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Phenotypes of patients with extensive tooth wear—A novel approach using cluster analysis

Wedad Hammoudi[a,b,*], Mats Trulsson[b,c], Jan-Ivan Smedberg[a,b], Peter Svensson[b,c,d]

[a] Dept. of Prosthetic Dentistry, Folktandvården Eastmaninstitutet, Stockholm, Sweden
[b] Dept. of Dental Medicine, Karolinska Institutet, Stockholm, Sweden
[c] Scandinavian Centre for Orofacial Neuroscience (SCON), Denmark
[d] Section of Orofacial Pain and Jaw Function, Department of Dentistry and Oral Health, Aarhus University, Aarhus, Denmark

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ABSTRACT

Objectives: Explore a new approach to identify phenotypes of tooth wear (TW) patients using an unsupervised cluster analysis model, based on demographic, self-report, clinical, salivary and electromyographic (EMG) findings.

Methods: Data was collected for 34 variables from 125 patients, aged 17–65 years, with a TW index > grade 2. Demographic information and presumed risk factors for chemical and mechanical TW were collected. A 14-item stress scale was completed and salivary flow rates, pH and buffer capacity were measured. Sleep bruxism was assessed with a portable single channel EMG device.

Results: The final cluster model comprised 16 variables and 103 patients and indicated two groups of TW patients; 61 participants in cluster A and 42 in cluster B. Cluster assignment was determined by several presumed mechanical risk factors and diseases affecting saliva. Cluster B had the highest percentage of sleep bruxism self-reports (A 1.6%, B 92.9%, $p \leq 0.001$), awake bruxism self-reports (A 45.9%, B 85.7%, $p \leq 0.001$), heavy sport exercises (A 1.6%, B 21.4%, $p = 0.001$); and highest percentage of diseases affecting saliva (A 13.1%, B 47.6%, $p \leq 0.001$). A notable finding was the lack of significant differences between clusters in many other presumed risk factors for mechanical and chemical TW.

Conclusion: TW patients can be clustered in at least two groups with different phenotypic characteristics but also with a large degree of overlap. Based on this type of algorithm, tools for clinical application may be developed and underpin TW classification and treatment planning in the future.

1. Introduction

Tooth wear (TW) has become more prevalent and severe in industrialised nations due to changes in lifestyle and nutritional habits, plus an aging population that retains more of its teeth for longer [1–3]. Several attempts to describe and classify the various types of TW have been presented in the past. The most commonly used classification is the one produced by Pindborg who proposed that attrition, erosion and abrasion are three etiological classifications that describe TW [4]. Clinically, the delineation of each etiology is frequently clouded because they often do not occur independently and may also occur concomitantly with other processes [5]. Prevalence studies on the different etiologies are few and difficult to compare due to different sampled populations and different indices that represent the actual degree of tooth loss and not the specific action or background of TW.

Extensive TW can result from a mechanical cause, a chemical cause, or a combination of both. Among the various background factors which have been suggested to associate with TW processes include functional activity (i.e. chewing), parafunctional activities (e.g. bruxism, nail biting), acidic diet, diseases and conditions that involve intrinsic acids (e.g. gastric reflux, eating disorders), acidic medicines, different aspects of a modern lifestyle, occupational environment, stress and salivary factors [6,7]. Many questions remain unanswered about the etiology of TW; the cause-effect relationship and the importance of each risk factor in relation to one another [8]. Nevertheless, there is growing evidence that erosion is the major cause of TW and the term “erosive tooth wear” is commonly used in contemporary European literature [9]. Overlooking possible risk factors for TW or failing to notice a treatable cause may hamper or delay treatment decisions of patients with worn dentition. The literature is awash with proposals and guidelines for classifications and systematic approaches to diagnose or manage TW. Yet, most of these studies summarise only existing knowledge of TW or do

* Corresponding author at: Folktandvården Eastmaninstitutet, Dept. of Prosthetic Dentistry, Box 6031, S-102 31 Stockholm, Sweden.
E-mail addresses: wedad.hammoudi@sll.se, wedad.hammoudi@ki.se (W. Hammoudi).

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not examine the diagnostic accuracy and feasibility of their own guidelines [10–12].

For decades, researchers in various medical fields have explored numerous methods to analyse data, such as to assemble objects based on their characteristics [13–15]. One of these methods is cluster analysis, a classification technique to form homogeneous groups within complex datasets depending on the similarity of the objects for a set of specified characteristics [16]. This enables the profiles of these groups to be studied, to establish tools for clinical use and form bases for disease classification and treatment modalities. However, this technique cannot differentiate relevant from irrelevant variables and only produces the most consistent, yet distinct, groups of objects across all the selected variables. For this reason, variables included in the analysis should be selected with regard to previous research in a specific field. There are many methods for cluster analysis and choosing the proper method depends on several factors such as data size and variable type (categorical or continuous) [17,18].

We hypothesised that there are different phenotypes among TW patients, and that these may be distinguished based on comprehensive datasets including self-reports, clinical findings, electromyographic (EMG) data and salivary characteristics. This study sought to identify phenotypes of TW patients with an unsupervised clustering model, based on demographic and self-report information, clinical findings, salivary and EMG measurements.

2. Materials and methods

2.1. Study population

From a consecutive series of patients referred to the Department of Prosthetic Dentistry at Folktandvården, St Erik's Hospital and Eastmaninstitutet, Stockholm, Sweden, 5000 referrals with different prosthodontic problems were screened between 2012–2017. Of these, 343 patients with TW aged 17–65 years old were initially selected for tentative inclusion by one investigator (WH) and were asked to participate in the study. A total of 44 refused to participate and 11 did not respond, despite 2 reminders. Thus, 288 patients agreed to participate. On further assessment, 125 patients fulfilled the inclusion criteria and were included in the study. No intention was made to create equal-sized groups according to age, gender, social or other categories. Criteria for inclusion were at least 10 teeth in the upper and lower arches, periodontal pocket depth ≤ 4 mm without bleeding on probing and at least TW $>$ grade 2 for any tooth surface on at least four teeth in the same arch, according to Smith and Knight's tooth wear index (TWI) [19]. In order to ensure that all participants fulfilled the inclusion criteria concerning the degree of TW, primary assessment was visually done first by one examiner (WH) while patients were sitting in a dental chair. Further, prior to the final inclusion, TW assessment was performed by two experienced examiners (WH and JI-S) who together went through standardized intraoral photos and study models for all participants. Patients with fixed and removable partial dentures; mineralisation disorders; gross malocclusion (severe Angel's Class II or III); pain on palpation of the temporomandibular joint; facial and widespread pain; pacemaker, and neurologic, psychiatric, or sleep disorders, were excluded from the study. Approval from the Regional Ethical Review Board, Stockholm, Sweden was obtained prior to study start (No 2012/263-31/2), and informed consent was signed by each participant.

2.2. Methods

At enrollment, participants in this study completed a similar comprehensive battery of questionnaires, clinical assessments and measurements as mentioned below.

2.2.1. Demographic characteristics

Demographic data on age, gender, height, weight, snuff use and medical history were collected at intake. Patient height and weight were used to calculate BMI values.

2.2.2. Self-report information

Possible background impact on TW was collected using two standardised forms and personal interviews. The first form included questions on possible risk factors for chemical and mechanical TW, while the second form included questions about mouth dryness and conditions and medications affecting saliva. Those questions were derived from literature review and clinical experience [6,7,20,21]. The same interviewer (WH) went through the questions using the two forms. Since there are multiple risk factors for TW, sets of individual risk factors were presumed that, in combination, represent sufficient component causes [22]. For this reason, the findings from the two forms and interviews were transcribed, by the same interviewer, to a standard form with three sections: Section A) presumed risk factors for chemical TW, Section B) presumed risk factors for mechanical TW, and Section C) presumed factors affecting saliva (Table 1). Diseases and conditions collected from study participants and presented in Table 1 were already diagnosed by their physicians. Subjects who indicated previous or ongoing history of eating/drinking the following products for ≥ 4 times/week considered as consumers of acidic diet: carbonated soft drinks (regular or diet), sport drinks or energy drinks, citreous fruit slices and fruit juices. Participants indicated previous or ongoing history of drinking alcohol for ≥ 4 times/week considered as frequent alcohol drinkers.

All participants completed the 14-item Perceived Stress Scale (PSS), used to evaluate whether appraised stress is a possible risk factor for extensive TW [23]. This 14-item questionnaire examines stressful feelings and thoughts experienced by a respondent during the past month. PSS-score was obtained for each patient by reversing the scores on the seven positively-stated items (i.e., 0 = 4, 1 = 3, 2 = 2, 3 = 1, and 4 = 0) and then summing across all 14 items. The positively-stated items were 4, 5, 6, 7, 9, 10 and 13.

2.2.3. Clinical findings

Clinical examination was performed by one of the authors (WH) to register number of teeth and the presence of torus mandibularis. Standardized intraoral photos were taken and used by one experienced examiner (WH) to grade TW, according to Smith and Knight's TWI [19]. This five-level ordinal index codes TW without regard to etiology on 5 surfaces (buccal, lingual, occlusal, incisal, cervical), where zero = no wear, and four = at or near pulpal exposure. According to Smith and Knight, the index can be recorded either clinically or from photographs. Extensive TW levels in this study were $>$ grade 2. Teeth with $>$ grade 2 TW on any scorable surface were registered and given only one score regardless of the number of worn surfaces. Missing, heavily restored and fractured teeth were also recorded and deemed unscorable due to lack of knowledge as to whether wear or caries would have been the primary cause of the TW. Later, photographs of 36 randomly selected patients were used to control intra-observer reproducibility for the examiner who graded TW in this study.

2.2.4. Determining salivary flow rates, pH, and buffering capacity

Unstimulated saliva was collected for 15 min and paraffin-stimulated saliva for 5 min. pH and buffering capacity were measured using commercially available colorimetric test kits (Saliva-Check BUFFER, GC, USA). All samples were collected between 8 AM and 12 AM and patients were requested to refrain from drinking, eating, tooth brushing and tobacco use for at least 1 h before saliva collection. Guidelines at the Department of Dental Medicine at Karolinska Institutet and manufacturer's instructions were followed.

2.2.5. EMG measurement

A portable single-channel EMG device (GrindCare Measure3, Medotech A/S, Herlev, Denmark) was used to assess sleep bruxism

Table 1
Collected presumed risk factors for chemical and mechanical tooth wear and presumed factors affecting saliva in 125 individuals.

Section		n (%)
A	**Presumed risk factors for chemical TW**	
	History of gastric reflux and conditions involving intrinsic acids	29 (23.2)
	Previous conditions of dietary alterations (Bulimia nervosa and anorexia nervosa, weight loss and gain)	10 (8.0)
	Acidic diet	82 (65.6)
	Frequent alcohol intake	17 (13.6)
	Wine testers/club- and restaurant workers	5 (4.0)
	Acidic medication	23 (18.4)
B	**Presumed risk factors for mechanical TW**	
	Self-report of sleep bruxism	51 (40.8)
	Self-report of awake bruxism	74 (59.2)
	Nail biting, lip or cheek biting, pencil biting, etc.	9 (7.2)
	Working in a dusty environment	21 (16.8)
	Heavy labour (Builders, carpenters, truck drivers, etc.)	22 (17.6)
	Heavy sport exercisers (body builders)	11 (8.8)
	Snuff	33 (26.4)
C	**Presumed factors affecting saliva**	
	Diseases like asthma, depression, diabetes mellitus, hypertension	34 (27.2)
	Drugs affecting salivary protection	16 (12.8)
	Sports enthusiast (> 3 times/week)	51 (40.8)

Values represent number (%) of individuals.

[21,24]. The device recorded EMG activity of the anterior temporalis muscle (unilaterally). Participants were instructed and carefully taught to use the device for at least 7 days in their own home during sleep. A minimum of 4 nights' error-free recordings were required for each participant. The following parameters were collected from the EMG device: number of nights, total number of EMG grinds, number of EMG grinds/h, intensity, total number of EMG bursts, number of EMG bursts/h, average EMG burst duration, total number of EMG episodes and number of EMG episodes/h.

2.2.6. Clustering and statistical analysis

To ensure that the collected variables were independent from each other, Pearson's correlation, Spearman's correlation, cross tabulation and *T*-tests, where appropriate, were used to study the degree of relationship between the pairs of variables. Outliers were detected by visual inspection and calculation of descriptive statistics. No outliers were detected. For the clustering procedure, two-step cluster analysis was considered to be a suitable clustering algorithm for the present study [25,26]. This was attributed to the large number of variables that were a mixture of categorical and numerical variables. In the first step of the two-step cluster analysis, pre-clusters (based on non- hierarchical clustering) were formed from the participants to reduce the size of the matrix that contained distances between pairs of cases. The pre-clusters were used as cases in the second step (based on hierarchical clustering), where new clusters were formed and switching of cluster membership was allowed. Variable selection for cluster analysis was considered to be a novel aspect. Attempting to use all the available variables to identify clusters might decrease the quality of the resulting clusters, for instance the irrelevant variables would add "noise" to the clusters [27]. Our strategy for variable selection was based on several factors; variables most strongly associated with the outcome of interest according to previous knowledge, identification of the most relevant numerical variables using binary logistic regression, and exclusion of some variables with low frequencies and variables that impaired the quality of the cluster model. Some variables were aggregated by combining two self-reported symptoms for SB (self-report of grinding or clenching

Table 2
. Comparison between clusters.

	Cluster A (n = 61)	Cluster B (n = 42)	*P*
Self-report of sleep bruxism	1(1.6%)	39 (92.9%)	≤0.001*
Self-report of awake bruxism	28 (45.9%)	36 (85.7%)	≤0.001*
Diseases affecting saliva (Asthma, diabetes, hypertension, diabetes mellitus)	8 (13.1%)	20 (47.6%)	≤0.001*
Heavy sport exercisers (body builders)	1 (1.6%)	9 (21.4%)	0.001*
Heavy labour (builders, carpenters, truck drivers, etc.)	6 (9.8%)	13(31%)	0.007
Salivary buffering capacity	10.6 ± 1.7	11.4 ± 1.0	0.006
Working in a dusty environment	6 (9.8%)	12 (28.6%)	0.014
Age	41.1 ± 10.16	46.0 ± 9.7	0.015
Sport Enthusiast	17 (27.9%)	21 (50%)	0.022
Torus mandibularis	45 (73.8%)	22 (52.4%)	0.025
Median number of episodes per hour	4.1 ± 2.5	4.6 ± 2.3	0.332
Acidic diet	43 (70.5%)	27 (64.3%)	0.507
Non-stimulated saliva	0.3 ± 0.2	0.3 ± 0.2	0.532
PSS-14 score	21.3 ± 8.3	22.0 ± 6.9	0.679
Median number of grinds per hour	14.1 ± 19.7	13.1 ± 12.6	0.739
History of gastric reflux and conditions involving intrinsic acids	15 (24.6%)	10 (23.8%)	0.928

n = number of participants.
Values represent number (%) of participants or mean ± standard deviation.
* Significant difference after Bonferroni correction with adjusted significance level of $P < 0.003$.

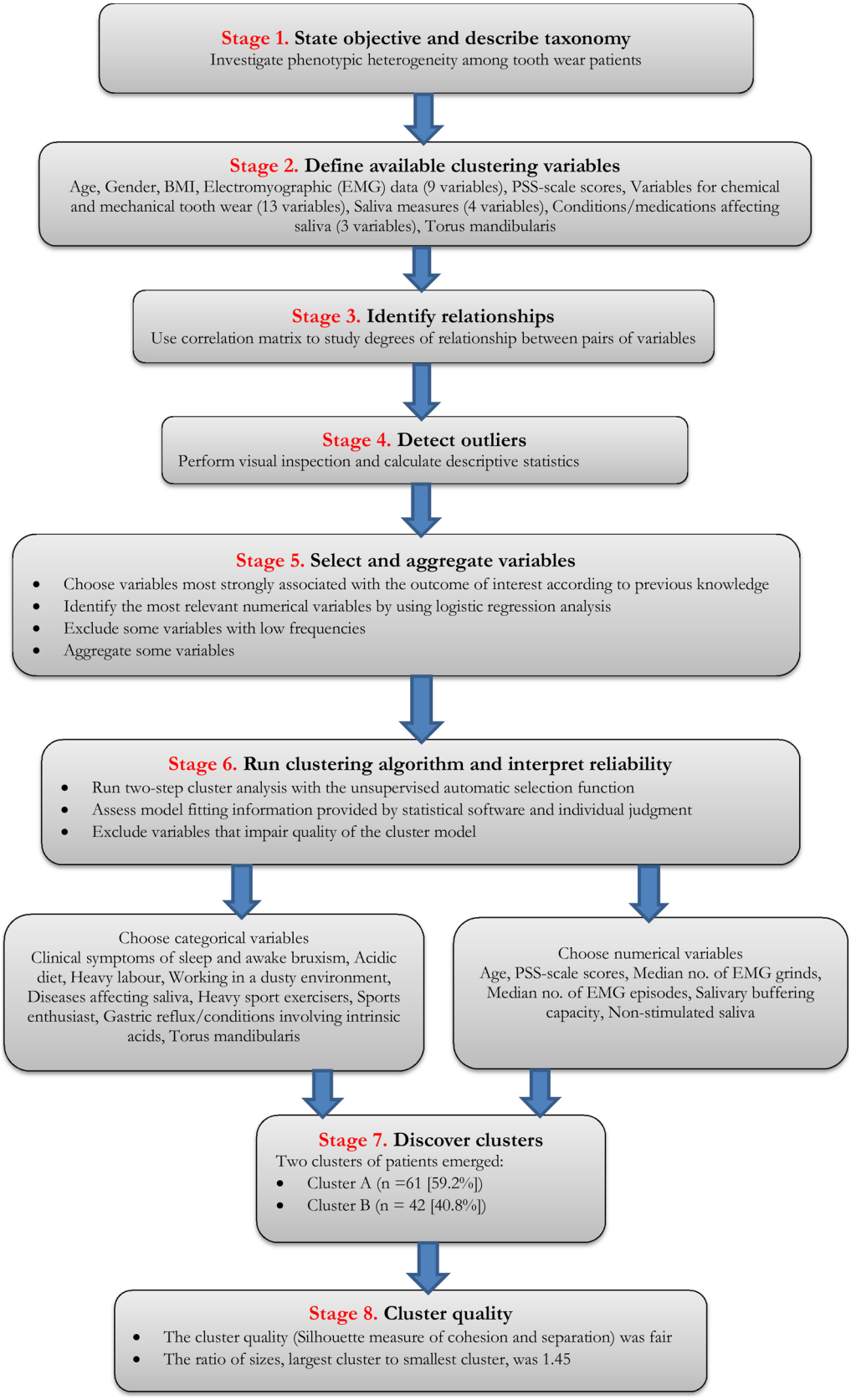

Fig. 1. The clustering procedure.

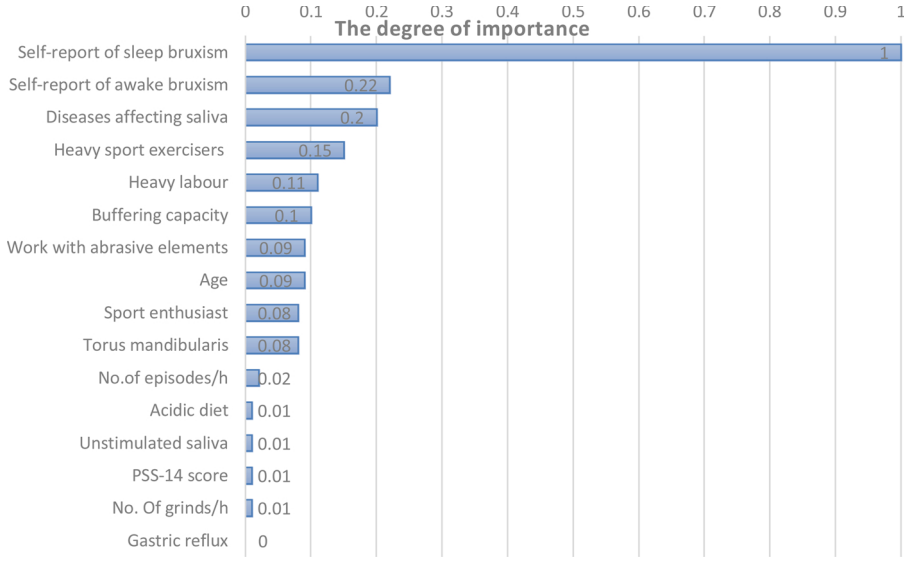

Fig. 2. Degree of predictor importance as revealed by SPSS.

during sleep, report by bed partner of tooth grinding or clenching habits during sleep) into one variable. The same was done with two self-reported symptoms for awake bruxism (self-report of tooth grinding during wakefulness, self-report of tooth clenching during wakefulness). Numerical variables were standardised. The Log-Likelihood function was used to derive distance between two clusters. Bayesian information criterion (BIC) was used to find the best cluster solution [28]. To determine the appropriate number of clusters, an unsupervised automatic selection function was used. Reliability of generated clusters was assessed using model fitting information from the statistical software and individual judgment. The final cluster model consisted of 16 different variables (Table 2).

Overall comparisons between clusters were performed using Chi-Square test and Fisher's exact test for categorical variables and T-test for continuous variables. Significance level was set at $P < 0.05$. As multiple pairwise tests were used on a single set of data, the Bonferroni correction was performed to reduce the chances of obtaining false-positive results (type I error) [29]. This correction gave an adjusted significance level of $P < 0.003$. Cohen's kappa was used to measure intra-examiner reliability for TW grading for the examiner who re-graded TW in 36 randomly selected patients. IBM SPSS version 21 was used.

3. Results

3.1. Study population

A total of 125 consecutively referred patients (29 females, 96 males) with a mean (SD) age of 43.1 years (10.2) participated in this study. For the whole group, the mean (SD) number of teeth present was 27.1 (1.3) and the mean (SD) number of teeth with TW > grade 2 was 15.9 (6.0). The number (%) of individuals with different presumed chemical or mechanical risk factors and factors affecting saliva are shown in Table 1. Participants could have one or more of the listed risk factors. Intra-examiner reproducibility for the examiner who re-graded TW in 36 randomly selected patients was very good ($K = 0.8–1.0$/tooth).

3.2. Construction and quality of clusters

Unsupervised two-step clustering was applied to 125 individuals and the entire clustering procedure and variables selection is illustrated in Fig. 1. Variable selection and cluster discovery resulted in exclusion of 22 participants from the final cluster model due to incomplete data concerning PSS-scale, salivary and/or EMG measurements. The final cluster model consisted of 103 individuals (men = 80 [77.7%], women = 23 [22.3%]) and 16 variables. The analysis revealed two groups of patients; cluster A (n = 61 [59.2%], men = 47 [77.0%], women = 14 [23.0%]) and cluster B (n = 42 [40.8%], men = 33 [78.6%], women = 9 [21.4%]). The Silhouette measure of cohesion and separation was = 0.2, which indicates a fair cluster quality. The ratio of sizes, largest cluster to smallest cluster, was 1.45. Overall, the cluster analysis resulted in two relatively well-separated groups of clinical interest.

3.3. Characteristics of the clusters

Comparison between the two clusters is shown in Table 2 and the degree of predictor importance in the clustering procedure is shown in Fig. 2. The most important predictor that ruled the clustering process was the self-report symptom of sleep bruxism, and the least important predictor was history of gastric reflux and conditions involving intrinsic acids. Interpretation of the results after Bonferroni correction with the adjusted significance level of $P < 0.003$ showed significant difference between the clusters for 4 variables. The smaller cluster, cluster B, had the highest percentage of mechanical risk factors, self-reports of sleep bruxism ($P \leq 0.001$), self-reports of awake bruxism ($P \leq 0.001$) and heavy sport exercises ($P = 0.001$). Cluster B also had the highest percentage of diseases affecting saliva ($P \leq 0.001$). No statistical significant difference could be found between the two clusters concerning the remaining 12 variables. It was clear that a high percentage of individuals in both clusters had both a frequently acidic diet and a high percentage of torus mandibularis.

4. Discussion

4.1. Important variables for TW

In the current prospective study, TW patients were clustered based on demographic and self-report information, clinical findings, salivary and EMG data, to investigate possible variations in TW phenotypes. Two clusters of patients were identified; cluster A (the largest cluster) and cluster B (the smallest cluster). Cluster B was characterised by high prevalence and percentage of factors related to a mechanical background (sleep and awake bruxism, heavy sport exercise) and diseases affecting saliva (Table 2).

Current literature emphasises the multifactorial etiology of TW, and that dietary habits and saliva are now important factors, while bruxism

and other factors are less important [24,30]. Such presumption may lead to different preventive and restorative treatment flows of patients with worn dentition. A high percentage of individuals in both clusters frequently consumed an acidic diet. However, the present analysis showed that the presumed mechanical risk factors could be important for classification and identification of at least two phenotypes of TW patients since individuals reporting bruxism and those practicing heavy sports are clustered together and define a distinct group. Cluster B had the highest percentage of diseases affecting saliva (Table 2). Yet, the present analysis showed no difference between the two clusters regarding salivary flow rates, pH and buffering capacity. Results from the present study and conflicting results from previous studies indicate that salivary parameters such as flow rate, pH and buffer capacity could be difficult predictors for dental wear [31]. Searching for biological markers in salivary proteins and dental acquired pellicle may be needed, since these have been reported as important factors in other studies [32,33].

The study sample was collected from a consecutive series of patients referred to the Department of Prosthetic Dentistry, and most participants were men. This was partially attributed to the exclusion of women with ongoing neurologic and psychiatric disorders (e.g. anorexia, bulimia, depression and widespread pain). Yet, other studies show that men, because of a more acidic diet and higher forces exerted by masticatory muscles, have more extensive TW than women [34–36]. This is supported by Donachie and Walls, who examined 586 participants and found that mean wear scores were greater in men than in women [37].

It has been suggested that clinical assessment together with study models and clinical photos can provide an appropriate baseline reference point for the assessment of the severity of TW [24]. A combination of visual clinical examination under good lighting, standardized clinical photos and study casts were used under recruitment. This was to ensure that all participants had at least TW > grade 2 for any tooth surface on at least four teeth in the same arch, according to Smith and Knight's TWI. As the level for extensive TW in this study were > grade 2, teeth with > grade 2 TW on any scorable surface were registered and given only one score regardless of the number of worn surfaces. Scoring of those extensive lesions was performed by using the standardized intraoral photos as the lesions were considered large enough to be detected in clinical photos by an experienced examiner and as a simplified variant for TWI was used. Results of intra-examiner reproducibility for the examiner who re-graded TW was very good (K = 0.8–1.0/tooth). Recent European consensus statement on management guidelines of TW suggested the use of only two terms; severe TW which is represented by dentin exposure and significant loss (≥1/3) of the clinical crown, and pathological TW where TW is considered atypical for the age of the patient, causing pain or discomfort, functional problems, or deterioration of esthetic appearance [38].

The most important predictor that ruled the clustering process was the self-report symptom of sleep bruxism (Fig. 2). Accurate diagnosis of sleep bruxism and its severity is still difficult in a dental setting. Although several diagnostic techniques are available, they each have advantages and limitations [39]. In this current study, in addition to self-reports, a portable home ambulatory EMG device was used to assess sleep bruxism, with a minimum of 4 nights' error-free recordings required for each participant [21]. Comparison between this type of device and the gold standard method, Polysomnographic recording (PSG), to validate sleep bruxism activity, demonstrated acceptable correlation [40]. No difference in EMG activity was found between individuals in the two clusters, in line with a recent study that compared individuals with and without an attrition type of TW using the same device [24]. This might be because EMG and PSG simply give a random indication of a disorder that may fluctuate over time, and that self-reported bruxism may reflect a problem in the past rather than the present [41]. Previous studies question the relationship between the degree of bruxism, muscle activity and the severity of TW, and so it is not recommended to use TW as a direct indication of active sleep bruxism [42,43].

Table 3
Examples of cluster models gained by using unsupervised modelling.

Cluster model	No. of variables	No. of emerged clusters	Cluster quality*
1	13	3	0.2
2	12	2	0.2
3	11	3	0.2
4	10	5	0.3
5	10	5	0.2
6	9	5	0.3
7	8	2	0.3
8	7	3	0.3
9	6	2	0.3
10	4	7	0.7
11	3	7	1
12	2	4	1

No. = number.
* Silhouette measure of cohesion and separation.

Although increased sleep bruxism as a direct outcome of diurnal stress could not be proven, most studies propose an association between stress and sleep bruxism [44,45]. One suggested explanation is that sleep bruxism is a side-effect of micro-arousals arising from increased transitions between deep sleep and lighter sleep, since emotional stress disturbs the quality of sleep [46]. The international 14-item stress scale was used in the current study and no significant difference could be detected between participants fitted into the two clusters. The numerous methods used in previous studies for the assessment of sleep bruxism differ widely in their validity, which makes it difficult to compare different studies and draw conclusions from the current results.

Participants in both clusters had a high prevalence and percentage of torus mandibularis (Table 2). Since occlusal overload was suggested to be involved in the pathogenesis of mandibular torus, it was proposed that the association between signs and symptoms of bruxism and tori could help in recognising patients susceptible to bruxism [47]. However, this study found no sufficient evidence to support the hypothesis that bruxism identified by self-report is associated with torus mandibularis. On the other hand, based on available evidence and results from this study it seems that torus mandibularis might be associated with extensive TW [48].

4.2. Methodological issues

The modelling procedure used in this study, two-step cluster analysis, is an exploratory tool designed to reveal natural groupings (or clusters) within a dataset that would otherwise not be apparent. The main goal was to partition a set of TW individuals into two or more groups based on the similarity for a set of easily measured clinical variables. Its advantage is that a clustering procedure requires only one pass of data, and clusters can form rapidly on the bases of mixed categorical and continuous data. Clustering methods provide the opportunity to study the degree of homogeneity or heterogeneity within the same cohort and does not demand a control group, e.g. unsupervised spectral clustering methods have been used by some authors to investigate phenotypic heterogeneity amongst periodontitis patients [17]. One difficulty with this analysis is, however, that it is not reproducible. Excluding the least important predictor from one model will not guarantee a better cluster quality or the same sequence of predictors in the next generated model. Adding or excluding variables will change the heterogeneity and homogeneity of the cohort and individuals gain new chances to group in an already existing cluster or build a new cluster (Table 3). Thus our strategy for variable selection in this study was considered to be efficient and beneficial.

Selection of appropriate variables for clustering is, indeed, of utmost significance. It is recommended to choose variables that can be

expected to differ across the clusters and can provide a clear cut differentiation as well as make it possible to offer a description of the characteristics of the members of the cluster. By running different cluster models, using the unsupervised modelling, and monitoring the outcomes we could identify that the categorical mechanical variables and diseases affecting saliva were the variables that could provide a differentiation between the study members. Further, it was attempted to include both chemical and mechanical background factors [6,7] in the final cluster model in order to be able to describe the final cluster members and to avoid misapplication or abuse of this technique.

Unfortunately, there is no standard objective procedure for the selection of the number of variables and it still falls to the researcher to decide as to the number of clusters to accept as the final solution [16]. The present attempts to reduce the number of clusters did not improve the quality of the produced cluster models considerably and/or complicated the clinical interpretability (Table 3). In some occasions, the procedure selected a large number of clusters that were even more than the selected variables (Table 3, cluster model $10-12$). Large number of clusters might give better results because the cases are more similar in a cluster, however the explored cluster solutions might not be interpretable even though they have a good cluster quality.

Two-step clustering offers an overall goodness-of-fit measure called silhouette measure of cohesion and separation. The measure is based on the average distance between the objects and may vary between -1 and $+1$. A silhouette measure of < 0.20 indicates a poor solution quality, a measure between 0.2 and 0.50 a fair solution, and values of > 0.50 indicate a good solution. However, one should not solely rely on the silhouette measure, but each solution should be evaluated on practical grounds as well as solution's interpretability [16].The quality of the final cluster model was fair. It is clear that individuals in the present cohort share many characteristics and that their TW lesions had multiple backgrounds. Further, simply because no statistical significant difference was detected for 12 variables in the head-to-head comparisons between clusters, it does not mean that those 12 variables are clinically insignificant predictors for TW. Rather, the degree of separation between the 2 clusters was not large enough to reach a statistically significant difference. Although it's known that the processes of chemical and mechanical TW clinically do not occur independently, the present study indicated some differences and two clusters of patients could be identified. Further studies will be needed to examine for e.g. differences in the clinical presentation of TW lesions in these proposed clusters which will support the clinical value of a differentiation of patients into at least two clusters.

A few more methodological limitations need to be addressed in the present study. Firstly, we tried to involve many variables in our cluster analysis. This enabled us to study the profile of these patients from different aspects, which gives an advantage when studying a multifactorial process like TW. However, including many variables may well decrease the importance of certain variables in clustering 125 patients. These limitations may be reduced with a larger study population and fewer variables. Fewer variables or more patients increase the chances of larger numbers of clusters with high internal homogeneity and, probably, increase the quality of the cluster model. On the other hand, there is no general accepted rule of thumb regarding minimum sample size and the rule that Forman (1984) recommends with a minimum sample size of 2^M, where M equals the number of clustering variables, can only provide rough guidance [49]. Increasing the sample size or decreasing the number of variables does not always guarantee an improvement in quality or clinical interpretability of the final cluster solution. As mentioned before, our attempts to reduce the number of variables did not improve the quality of the produced cluster models considerably and/or complicated the clinical interpretability (Table 3). Additionally, the achieved sample size in the current study is the total number of patients satisfying the inclusion criteria during approximately 53 months. Data collection demanded time and availability of several facilities, e.g. a dental office to perform the interviews, questionnaires, dental status, photographs and study models, a number of EMG devices and equipment for saliva tests. Nevertheless, many variables were included in the statistical analysis and the results showed two clusters of TW patients with different clinical profiles. As the achieved sample size could guarantee interpretable segments, it was considered to be large enough for this study. The Bonferroni correction was used to adjust the significance level in order to avoid exaggeration of the present results. Secondly, many of the categorical variables were based on patient self-report information. Data generated from these variables consisted of two alternatives. Though it was sought to balance the number of included continuous and categorical variables, the categorical variables were dominant in the emerged cluster model. Transforming questionnaires into scales that generate scores resembling results from psychological inventories, will form clusters based on continuous data instead of categorical data [50]. Such scales and speculations should be validated in future studies on TW patients.

4.3. Future perspectives on TW research

The current study is considered to be the first reported use of data mining and modelling to discover patterns in complex datasets to classify TW patients. The method could represent a new tool to identify phenotypic heterogeneity among TW patients. Data simplification and reduction can also be achieved by this method by using a large data set and instead of analysing all observations as unique, they can be viewed as a member of a cluster and profiled by its characteristics [16]. Although this study has produced two different clusters with logic profiles that have clinical implications, other types of results might be gained when examining other cohorts of TW patients depending on similarity of responses to collected variables. Additional research is needed to investigate whether these profiles can be replicated in other cohorts of TW patients. Further, developing interventions specific to the profiles, as well as testing them in randomised controlled trials, will give a greater clinical advantage to the current clustering outcome.

Factors like atypical occlusal loads in relation to varying intensity, modality and timing of masticatory muscle activities; eccentric occlusal overloads in terms of direction relative to tooth physiological axes; reduced occlusal tactile sensitivity and facial biotype are factors worth investigating in future studies since they have been mentioned in other references as presumed etiological factors for TW [6,51].

5. Conclusion

Based on demographic and self-report information, clinical findings, salivary and EMG measurements, TW patients can be clustered in at least two groups with different phenotypic characteristics. The two groups partially overlapped but also differed mainly in the prevalence and percentage of presumed mechanical background factors (sleep and awake bruxism, heavy sport exercise) and diseases affecting saliva. A new classification system and individualised treatment modalities may be initiated for TW patients based on these algorithms. However, further research is needed to investigate whether these profiles can be replicated in other TW patient cohorts. The hypothesis that there are different phenotypes among TW patients that can be distinguished based on comprehensive datasets including self-reports, clinical findings, EMG data and salivary characteristics was supported.

Conflict of interests

None.

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References

[1] A. Van't Spijker, J.M. Rodriguez, C.M. Kreulen, E.M. Bronkhorst, D.W. Bartlett, N.H. Creugers, Prevalence of tooth wear in adults, Int. J. Prosthodont. 22 (1) (2009) 35–42.

[2] T. Jaeggi, A. Lussi, Prevalence, incidence and distribution of erosion, Monogr. Oral Sci. 25 (2014) 55–73.

[3] D.W. Bartlett, A. Lussi, N.X. West, P. Bouchard, M. Sanz, D. Bourgeois, Prevalence of tooth wear on buccal and lingual surfaces and possible risk factors in young European adults, J. Dent. 41 (11) (2013) 1007–1013.

[4] J. Pindborg, Pathology of the Dental Hard Tissues, Munksgaard, 1970 Copenhagen.

[5] L.A. Litonjua, S. Andreana, P.J. Bush, R.E. Cohen, Tooth wear: attrition, erosion, and abrasion, Quintessence Int. 34 (6) (2003) 435–446.

[6] D.A. Paesani, M. Andersen, Bruxism: Theory and Practice, Quintessence Publishing, London, 2010.

[7] F. Khan, W.G. Young, Toothwear: The ABC of the Worn Dentition, Wiley-Blackwell, Chichester, West Sussex, UK, 2011.

[8] A. Johansson, A.K. Johansson, R. Omar, G.E. Carlsson, Rehabilitation of the worn dentition, J. Oral Rehabil. 35 (7) (2008) 548–566.

[9] T.S. Carvalho, P. Colon, C. Ganss, M.C. Huysmans, A. Lussi, N. Schlueter, G. Schmalz, P.R. Shellis, A. Bjorg Tveit, A. Wiegand, Consensus report of the European federation of conservative dentistry: erosive tooth wear diagnosis and management, Swiss Dent. J. 126 (4) (2016) 342–346.

[10] W.P. Holbrook, I.B. Arnadottir, E.J. Kay, Prevention. Part 3: prevention of tooth wear, Br. Dent. J. 195 (2) (2003) 75–81.

[11] R.G. Verrett, Analyzing the etiology of an extremely worn dentition, J. Prosthodont. 10 (4) (2001) 224–233.

[12] P. Wetselaar, F. Lobbezoo, The tooth wear evaluation system: a modular clinical guideline for the diagnosis and management planning of worn dentitions, J. Oral Rehabil. 43 (1) (2016) 69–80.

[13] T. Ahmad, M.J. Pencina, P.J. Schulte, E. O'Brien, D.J. Whellan, I.L. Pina, D.W. Kitzman, K.L. Lee, C.M. O'Connor, G.M. Felker, Clinical implications of chronic heart failure phenotypes defined by cluster analysis, J. Am. Coll. Cardiol. 64 (17) (2014) 1765–1774.

[14] F.J. Quintana, G. Getz, G. Hed, E. Domany, I.R. Cohen, Cluster analysis of human autoantibody reactivities in health and in type 1 diabetes mellitus: a bio-informatic approach to immune complexity, J. Autoimmun. 21 (1) (2003) 65–75.

[15] F.H. Borgen, D.C. Barnett, Applying cluster-analysis in counseling psychology research, J. Couns. Psychol. 34 (4) (1987) 456–468.

[16] L.G. Grimm, P.R. Yarnold, Reading and Understanding MORE Multivariate Statistics, American Psychological Association, 2000.

[17] C. Delatola, B.G. Loos, E. Levin, M.L. Laine, At least three phenotypes exist among periodontitis patients, J. Clin. Periodontol. 44 (11) (2017) 1068–1076.

[18] E. Bair, S. Gaynor, G.D. Slade, R. Ohrbach, R.B. Fillingim, J.D. Greenspan, R. Dubner, S.B. Smith, L. Diatchenko, W. Maixner, Identification of clusters of individuals relevant to temporomandibular disorders and other chronic pain conditions: the OPPERA study, Pain 157 (6) (2016) 1266–1278.

[19] B.G. Smith, J.K. Knight, An index for measuring the wear of teeth, Br. Dent. J. 156 (12) (1984) 435–438.

[20] C.D. Lofgren, P.E. Isberg, C. Christersson, Screening for oral dryness in relation to salivary flow rate addresses the need for functional tests of saliva, Oral Health Prev. Dent. 8 (3) (2010) 243–252.

[21] W. Yachida, E.E. Castrillon, L. Baad-Hansen, R. Jensen, T. Arima, A. Tomonaga, N. Ohata, P. Svensson, Craniofacial pain and jaw-muscle activity during sleep, J. Dent. Res. 91 (6) (2012) 562–567.

[22] K.J. Rothman, S. Greenland, Causation and causal inference in epidemiology, Am. J. Public Health 95 (2005) S144–S150.

[23] S. Cohen, T. Kamarck, R. Mermelstein, A global measure of perceived stress, J. Health Soc. Behav. 24 (4) (1983) 385–396.

[24] C. Jonsgar, P.A. Hordvik, M.E. Berge, A.K. Johansson, P. Svensson, A. Johansson, Sleep bruxism in individuals with and without attrition-type tooth wear: an exploratory matched case-control electromyographic study, J. Dent. 43 (12) (2015) 1504–1510.

[25] T. Zhang, R. Ramakrishnan, M. Livny, BIRCH: an efficient data clustering method for very large databases, ACM Sigmod Record (1996) 103–114.

[26] T. Chiu, D. Fang, J. Chen, Y. Wang, C. Jeris, A robust and scalable clustering algorithm for mixed type attributes in large database environment, Proceedings of the Seventh ACM SIGKDD International Conference on Knowledge Discovery and Data Mining (2001) 263–268.

[27] E. Bair, R. Tibshirani, Semi-supervised methods to predict patient survival from gene expression data, PLoS Biol. 2 (4) (2004) E108.

[28] G. Schwarz, Estimating the dimension of a model, Ann. Stat. 6 (2) (1978) 461–464, https://doi.org/10.1214/aos/1176344136.

[29] R.A. Armstrong, When to use the Bonferroni correction, Ophthal Physiol. Opt. 34 (5) (2014) 502–508.

[30] A.K. Johansson, R. Omar, G.E. Carlsson, A. Johansson, Dental erosion and its growing importance in clinical practice: from past to present, Int. J. Dent. 2012 (2012) 632907.

[31] V. Alaraudanjoki, M.L. Laitala, L. Tjaderhane, P. Pesonen, A. Lussi, J. Ronkainen, V. Anttonen, Influence of intrinsic factors on erosive tooth wear in a large-scale epidemiological study, Caries Res. 50 (5) (2016) 508–516.

[32] W.L. Siqueira, W. Zhang, E.J. Helmerhorst, S.P. Gygi, F.G. Oppenheim, Identification of protein components in in vivo human acquired enamel pellicle using LC-ESI-MS/MS, J. Proteome Res. 6 (6) (2007) 2152–2160.

[33] A.T. Hara, M. Ando, C. Gonzalez-Cabezas, J.A. Cury, M.C. Serra, D.T. Zero, Protective effect of the dental pellicle against erosive challenges in situ, J. Dent. Res. 85 (7) (2006) 612–616.

[34] P. Wetselaar, J.H. Vermaire, C.M. Visscher, F. Lobbezoo, A.A. Schuller, The prevalence of tooth wear in the Dutch adult population, Caries Res. 50 (6) (2016) 543–550.

[35] T. Heuer, C. Krems, K. Moon, C. Brombach, I. Hoffmann, Food consumption of adults in Germany: results of the German National Nutrition Survey II based on diet history interviews, Br. J. Nutr. 113 (10) (2015) 1603–1614.

[36] H.W. van der Glas, F. Lobbezoo, A. van der Bilt, F. Bosman, Influence of the thickness of soft tissues overlying human masseter and temporalis muscles on the electromyographic maximal voluntary contraction level, Eur. J. Oral Sci. 104 (2 (Pt. 1)) (1996) 87–95.

[37] M.A. Donachie, A.W. Walls, Assessment of tooth wear in an ageing population, J. Dent. 23 (3) (1995) 157–164.

[38] B. Loomans, N. Opdam, T. Attin, D. Bartlett, D. Edelhoff, R. Frankenberger, G. Benic, S. Ramseyer, P. Wetselaar, B. Sterenborg, R. Hickel, U. Pallesen, S. Metha, S. Banerji, A. Lussi, N. Wilson, Severe tooth wear: European consensus statement on management guidelines, J. Adhes. Dent. 19 (2) (2017) 111–119, https://doi.org/10.3290/j.jad.a38102.

[39] F. Lobbezoo, J. Ahlberg, A.G. Glaros, T. Kato, K. Koyano, G.J. Lavigne, R. de Leeuw, D. Manfredini, P. Svensson, E. Winocur, Bruxism defined and graded: an international consensus, J. Oral Rehabil. 40 (1) (2013) 2–4.

[40] J. Stuginski-Barbosa, A.L. Porporatti, Y.M. Costa, P. Svensson, P.C.R. Conti, Diagnostic validity of the use of a portable single-channel electromyography device for sleep bruxism, Sleep Breath. 20 (2) (2016) 695–702.

[41] F. Lobbezoo, J. van der Zaag, M.K. van Selms, H.L. Hamburger, M. Naeije, Principles for the management of bruxism, J. Oral Rehabil. 35 (7) (2008) 509–523.

[42] K. Baba, T. Haketa, G.T. Clark, T. Ohyama, Does tooth wear status predict ongoing sleep bruxism in 30-year-old Japanese subjects? Int. J. Prosthodont. 17 (1) (2004) 39–44.

[43] S. Abe, T. Yamaguchi, P.H. Rompre, P. De Grandmont, Y.J. Chen, G.J. Lavigne, Tooth wear in young subjects: a discriminator between sleep bruxers and controls? Int. J. Prosthodont. 22 (4) (2009) 342–350.

[44] M. Giraki, C. Schneider, R. Schafer, P. Singh, M. Franz, W.H.M. Raab, M.A. Ommerborn, Correlation between stress, stress-coping and current sleep bruxism, Head Face Med. 6 (2010).

[45] E. Winocur, N. Uziel, T. Lisha, C. Goldsmith, I. Eli, Self-reported Bruxism - associations with perceived stress, motivation for control, dental anxiety and gagging, J. Oral Rehabil. 38 (1) (2011) 3–11.

[46] D. Manfredini, N. Landi, F. Fantoni, M. Segu, M. Bosco, Anxiety symptoms in clinically diagnosed bruxers, J. Oral Rehabil. 32 (8) (2005) 584–588.

[47] G.D.L. Canto, S.T. De Freitas, G. Schuldt Filho, R. de Sousa Vieira, Association between mandibular torus and parafunctional activity, Int. J. Stomatol. Occlusion Med. 6 (2) (2013) 43–49.

[48] E. Bertazzo-Silveira, J. Stuginski-Barbosa, A.L. Porporatti, B. Dick, C. Flores-Mir, D. Manfredini, G.D. Canto, Association between signs and symptoms of bruxism and presence of tori: a systematic review, Clin. Oral Investig. 21 (9) (2017) 2789–2799.

[49] E. Mooi, M. Sarstedt, A Concise Guide to Market Research, Chapter 9: "Cluster Analysis" vol. 10, Springer-Verlag, Berlin, 2011 978-3-642-12541-6.

[50] K. Boersma, S.J. Linton, Screening to identify patients at risk - Profiles of psychological risk factors for early intervention, Clin. J. Pain 21 (1) (2005) 38–43.

[51] T. Kato, T. Yamaguchi, K. Okura, S. Abe, G.J. Lavigne, Sleep less and bite more: sleep disorders associated with occlusal loads during sleep, J. Prosthodont. Res. 57 (2) (2013) 69–81.