, CCI: Charlson comorbidity index.

DISCUSSION

Targeting elderly individuals aged 60 years or older in South Korea, the present study is the first to quantify the usefulness of the CCI as a tool for evaluating CDs that are predictive factors for PD. CDs refer to chronic diseases that coexist or are present at the time of diagnosis of the disease under consideration. More than 50% of patients with cancer are generally reportedly to have CDs, including hypertension, diabetes mellitus, pulmonary disease, and cardiovascular disease [18]. The present study similarly found that 51.2% of participants with PD had CDs that were included in the CCI.

Female participants showed a slightly lower risk of PD than male participants (HR, 0.92; 95% CI, 0.91–0.93; $P < 0.001$), which is consistent with the finding of a recent systematic review that male patients generally had a similar or a higher prevalence of PD than female patients [19]. Most studies have found that the morbidity rate of PD increased significantly with age [20,21]. However, the present study found that the HR for PD decreased with age, especially for the age range of 60–64 years; this might be attributable to fewer subjects visiting dentists and being diagnosed with PD compared to those visiting a hospital for CDs. In other words, this might have occurred because the proportion of participants who were diagnosed with PD by dentists decreased when they had severe concomitant physical or mental diseases that limited their access to dental services [22,23]. This is supported by the consistent observation of low HRs for PD among those with low income levels who lived in areas with a lower accessibility of dentists and had physical disorders.

The HR values for PD associated with CCIs of 1 and ≥ 2 were 1.11 (95% CI, 1.09–1.12; $P < 0.001$) and 1.12 (95% CI, 1.10–1.14; $P < 0.001$), respectively, meaning that PD appeared to be associated with an increase in the severity of — and mortality associated with — CDs. In particular, the results of the 12-year Kaplan-Meier analysis showed that the risk of PD increased significantly with the CCI. Analyzing the distribution of the CDs revealed the following distribution of increased risks for PD: 37% for peptic ulcer, 34% for pulmonary disease, 29% for liver disease, 25% for peripheral vascular disease, 19% for connective-tissue disorder, 18% for diabetes, 4% for cancer, and 1% for cerebral vascular accidents. Acute myocardial infarction, congestive heart failure, and dementia were CDs associated with lower risks of PD. Since acute myocardial infarction and congestive heart failure are diseases with high mortality rates, it can be postulated that individuals with those diseases would be unlikely to visit dentists to be diagnosed with PD, resulting in them showing lower risks in the present study [24]. Despite reports that tooth loss and PD worsen cognitive function, and the presence of shared inflammatory mediators with Alzheimer disease, a recent systematic review argued that the foundations for a direct correlation between PD and Alzheimer disease were insufficient and controversial [25].

Among the CDs included in the CCI, the HRs for peptic ulcer disease indicated that chronic gastritis, peptic ulcer, gastric carcinoma, and gastric mucosa-associated lymphoid tissue lymphoma showed the strongest associations with PD. *Helicobacter pylori* has been suspected to be one of the main causes of peptic ulcer disease [26]. Despite being easily treatable, *H. pylori* has a high re-infection rate, and the lifetime risk of peptic ulcer disease (once infection occurs) is as high as 10% to 20% [27]. The suspected major pathways of re-infection are dental plaque, poor oral hygiene, and PD [28]. Treating peptic ulcer disease in combination with periodontal treatment was approximately 30% more successful at eradicating gastric *H. pylori* than conventional triple therapy (antibiotics, antimicrobials, and

proton-pump inhibitors) without periodontal treatment [29]. Therefore, elderly participants, who tend to have poor oral hygiene and limited access to periodontal treatment, may be more likely to develop chronic PD; it is postulated that these factors may further increase the risk of the recurrence of peptic ulcer disease. No studies have investigated the effects of peptic ulcer disease on PD, meaning that the underlying mechanisms remain to be investigated.

The CDs with the second highest risk — pulmonary diseases such as pneumonia and chronic obstructive pulmonary disease — have also been found to be risk factors for PD in many studies, including a systematic review [30,31]. As with peptic ulcer disease, potential respiratory pathogens have been found in dental plaque, and they have been considered major sources of respiratory infection [32]. Sumi et al. [32] reported that the respiratory pathogens *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, and *Enterobacter cloacae* accounted for most of the pathogens in the dental plaque of elderly individuals. In particular, pneumonia is a life-threatening infection that is a significant risk factor for mortality in the elderly [33]. We found that pulmonary diseases, which are major contributors to morbidity and mortality, increased the risk of PD in the elderly by 34%. Although the study of pulmonary disease as a risk factor for PD is very limited, these observations suggest that pulmonary disease has substantial implications not only for oral health, but also for the entire public health sector.

Many researchers have confirmed that CDs are important predictive factors for health [34,35]. Chronic PD is rapidly becoming a global epidemic disease with an increasing prevalence worldwide, particularly in elderly populations. According to a report of the Health Insurance Review and Assessment Service in 2016, PD has been the most expensive health problem in South Korea (amounting to about US\$ 1 billion) and the second-most-frequent disease (about 26.3% [13 million] of the Korean population) among outpatients since 2011. In addition, consistent with the general trend in developed countries, the elderly population is rapidly growing in South Korea, which is predicted to be a super-aged society — defined as more than 20% of the population being aged 65 years or older — by 2020. In the present study, the risk factors for PD increased the incidence of CDs and healthcare costs to different extents, depending on the severity of the CDs, which suggests that more in-depth evaluation and management are required before establishing appropriate policies for dental health care. Thus, the risk of PD may be especially high for CDs associated with high CCI values (which are the most severe types of CDs), and so elderly participants with CDs should be actively informed of their elevated risk for PD and advised to seek appropriate medical and periodontal care.

This study was subject to several limitations. First, the analysis was unable to reflect various clinical outcomes due to the inherent limitations of the retrospective NHIS-EC data. It poorly reflected the detailed characteristics of the risk factors, particularly the severity and duration of PD and CDs. Second, another major weakness of this study is that smoking and remaining teeth were not assessed, although many previous studies have found these to be important confounding factors for PD [36]. Third, selection bias can occur due to the cohort design, and in particular the inclusion of only patients who visited dental and medical clinics and who were diagnosed with PD and CDs. Fourth, owing to the study design (which established the baseline as the period between 2002 and 2003), participants' sociodemographic and socioeconomic position could have changed during the follow-up period, which extended through 2013. We accept that this study failed to consider this point, making it a limitation of this study. Finally, the CCI used in this study was developed in 1986; it is currently recognized

for its usefulness and validity, but new weights should continuously be developed as medical technology evolves. Quantifying the usefulness of the CCI as a predictor of PD will require the development of novel evaluation tools for CDs based on the most recent medical knowledge.

This 12-year longitudinal cohort study provides evidence that a high CCI was significantly associated with a higher risk of PD in the South Korean elderly population. Although the significant associations reported here must be confirmed by further studies, these observations have potentially important implications not only for oral health, but also for the entire public health sector.

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