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# Oral Health-Related Quality of Life, A Proxy of Poor Outcomes in Patients on Peritoneal Dialysis

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**Introduction:** We sought to evaluate the associations of poor oral health hygiene with clinical outcomes in patients receiving peritoneal dialysis (PD).

**Methods:** As part of the multinational Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS), PD patients from 22 participating PD centers throughout Thailand were enrolled from May 2016 to December 2019. The data were obtained from questionnaires that formed part of the PDOPPS. Oral health-related quality of life (HRQoL) used in this study was the short form of the oral health impact profile (oral health impact profile [OHIP]-14, including 7 facets and 14 items). Patient outcomes were assessed by Kaplan-Meier analysis. Cox proportional hazards model regression was used to estimate associations between oral HRQoL and clinical outcomes.

**Results:** Of 5090 PD participants, 675 were randomly selected, provided informed consent, and completely responded to the OHIP-14 questionnaire. The median follow-up time of the study was 3.5 (interquartile range = 2.7–5.1 months) years. Poor oral health was associated with lower educational levels, diabetes, older age, marriage, and worse nutritional indicators (including lower time-averaged serum albumin and phosphate concentrations). After adjusting for age, sex, comorbidities, serum albumin, shared frailty by study sites, and PD vintage, poor oral health was associated with increased risks of peritonitis (adjusted hazard ratio [HR] = 1.45, 95% confidence interval [CI]: 1.06–2.00) and all-cause mortality (adjusted HR = 1.55, 95% CI: 1.04–2.32) but not hemodialysis (HD) transfer (adjusted HR = 1.89, 95% CI: 0.87–4.10) compared to participants with good oral health.

**Conclusion:** Poor oral health status was present in one-fourth of PD patients and was independently associated with a higher risk of peritonitis and death.

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Oral health directly affects one's physical and mental health. Kidney failure (KF) patients with poor oral health are more at risk of overall and cardiovascular-related deaths due to the systemic effects of this condition, such as inflammation, infections, protein-energy wasting, and atherosclerosis.[1] In addition, oral health could have a psychological effect on individuals' and patients' lives by affecting speech, chewing, taste, swallowing, and self-confidence.

Several studies show that KF patients have higher rates of decayed, missing, and filled teeth, dental plaque, loss of attachment, xerostomia, gingivitis, periodontitis, as well as mouth and jaw-bone lesions than the general population.[2-7] Moreover, the consequences of poor oral health are worse for KF patients due to advanced age, diabetes, polypharmacy, and impaired immune function.[1]

Nevertheless, oral health evaluation is often not a high priority in the PD care setting. Similarly, there is a high discordance between symptoms reported by patients and those identified by their medical team. Currently, the International Society for Peritoneal Dialysis (ISPD) endorses the practice of reporting patient-reported outcomes as one of the essential indices that should be assessed routinely to help ensure the delivery of high-quality PD care.[8] Patient-reported oral health has been widely explored in patients receiving HD,[9-20] but less so in patients receiving PD.[21-27] Almost all studies were done in less than 120 PD participants and assessed only the physical dimension. A few studies have specifically explored the association between oral health and clinical outcomes. A single study conducted in Finland found no relationship between oral health and subsequent PD-related peritonitis,[24] and no other hard clinical outcomes were explored. Nevertheless, these results might be imprecise because the analyses were based on only 77 peritonitis episodes in 46 PD patients (a median follow-up time of 23 months).

The PDOPPS is a prospective international cohort study in PD, in collaboration with the ISPD, which has recruited participants from many countries, including Thailand.[28] To overcome the limitations of past studies, we leveraged this rich database with information from 22 facilities in Thailand to conduct adequately powered and multivariable-adjusted comparisons of self-reported oral health hygiene among patients on PD in order to better elucidate the relationship between oral health and patient outcomes.

## METHODS

### Study Design and Population

This prospective cohort study was conducted among patients 18 years and older who were receiving maintenance PD in Thailand according to the global PDOPPS protocol with minor modifications to meet Thailand's specific situation. Both incident ($n = 10$–$15$) and prevalent ($n = 20$–$30$) participants were randomly selected from 22 PD centers providing treatment to at least 20 PD patients at the time of selection. The study centers were selected from a complete list of 140 eligible PD facilities in Thailand. The study rationale and methods have been published previously.[28,29] All reporting adhered to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines (Supplementary Item S1).[30] The study was approved by the Chulalongkorn University institutional review board and local ethics committees. Informed consent was obtained from all participants prior to study enrolment.

### Data Collection

The PDOPPS collected patient-level and facility-level data using a standard protocol and data collection instruments in all participating facilities between 2 May 2016 and 1 December 2019. Participant demographics and comorbidities were captured at study enrolment. Blood chemistries were tested bimonthly, whereas all-cause mortality, cause-specific PD technique failure, hospitalizations, and PD-related complications were collected continuously during study follow-up. Patient-reported data, including HRQoL were collected at study enrolment and annually thereafter via self-administered surveys. The returned surveys were coded and entered into an electronic data file with a double-entry cross-checking process.

### Self-reported Oral Health Status and HRQoL

Oral HRQoL was evaluated in this study by using the short form (14 items, 7 facets) of the 49-item OHIP developed by Slade *et al*.[31,32] The short form OHIP-14 has been widely used across the globe for various research purposes and verified among HD[9] and PD patients.[23] The OHIP-14 measures limitation, discomfort, and disability attributed to oral conditions and is a self-filled questionnaire that focuses on 7 domains of impact (functional limitation, pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap), with participants being asked to respond according to the frequency of impact on a 5-point Likert scale coded as follows: never (score 0), hardly ever (score 1), occasionally (score 2), fairly often (score 3) and very often (score 4) using a few-months recall period. All 2 items of each facet of the questionnaire were aggregated and averaged to generate facet scores. Complete response was defined by the response to all 14 items of the questionnaire. The total OHIP-14 score was summed up from all 14 items. The higher the average value of the 7 dimensions and total OHIP score, the more negative the impact of oral health on the quality of life of an individual. The fourth quartile of OHIP-14 defined poor oral hygiene, whereas the first quartile of the OHIP-14 score was designated as good oral health. The second and third quartiles were collapsed and assigned to the

category of fair oral health. In Thailand, PDOPPS additionally collected OHIP-14 biennially.

HRQoL was assessed using the 12-item Short-Form (SF-12) of the original 36-item Kidney Disease Quality of Life survey. The SF-12 captured the 8 health domains and summarized them into a physical component summary score (PCS) and a mental component summary score (MCS). Higher PCS and MCS represented better physical and mental aspects of HRQoL, respectively.

### Statistical Analysis

Descriptive statistics were used to present the baseline characteristics of enrolled participants. Mean ± SD or median (interquartile range were used for continuous variables as appropriate, whereas categorical variables were presented as frequencies and percentages. One-way analysis of variance was used for comparison of continuous variables among the 3 groups of participants, whereas the $\chi^2$ test was used for comparison of categorical variables.

For time-to-event analyses, follow-up started at the participant's enrolment date. Follow-up ended at death, kidney transplantation, 7 days after a permanent shift to HD, loss to follow-up, or study end, whichever came first. Peritonitis was diagnosed according to the 2016 ISPD guidelines by employing at least 2 of the following criteria: (i) clinical features consistent with peritonitis, including abdominal pain and/or cloudy effluent; (ii) PD effluent leukocyte count more than 100/μl with polymorphonuclear cell predominance (after dwell time at least 2 hours); (iii) positive microbial culture from PD effluent.[33] HD transfer (defined as transfer to HD for greater than 84 days [12 weeks], or planned modality switch [clinically reported] and was censored for kidney transplantation and death). Death within 7 days of transfer to HD was counted as death on PD (outcome event), not HD transfer. Relapsing peritonitis (defined as a peritonitis episode that occurred within 4 weeks of completion of therapy of a prior episode with the same organism or no growth) was only counted once.[33]

Patient, peritonitis-free, and PD technique survivals were analyzed as time-to-event outcomes using the Kaplan-Meier method and multivariable Cox proportional hazard regression models, whereas peritonitis-free survival and HD transfer were analyzed as time-to-event outcomes adjusted for participant age, gender, PD vintage, comorbidities including (diabetes, coronary artery disease, congestive heart failure, and cerebrovascular disease), shared frailty by study sites, and serum albumin using cause-specific hazards models in the presence of competing events. The proportional hazards assumption of the Cox regression model was checked using Schoenfeld residuals and a log-log plot.

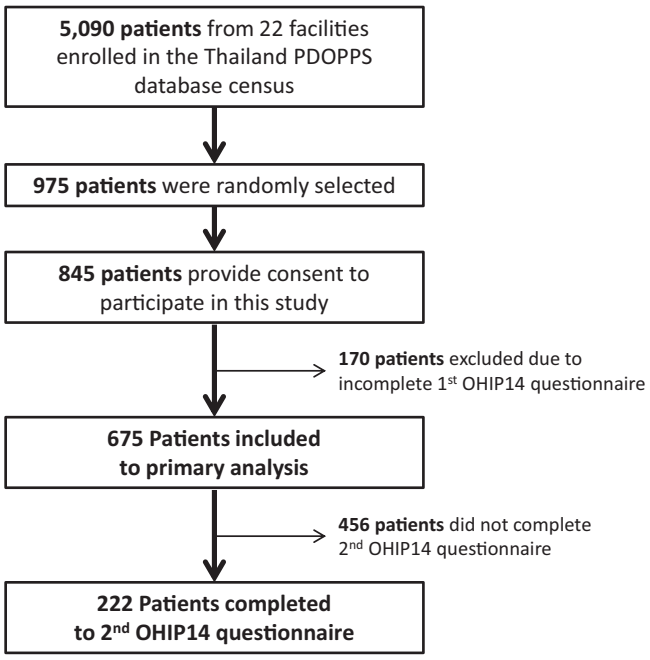


**Figure 1.** Patient flow diagram. OHIP, oral health impact profile; PDOPPS, peritoneal sialysis outcomes and practice patterns study.

Covariates were treated as time-varying if the assumption was not met. Sensitivity analyses were also conducted to calculate subdistribution (hazard ratios) HRs using Fine and Grey subdistribution hazard models,[34] and generate cumulative incidence curves for peritonitis considering HD transfer and death as competing events, and for HD transfer considering death as a competing event. Peritonitis was calculated as incidence (episodes per participant-year) and compared among groups using multivariable Poisson regression with adjustment for relevant variables mentioned earlier. All models accounted for PD facility clustering using robust sandwich covariance estimators. Multiple imputations were used to manage covariate variables with missing values. Assuming the missingness occurred randomly, we used sequential imputation by chained equations with 20 imputations added. All statistical analyses were performed using STATA/IC version 16.1 (StataCorp, College Station, TX).

## RESULTS

### Study Population

Of 5090 PD patients from 22 facilities in the Thailand PDOPPS database census, 975 patients were randomly selected. Of these, 848 patients provided written informed consent to participate in the study, while 53 (6%), 117 (14%), and 675 (80%) participants provided none, incomplete, and complete responses, respectively, to the OHIP-14 questionnaires. Only participants who completed all 14 items of the questionnaires

**Table 1.** Baseline characteristics

| Clinical parameters | Total (675) | Oral hygiene | | | *P*-value[a] |
|---|---|---|---|---|---|
| | | Good (171) | Fair (338) | Poor (166) | |
| Total OHIP-14 score | 13.4 ± 11.8 | 0.6 ± 0.9 | 11.6 ± 5.8 | 30.3 ± 6.3 | <0.001 |
| Age, yrs | 55.4 ± 13.4 | 52.1 ± 15.1 | 56.3 ± 13.2 | 57.0 ± 11.2 | <0.001 |
| Male gender | 337 (50%) | 83 (49%) | 173 (51%) | 81 (49%) | 0.81 |
| Marriage status | 485 (72%) | 106 (62%) | 247 (73%) | 132 (80%) | 0.001 |
| Education | | | | | 0.004 |
| Elementary school or lower | 51 (8%) | 22 (13%) | 21 (6%) | 8 (5%) | |
| High school graduate | 463 (69%) | 104 (61%) | 228 (67%) | 131 (79%) | |
| Bachelor's degree of higher | 108 (16%) | 31 (18%) | 57 (17%) | 20 (12%) | |
| Unknown | 53 (8%) | 14 (8%) | 32 (9%) | 7 (4%) | |
| Employed status | 271 (40%) | 71 (42%) | 140 (41%) | 60 (36%) | 0.5 |
| Caregiver dependency | 294 (44%) | 61 (36%) | 157 (46%) | 76 (46%) | 0.06 |
| Diabetes | 332 (49%) | 70 (41%) | 169 (50%) | 93 (56%) | 0.02 |
| Coronary heart disease | 54 (8%) | 14 (8%) | 27 (8%) | 13 (8%) | 0.99 |
| Congestive heart failure | 77 (13%) | 16 (11%) | 38 (13%) | 23 (15%) | 0.5 |
| Cerebrovascular disease | 25 (4%) | 3 (2%) | 15 (5%) | 7 (5%) | 0.3 |
| Smoking status | | | | | 0.4 |
| Active smoker | 7 (1%) | 2 (2%) | 5 (2%) | 0 | |
| Former smoker | 148 (9%) | 31 (25%) | 73 (29%) | 44 (33%) | |
| Never | 359 (70%) | 91 (73%) | 177 (6%) | 91 (67%) | |
| Kidney failure vintage, yrs | 1.0 ± 1.7 | 1.0 ± 1.8 | 0.9 ± 1.6 | 1.2 ± 1.8 | 0.2 |
| PD vintage, yrs | 0.8 ± 1.6 | 0.8 ± 1.5 | 0.8 ± 1.6 | 1.0 ± 1.7 | 0.3 |
| 24-h urine volume, l | 0.6 ± 0.6 | 0.7 ± 0.6 | 0.6 ± 0.7 | 0.5 ± 0.5 | 0.6 |
| CAPD modality | 654 (97%) | 161 (94%) | 330 (98%) | 163 (98%) | 0.06 |
| Laboratories[b] | | | | | |
| Serum creatinine, mg/dl | 9.4 ± 3.8 | 9.9 ± 4.2 | 9.2 ± 3.5 | 9.4 ± 3.8 | 0.2 |
| Serum sodium, mEq/l | 136.5 ± 3.3 | 136.7 ± 3.4 | 136.4 ± 3.3 | 136.3 ± 3.1 | 0.5 |
| Serum potassium, mEq/l | 3.7 ± 0.6 | 3.8 ± 0.5 | 3.7 ± 0.6 | 3.8 ± 0.5 | 0.2 |
| Serum bicarbonate, mEq/l | 27.4 ± 2.8 | 27.1 ± 2.9 | 27.6 ± 2.9 | 27.4 ± 2.7 | 0.3 |
| Serum calcium, mg/dl | 8.8 ± 0.8 | 8.7 ± 0.9 | 8.7 ± 0.8 | 8.8 ± 0.8 | 0.4 |
| Serum phosphate, mg/dl | 4.2 ± 1.4 | 4.5 ± 1.4 | 4.0 ± 1.4 | 4.1 ± 1.4 | 0.009 |
| Serum albumin, g/dl | 3.3 ± 0.6 | 3.4 ± 0.7 | 3.2 ± 0.6 | 3.3 ± 0.5 | 0.03 |
| Hemoglobin, g/dl) | 10.3 ± 1.5 | 10.4 ± 1.6 | 10.2 ± 1.4 | 10.5 ± 1.3 | 0.2 |
| Total Kt/V urea | 2.4 ± 1.1 | 2.3 ± 0.9 | 2.3 ± 0.9 | 2.6 ± 1.6 | 0.4 |
| Physical component status | 39.1 (33.5–44.9) | 40.8 (35.4–47.2) | 38.5 (32.8–45.4) | 37.8 (33.1–42.1) | 0.03 |
| Mental component status | 41.1 (36.6–47.6) | 43.0 (38.1–51.6) | 41.2 (36.1–47.6) | 40.2 (36.3–45.6) | 0.03 |

CAPD, continuous ambulatory peritoneal dialysis; OHIP, oral health impact profile; PD, peritoneal dialysis.
[a]Test of difference using ANOVA and $\chi^2$ test for continuous and categorical measures, respectively.
[b]Time averaged values over the first 4 months.
Parameter missingness varied from 13% (PD vintage) to 24% (smoking status).
All data are presented as mean±SD or median (IQR) for continuous measures, and *n* (%) for categorical measures.

were included in the analysis (Figure 1). One-fourth (25%) of the participants reported poor oral health at baseline. The OHIP-14 questionnaire was repeated in the following 2 years among 222 participants (33%).

## Participants' Demographics and Clinical Characteristics

Participant characteristics across different groups of oral health status are demonstrated in Table 1. Poor oral health at enrolment was associated with lower educational level, older age, marriage, diabetes, and worse nutritional indicators (including lower time-averaged serum albumin and phosphate concentrations). Other parameters were not significantly different among 3 groups. Parameter missingness varied from 13% (PD vintage) to 24% (smoking status), as demonstrated in Supplementary Table S1.

## Subscales of OHIP-14 and HRQoL

Different subscales of OHIP-14 measurements at the first and subsequent surveys are demonstrated in Supplementary Table S2 and S3. The most common concerning facet was physical pain while eating or at rest. Although comparability was limited, functional or psychological impairments and pain were the predominantly affected subscales. Of note, functional and social handicaps were also present but were comparably lower than the other facets. More than half (65%) of the participants did not consider their oral hygiene as a significant handicap. All subscales and total OHIP-14 scores were consistently and significantly worse in

**Table 2.** Adjusted hazard ratio for the estimated effect of self-reported oral health status on crucial patient outcomes

| | Oral hygiene | | |
|---|---|---|---|
| **Outcomes** | **Good ($n$ = 171)** | **Fair ($n$ = 338)** | **Poor ($n$ = 166)** |
| Peritonitis[c] | | | |
| Incidence proportion ($n/N$) | 42% (71/171) | 43% (147/338) | 57% (94/166) |
| Incidence rate (episodes per pt-years) | 0.17 | 0.24 | 0.27 |
| Unadjusted HR[a] | reference | 1.14 (0.86–1.52) | 1.51 (1.11–2.05) |
| Adjusted HR[a,b] | reference | 1.08 (0.82–1.44) | 1.45 (1.06–2.00) |
| Hemodialysis transfer | | | |
| Incidence proportion (n/N) | 6% (11/171) | 9% (31/338) | 11% (18/166) |
| Incidence rate (episodes per pt-yrs) | 0.019 | 0.029 | 0.033 |
| Unadjusted HR[a] | reference | 1.54 (0.78–3.07) | 1.73 (0.82–3.66) |
| Adjusted HR[a,b] | reference | 1.61 (0.88–2.94) | 1.89 (0.87–4.10) |
| Death | | | |
| Incidence proportion ($n/N$) | 21% (36/171) | 30% (100/338) | 36% (60/166) |
| Incidence rate (episodes per pt-yrs) | 0.06 | 0.09 | 0.11 |
| Unadjusted HR[a] | reference | 1.53 (1.04–2.24) | 1.75 (1.16–2.65) |
| Adjusted HR[a,b] | reference | 1.20 (0.73–1.98) | 1.55 (1.04–2.32) |

HR, hazard ratio; pt, patient.
[a]Cox proportional hazard regression.
[b]Adjusted for age, gender, PD vintage, comorbidities (diabetes, congestive heart failure, coronary artery disease, and cerebrovascular disease), shared frailty by study sites, and serum albumin, and after multiple imputations and accounting for facility clustering.
[c]Relapsing episode was counted at once.

the subsequent evaluation ($P < 0.001$) (Supplementary Table S4 and S5). MCS and PCS were significantly different among the OHIP groups. Patients with better oral health had higher MCS and PCS. By spearman correlation analysis, both MCS and PCS showed significant negative correlations with OHIP score (rho = −0.18, $P = 0.0006$, and rho = −1.69, $P = 0.0014$, respectively) (Supplementary Table S6).

## Oral Health and Subsequent Peritonitis, HD Transfer, and Death

Of 675 enrolled participants, 312 (46%) developed at least 1 episode of peritonitis, 60 (9%) experienced permanent HD transfer, and 196 (29%) died during a median follow-up time of 3.5 years (interquartile range 2.5–5.1). Peritonitis rates were 0.24 episodes per patient-year (overall), 0.17 episodes per patient-year in the good oral health group, 0.24 episodes per patient-year in the fair oral health group, and 0.27 episodes per patient-year in the poor oral health group. Many oral and nonoral pathogens, including *Bacillus*/*Corynebacterium*, *Streptococcus*, *Pseudomonas*, fungi and mycobacterium, demonstrated trends toward graded increases in peritonitis rates due to these organisms across OHIP levels; however, none individually reached the level of statistical significance (Supplementary Table S7).

Using a time-to-event analysis with a multivariable Cox proportional hazards model adjusted for age, gender, comorbidities, shared frailty by study sites, serum albumin, and PD vintage, patients who reported poor oral health at study entry were associated with higher risks of peritonitis (adjusted HR 1.46, 95% CI 1.06–2.01) and all-cause mortality (adjusted HR 1.55, 95% CI 1.04–2.32), but not HD transfer (adjusted HR 2.00, 95% CI 0.88–4.52) compared to those who reported good oral health. Patients with fair oral health showed an increased risk; however, it was not statistically significant (Table 2). Kaplan-Meier curves for peritonitis-free survival, PD technique survival, and patient survival are demonstrated in Figure 2, 3, and 4. The findings were consistent in sensitivity analyses using Fine and Grey subdistribution hazard models for peritonitis and HD transfer. The results of the competing risk regression and cumulative incidence curves are shown in Supplementary Table S8 and Supplementary Figure S1, respectively. In addition, the proportion of peritonitis-free participants was significantly lower in the poor oral health group (43% [72/166] vs. 59% [100/171], $P = 0.006$).

# DISCUSSION

In this large and multicenter study evaluating self-reported oral health among PD patients, poor oral health was common in the PD population, particularly among patients of older age, marriage, diabetes, lower educational level, and worse nutritional status (including lower time-averaged serum albumin and phosphate concentrations). Interestingly, self-reported poor oral health at baseline was significantly associated with shorter time to first peritonitis and death as well as higher rates of peritonitis and death but not HD transfer after adjusting for age, gender, PD vintage, comorbidities, shared frailty by study sites, and serum albumin. Oral health (in all dimensions) became worse with prolonged PD vintage.

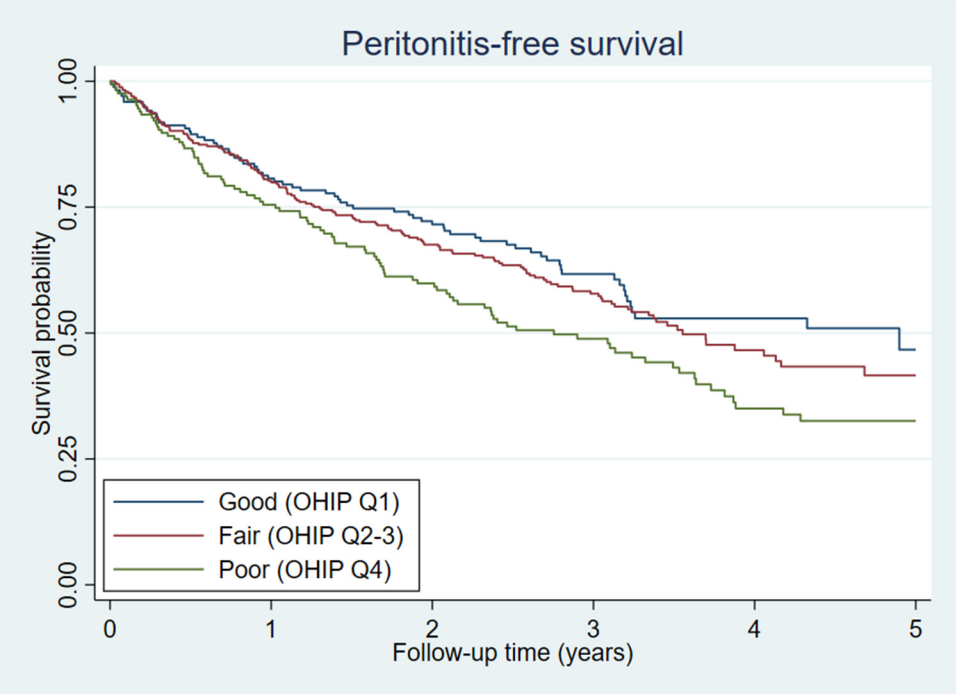


**Figure 2.** Kaplan-Meier survival curves demonstrating peritonitis-free survival among PD patients with good, fair, and poor self-reported oral health hygiene at the study entry. OHIP, oral health impact profile. After adjustment for participant age, gender, PD vintage, comorbidities, shared frailty by study sites, and serum albumin using cause-specific hazards models in the presence of competing events, peritonitis-free survival was significantly lower for poor oral health (adjusted hazard ratio 1.45, 95% confidence interval 1.06–2.00, $P = 0.03$) but not fair oral health (adjusted hazard ratio 1.08, 95% confidence interval 0.82–1.44, $P = 0.59$) compared with good oral health (reference).

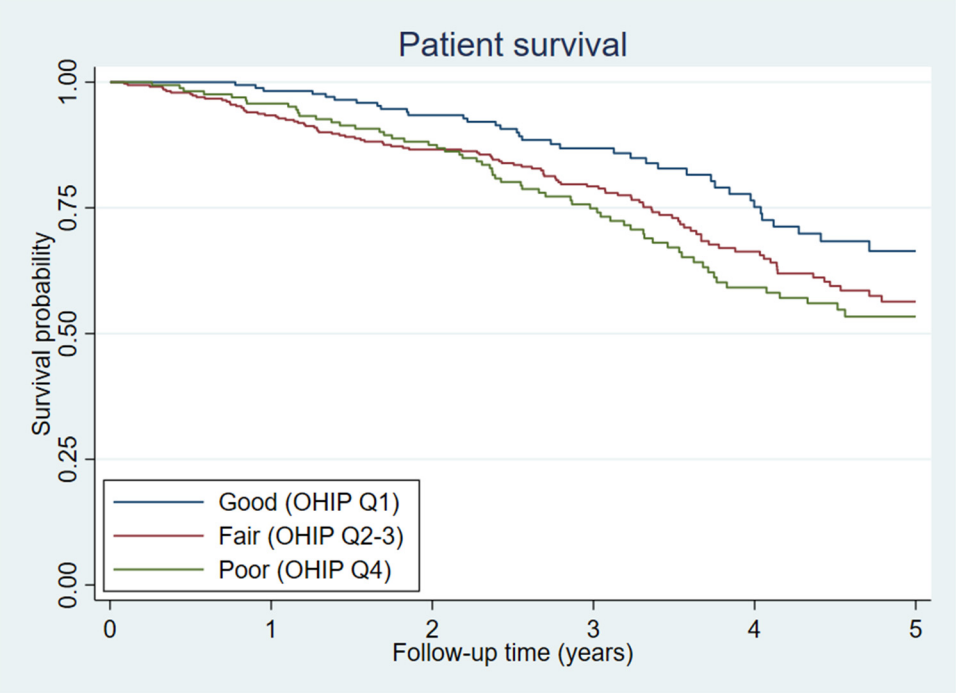


**Figure 3.** Kaplan-Meier survival curves demonstrating patient survival among PD patients with good, fair, and poor self-reported oral health hygiene at the study entry. OHIP, oral health impact profile. After adjustment for participant age, gender, PD vintage, comorbidities, shared frailty by study sites, and serum albumin using cause-specific hazards models in the presence of competing events, peritonitis-free survival was significantly lower for poor oral health (adjusted hazard ratio 1.55, 95% confidence interval 1.04–2.32, $P = 0.03$) but not fair oral health (adjusted hazard ratio 1.20, 95% confidence interval 0.73–1.98, $P = 0.46$) compared with good oral health (reference).

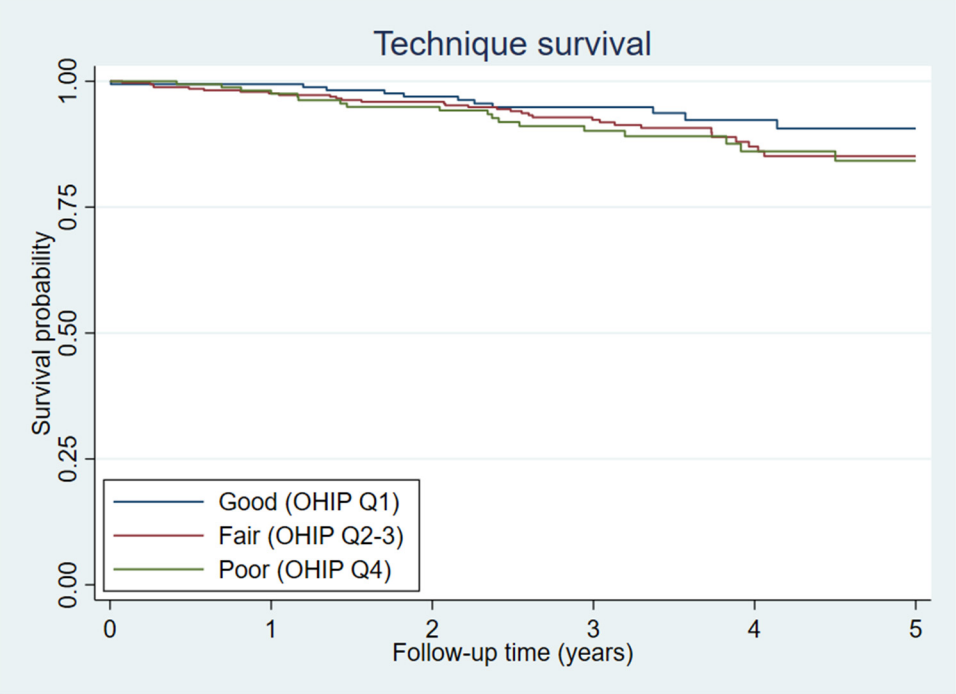


**Figure 4.** Kaplan-Meier survival curves demonstrating technique survival among PD patients with good, fair, and poor self-reported oral health hygiene at the study entry. OHIP, oral health impact profile. After adjustment for participant age, gender, PD vintage, comorbidities, shared frailty by study sites, and serum albumin using cause-specific hazards models in the presence of competing events, peritonitis-free survival was significantly lower for poor oral health (adjusted hazard ratio 1.61, 95% confidence interval 0.88–2.94, $P = 0.14$) but not fair oral health (adjusted hazard ratio 1.89, 95% confidence interval 0.87–4.10, $P = 0.14$) compared with good oral health (reference).

Poor oral health has previously been reported as common in pre-KF and HD patients, with 30% to 70% prevalence.[18–20] Nevertheless, only a few studies have examined oral health as a primary focus among PD patients. They reported poor oral health and gingivitis in 43% and 67% of patients,[21,25] respectively, but small sample sizes and single-center designs limited the reliability of their estimates. In contrast, the present study involving 675 patients from 22 PD facilities is by far the largest cohort to address this issue and observe a 24% prevalence of poor oral health. Nevertheless, the prevalence was seemingly lower than the previous reports in pre-KF and dialysis patients.[18–21,25] The explanation might be related to different tools or cut-points for poor oral health used in different studies. If we applied the OHIP-14 cut-point of 11 as recommended by Roumani *et al.*,[35] the prevalence of poor oral health was much higher, 333 of 675 (49%). The other possibility of this discrepancy is that oral health might be of less concern in our population. In fact, more than half (65%) of the participants did not consider their oral hygiene a significant handicap. Previously published data from our group demonstrated that most (54%) PD patients brushed their teeth less than twice a day. Most of the patients brushed their teeth for only 1 to 2 minutes, and none of them used dental floss or mouthwash for additional cleansing. Most participants sought the dentist's advice only when problems existed. One-third of the PD patients never had an oral examination or dental treatment.[26]

Poor oral health also appeared to associate with older age and some specific comorbid conditions, such as diabetes and malnutrition. The association between underlying diabetes and poor oral health in the present study is consistent with previous findings from a Turkish study.[22] Diabetes is closely related to oral health in dialysis patients.[25] The level of glycemic control is an essential determinant in that relationship.[36] Oral health status showed a significant negative correlation with serum albumin[21] and other nutritional indices.[5] Several proposed mechanisms underlying the association of malnutrition with poor oral health include the following: (i) dryness, pain, or abnormal taste in the mouth leading to anorexia and poor intake; (ii) tooth loss contributing to mastication dysfunction; and (iii) gingivitis and periodontitis associated with systemic inflammation and increased anorectic cytokines.[1] It is also possible that poor oral health may be a marker of poor general health or poor lifestyle and health-related behaviors.

Although the association between poor oral health and peritonitis has long been mentioned in the literature, the evidence supporting this assumption is weak,

usually limited to case reports or series observing that a concomitant oral infection (gingivitis, periodontitis, or dental root abscess) is established during peritonitis after carefully excluding other potential sources of peritonitis. The 2016 ISPD Peritonitis Guidelines mention that *Streptococci* frequently originate from the mouth and that transient bacteremia is common after dental procedures and may lead to peritonitis. Prophylactic antibiotics before extensive dental procedures may be reasonable (without grading).[33] These statements are based on 2 retrospective studies that demonstrated streptococcal peritonitis after dental treatment in 1 and 3 cases.[37,38] Arenius *et al*.[24] recently observed no relationship between oral health evaluation by complete oral and radiographic examinations and subsequent peritonitis. Our study is the first to demonstrate a relationship between poor oral health and peritonitis. Our finding is supported by a Japanese observational study[23] that reported that improving oral hygiene habits (increased duration of daily oral care and more frequent toothbrush replacement) was significantly associated with less frequent peritonitis among 75 PD patients, mainly caused by *Streptococci*.

The proposed mechanisms of the association between poor oral hygiene and peritonitis may be related to the presence of an increased reservoir of pathogens in the oral cavity, particularly gingiva and surrounding tissues (periodontal pockets), or indirect effects caused by poor nutritional status resulting in impaired host immunity. Most dental manipulations, including tooth brushing, dental flossing, and oral irrigation, can engender transient and inconsequential bacteremia for healthy individuals but may contribute to persistent and clinically significant bacteremia in immunocompromised patients in the presence of accumulated plaque and gingivitis.[1] The overall area of periodontal lesions can be as large as 1500 to 2000 $mm^2$,[39] and the number of bacteria can exceed 100 million in a single cubic millimeter of dental plaque.[1] Greater severity of gingival inflammation correlates with a higher likelihood of detectable bacteremia.[40] Odontogenic pathogens might enter the blood circulation and invade the PD system, thereby causing peritonitis.

On the OHIP-14 scale, the most common concerning facet raised by the participants in this study was physical pain while eating or at rest. This problem potentially disturbed their quality of life, created emotional stress, and contributed to insufficient food intake. Any difficulty in eating solid foods may reduce protein intake and contribute to overhydration due to consuming a softer or higher fluid-containing diet as compensation. Chewing affects both quality and quantity of food intake, contributing to malnutrition and potentially a higher peritonitis rate and worse survival.

The association between poor oral health and mortality remained significant even after adjustment for various clinical parameters; the adjusted HR was 1.55 [95% CI 1.04–2.32]. This result is consistent with what has been reported among HD patients. In the Oral-D study,[6,7] dental health status and habits were associated with increased risks of all-cause and cardiovascular death among patients receiving HD. The oral disease was associated with inflammation and malnutrition, which might have accelerated cardiovascular disease and therefore represents a testable risk factor for cardiovascular events in the context of KF.[1] Not only does oral infection drive local inflammation within the gingival epithelium, but it also stimulates systemic inflammation through bacteremia, circulating oral microbial toxins, and immunologic responses to the microorganism.[1,40] It is also worth emphasizing the role of oral hygiene in systemic inflammation, which plays a crucial role in the progression of cardiovascular system disease, one of the leading causes of death in dialyzed patients.

The oral-health dimension of life participation assessment allows a shift from the traditional physical dental evaluation to the individual social, emotional, and physical functioning of a patient in caring for oral health. It may also be a proxy of overall personal hygiene habits, such as washing, grooming, trimming fingernails, regularly changing clothing, removing visible nail dirt, hand washing, etc. In our view, such overall personal cleanliness, rather than just simply considering hand hygiene, is vital for preventing peritonitis in PD patients. Furthermore, we postulate that oral hygiene might be a good indicator of long-term personal hygiene status with the ability to reflect the cumulative poor personal hygiene of the preceding several months to years. The 2016 ISPD guidelines only state that meticulous hand hygiene during the dialysis exchange is essential and should be emphasized during patient training but do not generalize to personal hygiene.[33] Therefore, the role of overall personal hygiene in preventing PD-related infections is worthy of further exploration.

The strengths of our study include the length of follow-up (median 40.3 months, interquartile range 29.5–59.8), multicenter design, large sample size (678 patients), and high cumulative number of peritonitis, HD transfer, and death events, which helped to augment statistical power. Nevertheless, some limitations also need to be highlighted. First, the OHIP-14 used a subjective measure to assess oral health among PD patients. Future research might benefit from more objective measures of oral health, a dental examination, and radiographic studies. Second, the questionnaire was collected voluntarily and self-

administered such that the patients with inferior functional status may have been less likely to respond to the questionnaire and be under-represented in the cohort. Despite adjusting for several demographic and clinical factors, the possibility of residual confounding cannot be excluded. Finally, the observational design of this study meant that causal inferences could not be drawn.

In conclusion, poor oral health status was common among PD patients and was independently associated with a higher risk of peritonitis and death but not HD transfer and may be a proxy of poor overall personal hygiene. These associations may have important clinical implications for clinicians by using a simple oral health assessment to predict PD patients at risk of peritonitis and death and prioritizing them for full dental assessment and intervention. Further exploration of whether poor oral health is a proxy of overall personal hygiene and provides valuable guidance for prioritizing home visits and more intensive PD training is warranted.

## APPENDIX

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## DISCLOSURE

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## SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

**Figure S1.** Cumulative incidence curves for peritonitis and HD transfer.

**Table S1.** Missing values of demographics and laboratory values.

**Table S2.** Individual scores of OHIP-14 measures at the first survey.

**Table S3.** Individual scores of OHIP-14 measures in the following survey.

**Table S4.** Comparison of OHIP facets between the first and second surveys.

**Table S5.** Differences between the first and second surveys on total and individual OHIP facets ($N = 222$).

**Table S6**: PCS and MCS assessed by 12-item Short-Form (SF-12) and oral health hygiene status.

**Table S7.** Causative organisms and oral health hygiene status.

**Table S8.** Competing risk regression for key clinical outcomes according to self-reported oral health status.

**Supplementary Item S1.** Strengthening the Reporting of Observational Studies in Epidemiology
**(STROBE) Statement checklist**

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