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The risk of temporomandibular disorder in patients with depression: a population-based cohort study

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Abstract – *Objectives:* This study used a population-based retrospective cohort design to examine whether depression is a risk factor of temporomandibular disorder (TMD). *Methods:* From a universal insurance database, we identified 7587 patients who are newly diagnosed individuals with depression in 2000 and 2001. A total of 30 197 comparison subjects were randomly selected from a nondepression cohort. Both groups were followed until the end of 2008 to measure the incidence of TMD. *Results:* The incidence of TMD was 2.65 times higher in the depression cohort than in the nondepression cohort (6.16 versus 2.32 per 1000 person-years). The hazard ratio (HR) measured by multivariate Cox's proportional hazard regression analysis of TMD for the depression cohort was 2.21 (95% confidence interval (CI) 1.83–2.66), after controlling for socio-demographic factors and other psychiatric comorbidities. Women had higher risk to develop TMD than men (HR 1.61, 95% CI 1.36–1.92 for women without depression; HR 3.54, 95% CI 2.81–4.45 for women with depression). *Conclusions:* This study demonstrates that patients with depression are at an elevated risk of developing TMD.

Key words: depression; hazard ratio; population-based study; retrospective cohort design; temporomandibular disorder

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Temporomandibular disorders (TMD) are quite common among the general population, with a lifetime prevalence of up to 93% in an epidemiological study (1). These disorders include complaints of the temporomandibular system, consisting of the temporomandibular joint (TMJ) and the associated neuromuscular system (2). A national survey among Dutch adults showed that 21.5% of the adult population had temporomandibular dysfunction but only 15% of those sought treatment (3). Most patients seek treatment because of TMD pain (4), in the temporomandibular region or involving the eyes, face, shoulder, neck, back, and head (5, 6). Patients with TMD have a decreased quality of life because of orofacial pain, particularly for patients with severe TMD (7). The etiology of TMD has been regarded as multifactorial. Dworkin and LeResche (8) designed a two-axis diagnostic scheme to evaluate the patient's condition. The psychological variables were assessed with Axis II, emphasizing the relevant factors of TMD. Gracely (9) reported that individuals can have different levels of pain perception, which can be influenced by emotional factors. Hotopf et al. (10) have noted the psychiatric disorder may promote 40% cases of multiple symptoms including arthritis, rheumatism, and headache. Magni et al. (11) found in a prospective study that the relationship between depressive systems and chronic musculoskeletal pain may operate in both directions.

Depressive symptoms are significantly related to the severity of pain in the TMD patients (12). Moreover, TMD pain and depression are often co-existent (13–15). Macfarlane et al. (15) found in a

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case–control study that patients with pain dysfunction syndrome had high levels of psychological distress. Depression has now become a global burden disorder and the fourth leading cause of disability worldwide (16). Major depressive disorder presents in 5–10% of patients seeking primary care (17). The prevalence of depression may well be higher among the general population because some people may have depressive disorders which do not fully meet the diagnostic criteria for major depressive disorder of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.

Among studies on the relationship between depressive systems and pain, there is a convergent association between depression and TMD pain, especially in the chronic pain group (2). Several studies on the relationship between depression and TMD have evaluated the mood condition among TMD patients (13–18). However, those studies were unable to answer whether depression is a source or consequence of TMD pain because of case–control and cross-sectional designs.

Slade et al. have recently conducted a prospective cohort study of 238 healthy female volunteers aged 18–34 years investigating the psychological influence on the risk of TMD. They found that depression, perceived stress, and mood are associated with pain sensitivity with a two- to threefold increase in the risk of TMD ($P < 0.05$) (19). But, this study was limited to a small sample size with only one gender and a short follow-up period. We therefore designed a population-based cohort study with higher statistical power to detect the development of TMD among the depressive patients. Not all patients with TMD complaints visit the dentists. We hypothesized that patients with depressive disorder would have a higher risk of TMD complaints, leading to a greater likelihood to seek dental services than the general population. To gain a better understanding of the relationship between depression and TMD, we conducted a population-based retrospective cohort study using claims data from the universal insurance program. The incidences of dentist-diagnosed TMD were compared between patients with depression and without depression.

Materials and methods

Data resources

This study used the reimbursement claims data of The National Health Insurance program of Taiwan that reformed in March 1995 from 13 insurance systems. The insurance program has covered more than 96% of the 23 million population and contracted with more than 90% of hospitals and clinics in Taiwan since 1996 (20, 21). The Department of Health National Health Research Institute (NHRI) managed all medical claims data reported from the contracted health care facilities. With approval from NHRI, we were able to use a representative sub-datasets of 1 million insured persons randomly selected from all beneficiaries enrolled in the insurance program (21). This dataset consisted of the registry of medical facilities, details of inpatient orders, ambulatory care, dental services, and prescriptions linked with scrambled patient identification. Because all patient identifications were surrogated, this study was conducted with patients privacy secured and with a waiver from the institutional review board.

Study sample

We used the coding of the International Classification of Disease Diagnoses, Ninth Revision of Clinical Modification (ICD-9-CM), to identify 7587 patients with depression (ICD-9-CM 296.2, 296.3, 300.4 and 311) newly diagnosed in 2000 and 2001 as the study cohort. To ensure the validity of the diagnosis, only new patients with at least three visits for depression care during the follow-up period after the index date were eligible for inclusion. For each case with depression identified, we used simple random sampling methods to select four persons without depression in the same period for the comparison cohort ($N = 30\,348$). We excluded 102 subjects from the depressive cohort and 151 subjects from the comparison cohort. They were excluded because of a history of TMD diagnosis by the baseline index date (defined as the date the subject identified and selected) or missing information on age or sex. Our final sample includes 7485 subjects in the depression cohort and 30 197 subjects in the nondepression cohort.

Socio-demographic variables and comorbidities

The socio-demographic variables, including sex, age, occupation, employment category, residential area, and monthly income, were available. The age of each study subject was measured by the difference between the index date and the date of birth. Using the National Statistics of Regional Standard Classification (22), we grouped all study subjects into four geographic areas (North, Central, South,

and East and off Islands) and three urbanization levels (low, medium, and high).

We considered anxiety state (ICD-9-CM 300.00), panic disorder (ICD-9-CM 300.01), generalized anxiety disorder (ICD-9-CM 300.02), obsessive-compulsive disorders (ICD-9-CM 300.03), and psychiatric diseases (ICD-9-CM 290-319, except the main effect in this study – depression) as other psychiatric comorbidities.

Study end point

We linked study subjects to the inpatient and outpatient claims data of dental clinics to identify the newly diagnosed cases of TMD (ICD-9-CM 524.6) as the outcome of the study, using the scrambled patient identification number. We calculated person-years for each study subject until TMD was diagnosed, or until December 31, 2008, for those uncensored, or the censoring date because of death, emigration, termination of insurance, or loss to follow-up.

Statistical analysis

We compared the distributions of categorical socio-demographic variables and comorbidities between depression patients and nondepression patients using the Chi-square test. We also calculated the incidence density with person-years for these variables in the study cohort and comparison cohort. The rate ratio of TMD was calculated by each variable.

Cox's proportional hazard regression analysis was used to assess the risk of TMD associated with depression, adjusting for variables that were significantly related to depression from the prior Chi-square analyses. Hazard ratio (HR) and 95% confidence interval (CI) were calculated in the model. The sex and age stratification analyses for the risk of TMD in association with depression were also examined using Cox's proportional hazard regression analysis.

All analyses were performed with SAS statistical software (version 9.1 for Windows; SAS Institute, Inc., Cary, NC, USA). Significance level was set to 0.05.

Results

Table 1 compares socio-demographic characteristics between the depression cohort and the nondepression comparison cohort. There were more women in the depression cohort than in the comparison cohort (60.6% versus 48.1%). The depression cohort was also older, less white collar employment and had middle income.

Table 1. Comparisons in demographic characteristics between patients with and without depression at baseline in 2000–2001

	Depression*	
	No[a] *N* = 30 197	Yes *N* = 7485
Variables	*n* (%)	*n* (%)
Sex		
Female	14 529 (48.1)	4536 (60.6)
Male	15 668 (51.9)	2949 (39.4)
Age, years		
<20	9240 (30.5)	363 (4.9)
20–39	10 558 (35.0)	2307 (30.8)
40–59	6995 (23.2)	2672 (35.7)
≥60	3404 (11.3)	2143 (28.6)
Occupation		
White collar	16 977 (56.2)	3440 (46.0)
Blue collar	9412 (31.2)	2675 (35.7)
Others[b]	3808 (12.6)	1370 (18.3)
Urbanization[a]		
Low	3627 (12.1)	1007 (13.5)
Moderate	6337 (21.1)	1458 (19.6)
High	20 092 (66.9)	4978 (66.9)
Region		
North	14 215 (47.0)	3148 (42.1)
Central	6162 (20.4)	1534 (20.5)
South	7535 (25.0)	2104 (28.1)
East and Island	2284 (7.6)	699 (9.3)
Income		
<15 000	15 164 (50.2)	3138 (41.9)
15 000–29 999	11 257 (37.3)	3505 (46.8)
≥30 000	3776 (12.5)	842 (11.3)

Depression: ICD-9 codes: 296.2, 296.3, 300.4, and 311.
[a]Urbanization: low = 1st and 2nd lowest quartile of population density, moderate = 3rd quartile of population density, high = 4th highest quartile of population density.
[b]Unemployed, retired and low income.
*Chi-square test, all *P* values are <0.001.

Table 2 presents the incidence and crude hazard ratios of TMD by socio-demographic status. The overall incidence rate of TMD in the depression cohort was 2.65 times higher than that in the comparison cohort (6.16 versus 2.32 per 1000 person-years). The crude hazard ratios measured by categorized socio-demographic status ranged from 2.35 to 3.64, with the depression cohort of those more than 60 years of age having the highest hazard ratio. Older men in the nondepression cohort had the lowest risk of having TMD.

The multivariate Cox proportional regression analysis showed that the risk of TMD was significantly greater in the depression cohort than in the

Table 2. Comparisons of incidence of temporomandibular disorder between cohorts with and without depression by socio-demographic factor

	Depression						
	No			Yes			
Variables	Cases	Person-years	Rate[a]	Cases	Person-years	Rate[a]	Crude HR (95% CI)
All	533	229 485	2.32	338	54 872	6.16	2.64 (2.30–3.03)
Sex							
Female	319	110 865	2.88	241	33 785	7.13	2.49 (2.10–2.95)
Male	214	118 619	1.80	97	21 087	4.60	2.49 (1.95–3.18)
Age, years							
<20	149	72 808	2.05	15	2787	5.38	2.78 (1.63–4.73)
20–39	207	79 699	2.60	109	17 558	6.21	2.36 (1.86–2.99)
40–59	137	53 806	2.55	123	20 276	6.07	2.35 (1.84–3.01)
≥60	40	23 172	1.73	91	14 252	6.39	3.64 (2.50–5.30)
Occupation							
White collar	313	129 644	2.41	172	25 691	6.69	2.70 (2.23–3.26)
Blue collar	163	71 273	2.29	105	19 628	5.35	2.42 (1.89–3.10)
Others	57	28 569	2.00	61	9553	6.39	3.15 (2.19–4.53)
Urbanization							
Low	57	27 151	2.10	44	7138	6.16	2.93 (1.97–4.36)
Moderate	109	47 877	2.28	74	10 664	6.94	3.01 (2.23–4.07)
High	367	153 372	2.39	219	36 748	5.96	2.48 (2.09–2.94)
Region							
North	244	107 867	2.26	141	23 217	6.07	2.61 (2.11–3.23)
Central	110	46 962	2.34	65	11 327	5.74	2.39 (1.75–3.27)
South	145	57 316	2.53	107	15 253	7.02	2.84 (2.21–3.66)
East and Island	34	17 332	1.96	25	5075	4.93	2.57 (1.54–4.32)
Income							
<15 000	260	116 460	2.23	135	22 391	6.03	2.70 (2.19–3.34)
15 000–29 999	196	83 606	2.37	162	26 066	6.21	2.65 (2.15–3.27)
≥30 000	77	29 419	2.62	41	6415	6.39	2.35 (1.59–3.47)

[a]Per 1000 person-years.

nondepression cohort (HR 2.21, 95% CI 1.83–2.66) after controlling for covariates (Table 3).

Table 4 shows that women were at greater HRs to develop TMD than men. Compared with men without depression, women without depression had a HR of 1.61 (95% CI 1.36–1.92) and women with depression had the HR increased to 3.54 (95% CI 2.81–4.45). Compared with the nondepression cohort ≧60 years of age, the HRs of TMD increased in patients with depression, and in particular, the highest risk was noted in depression patients ≧60 years of age (HR 3.22, 95% CI 2.20–4.73).

Discussion

Studies investigating whether the risk of TMD is higher in patients with depression using cohort designs are limited. Our study aimed at exploring

Table 3. Hazard ratio of temporomandibular disorder in association with depression in Cox's proportional hazard models

	Model 1	Model 2	Model 3
Variables	HR (95% CI)	HR (95% CI)	HR (95% CI)
Depression			
No	1.00 (reference)	1.00 (reference)	1.00 (reference)
Yes	2.64 (2.30–3.03)*	2.42 (2.09–2.81)*	2.21 (1.83–2.66)*

Model 1: unadjusted.
Model 2: adjusted for age, sex.
Model 3: adjusted for age, sex, area, occupation, urbanization, income, and other psychiatric comorbidity.
*$P < 0.0001$.

Table 4. Sex- and age-specific hazard ratio of temporomandibular disorder associated with depression measured with multivariable Cox method

	Depression	
Variables	No[a] HR (95% CI)	Yes[a] HR (95% CI)
Sex*		
Female	1.61 (1.36–1.92)***	3.54 (2.81–4.45)***
Male	1.00 (reference)	2.23 (1.70–2.94)***
Age, years[a]		
<20	1.25 (0.87–1.81)	2.70 (1.48–4.94)**
20–39	1.55 (1.09–2.19)*	3.05 (2.10–4.45)***
40–59	1.49 (1.04–2.13)*	2.98 (2.05–4.33)***
≥60	1.00 (reference)	3.22 (2.20–4.73)***

[a]Multivariable model including also area, occupation, urbanization, income, and other psychiatric comorbidity. *$P < 0.05$; **$P < 0.01$; ***$P < 0.0001$.

whether depression is a risk factor related to subsequent TMD problems. We measured the incidence of dentist-diagnosed TMD in depressive patients compared with that of a nondepression cohort, using a population-based retrospective cohort study design. This approach overcomes the major limitation of cross-sectional and case–control study designs by providing incidence information.

Temporomandibular disorder disorders have a high degree of comorbidity with depression (13, 14, 23). Previous studies on TMD and depression have been unclear as to whether depression occurred prior to the onset of TMD or as a consequence of it. Slade et al. (19) found that depression was one of the predicted risk factors of the first onset of TMD among healthy women with a small sample size. These studies collected information on depression based on self-reported questionnaires, which is different from clinically verified depressive disorder. Our population-based study on the association between depression and subsequent TMD found that there is a 2.21- to 2.64-fold higher risk of a diagnosis of TMD among patients with a physician-diagnosed depressive disorder, compared with the control group within an 8-year follow-up period, after adjusting for demographic characteristics and comorbid anxiety disorders.

Temporomandibular disorder are a heterogeneous group of disorders affecting TMJ, the masticatory muscles, or both, and might present with joint sounds or severe dysfunction. The most common symptom was pain, and most patients sought help because of it. TMD has also been a chronic pain condition in many cases (24). Not only is depression prevalent among patients with chronic TMD-related pain conditions, but patients with TMD and comorbid psychological factors had a poor response to dental treatment alone (25). This could be explained by depression possibly increasing pain-perception thresholds (26, 27) and affecting the expression of TMD signs and symptoms (28). Therefore, depressive patients might have more TMD problems, which lead them to seek dental services.

In our study, the incidence of TMD among the depression group was 4.5% in the 8-year follow-up, which is higher than the incidence in a previous study (3.1%) for a Dutch adult population (3). This reflects a higher risk of TMD problems among the depressive population. Our definition of TMD was based on the information from patients who had visited a dental clinics rather than from case–control study or general cross-sectional survey among the general population. Therefore, in our study, the difference in TMD incidences between the depressive patients and the general population without depression is more valid. However, our diagnosis of depression included both minor and major depressive disorders (ICD 296.2, ICD 296.3, ICD 300.4, and ICD 311) and may have identified subjects with a broader spectrum of depressive disorders. It still is likely that depression is underestimated in the general population, because not all patients seek help from physicians when depressed.

Our study was compatible with the previous reports that found that women had a higher rate of TMD than men (29–31). Elderly depressive patients are also found to have a higher risk of TMD, which lead them to seek dental services. However, the nondepressive elderly had the least risk of TMD. Further research to evaluate TMD among geriatric patients is needed.

There are some limitations to interpret the results of our study. First of all, the diagnoses of depression, TMD, and comobidity relied on claims data, so there may be missing information made under a standardized diagnostic process. Obtaining this kind of information for a large population-based cohort study would be extremely difficult. But our strength in this study was that working from a clinical diagnosis made it possible to avoid the limitations of self-reported questionnaires. To increase the diagnostic validity, all cases were diagnosed with depressive disorder at least three times, which provided a reliable cohort assessment. Second, some studies found that a myofascial type of TMD have a higher comorbidity of depression

and required health care more frequently (32, 33). But, we did not have the type and severity of TMD, and the stress and mood status among our study cohort. We, therefore, could not further evaluate the impact among them. Even though, we found a higher risk of developing TMD among the depressive patients than the general population, which supports the temporal relationship between depressive disorder and TMD. In addition, we could not definitively identify the real onset time of depression from the database. However, we still could hypothesis that lifetime depression is one risk factor of TMD.

In conclusion, a temporal relationship between depression and TMD seems to exist. These results imply that dentists involved in the management of TMD need to be aware of the comorbidity of depression in these patients. Further research on the clinical efficacy of decreasing dental services for TMD after the treatment of depression is needed.

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