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Persistent Pain among Registrants in the National TMJ Implant Registry and Repository

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Abstract

The aim of this study was to evaluate the association of persistent facial pain with tissue injury among subjects in the National TMJ Implant Registry and Repository. This case-control analysis included three groups: No surgery and no implant, TMJ surgery only and TMJ implant surgery. Unconditional binary logistic analyses were used to assess the association of tissue injury (by implant or surgery), comorbid conditions, and gender with persistent facial pain. Persistent pain was reported by the majority (64%) of the 645 subjects, and there was no difference among age groups. Number of surgeries was related to persistent pain, irrespective of whether the surgery involved an implant. When adjusted for number of TMJ surgeries, TMJ surgery without implant was associated with persistent pain while implant surgery had a weak and insignificant association with persistent pain. Among the comorbidities studied, headache, low back pain, and fibromyalgia were most frequently reported, followed by chronic fatigue syndrome and rheumatoid arthritis. The increased odds of persistent pain remained when the model was adjusted for depression, anxiety, and number of comorbid conditions. These data indicate the number of surgical procedures a patient underwent was related to persistent facial pain irrespective of type of surgery or comorbidities.

Keywords: Implants; Temporomandibular joint disorders; Persistent pain; Tissue injury; Surgery

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Introduction

Temporomandibular Joint Disorder (TMJD) is a major cause of non-odontogenic, chronic pain in the craniofacial region second only to headache [1]. There are a variety of approaches for management of TMJD, including TMJ surgery with or without implants. The US Food and Drug Administration (FDA) analyzed TMJ implant-related adverse event reports between 2004-2010 to determine the length of time for implant removal or replacement due to pain or other reasons and found that over half of TMJ implants had to be removed within the first three years because of severe pain and other problems [2]. Similar symptoms were described by patients who have had multiple TMJ operations, but have not received alloplastic devices as part of joint reconstruction [3]. In a cross-sectional study of patients with Proplast-Teflon (Vitek) and Silastic® (Dow Corning, Arlington, TX) implants, patients reported pain that persisted long after removal of their implants [4]. A study of prospective pre and postoperative outcome data from a set of patients with multiple TMJ reconstructions found that the greater the number of surgical procedures performed on the TMJ reduced the chance of subjective improvement [5]. A separate study correlated increased pain severity with the increasing frequency of surgeries and found that nearly 80% of patients who reported severe pain also had overall bodily pain [6]. Taken together, these findings suggest that either TMJ surgery, or the implants themselves, impart sufficient tissue injury to lead to sensitization resulting in hyperalgesia, manifesting as persistent pain, and possibly widespread body pain. Furthermore, little is known about overlapping risk factors that may be shared between painful conditions, such as fibromyalgia and TMJD (e.g., comorbidities). Comorbid conditions may contribute to TMJD and treatment failure [7]. Comorbid complaints self-reported by TMJD patients include: headaches, ear pain, fibromyalgia, irritable bowel syndrome, rheumatoid arthritis, osteoarthritis and interstitial cystitis [8]. The number of these comorbidities present has been found to be positively associated with TMJD pain intensity and duration [9]. The primary aim of this case-control study was to evaluate the association of persistent facial pain among subjects from the Temporomandibular Joint Implant Registry and Repository (TIRR) database who had a history of any type of TMJ surgery (including implants) and subjects who did not have TMJ surgery (controls) based on the working

Table 1: Demographic data for TIRR participants, n (%).

Characteristics[a]	Group I TMJ Implant Surgery		Group II Non-implant Surgery		Group III Non-Surgical Group (control group)		Total	
	n=269	%	n=152	%	n=310	%		%
Gender								
Female	245	91	133	88	256	83	634	87
Male	24	9	19	13	54	17	97	13
Ethnicity								
Hispanic	10	4	4	3	7	2	21	3
Non-Hispanic	205	88	125	91	269	93	599	91
Other	19	8	8	6	12	4	39	6
Mean age (95% CI)	44.8 (43.1-46.7)		37.5 (35.9-39.9)		41.2 (39.5-42.9)			

[a]Excluding cases with missing information

hypothesis that persistent pain was positively associated with tissue injury. We hypothesized that those reporting persistent pain were more likely to have a history of TMJ surgery when compared to the non-surgical treatment group. We also evaluated the relationship of self-reported comorbidities to persistent facial pain among these groups. We hypothesized that persistent facial pain is positively associated with number of comorbidities.

Materials and Methods

The protocol for this study was approved by the University of Maryland, Baltimore Institutional Review Board for Human Subjects Research where both authors were affiliated at the time that the research was conducted. We analyzed data from the National Institute of Dental and Craniofacial Research (NIDCR) sponsored TIRR database maintained by the University of Minnesota [10]. The repository contains clinical information and biological specimens from patients throughout the United States with TMJD. All TIRR registrants completed a questionnaire and underwent standardized examination following the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) protocol [11]. The database contains extensive demographic and clinical information on TMJD patients, including pain and jaw function, primary diagnosis, medical conditions, functional status, and information on treatments, including surgeries and implant data. The primary outcome variable for this study was persistent pain, taken from the subjects' most recent self- reported response to the question, "What is the pattern for the worst jaw pain problem?"

Data collected and measures

Study population: TIRR patients were recruited from two sources: 1) clinicians and surgeons who treat TMJD patients; and, 2) patients who participated in facial pain clinical studies at the University of Minnesota. Excluded were those with presence of infection, tumor, or any other disease unrelated to TMJ disorder that could cause jaw symptoms or dysfunction; a primary TMJ diagnosis other than TMJ disc displacement or osteoarthritis; and surgical treatment not directed at the joint (such as orthognathic surgery). Calibrated examiners performed a comprehensive TMJ diagnostic examination including the RDC/TMD, and the findings were entered into the TIRR database. Diagnoses were corroborated using a combination of symptoms, signs, and radiographic evidence retrieved from the patients' records descriptions. Details of the TIRR have been published elsewhere [10]. Patients included in this case-control study are a subpopulation of 985 subjects from the TIRR database with and without history of TMJ surgery. Subjects without

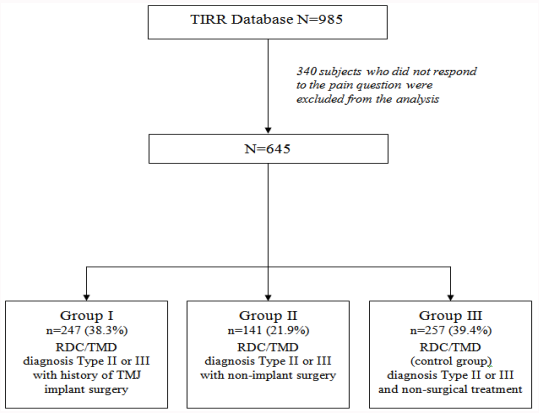

Figure 1: CONSORT flow diagram of the study subjects groups according to RDC/TMD classification.

response to the persistent pain question were excluded from the analysis, for a total of 645 subjects. For the case control analysis, the study population was divided into three groups of participants with Type II (disc displacement) or Type III (arthralgia, osteoarthritis, osteoarthritis) diagnoses. Patients were classified as: 1) Group I-RDC/TMD diagnosis Type II or III with a history of TMJ implant surgery; 2) Group II-RDC/TMD diagnosis Type II or III with non-implant TMJ surgery; and 3) Group III- RDC/TMD diagnosis Type II or III with non- surgical treatment (control group) (Figure 1).

Statistical analyses: Chi-square, Fisher's exact test, Analysis of Variance (ANOVA) and student's t-test were used to test differences between study groups. Unconditional binary logistic regression (proc logistic; SAS Institute Inc., Cary, NC) was used to assess the factors associated with persistent pain. The dependent variable was persistent pain (yes/no); the independent variables were study groups (i.e., TMJ surgery with and without implant, no surgery or implant), number of surgeries, and sum of comorbid conditions, age, and gender. The sum of comorbid conditions was created by summing the number of times the subject responded "yes" to the presence of any of the listed comorbidities, including fibromyalgia, headache, chronic fatigue syndrome, rheumatoid arthritis, and low back pain. In addition, we evaluated the relationship between each pain comorbidity and persistent TMJD pain. The multivariable logistic regression model also included number of surgeries, study groups, depression, and anxiety.

Results

Participants were classified according to socio-demographic

Table 2: Distribution of persistent pain by group; n (%).

	Persistent Pain[a]		Other Response[b]		Total
	n=416	%	n=229	%	n=645
Group I TMJ implant surgery	171	70	76	30	247
Group II Non-implant surgery	110	38	31	22	141
Group III Non-surgical treatment control group	135	53	122	47	257

[a]Self- reported response to pattern of worst pain problem
[b]Other response includes "no pain" or "one-time pain"

Table 3: Results of logistic regression analysis accessing the association between persistent pain and sum of comorbid conditions and surgery.

.	Persistent Pain n (%)		Crude OR (95% CI)	Adjusted OR (95% CI)[a]
Group I (TMJ implant surgery)	No	76 (30.8)	1 (referenced)[b]	1 (reference)[b]
	Yes	171 (69.2)	3.00 (2.00-5.10)[c]	1.45 (0.87-2.26)
Group II (Non-implant surgery)	No	31 (21.1)	1 (reference)[b]	1 (reference)[b]
	Yes	110 (78.0)	2.00 (1.40-2.90)[c]	2.00 (1.14-3.51)
Number of surgeries	No	230 (36.5)	1.24 (1.13-1.35)	1.11 (1.00-1.24)
	Yes	401 (63.6)		
Sum of comorbid conditions	No	226 (35.7)	1.29 (1.11-1.50)	1.36 (1.14-1.63)
	Yes	408 (64.7)		
Mean age (Years)	No	43.7	0.97 (0.96-0.96)	0.97 (0.96-0.96)
	Yes	40.8		
Gender				
Female	No	48 (10.1)	1.00 (0.60-1.60)	0.80 (0.46-1.39)
	Yes	390 (89.1)		
Male	No	27 (10.1)		
	Yes	219 (89.2)		

[a]After adjusting for number of surgeries
[b]Group III is the reference group
[c]Indicates statistical significance p<0.001

characteristics as shown in Table 1. The majority of the subjects were women (86.7%), and the mean age of all subjects was 45 years. Non-Hispanics constituted 91.3% of the ethnicity of the study population, followed by Hispanics (3.2%). Self-disclosed as "other" was 5.9%. The distribution of persistent pain among the groups is shown in Table 2. Women were no more likely than men to report persistent pain (Table 3, adjusted Odds Ratio [OR] =0.80, 95% Confidence Interval [CI] = 0.46-1.39). Among females, 390 (64%) reported persistent pain and among males, 48 (64%) reported persistent pain. In the crude logistic regression analysis, subjects receiving any type of surgery, including implant, had higher odds of reporting persistent pain than those who did not undergo surgery (Table 3). In the multivariable model adjusted for age, gender, and number of surgeries, surgery (Group II) remained associated with persistent pain, whereas surgery with implant (Group I) did not. The increased odds related to surgery and number of surgeries did not substantially change when the model was also adjusted for depression, anxiety, and number of comorbid pain conditions (Table 3). Table 4 shows the distribution of painful comorbidities across the groups. Among comorbidities, there was higher frequency of headaches, low back pain and fibromyalgia reported, followed by chronic fatigue syndrome and rheumatoid arthritis. Subjects with higher numbers of comorbid pain conditions had slightly increased (non-significant) odds of reporting persistent pain (Table 3). A positive, but weak correlation was noted between persistent pain and headache (r=0.20, p<0.0001), chronic fatigue syndrome (r=0.12, p=0.002) and anxiety (r=0.12, p=0.002). In the multivariable logistic regression analysis including all comorbid conditions, higher odds of persistent pain were only significantly related to headache and rheumatoid arthritis (Table 5). In a parsimonious model including only comorbidities with p-values ≤ 0.20 (headache, chronic fatigue syndrome and anxiety), study groups, age and number of surgeries, headache (adjusted OR=1.70, 95% CI=1.13-2.56) remained the only significant comorbidity related to persistent pain. A borderline association was noted with chronic fatigue syndrome (adjusted OR=1.69, 95% CI=0.70-4.10, p=0.08).

Discussion

Following tissue injury the release of inflammatory mediators, pro-inflammatory cytokines, and other substances sensitize peripheral nociceptors [12]. This phenomenon of peripheral sensitization contributes to pain hypersensitivity at the site of tissue injury [13]. Earlier studies and case reports suggested that inflammatory cell types in TMJ tissues with implant wear debris showed a significant increase in the number of localized multinucleated giant cells and lymphocytes in patients with a history of implant when compared to non-implant surgery and control TMJ tissues [14]. Another study found reduced conditioned pain modulation in patients who had received total TMJ prostheses compared to healthy controls, suggesting somatosensory abnormalities in TMJ prosthesis patients [15]. Sensitization alters the relationship of nocioceptive neurons resulting in signal amplification [13]. Occasionally, this sensitization does not reverse when the tissue is healed, resulting in central sensitization. Following repeated injury,

Table 4: Distribution of comorbidities across groups.

Comorbidities[a]	Headache	Low Back Pain	Fibromyalgia	Chronic Fatigue Syndrome	Rheumatoid Arthritis
	n	n	n	n	n
Group I TMJ implant surgery	95	85	48	32	20
Group II Non-implant surgery	53	50	13	9	12
Group III Non-surgical treatment (control group)	87	108	29	10	13
Total	235	243	90	51	45

[a]Subjects could report more than one painful comorbidity

Table 5: Association between persistent pain and various comorbidities.

	Persistent Pain		Crude OR	Adjusted OR[a]
	n (%)			
Fibromyalgia	No	223 (35.70)	1 (reference)	1 (reference)
	Yes	402 (64.30)	1.60 (0.90-2.70)	1.41 (0.75-2.67)
Headache	No	199 (37.20)	1 (reference)	1 (reference)
	Yes	326 (62.10)	2.30 (1.60-3.40)[b]	1.70 (1.13-2.56)[b]
Chronic fatigue syndrome	No	239 (36.70)	1 (reference)	1 (reference)
	Yes	422 (63.80)	3.00 (1.40-6.20)[b]	1.69 (0.70-4.10)
Rheumatoid arthritis	No	222 (35.60)	1 (reference)	1 (reference)
	Yes	401 (64.40)	1.40 (0.70-2.70)	1.51 (0.70-3.29)
Low back pain	No	200 (38.10)	1 (reference)	1 (reference)
	Yes	326 (61.10)	1.30 (0.90-1.90)	1.07 (0.70-1.62)
Depression	No	222 (35.50)	1 (reference)	1 (reference)
	Yes	404 (64.50)	1.60 (0.99-2.58)	1.50 (0.70-1.70)
Anxiety	No	219 (35.80)	1 (reference)	1 (reference)
	Yes	390 (64.10)	1.02 (0.67-1.54)	1.40 (0.90-2.50)

[a]After adjusting for number of surgeries
[b]Indicates statistical significance p<0.001

as with multiple surgeries, central nervous system hyperexcitability can alter the synaptic connections between the nociceptors and the neurons of the spinal cord, which may lead to persistent pain [16]. TMJ implant patients who had undergone multiple surgeries report persistent pain not only localized to the overlying surgical regions of the preauricular region, but often diffused to distant regions of the head, neck, upper back, and upper extremities indicating central sensitization [17]. Pain is often reported by TMJD patients at other body sites [18]. For example, TMJD pain has been frequently observed with fibromyalgia [19-21]. Central sensitization has been implicated in several chronic pain states such as fibromyalgia, low back pain and headache [22]. A prospective cohort study has also shown the persistence of clinically significant TMJD pain related to fibromyalgia and depression [23]. The main finding of this present study is association between number of TMJ surgeries and persistent pain. However, when adjusted for number of surgeries, the association between implant surgery and persistent pain did not remain statistically significant, consistent with results of a number of prospective studies [24-26]. The majority of subjects reported persistent pain suggesting that chronic pain is common among TMJ surgery patients or our sample population was skewed towards patients with delayed recovery. Pain is often reported by TMJD patients at other body sites [18]. For example, TMJD pain has been frequently observed with fibromyalgia [19-21]. A prospective cohort study has also shown the persistence of clinically significant TMJD pain related to fibromyalgia and depression [23]. Comorbidities were associated with persistent pain independent of type and number of surgeries. Interestingly, the increased odds of persistent pain remained when the model was adjusted for depression, anxiety, and number of comorbid conditions. This study confirms previous reports of comorbidities between TMJD and headache, low back pain, and rheumatoid arthritis [27,28]. Thus, numbers of surgeries are related to persistent facial pain irrespective of comorbidities. Indicating that central sensitization is the main mechanism for persistent pain in this study population. This case control study examined the distribution of persistent pain among a cohort of TMJ implant patients. Similar to other reports, we observed an association between persistent pain and number of surgeries. However, it was not possible to address the mechanisms by which numbers of surgeries were related to persistent pain in this retrospective analysis. Similarly, other limitations include the temporal relationship between the exposure and outcome variables, and absence of concomitant medication use which might have influenced the pain pattern. Further prospective studies are needed to better understand mechanisms of tissue injury and persistent pain.

Ethical Approval

The protocol was approved by the University of Maryland, Baltimore Institutional Review Board for Human Subjects Research.

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