Journal of Dental Sciences (2014) 9, 394—399

Available online at www.sciencedirect.com
SciVerse ScienceDirect
journal homepage: www.e-jds.com

ORIGINAL ARTICLE

Clinical evaluation of maxillary edentulous patients to determine the prevalence and oral risk factors of combination syndrome

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Final revision received 27 January 2012; accepted 8 April 2012
Available online 21 November 2012

KEYWORDS
combination syndrome;
edentulous jaw;
logistic regression;
removable partial dentures

Abstract *Background/purpose:* Destructive changes in maxillary edentulous patients with different mandibular occlusal schemes were first described many years ago. However, little is known about the causative factors for "combination syndrome". The aim of the present study was to determine the prevalence and distribution of symptoms associated with combination syndrome among maxillary edentulous patients with different mandibular occlusal schemes.
Materials and methods: This study examined the clinical and prosthetic status of 100 maxillary edentulous patients with four different mandibular occlusal schemes to evaluate the prevalence of and oral risk factors for combination syndrome. Data were analyzed using logistic regression analysis.
Results: Only nine patients were found to have all five symptoms of combination syndrome. All of these patients used dentures. Eight of them had Kennedy class I and one had Kennedy class II mandibular occlusal schemes.
Conclusion: Development of symptoms associated with combination syndrome, especially mandibular posterior alveolar bone loss, cannot be prevented by the use of removable partial dentures.

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1991-7902/$36
http://dx.doi.org/10.1016/j.jds.2012.04.004

Introduction

Treatment of patients with an edentulous maxilla and a partially edentulous mandible is common in clinical practice. In general, only the mandibular anterior teeth remain in these patients, and specific degenerative changes are often seen.[1,2] Destructive changes in the hard and soft tissues of the jaws were reported in patients with complete maxillary dentures opposed by mandibular natural anterior teeth, and a mandibular bilateral distal extension removable partial denture (RPD).[3–6] Changes consisting of bone loss from the anterior part of the maxillary ridge, overgrowth of maxillary tuberosities, papillary hyperplasia of the palate, extrusion of the lower anterior teeth, and loss of bone under the RPD bases were first described by Kelly[3] as comprising what he referred to as "combination syndrome". Combination syndrome is the evolution over time of pathological conditions of the stomatognathic system.[1] Saunders et al[4] subsequently described six additional changes associated with combination syndrome as follows: loss of the vertical dimension of occlusion; an occlusal plane discrepancy; anterior spatial repositioning of the mandible; poor adaptation of the prosthesis; epulis fissuratum; and periodontal changes. They also noted that patients with combination syndrome experienced progressive difficulties in wearing dentures and eventually required surgical correction to improve prosthetic functioning.[7,8]

Shen and Gongloff[9] investigated the prevalence of combination syndrome in patients with complete maxillary dentures and found that 7% of patients experienced pathological alveolar ridge changes consistent with a diagnosis of combination syndrome. Although these changes are recognized by many clinicians and many treatment modalities are recommended,[2,10–17] there is very little documentation to be found in the literature.[1,9,10]

The aim of the present study was to determine the prevalence and distribution of symptoms associated with combination syndrome among maxillary edentulous patients with different mandibular occlusal schemes (MOSs) in order to identify which parameters represent oral risk factors for the development of combination syndrome.

Materials and methods

In total, 100 maxillary edentulous patients were randomly selected among patients applying for treatment at the Ankara Dental Hospital clinic. They had been edentulous for 10–20 years. Patients with parafunctional occlusal forces or a history of systemic disease that could affect bone metabolism or accelerate the resorption process were excluded.

Clinical examinations were conducted to assess five parameters that represent possible risk factors for combination syndrome as well as five symptoms associated with combination syndrome. In this study, neither medical nor invasive treatment was applied to patients, and a confirmation form was submitted by each patient. Clinical inspections of patients were conducted after receiving written informed consent from each of them. All examinations were conducted by the same dentist.

The following five parameters were examined: MOS; the presence of dentures (PD); denture retention (DR); denture stability (DS); and vertical dimension (VD) (Table 1). Prostheses were checked for stability and retention using conventional procedures for complete dentures and RPDs. Patients were judged to have poor retention when an examination showed no resistance to vertical pull and lateral forces, and the prosthesis fell out of place. Patients with protrusive and laterally balanced occlusions and only slight or no rocking of the prosthesis on its supporting structures when pressure was applied were judged to have adequate stability. Patients without protrusive or laterally balanced occlusions and with extreme rocking of the prosthesis on its supporting structures when pressure was applied were judged to have poor stability. Niswonger's physiological resting position and Silverman's phonetic tests were used to classify vertical dimensions of occlusion as normal, high, or low.

The following five symptoms were examined: maxillary anterior alveolar bone loss (MABL); overgrowth of maxillary tuberosities (OMT); papillary hyperplasia (PH); extrusion of the lower anterior teeth (ELAT); and mandibular posterior alveolar bone loss (MPBL). Patients with all five symptoms were considered to have combination syndrome.

Binary logistic regression analysis was used to identify any relationships between the parameters and symptoms studied in order to determine whether specific parameters could be considered risk factors for the development of the symptoms associated with combination syndrome. Binary

Table 1 Definitions of the clinical and prosthetic status of patients.

Parameter		Status	Level
	Mandibular occlusal scheme	Natural dentition	1
		Kennedy class II	2
		Kennedy class I	3
		Edentulous	4
	Presence of dentures	Upper and lower	1
		None	2
		Only upper	3
	Denture retention	Absence	0
		Presence	1
	Denture stabilization	Absence	0
		Presence	1
	Vertical dimension	Normal	1
		High	2
		Low	3
Symptoms			
	Maxillary anterior alveolar bone loss	Absence	0
		Presence	1
	Overgrowth of maxillary tuberosities	Absence	0
		Presence	1
	Papillary hyperplasia	Absence	0
		Presence	1
	Extrusion of the lower anterior teeth	Absence	0
		Presence	1
	Mandibular posterior alveolar bone loss	Absence	0
		Presence	1

logistic regression analyses were used to inspect the relationship between dichotomous dependent variables and several discrete and/or continuous independent variables.[18]

Results

The distribution of patients according to their clinical and prosthetic status is shown in Table 2. In total, 20% of patients retained their natural dentition in their mandibular arch, 22% had Kennedy class I mandibular occlusion, 16% had Kennedy class II mandibular occlusion, and 42% were totally edentulous. The majority of patients (87%) used both upper and lower prostheses, 8% used only lower dentures, and 5% used neither upper nor lower dentures. The majority of patients had good denture retention (67.82%) and stability (75.64%). Vertical dimensions were either normal (65.12%) or low (26.74%).

When the symptoms of combination syndrome were examined, 50% of patients were found to have MABL, 39% had OMT, 16% had PH, 18% had ELAT, and 47% had MPBL. All five symptoms were identified in 9% of the patients studied, who were thus diagnosed as having combination syndrome.

Table 3 shows the distribution of patients with combination syndrome according to their clinical and prosthetic status. Of the nine patients found to have combination syndrome, eight patients had class I and one patient had class II MOSs. All of the patients with combination syndrome were found to use both their upper and lower prostheses, and most of the patients (85.7%) had poor denture stability. The majority (62.5%) of patients with combination syndrome had normal VDs.

Table 2 Distribution of patients according to their clinical and prosthetic status.

Parameter and Symptom	Level	*n*	Percentage of total	*n*
Mandibular occlusal scheme	1	20	20.0	
	2	16	16.0	
	3	22	22.0	100
	4	42	42.0	
Presence of dentures	1	87	87.0	
	2	5	5.0	100
	3	8	8.0	
Denture retention	0	28	32.18	87
	1	59	67.82	
Denture stabilization	0	19	24.36	78
	1	59	75.64	
Vertical dimension	1	56	65.12	
	2	7	8.14	86
	3	23	26.74	
Maxillary anterior bone loss	0	50	50.0	100
	1	50	50.0	
Overgrowth of maxillary tuberosities	0	61	61.0	100
	1	39	39.0	
Papillary hyperplasia	0	84	84.0	100
	1	16	16.0	
Extrusion of the lower anterior teeth	0	82	82.0	100
	1	18	18.0	
Mandibular posterior bone loss	0	53	53.0	100
	1	47	47.0	

Table 3 Distribution of patients with combination syndrome with regard to the examined parameters.

Parameter	Level	No. of patients with combination syndrome	Percentage within each group
Mandibular occlusal scheme	2	1	11.1
	3	8	88.9
Presence of dentures	1	9	100
Denture retention	0	4	44. 4
	1	5	55.6
Denture stabilization	0	6	85.7
	1	1	14.3
Vertical dimension	1	5	62.5
	2	1	12.5
	3	2	25.0

Univariate binary logistic regression analysis indicated the relationship between parameters and symptoms examined (Table 4). The probability of a Wald statistic of <0.05 indicates that a specific parameter is a risk factor for a particular symptom. The probability of a G statistic of <0.05 indicates that the logistical regression model can adequately explain the symptoms in terms of the parameters used.

As Table 4 indicates, univariate binary logistic regression analysis showed that none of the parameters studied could be considered risk factors for MABL or PH. However, MOS was found to be a risk factor for OMT ($P < 0.05$), DR was found to be a risk factor for ELAT ($P < 0.05$), and both MOS ($P < 0.01$) and PD ($P < 0.05$) were found to be possible risk factors for MPBL. When the multivariate binary logistic regression analysis was conducted (Table 5), only MOS was found to be a risk factor for MPBL ($P < 0.05$).

The following logistic regression models for OMT, MPBL, and ELAT were formed using the estimated coefficients found in Tables 4 and 5: $\text{OMT} = -1.708 + 0.445\ \text{MOS}$; $\text{MPBL} = -2.308 + 1.096\ \text{MOS}$; and $\text{ELAT} = -2.005 + 1.258\ \text{DR}$.

These models could be used to calculate the probability of developing symptoms of combination syndrome. For example, the probability of developing OMT according to MOS was calculated using the following two equations:

$$\text{OMT} = -1.708 + 0.445\ \text{MOS}$$ and

$$P_r = \frac{e^{OMT}}{1 + e^{OMT}}$$

In the first equation, the OMT value was calculated using the value for the parameter being tested; in this case, the patient's MOS. In the second equation, the risk factor (P_r) was calculated, with a P_r value ≥ 0.50 indicating that the patient was likely to develop the symptom; in this case, OMT.

Probability calculations for developing OMT and MPBL using MOS values are given in Table 6. As the table shows,

Table 4 Univariate binary logistic regression analysis.

Symptom	Parameter	β_0	β	SE(β)	Wald	Significance	$G_{(1)}$
Maxillary anterior alveolar bone loss	MOS	0.112	−0.025	0.173	−0.14	0.885	0.021
	PD	−0.234	0.229	0.362	0.63	0.527	0.408
	DR	0.034	0.401	0.466	0.86	0.389	0.749
	DS	0.102	0.437	0.542	0.81	0.420	0.662
	VD	−0.208	0.276	0.253	1.09	0.277	1.208
Overgrowth of maxillary tuberosities	MOS	−1.708	0.445	0.192	2.32	0.020*	5.786*
	PD	0.301	−0.609	0.444	−1.37	0.170	20248
	DR	−0.744	0.457	0.473	0.97	0.334	0.928
	DS	−0.377	−0.652	0.585	−1.12	0.264	1.316
	VD	−0.984	0.250	0.252	0.99	0.321	0.979
Papillary hyperplasia	MOS	−2.064	0.147	0.243	0.61	0.542	0.382
	PD	−1.225	−0.350	0.587	−0.60	0.551	0.413
	DR	−1.715	0.416	0.586	0.71	0.478	0.493
	DS	−1.715	0.041	0.726	0.06	0.955	0.003
	VD	−2.287	0.329	0.324	1.01	0.311	1.001
Extrusion of the lower anterior teeth	MOS	−0.818	−0.247	0.220	-1.12	0.261	1.256
	PD	−1.572	0.067	0.444	0.15	0.881	0.022
	DR	−2.005	1.258	0.571	2.20	0.028*	4.903*
	DS	−1.589	−0.085	0.719	−0.12	0.906	0.014
	VD	−1.336	−0.088	0.322	−0.27	0.786	0.075
Mandibular posterior alveolar bone loss	MOS	−3.474	1.157	0.245	4.72	0.000**	31.465**
	PD	1.140	−1.050	0.508	−2.07	0.039*	6.113*
	DR	−0.238	0.382	0.461	0.83	0.408	0.688
	DS	0.034	−0.139	0.528	−0.26	0.792	0.07
	VD	−0.869	0.451	0.252	1.79	0.074	3.286

β_0 is the constant of the logistic regression model, β is the estimated logistic regression coefficient, and SE(β) is the standard error of the estimated regression coefficient.
*$P < 0.05$; ** $P < 0.01$.
DR = denture retention; DS = denture stability; MOS = mandibular occlusal scheme; PD = presence of dentures; VD = vertical dimension.

patients with an edentulous MOS had a 2.34-fold higher risk of developing OMT than patients with natural dentition (as calculated by the odds ratio of 0.518/0.221). Patients with an edentulous MOS also had a 3.88-fold higher risk of developing MPBL (odds ratio, 0.889/0.229) than patients with natural dentition.

Probability calculations for developing ELAT using DR values are given in Table 7. As the table shows, patients with denture retention were at twice the risk of developing ELAT than patients without denture retention.

Discussion

A review of the literature found no epidemiological studies of combination syndrome.[1] Findings such as PH of the hard palatal mucosa seem rare compared to bone loss in the anterior portion of the edentulous maxilla, which is the main symptom of combination syndrome.[19,20] In the present study, the most frequently encountered symptoms were MABL (50%) and MPBL (47%), whereas PH was the least frequently encountered symptom (16%).

Enlarged tuberosities may have other causes than those described by Kelly[3] as part of combination syndrome. Enlarged tuberosities are often seen together with supraerupted maxillary molars. In situations where mandibular molars have been lost, the opposing maxillary molars may supraerupt as part of the alveolar process,[21] resulting in enlarged tuberosities that are unrelated to denture use. In this study, the MOS was the only parameter found to be related to OMT, with totally edentulous patients found to

Table 5 Multivariate binary logistic regression analysis for mandibular posterior alveolar bone loss.

Symptom	Parameter	β	SE(β)	Wald	Significance	$G_{(2)}$
Mandibular posterior alveolar bone loss	MOS	1.096	0.242	4.53	<0.001**	34.235**
	PD	−0.840	0.577	−1.46	0.145	
	Constant	−2.308	1.038	−2.22	0.026*	

β is the estimated logistic regression coefficient, and SE(β) is the standard error of the estimated regression coefficient.
*$P < 0.05$; ** $P < 0.01$.
MOS = mandibular occlusal scheme; PD = presence of dentures.

Table 6 Probability of having overgrowth of maxillary tuberosities and mandibular posterior alveolar bone loss for levels of the mandibular occlusal scheme.

Mandibular occlusal scheme status		Risk probability of	
	Level	Overgrowth of maxillary tuberosities	Mandibular posterior alveolar bone loss
Natural dentition	1	0.221	0.229
Kennedy class II	2	0.306	0.471
Kennedy class I	3	0.408	0.727*
Edentulous	4	0.518*	0.889*

* $P < 0.05$.

be the only group at risk. No differences in OMT were found between patients according to denture usage.

ELAT was found at a very low rate (18%) in the present study. DR was found to be a risk factor ($P < 0.05$) for developing ELAT independent of the MOS; moreover, good retention did not prevent the appearance of ELAT.

Previous studies reported much lower rates of maxillary bone loss among patients with immediate denture use compared to those who delayed use until after a healing period,[22,23] whereas differences in mandibular resorption rates were smaller or nonexistent between the two groups.[23,24] Resorption under dentures was shown to occur in the alveolar bone and basal bone.[25,26]

Although both the type and amount of bone loss vary greatly between individuals, and factors other than the wearing of removable dentures may be involved in the resorption process,[27,28] there is little doubt that removable dentures play an important causative role in bone resorption. Studies have shown that edentulous patients who do not wear removable dentures have significantly more residual alveolar bone than those who do wear removable dentures.[29,30] Continuous bone resorption in the mandible posterior to the remaining anterior teeth was demonstrated in two groups of patients wearing different types of class I mandibular RPDs, whereas no change in posterior bone levels was noted in a group not wearing RPDs.[31,32] In groups of patients who wore complete mandibular dentures for different lengths of time, continuous bone resorption in areas distal to the mandibular foramina ceased after patients were given fixed prostheses supported by implants placed anterior to the foramina[33]; however, resorption in the same areas continued when patients were given an overdenture supported by implants.[34]

Table 7 Probability of having extrusion of the lower anterior teeth for levels of denture retention.

Status of denture retention	Level of denture retention	Risk probability of extrusion of the lower anterior teeth
Absence	0	0.321
Presence	1	0.625*

* $P < 0.05$.

Denture retention and stability play important roles in alveolar bone loss. In the present study, all of the patients with combination syndrome were using their dentures and had relatively poor retention and stability; therefore, the finding of MABL among these patients is not surprising. The literature also indicates that an RPD is more often associated with mandibular bone loss than no RPD or a fixed prostheses supported by anterior implants.[31–35] In the present study, a univariate binary logistic regression indicated that both MOS and PD could be risk factors for MPBL; however, when these two parameters were evaluated using multivariate binary logistic regression, the contribution of PD as a risk factor for MPBL was not found to be statistically significant ($P > 0.05$).

Bone resorption in the anterior portion of an edentulous maxilla has been the subject of many clinical reports. In one study[36] comparing bone resorption of the anterior maxilla in patients with complete maxillary dentures but varying mandibular status, no statistically significant differences were found between groups. Similarly, two other clinical studies reported no significant differences in maxillary bone resorption between patients wearing a complete mandibular denture and those with natural teeth and an RPD or overdenture supported by the roots of the mandibular canines.[37,38] In another study, the authors found no significant differences in pathological alveolar changes related to use of an RPD.[7] This was supported by the findings of the current study that showed no statistically significant changes in MABL related to either MOS or PD.

In a study examining the prevalence of symptoms associated with combination syndrome in 150 consecutive denture patients with complete maxillary dentures but different mandibular status, changes associated with combination syndrome were found to be prevalent in <7% of the total sample, but were found in 24% of patients with a bilateral distal-extension RPD.[9] In the current study, combination syndrome, as indicated by the presence of all five symptoms examined, was found in only 9% of patients; the majority (88.89%) of whom were class I partially edentulous and the remainder (11.11%) were class II partially edentulous.

In a long-term study conducted with patients wearing complete maxillary dentures over a 21-year period, no support was found for any systematic development of combination syndrome[26]; however, the author emphasized the negative effects of mandibular RPDs. Keltjens et al[39] also stressed the fundamental inadequacy of a complete maxillary denture and a class I mandibular RPD for treating an edentulous maxilla opposed by a partially edentulous mandible.

In conclusion, the lack of epidemiological studies and the rare occurrence of combination syndrome in the population have prevented it from achieving full acceptance as a medical syndrome. However, as this study shows, the presence of individual symptoms that are associated with combination syndrome in maxillary edentulous patients cannot be ignored. Moreover, the study findings indicate that the development of symptoms associated with combination syndrome, especially MPBL, cannot be

prevented by an RPD. However, the use of an alternative prosthesis that can alter a patient's MOS from bilateral distally extended, and/or totally edentulous mandible may prevent the development of symptoms such as MPBL and OMT. In order to be able to say how many years are necessary for combination syndrome to occur in edentulous patients, a follow-up study should be planned to observe patients from the time they first became edentulous. In this way, symptoms related to combination syndrome can be confirmed by future research, including long-term clinical studies.

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