Patients profiles and outcomes of care in temporomandibular disorders

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CHAPTER 1

General Introduction

Temporomandibular disorders (TMDs) are a collective term for pain and dysfunction of the masticatory muscles and temporomandibular joints (TMJs) [1]. TMDs are regarded as the second most common cause of orofacial pain, following odontogenic pain [2,3]. The prevalence of TMDs in an adult population is estimated to be around 18% [4]. Furthermore, based on the Orofacial Pain Prospective Risk Evaluation and Assessment (OPPERA) prospective cohort study in the USA, the average incidence of first onset painful TMDs is about 4% per year [5].

Temporomandibular joint osteoarthritis (TMJ OA) is one of the subtypes of TMDs and the most common form of arthritis occurring in TMJs [6,7]. TMJ OA has an estimated prevalence of about 4-5% in the general population [8-10], while that in TMD patients ranges up to 22% [11-13]. Chronic orofacial pain is the main symptom of TMDs, including TMJ OA, and also the main reason for TMD patients to seek treatment [14]. Chronic orofacial pain is generally defined as a pain that occurs for at least 15 days during each month for more than 3 months [15,16]. The pain is either continuous or occurs in episodes lasting for more than 4 hours each time [15,16]. Disc displacement (DD) is one of the most common internal derangement of TMJs, which is caused by a disc displaced from its normal position between the condyle and the articular eminence [17]. The prevalence of DD in the general population is around 8% [10], while that in TMD patients ranges from 38% to 73% [13,18,19].

Diagnosis

In both clinical practice and research, TMDs and its subtypes are commonly diagnosed with dual-axis Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) or new dual-axis Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) [20,21]. The DC/TMD optimized the diagnostic algorithms of TMDs on the basis of RDC/TMD, which seems to be more applicable in the clinical practice and research [21-23]. However, in both RDC/TMD and DC/TMD, the validity for the diagnosis of a DD is inadequate without imaging [21,22]. For most cases, DD is a stable, pain-free, and lifelong condition of the joints, but in a small minority of patients, a DD may cause reduced mouth opening and may be associated with pain. Therefore, in case there is an urge of an objective diagnosis of a suspected DD, the presence of a DD needs to be confirmed by TMJ imaging. In clinical practice, Magnetic Resonance

Imaging (MRI) was so far described as the gold standard for diagnosis of DDs [24]. It is reported that the diagnostic accuracy of MRI is 95% and 93% in determining the disc position and bone changes, respectively, when compared to cryosectioning of TMJs [25]. However, MRI has several drawbacks in clinical practice. For example, MRI cannot be carried out in patients with pacemakers or metallic prosthesis, or in claustrophobic patients [26,27]. Also, the use of MRI is limited by the required centralized facilities, the high costs, and the long time it takes for scanning compared to other imaging modalities like computed tomography (CT) [27]. Therefore, more advanced imaging techniques are required for the diagnosis of DD. Ultrasonography (US) can be used for the visualization of the disc for both research purposes and patient care, which has gained increasing attention in the recent decades. Compared to other imaging techniques like MRI or CT, US is less expensive, less time-consuming, and easily accessible [28]. Besides, it can be used to directly observe the disc movement during opening and closing of the mouth, thus allowing the investigators to detect disc positions more accurately [29]. However, the interpretation of US is reported to be highly dependent on the operators, and the visualization of the disc with US is difficult, because the disc can be visualized only through the small gap between the zygomatic process of the temporal bone and the head of the condyle [24]. Also, the standardized diagnostic criteria of US for the diagnosis of DD have not yet been well-established. Therefore, despite an increasing number of studies focusing on the diagnostic accuracy of US for the diagnosis of DD, it is still controversial whether US has sufficient added diagnostic values over MRI and whether US can replace MRI for the diagnosis of DD in clinical practice.

Oral health related quality of life (OHRQoL)

Nowadays, OHRQoL is regarded as an important outcome measure for assessment of the effectiveness of dental treatment. Traditionally, effectiveness of dental treatment was usually based on objective clinical parameters such as success or failure. However, such a point of view does not take into consideration the patients' subjective expectations, experience or feelings. To illustrate, a partial prosthetic denture may be manufactured perfectly from a technical point of view, but the patient may not wear at all

because he/she feels painful or discomfortable when eating and speaking while wearing the denture. Patients' subjective evaluation, like OHRQoL, seems to be increasingly important for the assessment of the effectiveness of dental treatment. This is because patients' subjective evaluation can truly reflect patients' feelings of the effectiveness of treatment with regard to their own health. Clinicians' increasing importance placed on patients' subjective evaluation makes patients more active in the decision-making process of treatments, thus making the assessment of treatment effectiveness more comprehensive and patient-oriented [30]. The concept of "Quality of life (QoL)" is broad, diverse and dynamic over time, but the conceptualization that considers QoL on the basis of life satisfaction is the most recommended [31]. Health related quality of life (HRQoL) is one aspect of QoL, which specifically focuses on an individual's subjective experience which relates to health, disease, disability, impairment, and effectiveness of treatment [32]. The definition of OHRQoL by the National Institute of Health (NIH) is "a multidimensional construct that reflects people's comfort when eating, sleeping, and engaging in social interaction; their self-esteem; and their satisfaction with respect to their oral health" [33], which is a result of the interaction of oral health conditions, social and contextual factors, and the rest of the body [34].

Pain is a key symptom related to possible impairment of OHRQoL, not only because pain directly affects patients by hurting them physically, but also because patients with chronic pain are very likely to have a variety of psychosocial and behavioral comorbid conditions. This can negatively affect patients' interpersonal relationships with friends, family, and health care providers as well as patients' daily life, activities, and work [35,36]. Also, other clinical signs and symptoms of TMDs, including limitation of jaw movement, are thought to impair OHRQoL of TMD patients [36,37]. As such, OHRQoL was demonstrated to be negatively influenced among TMD patients based on a systematic review [38]. Barros Vde et al. reported that TMD patients with muscular disorders (Group I based on axis I of RDC/TMD) or TMJ OA (Group IIIb) had a greater impaired OHRQoL than those without muscular disorders or TMJ OA [39]. Reissmann et al. reported that patients with diagnoses of Group I (myofascial pain) or Group III (arthralgia, osteoarthritis, or osteoarthrosis) had a significantly worse OHRQoL than patients with a Group II (DD) TMD diagnosis, while there was no significant difference between Group I and Group III in OHRQoL [40]. He also re-

ported that compared with mean scores of OHIP-49 for general population subjects without any sign or symptom or for general population subjects without any RDC/TMD diagnoses, the score of OHIP-49 for patients with TMJ OA tended to be higher but without statistical significance [40]. John et al. reported that compared with the norms of OHIP-49 in the general population, the mean scores of OHIP-49 for all subtypes of TMDs based on the RDC/TMD except for DD with reduction was significantly higher [41]. This indicated that OHRQoL of patients with TMJ OA was significantly impaired. Therefore, it can be hypothesized that patients with pain-related TMD or osteoarthrosis (Group I and Group III of RDC/TMD) are more likely to have lower OHRQoL than patients with other subtypes of TMD. However, the studies that specifically focused on the effect of TMJ OA on patients' OHRQoL is scared [40,41].

Chronic pain and psychological wellbeing

It has been mentioned that patients with chronic pain are more likely to have psychological disorders than patients without chronic pain [35,36]. Chronic orofacial pain is highly prevalent in TMD patients. It is reported that the prevalence of orofacial pain in the general population ranges from 4.0% to 15.0% [42-45]. In TMD patients, it is reported that 12% of patients experienced a singular-episode of orofacial pain or headache, 65% experienced recurrent orofacial pain or headache, and 12% experienced persistent orofacial pain or headache [46]. Recently, several studies have found positive associations between pain-related disability and certain psychological problems like depression, somatization, sleep dysfunction, worry, and catastrophizing [47-49]. This may provide clinicians with some important clues in clinical practice that if TMD patients have severe pain-related disability, these groups of patients may be more likely to have psychological disorders. Therefore, clinicians should pay more attention to the psychological wellbeing of these patients and give them psychological support if necessary. However, the available information on the associations between pain intensity and psychological problems or on the association between pain-related disability and other psychological problems like stress, optimism, or daytime sleepiness in TMD patients is absent.

Management

Given the multidimensional nature of TMDs, recently, several types of physical and psychological treatments have been advocated for treating TMDs in clinical practice. Clinicians who manage patients' treatment should decide which type of treatments are most cost-effective and evidence-based, and which have the greatest potential to bring patients long-term symptom relief [50]. Based on international consensus reached in 1995 and 2010, reversible and conservative treatments should be recommended for the first-line intervention for TMD patients [51,52]. So, various reversible and conservative treatments like physiotherapy, splint, and psychological treatment have been adopted widely for most TMD patients. It has been shown that splints are beneficial for masticatory muscle pain, TMJ pain, TMJ noises, restricted jaw mobility, and TMJ dislocation in those who grind or clench their teeth at night [51,53]. Physiotherapy, which includes massage or targeted exercises, aims to decrease pain, enable muscle relaxation, reduce muscular hyperactivity, and re-establish muscle function and joint mobility [53,54]. Psychological treatment is also well-established nowadays as a supplemental treatment for TMD patients with possible psychological disorders to relieve their pain and improve their psychological wellbeing [55,56]. However, not all types of treatments are equally effective for all patients. Therefore, clinicians' decision-making of which treatment is optimal for which groups of individual patients, is of great importance. As such, the process of clinicians' decision-making is complicated and influenced by multiple factors, including patient and disease characteristics, the clinicians' knowledge, profession traditions, clinical judgment, clinical routines, and even clinicians' psychological status [57]. As the number of subjective factors that goes into formulating a treatment plan increases, the possibility of inaccuracy and variability in clinical decision-making among clinicians increases [58], which may negatively affect patients' health and clinicians' reputation. Therefore, a standardized model, driven by valid data from patient care which are objective and easy-to-collect, is necessary to develop in order to make the process of decision-making more standardized, transparent, accurate, and easier for clinicians.

Although reversible and conservative treatments are recommended for most TMD patients, there is a small proportion of patients who may require a surgical intervention [59]. One surgical intervention is arthrocentesis, which is a simple and minimally

invasive procedure with the purpose of removing inflammatory and pain mediators from the joint cavity, simply by intraarticular injection of saline [60,61]. Arthrocentesis is widely used as a treatment option for various types of TMDs, including TMJ OA [62]. Hyaluronic acid (HA) is one of the components of synovial fluid (SF), which is related to the physical and functional features of TMJs [63] and has an important role in impairing the lubricating properties of SF and the cartilage in the TMJs [64,65]. Several previous studies have shown that arthrocentesis with HA is safe and can reduce orofacial pain in patients with TMJ OA [62,66-68]. Besides, oral medication is regarded as a supplement treatment to reduce orofacial pain and improve jaw functions [69]. Glucosamine has recently been suggested to relieve the symptoms of patients suffering from OA by supplying the components for cartilage repair, thus alleviating pain and disability [70]. For TMJ OA, oral glucosamine hydrochloride (GH) can be regarded as a supplement to other types of treatment [7]. Li et al. compared the effectiveness and safety between an intervention group (combined oral GH and arthrocentesis with HA injections) and a control group (combined oral placebo and arthrocentesis with HA injections) for TMJ OA patients based on a randomized controlled trial [62]. The study found that the intervention group had significantly larger improvement in maximal mouth opening and pain on opening than the control group [62]. Additionally, no serious drug events were detected in both groups, and patients' OHRQoL was equally improved in both groups [62]. However, the studies assessing the effectiveness of oral GH for TMJ OA are still scarce [62]. Furthermore, no studies focused on how oral GH with arthrocentesis with HA affects the OHRQoL of TMJ OA patients in short and long term after the treatment. In addition, arthrocentesis with HA is a widely used treatment for TMJ OA, but it is invasive and not always effective for improving chronic orofacial pain for all patients with TMJ OA. So, in clinical practice, it is very important for clinicians to predict whether the OHRQoL of individual patients can be improved after completion of arthrocentesis with HA.

Aim and structure of thesis

The purpose of the present thesis is to increase the currently available knowledge about patient profiles and outcomes of care in TMDs. To this end, the following studies will be performed:

The aim of the study in ***Chapter 2*** is to assess the effect of arthrocentesis with HA injections, combined with orally administered GH, on short and long-term OHRQoL, in patients with TMJ OA. The OHRQoL of patients with TMJ OA is recorded at baseline, at the first month, third month, and sixth month after baseline using the Chinese version of the 14-item Oral Health Impact Profile (OHIP-C14). Possible changes in OHRQoL across these time points are assessed.

The aim of the study in ***Chapter 3*** is to assess the association between OHRQoL and severity of clinical symptoms and signs in patients with TMJ OA. The patients' OHRQoL is assessed with the OHIP-C14. The severity of clinical symptoms and signs of the patients is assessed with the Helkimo clinical dysfunction index (HDI).

The aim of the study in ***Chapter 4*** is to develop two prediction models for OHRQoL in patients with TMJ OA one month and six months after arthrocentesis with HA injections. Patient characteristics and history data, outcomes of clinical examinations, and questionnaire data are recorded at baseline as potential predictors in the models. Patients' OHRQoL at one and six months after completing treatment is regarded as the outcome in both models. Logistic regression analyses are used to develop the prediction models.

The aim of the study in ***Chapter 5*** is to assess the association of several psychological and socio-demographic factors with pain intensity and pain-related disability in TMD patients. The psychological status of patients is assessed with several questionnaires including the 7-item general anxiety disorder (GAD-7) for anxiety, the 15-item Patient Health Questionnaire (PHQ-15) for somatization, the 9-item Patient Health Questionnaire (PHQ-9) for depression, a 7-item questionnaire for stress, the Epworth Sleeping Scale (ESS) for daytime sleepiness, and the Life Orientation Test-Revised (LOT-R) for optimism. The pain intensity and pain-related disability of patients are assessed with the characteristic pain intensity (CPI) scale and disability points from the Graded Chronic Pain Scale (GCPS), respectively.

The aims of the study in ***Chapter*** 6 are twofold. The first aim is to identify which potential predictors in patient profiles are significantly associated with the types of treatment indicated for TMD patients. In this aim, the differences and similarities of predictors that are associated with different types of treatment are found out and compared. The second aim is to derive weights of the predictors and then develop

a clinical prediction model to predict types of treatment indicated for future TMD patients in clinical practice. Patients' characteristics and disease characteristics are recorded at baseline as the potential predictors of the model. Types of treatments including no treatment (NT), physical treatment only (PTO) including splint and/or physiotherapy, and combined physical and psychological treatment (CPPT) are regarded as the outcomes of the model. Multinomial logistic regression analyses are used to identify the similarities and differences of predictors in patient profiles for differentiation of types of treatment indicated for TMD patients and are used to develop a prediction model for types of treatment indicated for TMD patients.

The aim of the study in ***Chapter 7*** is to assess the added diagnostic value of ultrasonography (US) for detection of disc displacement (DD) in the temporomandibular joints (TMJs) based on a systematic review. Pubmed and EMBASE are searched electronically to identify diagnostic accuracy studies that assessed the diagnostic value of US for the diagnosis of DD, using MRI as the reference standard. Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) is used to assess the risk of bias of the included studies. Meta-analyses are performed with Metadisc 1.4 and RevMan 5.3.

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