



Oral symptoms and oral health-related quality of life in patients with chronic kidney disease from predialysis to posttransplantation

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Abstract

Objective This prospective follow-up cohort study analyzed chronic kidney disease (CKD) patients' oral symptoms, health habits, and oral health-related quality of life (OHRQoL), from predialysis to posttransplantation. A simplified questionnaire method (Oral Health Quality Score, OHQS), based on these and clinical findings, was constructed and tested for identifying patients in need for referral to a dentist.

Material and methods Fifty-three CKD patients were followed up for a mean of 10.3 years. Clinical oral, radiological, and salivary examination was performed at baseline and posttransplantation. Total Dental Index (TDI) indicating inflammation was calculated. The patients filled out a questionnaire on symptoms, oral hygiene and health care habits, smoking, alcohol use, and medication. General health-related quality of life was assessed with the 15-dimensional (15D) instrument at posttransplantation. Descriptive and analytical methods were used in statistics.

Results OHQS significantly correlated with high TDI ($p = 0.017$), number of teeth ($p = 0.031$), and unstimulated salivary flow rate ($p = 0.001$) in transplanted patients. Number of daily medications showed a negative correlation with the OHQS ($r = -0.30$; $p = 0.028$). The prevalence of oral symptoms was slightly, but not significantly, more common posttransplantation compared with predialysis stage.

Conclusion OHQS identified patients with high oral inflammatory score thus confirming our study hypothesis.

Clinical relevance Use of OHQS and measuring salivary flow indicate patients at risk for oral diseases. These markers might be easy to use chair-side also by auxiliary personnel.

Keywords Burning mouth sensation · Kidney diseases · Oral health · Organ transplants · Self-care · Xerostomia

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Introduction

Chronic kidney disease (CKD) is a worldwide public health problem. Its prevalence is over 10% in many countries, and the number of patients is rising at an alarming rate [1]. While the main risk factors for CKD are hypertension, diabetes, and obesity, periodontal disease has also been proposed as a non-traditional risk factor [2–4]. CKD or its treatment may affect salivary flow rate and cause hyposalivation and thus increase susceptibility to symptoms and discomfort such as xerostomia, dysphagia (difficulty of swallowing), dysgeusia (an alteration in taste sensation), and burning mouth sensation (BMS) [5]. Hyposalivation also predisposes patients to oral and dental problems such as caries, periodontal disease, and *Candida* infections [6].

Previous studies on the oral health of patients with CKD have shown that they indeed have a high prevalence of oral infections at the predialysis stage [7, 8]. They also are susceptible to oral diseases after transplantation due to immunosuppression. We have previously conducted a clinical study on CKD patients at the predialysis stage where we also examined, using a questionnaire, oral symptoms such as BMS, xerostomia, dysphagia, and dysgeusia, together with various background characteristics like education, working status, and the patients' perception of their own oral health [5].

Oral health can affect the patients' quality of life [9–15]. Locker and Allen [9] are the pioneers in the field of measuring perceived oral health-related quality of life (QoL). There are studies in the general population showing that patients with periodontal disease have lower levels of joy [10], greater shame when talking and showing their teeth, fear of losing them, and anger against the previous dentist who did not alert them about periodontal disease [11]. Oral health-related QoL has previously been studied and measured using the General Oral Health Assessment Index (GOHAI), the Oral Health Impact Profile (OHIP), and the oral health-related quality of life-OHRQoL-UK (W) [12–15]. However, these scorings are based on a combination of oral symptoms with general QoL scores. The general evaluation using these scorings includes psychosocial components, financial situation, and evaluation of general health with only a single question. In particular, the original version of the OHIP consists of 49 items to evaluate, making the OHIP very laborious in the clinical setting. This drawback led to the development of a simplified version, the 14-OHIP, which includes only the most significant variables from the original instrument but still mixes parameters from very different areas [16].

Health-related quality of life (HRQoL) is affected by the presence of an acute or chronic condition [17] such as CKD or organ transplantation. Of note, HRQoL is a dynamic construct that may change over time. The impact of oral health on the HRQoL in patients with a particular medical condition demands an evaluation of both these aspects separately. Thus, it is crucial to evaluate HRQoL with a generic instrument and separately evaluate the OHRQoL. Clinicians should be able to evaluate OHRQoL with a short and easily applicable questionnaire in the clinical setting. Such a questionnaire should also be easily repeatable and accurate enough to distinguish even small changes over time. Because poor oral health is known to be associated with CKD [7, 8], patients at risk for oral diseases should be easily identified already by auxiliary personnel before seeing the doctor.

Against this background, the objectives of the present study were (1) to investigate the prevalence of CKD patients' oral symptoms and health care habits comparing results from predialysis with posttransplant stage, (2) to prospectively analyze the self-reported OHRQoL in the patients, and (3) to construct and test a simplified questionnaire scoring system

based on the reported symptoms and clinical oral findings. Our hypothesis was that this instrument would easily identify patients in need for referral to a dentist.

Subjects and methods

The study is part of an ongoing longitudinal clinical prospective cohort study that focuses on comparing oral health variables from predialysis to subsequent follow-up stages. At the beginning, 144 adult CKD patients at predialysis stage in 2000–2005 (97 males, 47 females, aged 23 to 83 years) were referred from the Department of Nephrology to the Department of Oral and Maxillofacial Diseases (Helsinki University Hospital, Helsinki, Finland) for diagnosis and treatment of oral infection foci. Inclusion criterion was glomerular filtration rate (GFR) ≤ 20 mL/min/1.73 m² corresponding to midpoint of chronic kidney disease stages 4 and 5 as it is the definition for predialysis at our clinic. Exclusion criteria were based on guidelines from the Ethical Committee of the Helsinki and Uusimaa Hospital District, Helsinki, Finland and were (1) children, (2) pregnant or breast-feeding women, (3) handicapped, and (4) prisoners. All oral infection foci of the patients had been treated at the predialysis stage. The follow-up study was conducted in 2013–2015 and all the original patients were asked to participate. Out of the 144 patients, 65 patients were deceased, and the 79 survived patients were then invited to the re-examination between 2013 and 2015. Of these, 26 patients dropped out (declined participation). We thus included all the 53 end-stage CKD adult patients (estimated glomerular filtration rate < 20 mL/min/1.73 m²) who participated to the original study conducted 2000–2005 and who were followed at the Department of Nephrology. Most of these patients (51 patients) later received a kidney transplant. The mean follow-up time was 124 months. Study profile is given in Fig. 1.

Medical history was recorded from hospital files. Oral and dental examinations were performed by the same periodontist (HR) both at the predialysis and follow-up stages in a conventionally equipped dental unit at the Department of Oral and Maxillofacial Diseases in the hospital. The examination included taking a panoramic radiograph of the jaws from all patients. Focus radiographs including bitewings were taken when needed. Radiographs were analyzed by a hospital radiologist specialized in dental and oral radiology. Subsequent oral examination recorded caries lesions and periodontal and mouth mucosal findings. The results of the clinical oral examination have been published earlier [6]. The number of teeth and implants and fixed or removable prostheses and their condition were also recorded. Decayed, missing, filled teeth index (DMFT) [18, 19], Total Dental Index (TDI) [20], and periodontal inflammatory burden index (PIBI) [21] were calculated to describe oral inflammatory burden. TDI was calculated

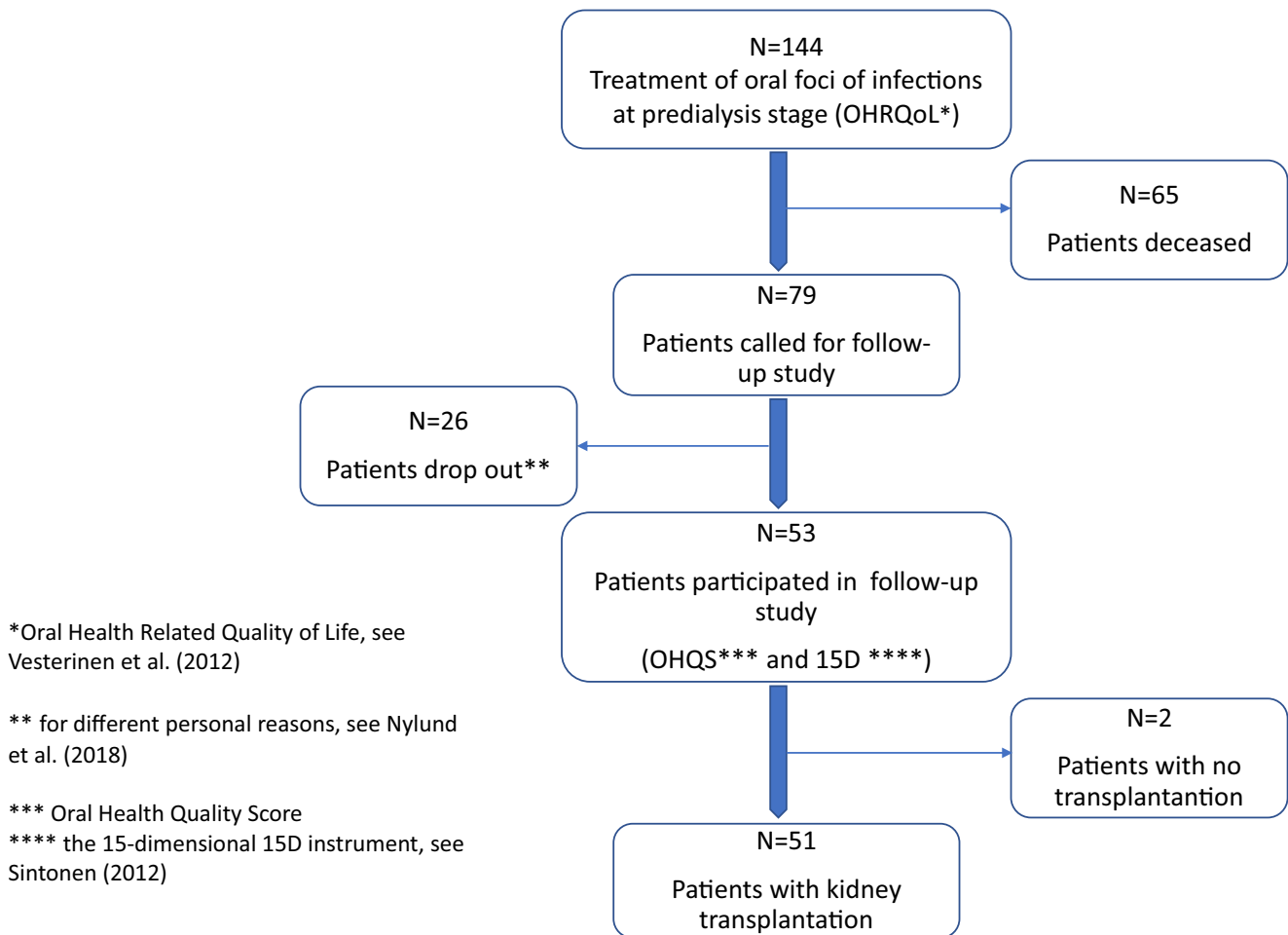


Fig. 1 Study profile of the oral health quality score

from 32 teeth. The scoring takes into account carious, periodontal, periapical, and pericoronitis lesions, and the index ranges from 0 to 10 [20]. The PIBI was calculated from 28 teeth. This index adds moderate periodontal pockets (4–5 mm) to the weighted number ($\times 2$) of deep (≥ 6 mm) periodontal pockets [21].

Unstimulated and stimulated salivary flow rates were also measured at both examinations. Saliva samples were collected for 5 min in graded test tubes to record salivary flow rates (ml/min). Patients were asked not to eat or smoke for at least 60 min before the examination. Unstimulated saliva was first collected. Paraffin wax was subsequently used to stimulate salivary flow.

The oral health quality score (OHQS) was constructed based on the oral health-related questionnaire described by Vesterinen et al. [5]. This structured form was used for recording the patients' oral symptoms, such as BMS, xerostomia, dysphagia, and dysgeusia. We also included questions regarding dental care visits and oral health risk factors, such as smoking and daily alcohol consumption. The OHQS has been updated with two questions added to the survey during follow-up (question no. 3 on tooth brushing and no. 10 on alcohol

consumption). The OHQS questionnaire in its actual version is given in Table 1. Each "b" answer gives one point. The score ranges from 0 to 10, where score 10 represents the best OHQS and 0 the worst. The OHQS results were then analyzed together with the dentist's clinical and radiographic examination records.

Furthermore, we chose the 15D for measuring general HRQoL [22]. This tool scores individuals through 15 dimensions, has been validated in a myriad of several chronic diseases to assess their impact on general health, and also tested in kidney transplant patients [23]. It is quick and easy to apply in the clinical setting, and it allows both a comparison between the impact of different diseases on general health and possible changes of it across time. For each of the 15 dimensions (moving, seeing, hearing, breathing, sleeping, eating, speech, excretion, usual activities, mental function, discomfort and symptoms, depression, distress, vitality, and sexual activity), the respondent chooses the level that best describes his or her present health status. The single-index scores (15D score), which represent the overall HRQoL, and the dimension level values, which reflect the goodness of the levels relative to no problems on the dimension and to being dead, are calculated

Table 1 Oral health quality score (OHQS)

Patient's oral care	
1. When was your last check-up with a dentist?	a. over 1 year ago b. less than a year ago
2. Do you consider your oral health important in relation to your kidney disease?	a. not very important b. very important
3. How do you brush your teeth?	a. with a fluoride-containing toothpaste b. and also using dental floss, small interdental brushes, or both
Symptoms	
4. How do you consider your oral health right now?	a. not good b. good
5. Have you experienced pain in your mouth, apart from tooth pain?	a. yes b. no
6. Do you experience dryness of your mouth?	a. yes b. no
7. Do you experience difficulties swallowing?	a. yes b. no
8. Has your ability to taste been affected lately?	a. yes b. no
Risk factors	
9. Do you smoke?	a. yes b. no
10. Do you drink alcohol every week or daily?	a. yes b. no
Total OHQS score	

Each "b" answer gives 1 point. The maximum score is 10 points

from the health state descriptive system using a set of population-based preference or utility weights. The 15D score ranges from 0 to 1, where 0 equals death and 1 reflects the best possible HRQoL. The 15D has been used both in the general population and in patients with a variety of diseases including hemodialysis and kidney transplantation [23]. In the present study, the 15D was only used for patients at the follow-up stage.

Ethical consideration

The study was approved by the ethical committee of the Helsinki and Uusimaa Hospital District (HUH) (Dnro 305/

13/03/02/2012). The study was conducted in agreement with the Declaration of Helsinki and is registered in the HUH database for clinical trials.

Statistical analyses

Descriptive statistics are presented as mean and standard deviation, unless otherwise stated. Between groups comparison for continuous variables was analyzed with T test after testing for normality with Shapiro-Wilk's test. In case of non-normal distribution of the variables, the Mann-Whitney *U* test was used. Chi-square was applied for categorical variables. We chose the median value to group the following variables: TDI (below and over 1), DMFT (below and over 23), and PIBI (below and over 1). A Pearson's product-moment correlation was used to test the correlation between OHQS and 15D. Multivariate testing with linear regression was applied to identify variables affecting oral health quality of life. A *p* value < 0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS for Windows, version 22 (IBM Corp., Armonk, N.Y., USA).

Results

Demographics

From the original study of 144 patients examined between 2000 and 2005, 79 had survived. Out of the 79 patients, 53 were willing to participate in follow-up study in 2013–2015. The remaining 26 patients declined participation, mainly because they live too far from Helsinki University Hospital and were not willing to travel. The longest follow-up time of the participants was 157 months or 13.1 years (range 20 to 157 months, median 128 months).

The median patient age was 61 years (range 31 to 86 years) at the posttransplant stage; 67% of them were men. All patients were Caucasian. The median time since transplantation was 7.1 years (range 1 to 11 years). The most common diagnoses for the etiology of the kidney disease were diabetes (21%), autosomal dominant polycystic kidney disease (28%), and IgA nephropathy (19%). The mean number of daily medications was 7.9 (SD 2.4) and 10.2 (SD 3.8) at predialysis and posttransplant stages, respectively. The immunosuppressive regimen comprised a calcineurin inhibitor plus an antimetabolite in 80% of the transplanted patients, and monotherapy with a calcineurin inhibitor in 13%. Steroids were used by only 7% of the patients. Figure 1 and Table 1.

Comparison of the oral health findings and symptoms between predialysis and posttransplantation stages

Overall clinical oral health was better at the posttransplantation stage compared with the predialysis stage. Most patients (51 of 53, 96.2%) received a kidney transplant. The mean number of teeth before the transplantation was 26.6 (± 3.7) and after the transplantation 21.7 (± 6.8). Infection was the main reason for tooth extraction. In the predialysis stage, the patients had more often calculus, deep periodontal pockets, and higher TDI and PIBI scores. The clinical oral examination results have been presented in more detail in our previous study [6]. In the posttransplant stage, the patients suffered more often from BMS (15.1% vs. 6.0%), xerostomia (41.5% vs. 38%), dysphagia (18.9% vs. 16.3%), and dysgeusia (9.4% vs. 4.0%), respectively, than in the predialysis stage. The comparison of oral symptoms and salivary flow rates in both examinations is detailed in Table 2. Unstimulated salivary flow rates correlated between predialysis and posttransplant states ($r = 0.65$, $p = 0.039$) while stimulated salivary rates did not ($r = 0.28$; $p = 0.433$).

Oral health-specific health-related quality of life

OHQS described in the methods section had been modified by adding two questions at the follow-up examination (question no. 3 on tooth brushing and no. 10 on alcohol consumption). For this reason, the maximum score with the previous OHQS survey is 8, while with the two questions added the maximum score increased to 10. Thus, for the analysis, we calculated the percentage of the maximum scores obtained at each time point. At predialysis, 71.5% of the maximum OHQS score was observed while at posttransplantation, it increased to 75.1%. This indicates a slight improvement in the oral health-related quality of life after transplantation.

We investigated, using a linear regression model, the relationship between OHQS and the following independent variables: number of periodontal pockets, TDI and PIBI scores,

Table 2 Prevalence of burning mouth sensation (BMS), xerostomia, dysphagia and dysgeusia (expressed in % of population), and salivary flow rates at predialysis and posttransplantation. Group comparison analyzed Chi square

	Predialysis	Posttransplantation	<i>p</i>
BMS	6.0	16.0	0.414
Xerostomia	38.0	40.0	0.129
Dysphagia	16.3	20.4	0.197
Dysgeusia	4.0	10.0	0.192
Salivary flow rates (ml/min)			
Unstimulated	0.41	0.32	0.328
Stimulated	1.22	0.95	0.397

salivary flow rates, and the number of teeth. At predialysis, we were unable to detect any significant correlation between these parameters and OHQS. However, after transplantation, unstimulated salivary secretion rates ($r = 0.45$; $p = 0.001$), number of teeth ($r = 0.29$; $p = 0.031$), and TDI scores ($r = -0.32$; $p = 0.017$) were significantly associated with OHQS. The number of medications used posttransplantation (mean 10 drugs each day), showed a negative correlation with the OHQS ($r = -0.30$; $p = 0.028$).

Oral health-specific and general health-related quality of life measures at posttransplantation

To study whether a lower oral health scoring was related to lower general health-related quality of life, we asked the patients to fill in the 15D questionnaire at the posttransplantation examination. The lowest 15D score was 0.56 while the highest was 1. The score was not affected by the etiology of the kidney disease. We were unable to find any clinically relevant difference in the mean 15D scores in patients with low vs. high PIBI score, periodontal pockets, or TDI scores. However, we found a modest correlation between 15D and the constructed OHQS at the posttransplant stage ($r = 0.40$; $p = 0.003$).

We also compared the results of the OHQS and 15D scores in patients with > 4 mm periodontal pockets and in patients with ≥ 6 -mm deep periodontal pockets at the posttransplant stage. We chose the median value to group the following variables: TDI (below and over 1), DMFT (below and over 23), and PIBI (below and over 1). The different areas of the OHQS (such as patient care, symptoms, and risk factors) were also compared with the unified HRQoL score obtained by the addition of the 15D and OHQS scores. Results are given in Table 3. In the multivariate analysis, we included TDI score, age at follow-up, number of medications, being diagnosed with diabetes, and 15D score. All the variables, except age, turned out to affect the oral health quality of life in a statistically significant manner (TDI score $p = 0.017$; age $p = 0.966$; number of daily medications $p = 0.028$; diabetes $p = 0.034$; and 15D score $p = 0.003$, respectively).

Discussion

In the follow-up stage, i.e., in most patients after kidney transplantation, oral health was better when compared with respective findings at predialysis, which partly confirmed our study hypothesis. This was not surprising because all oral infection foci had been treated at the predialysis stage. In predialysis stage, the patients had had more often dental calculus, periodontal deep pockets, and higher TDI scores. However, the prevalence of oral symptoms was slightly, but not significantly, higher at posttransplantation compared to what was recorded at predialysis stage.

Table 3 Comparison between clinical oral health scores with oral quality of life scores at posttransplantation phase

	PPD (4 mm) (no/yes)	PPD (6 mm) (no/yes)	DMFT (<23 vs ≥23)	PIBI (<1 vs ≥1)	Dental calculus (no/yes)	TDI (<1 vs ≥1)
<i>N</i>	28/25	50/3	24/29	28/25	12/41	16/37
15D	0.170	0.814	0.617	0.170	0.710	0.473
OHQS	<i>0.013</i>	0.427	0.862	<i>0.013</i>	0.082	<i>0.050</i>
Patients' care	<i>0.954</i>	0.089	0.162	0.954	0.357	0.171
Symptoms	<i>0.012</i>	0.758	0.220	<i>0.012</i>	0.178	0.142
Risk factors	0.659	0.871	0.273	0.659	0.579	0.649
15D + OHQS	<i>0.010</i>	0.713	0.886	<i>0.010</i>	0.131	<i>0.050</i>

PPD pocket probing depth, OHQS oral health quality score. Patient's care, symptoms, and risk factors are the areas comprising the OHQS. The grouping criteria was the median value for DMFT decayed/missing/filled teeth, PIBI periodontal inflammatory burden index, and TDI total dental index. Group comparison was analyzed with Mann-Whitney *U* test. Statistically significant *p* values are in italic

OHQS was better at the posttransplant stage compared with the predialysis stage which also confirmed our hypothesis.

The importance of dental examination in CKD patients is emphasized in our hospital due to the anticipated side effects of immunosuppression and hence potential danger for oral infection spread. This might explain the good oral health observed even several years after transplantation. After transplantation, the patients themselves more often considered their oral health as good compared with their conception at the predialysis stage, even though they more often reported symptoms like BMS, xerostomia, dysphagia, and dysgeusia.

The prevalence of oral symptoms could also be due to the lower salivary flow rates found among the posttransplant patients since dry mouth renders the patient susceptible to these nonspecific symptoms. Patients with xerostomia or hyposalivation have been reported to have reduced oral QoL compared to those without these symptoms [24]. At the posttransplant stage, the high number of daily medications may also explain these results. Namely, patients taking multiple prescribed drugs daily are known to have significantly lower stimulated and unstimulated salivary flow rates than those taking fewer drugs daily [25, 26]. After kidney transplantation, overall HRQoL has been reported to improve but not in all patients; low number of medication and employment were linked to better quality of life [23]. In previous studies of kidney transplant patients, it was concluded that age, diabetes, and comorbidities affect HRQoL [27, 28].

We used the 15D instrument for assessing HRQoL at follow-up. This assessment was not made at baseline, which is a limitation of the study. However, we did not find any clinically relevant difference in the mean 15D scores in patients with low vs. high dental index scores. This is explained by the fact that the 15D is a generic tool for measuring HRQoL and it does not focus on aspects of oral health. For this reason, we constructed the current scoring system which can be used to assess specifically oral health-related QoL. It should be emphasized, however, that oral health is an integral part of

general health and well-being. Accordingly, a comprehensive QoL assessment should always include more variables than here recorded. These variables may include biological, social, educational, and psychological markers and factors linked to clinical variables [12].

The strengths of our study were the longitudinal design and the fact that the same clinicians performed both the clinical and radiographic examinations. This ensured low inter-observer variation when analyzing changes in scores between the predialysis and posttransplant stage recordings.

The limitations of this study were the lack of a healthy, age- and sex-matched control group and the relatively small cohort size. Since this was part of the continuing investigation since of our baseline study conducted in 2000–2005, these limitations could not be avoided. Also, this can be regarded as a pilot study to test the constructed OHQS in the hospital environment.

Combining both generic and disease-specific HRQoL measures gives the clinician a global view on the well-being of the patients. Even though the OHQS was specifically constructed to identify symptoms associated with oral health in CKD patients, we recommend that it should be used in conjunction with a general QoL tool, such as the 15D. Namely, concomitant use of both general and oral health-specific QoL measurements may still better identify patients who are at greater risk for dental and oral health problems. In a busy clinical environment, however, the simplified assessment using OHQS alone may be sufficient and might even be delegated to the auxiliary.

Conclusion

Kidney transplant patients considered their oral health improved compared to the predialysis stage. Nevertheless, symptoms like BMS, xerostomia, dysphagia, and dysgeusia were common after transplantation. In particular, xerostomia is the

symptom that most significantly affects the patients' QoL. OHQS here presented is a new tool targeted to CKD patients. However, it may also be suitable for identifying dental treatment needs of any patient group.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants in the study.

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