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Faculty of Medicine, University of Tartu, Tartu, Estonia.

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Contribution of Oksana Jagur to original publications:

Paper I: Study design, data collection and analysis. The author wrote the manuscript.

Paper II: Study design, data collection and analysis. The author wrote the manuscript.

Paper III: Clinical evalution and treatment of patients. The author was one of the writers of the manuscript.

Paper IV: The author was one of the writers of the book chapter.

2. LIST OF ABBREVIATIONS

ADL	Activities of daily living
BMD	Bone mineral density
CT	Computed tomography
CTX-1	C-telopeptide crosslaps of type I collagen
DXA	Dual energy X-ray absorptiometry
FT- score	Femur neck T-score
5-HT	5-hydroxytryptamine, serotonin
IQR	Interquartile range: the numerical difference between the 75 and 25 percentile
LT-score	Lumbar T-score
MIO	Maximal interincisal opening
MRI	Magnet resonance imaging
NSAID	Non-steroidal anti-inflammatory drug
OA	Osteoarthritis
OPTG	Orthopantomography
P1NP	Procollagen type I N-terminal propeptide
SD	Standard deviation
TMJ	Temporomandibular joint
TMD	Temporomandibular joint disorders
VAS	Visual analogue scale
WHO	World Health Organization

3. INTRODUCTION

Temporomandibular joint disorders (TMD-s) present an important health problem. It has been estimated that approximately 20% to 30% of the adult population will experience temporomandibular joint (TMJ) dysfunction (Guo et al. 2009).

The common signs and symptoms include facial and jaw pain which can be aggravated by jaw movements, TMJ sounds (clicking or crepitus) and restriction of mandibular movements. Radiological investigation often shows the displacement of the disc from its normal location, or osteoarthritic changes in the articular portion of the temporal bone or condyloid heads. Patients with TMD can experience significant reductions in quality of life, affecting both personal life and work; everyday activities such as eating, talking, yawning, and laughing can become painful (Voog et al. 2003a, Bessa-Nogueira et al. 2008). Contemporary researchers focus on the role of biochemical mediators in development and progression of TMJ pain and dysfunction. There has been found association between some bone markers and TMD (Israel et al. 2006, Vlasiadis et al. 2008). Several biochemical markers of bone turnover can be used to predict individual bone loss on risk for TMJ pathologies (Garnero et al. 2003).

The globally increasing prevalence of TMD calls for a more detailed knowledge of the relationship between bone markers and Vitamin D in the pathogenesis of TMJ disorders. As Estonia is situated in Northen Europe the local population has a high risk for D-hypovitaminosis (Kull et al. 2009). There is still a lack of the knowledge of the specific impact of TMJ pain on daily activities in patients with clinical involvement of the TMJ. Hopefully, the new knowledge of the TMJ etiopathogenesis will help predict TMJ bone destruction. Additional vitamin D consumption might be suggested to avoid TMJ dysfunctions and thereby reduce pain level. A multidimensional understanding of the aetiopathogenesis of TMJ pathologies detected at an earlier stage would help improve diagnostics and apply evidence-based treatment.

4. REVIEW OF LITERATURE

4.1. Temporomandibular joint disorders and pain.

4.1.1 Temporomandibular joint (TMJ)

The temporomandibular joint is the articulation between the mandible and the cranium. The mandibular head (condyle), glenoid (mandibular) fossa, and articular eminence form the TMJ. These joints serve as one anatomic unit to control for both mandibular movement and occlusion, and are surrounded by a capsule, consisting of cells of endothelial origin, producing synovial fluid (Figure 1).

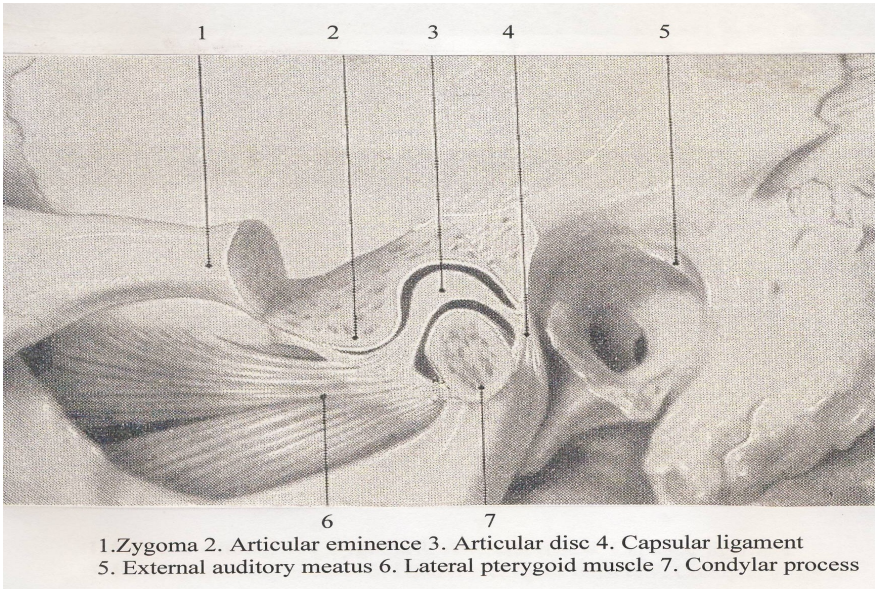

Fig. 1. A sagittal section of the left temporomandibular joint (by H. Stones, 1964).

The connective tissue capsule is reinforced by the strong lateral temporomandibular ligament and the medial ligament, incomplete at the medioanterior half of the joint. The articular disk divides the joint into two non-communicating compartments. It is composed of the fibrous connective tissue and the biconcave in shape with a thin intermediate zone bounded by thicker anterior and posterior bands. The disc is attached to the articular capsule anteriorly, medially, and laterally. Posteriorly, it is anchored to the tympanic plate and the condyle by the retrodiscal tissue which is highly vascular and innervated loose connective tissue. The joint extends posteriorly from the squamotympanic and petrotympanic fissures to the articular tubercle anteriorly.The articulating surfaces are covered with the fibrocartilage and the synovium lines the joint cavity.

The muscles of mastication are responsible for the complex movement of the jaw. The temporal, medial pterygoid, and masseter muscles facilitate jaw closure. Mouth opening is effected by the coordinated action of the lateral digastric, mylohyoid, and suprahyoid muscles (Oberz et al. 2006).
The lateral pterygoid muscle and part of the fibers of the masseter and medial pterygoid muscles effect the anterior translation of the mandible. The superior belly of the lateral pterygoid muscle originates from the greater sphenoid wing and inserts on the disc. Subsequently, the superior belly plays a key role in upholding the physiologic position of the disc as it pulls the disc forward when the jaw is opened, in a combined translation and rotation. The inferior head of the lateral pterygoid muscle stretches from the lateral lamina of the pterygoid process to the pterygoid fovea. The medial pterygoid muslcle originates from the pterygoid fossa and inserts near the medial aspect of the mandibular angle (Sommer et al. 2003).

The blood supply to the TMJ and to the outer and inner ear is provided mainly by branches from the internal maxillary artery as follows: temporal superficial artery,superior auricular artery, anterior tympanic artery and pterygoid artery. Innervation is provided by the auriculotemporal nerve (sensory branch of the mandibular nerve), deep temporal nerve and masseteric nerve (Figure 2). Sensory cervical sympathetic ramifications enter the disc and the capsule. Nerve receptors as the Ruffin receptors, the Golgi tendon organs and the Vater-Pacini corpuscules free nerve endings are in the capsule and substance P nerve fibres are also available in both the auriculotemporal and masseteric nerves, and have been demonstrated in the capsule and in the disc attachments but they are not present in the disc (Bumann et al. 2000).

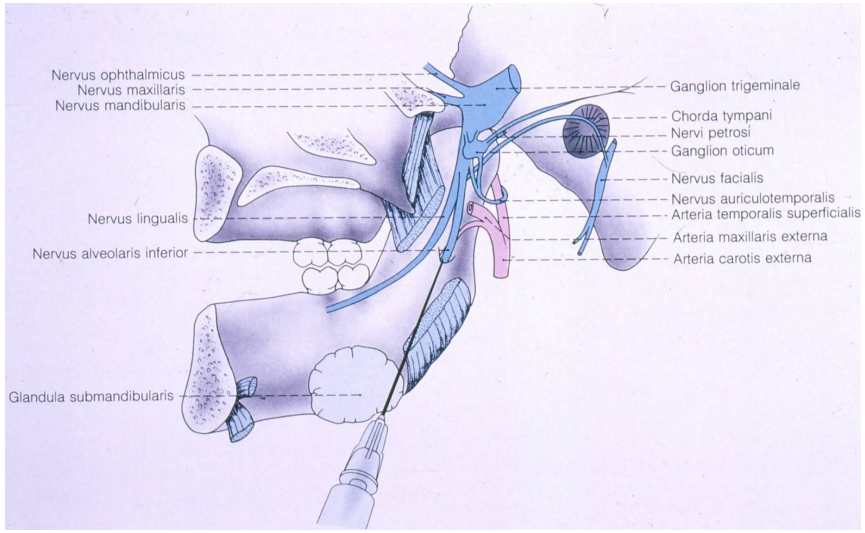

Fig. 2. Branches of the trigeminal nerve. Innervation and blood supply of the temporomandibular joint (by R. Schmelzle, 1989).

4.1.2 TMJ pain

Pain in the jaw musculature is the most commonly reported pain of nondental origin in the orofacial region (Okeson 2003).The TMJ pain is common among all age groups (Helkimo 1974). Chronic craniofacial pain conditions with a prevalence of approximately 10-15% are increasing in the adult population (Dworkin et al. 1990, LeResche 1997, John et al. 2005). The prevalence of TMJ pain across lifetime is still debated but there seems to be a peak of the pain at approximately 45 years of age for women, although also elderly people may suffer from TMD pain (Svensson et al. 2008). Pain is commonly accompanied by stiffness, sounds and functional limitations which result in a decreased quality of life, and thus exert a significant negative impact on activities of daily living. Many patients experience sleep disturbances, disruptions, decreased physical functioning, interference with activities of daily living, decreased productivity, increased anxiety and depression, and decreased quality of life (Katz et al. 2010). These clinical symptoms and signs in the TMJ produce an impact not only on specific aspects of daily living but also on the patients´ social life in general (De Boever et al. 2000, Voog et al. 2003a). Pain is always a subjective experience, and the impact of chronic pain is not just a sensory experience but also an emotional experience (Kelley et al. 1997, Thomas 2000, Tjakkes et al. 2010). Chronic pain may be nociceptive, neuropathic, ischemic, visceral or exhibit a combination of different aetiologies. Nociceptive pain may result from the stimulation of nociceptors at the nerve endings and is characteristically present in TMDs. Stress, somatic distress, and depression may be potential aetiological risk factors for TMDs related pain. In chronic pain, psychological factors may become more obvious and prominent (Zakrzewska et al. 2002).

Impairment in patients with arthritis is reflected in pain and restriction of a range of motion, while disability is reflected in difficulties in performing activities of daily living, according to the data of World Health Organisation (WHO 1980).

4.1.3. Temporomandibular joint disorders (TMD)

Temporomandibular joint disorders refer to several clinical conditions that involve muscles of mastication and TMJ or both (Keller et al. 2012). Also TMD are associated with disc displacement (Barkin et al. 2000).

The aetiology of TMD is multifactorial, being related to factors such as stress, muscle hyperactivity, arthrogenous factors, parafunctions or the anatomy of the TMJ (Yáñez-Vico et al. 2012).

The knowledge of the pathogenesis on a molecular level of disorders of the TMJ has been improved by allowing a possibility to use these data for the evidence-based treatment (Holmlund & Axelsson 1996, Kumagai et al. 2010, Guarda-Nardini et al. 2012).

Signs and symptoms of TMD may include pain, impaired jaw function, malocclusion, deviation or deflection, limited range of motion, joint noise, and locking. Headache, tinnitus, visual changes, and other neurologic complaints may also accompany TMD. It has been found that 28% of the adult population have signs of temporomandibular joint disorder, with higher prevalence in women at reproductive ages (LeResche 1997, Bagis 2012, Rezaii et al. 2012, Sipila et al. 2013). Women report more pain, TMJ pain of longer duration, higher clinical and experimental pain intensity, and lower pain thresholds (Rezaii et al. 2010).

Together with arthralgia of the temporomandibular joints it is collectively referred to as 'temporomandibular disorder'(Okeson 2003).

TMD can be classified as:

- Arthritis- acute, chronic, infectious (specific, nonspecific)
- Osteoarthritis (OA) – most frequent disorder
- Injuries – luxations, concussion, fracture
- Ankylosis (fibrous, fibro-osseous, osseous)
- Tumours (benign and malignant)
- Congenital disturbances: I & II branchial arch malformations, condylar hypo- hyperplasia
- Idiopathic condylar resorption
- Systemic conditions affecting the TMJ

The TMJ involvement occurs in systemic rheumatic diseases (rheumatoid arthritis, psoriatic arthritis etc.; Voog et al. 2004a), secondary from the neighbouring regions (otitis, maxillary sinusitis, tonsillitis), trauma (chronic), prevalence of dental arch defects e.g. missing of molar teeth, malocclusion, endocrinological disturbances, odontogenic infections (Tallents et al. 2002).
Many specific bacteria and several inflammatory mediators play an important role in the pathogenesis of TMJ diseases (Kim et al. 2003, Voog et al. 2003b, Hamada et al. 2008). These inflammatory mediators drive catabolic pathways, inhibit matrix synthesis, and promote cellular apoptosis. All bone loss at the TMJ condyle involves a common resorptive pathway: cytokine-activated osteoblasts promote the recruitment and activity of osteoclasts, which in turn, results in the secretion of enzymes that are responsible for the breakdown of hydroxyapatite and collagen (Gunson et al. 2012).

The most common form of TMJ arthritis is osteoarthritis. It is one of the few chronic diseases that involves TMJ (Lee 2012). The OA can be classified as primary (unknown causes) and secondary (local and systemic causes). Primary OA is considered idiopathic due to the absence of identical local or systemic aetiologic factors. In secondary OA, systemic causes are related to ethnicity, hormonal status, nutritional factors, genetics and bone metabolism, whereas local causes include obesity, mechanical environment, overloading of articular cartilage and acute joint injury (Jordan 2000, Kang 2007).

Most scientists regard osteoarthritis as an inflammatory process, being the most frequent TMJ disorder, characterized by proliferative changes in the syno-

via and primary degeneration of the cartilage and surrounding tissues with destruction of the bone structures (Holmlund and Axelsson 1996; Emshoff 2005). Nowadays, it is increasingly recognized that OA is a disease of the whole joint that affects all articular structures, including articular cartilage, subchondral bone, synovium, tendons, ligaments and menisci. The role of bone and articular soft tissues in the pathophysiology of OA has been widely overlooked (Brandt et al. 2003).

4.1.4. Activities of daily living (ADL) and the visual analogue scale (VAS)

The impact of pain on the health status and quality of life in patients with chronic inflammatory joint diseases has been recognized, but there is a lack of knowledge about the specific impact of TMJ pain on daily activities in patients with clinical involvement of the TMJ (Voog et al. 2003a).

Assessment of the individual level of daily activities is important in the evaluation of TMD. There are several scales for assessing patients´ TMJ functions and for describing the particulars of their disability and the fact how their current status reflects in their day to day activities. The term „activities of daily living“(ADL) has been used to denote activities undertaken as part of person´s daily functions (Bucks et al. 2002).

The ADL scale by Katz S et al. (1963) was primarily designed to measure the ability to carry out every day activities necessary for daily living. It has been validated and modified for specific use in patients with TMJ disorders (List et al. 1995, Voog et al. 2003a, Kaselo et al. 2007, Karibe et al. 2012).

The visual analogue scale (VAS) is a single-item scale to measure pain intensity (McCormack et al. 1988). The VAS is a continuous scale comprised of a horizontal or vertical line, usually 10 centimeters (100 mm) in length, anchored by 2 verbal descriptors, one for each symptom extreme. For pain intensity, the scale is most commonly anchored by “no pain” (score of 0) and “pain as bad as it could be” or “worst imaginable pain”(score of 100 [100-mm scale]; Burckhardt et al. 2003, Hawker et al. 2011).

The VAS was initially used in psychology by Freud in the early 1900s and was elaborated in rheumatology through a series of investigations by Huskisson et al in the late 1970s (Sokka 2003).

The scale has a high degree of sensitivity and validity because slight changes in pain intensity can be detected, however it can also be confusing in a way for both very young and elderly patients (Gagliese et al. 2005, Williamson et al. 2005). The VAS scale has been used in several TMJ studies (Ahn et al. 2011, Rusanen et al. 2011, Edefonti et al. 2012, Guarda-Nardini et al. 2012).

4.2. Radiographic imaging

Radiographic examination is commonly used for assessment of TMJ problems. Radiographic changes of the TMJ can be evaluated by orthopantomography, computed tomography and magnet resonance imaging (Ohnuki et al. 2003; Whyte et al. 2006) among other techniques, as well as by ultrasonography (Landes et al. 2007).

4.2.1. Orthopantomography (OPTG)

Orthopantomography (OPTG) is commonly used for assessment of bone changes in the TMJ. By evaluating OPTGs the following radiographic signs of bone structural changes can be detected, such as presence of erosions, flattening and osteophytes of the TMJ condyle as well as of temporal bone (Rohlin et al. 1986). Repeated assessments of radiographic changes provide a measure of the rate of progression (Sharp et al. 1989), which is important since progression of radiographic signs of joint damage can continue even despite well-planned general treatment (Gordon et al. 2001).

Many oral indices measured on OPTGs, such as the number of teeth present, alveolar bone resorption, mandibular bone mineral density (BMD), lamina dura width, cortical thickness of the mandible and morphology of the mandibular inferior cortex, may prove useful screening implements for low-skeletal BMD or increased risk for osteoporotic fractures (Leibur et al. 1995, Jeffcoat 2000, Jonasson et al. 2001, Krejc et al. 2002, Hardanti et al. 2011). The studies have shown that mandibular cortical shape on OPTG-s may be an indicator of bone turnover and spine BMD (Balcikonyte et al. 2004, Vlasiadis et al. 2007, Taguchi et al. 2009, Hastar et al. 2011). The most visible radiographic sign in the TMJ by OPTG is erosion.The mandibular cortical erosion has been significantly associated with increased N-telopeptide cross-links of type I collagen and alkaline phosphatase levels (Taguchi et al. 2003, 2006).

Recent investigations have shown that radiographic examination including OPTG may be an effective tool as primary changes appear most earlier in alveolar bone for the early diagnosis of osteoporosis (Bonnick et al. 2006, Jagelaviciene et al. 2006, Miliuniene et al. 2008, Vlasiadis et al. 2008, Khatoonabad et al. 2011).

4.2.2. Computed tomography (CT)

The first report of TMJ computed tomography (CT) was published by Suarez et al. (1980) and this method is superior to plain transcranial or transmaxillary imaging for detecting bone changes. CT allows detailed three-dimensional examination of the TMJ and it is capable to detect even small bone changes not demonstrable by conventional tomographic procedures (Larheim et al. 1990, 2001, Lee et al. 2012).

According to Rohlin and Petersson (1989): the changes can be investigated by CT as follows: erosion – a local area with decreased density of the cortical joint surface including or not including adjacent subcortical bone, sclerosis – a local area with increased density of the cortical bony joint surface that may extend into the subcortical bone, subchondral pseudocyst – a well defined local area of bone rarefication underneath an intact cortical outlining of the joint surface and flattening – a flat bony contour deviating from the convex form osteophyte – a marginal bony outgrowth. The CT allows to diagnose TMJ fractures, ankylosis, dislocation, neoplasms and growth abnormalities such as condylar hyperplasia (Barghan et al. 2012).

4.2.3. Dual energy X-ray absorptiometry (DXA)

Dual-energy X-ray absorptiometry (DXA) based densitometries were introduced in the 1980s. In Estonia the technology has been available since 1997 (Kull et al. 2009). The DXA is the best biophysical way to assess bone in clinical practice. It has been recommended by the International Osteoporosis Foundation to measure BMD by the DXA of the hip and lumbar spine (Baim et al. 2008, Kanis et al. 2008). For interpretation and aiming to reduce intermanufactural differences, the makers of DXA machines have implemented a derived measurement of bone density called the T-score, which is calculated using the peak bone mass of a young reference population and is expressed as a difference in standard deviation (SD) from the mean of young healthy adults. The WHO originally defined osteoporosis as a lumbal spine (L1-L4) or femur neck T-score of -2,5 SD below the mean of a young healthy population (WHO Study Group et al. 1994). Such recommendations are based on large prospective studies which have demonstrated that using of multiple regions and diagnosing by the lowest T-score does not improve fracture prediction when measured as a gradient of risk per standard deviation change (Kanis et al. 2006). In clinical practice DXA is the most commonly used technique for measurement of areal bone density (g/cm²) and it is a reliable method to examine BMD also in the mandible (Karayianni et al. 2007).

There are several studies dedicated to osteoporosis evaluating the data of the BMD of the lumbar spine in relation with mandibular cortical thickness. The data about the relationship are controversial. Some authors found relationship between skeleton BMD and mandible BMD (Horner et al. 1996, 1998, Taguchi et al. 1996, Jeffcoat 2005, Miliuniene et al. 2008) and between BMD and interproximal bone loss (Tezal et al. 2000), while other authors did not (Mohajery et al. 1992, Yasar et al. 2006). A significant relationship has also been found between mandibular bone mass, structure and thickness (Jonasson et al. 2007). Relationship has been shown between BMD and TMJ bone loss, periodontal diseases and tooth loss (Dervis et al. 2005, Jagelaviciene et al. 2006).

Until now, no studies has been performed to define the relationship between BMD and the TMJ bone status.

4.3. Bone markers, Vitamin D and Osteoporosis

4.3.1. C-telopeptide crosslaps of type I collagen (CTX-1) and procollagen type I N-terminal propeptide (P1NP)

Although several markers have been described to measure bone metabolism, it has been difficult to differ between the different mechanisms of bone resorption. These assays measure, in serum or in urine, enzymes or matrix proteins synthesized or degraded by bone cells (Garnero et al. 2003).

C-telopeptide crosslaps of type I collagen (CTX-1) and C-terminal telopeptide of type I collagen (1CTP) are currently considered the most sensitive markers of bone resorption and are released from bone by different enzymatic pathways. The CTX-1 is generated by cathepsin K, which is the key osteoclastic enzyme for systemic bone resorption. In contrast, 1CTP is generated by matrix-metalloproteinases whose activity plays an important role in collagen degradation associated with systemic inflammatory disease (Chopin et al. 2008).

Procollagen type I N-terminal propeptide (P1NP) is a sensitive marker of bone formation. P1NP is synthesized by osteoblasts from type I procollagen precursor proteins. These precursors have large extension domains at both ends. While type I collagen is being synthesized, type I aminoterminal and carboxy-terminal propeptides, PINP and PICP, respectively, are enzymatically removed and released into the circulation (Calvo et al. 1996). As bone is the major organ synthesizing type I collagen, PINP and PICP reflect bone formation (Delmas 1992).

Bone markers provide information beyond that of a single bone density measurement and on the cellular process leading to bone loss (Åkesson et al. 1993). However, some of the few studies have not reported relationship between biomarkers and BMD (Cosman et al. 1996). Used in combination with bone density, biochemical bone markers are more predictive of fracture and may strengthen indication for treatment. Serum bone biomarkers are associated not only with systemic BMD loss but also with alveolar bone loss (Payne et al. 2011). There are not enough data about the bone characteristics of patients with TMJ disorders. There still remains the question whether osteopenia in the TMJ area of the mandible is a local manifestation of osteoporosis having similar aetiology and risk factors, or it is an independent process depending primarily on factors that cause bone structural changes in the TMJ (Khatoonabad et al. 2011).

All this points to the need for additional studies which would evaluate the influence of potential contributing factors to further define the relationship between bone markers and TMJ disorders in population.

4.3.2. Vitamin D

Vitamin D plays also an important role in calcium and bone metabolism. The main circulating vitamin D metabolite is the 25(OH)D and it is used as an

indicator of vitamin D status. The 25(OH)D has been found to inhibit cytokine production and cell proliferation in various tissues (Dietrich et al. 2004). Low levels of vitamin D lead to compensatory elevation of parathyroid hormone, which can cause lowering of BMD and eventually osteoporosis (Kwon et al. 2007, Annweiler et al. 2009b). Vitamin D is related to musculoskeletal functioning and has been associated with a lower incidence of several cancers and autoimmune diseases. Studies have also shown that vitamin D has a role in neuromuscular function (Bischoff-Ferrari et al. 2001, 2004a,b, 2006).A majority of studies examined the association between serum 25(OH)D concentration and physical performance in community-dwelling older adults (Bischoff-Ferrari et al. 2004a, 2004b, Dukas et al. 2005, Gerdhem et al .2005, Houston et al. 2007, Annweiler et al. 2009a, 2009b, 2009c). In particular, elderly people are at a higher risk of vitamin D insufficiency but it affects all age groups (Chapuy et al. 1996, 1997, Lappe et al. 2006). Low levels of 25(OH)D in young people can be partly explained by inadequate dietary sources and low activity in the daytime. It is estimated that vitamin D inadequacy is present in 36% of healthy young adults and in 57% of general medicine inpatients in the United States (Holick et al. 2006, 2007). Vitamin D insufficiency seems a common health problem for people who live in countries at high latitudes where sunshine hours are short in the winter. Also Vitamin D levels are affected by modifiable and non-modifiable factors such diet, time outdoors, skin pigmentation, sunbathing habits, medications (Sherman et al. 1990, Budak et al. 2004, Bolek-Berquist et al. 2009).

Limited clinical research has focused on the specific effects of vitamin D deficiency on jaw pain. It is reported that vitamin D deficiency can cause predisposition to TMJ disorders (Abdel-Fattah 1992).A number of studies have addressed the relationship between sex hormones and TMDs and between low levels of vitamin D and pain all over the body but have not described the relationship between vitamin D and TMDs.

4.3.3. Osteoporosis

Osteoporosis is one of the most common human bone diseases affecting millions of people, including over one-third of females above the age of 65 years. Osteoporosis in generally characterized by low bone mass and micro-architectural deterioration of bone tissue, with increase in bone fragility and susceptibility to fracture. According to the World Health Organization, osteoporosis is considered to be present when BMD is 2.5 SD below the young normal. Osteopenia is defined as bone density levels between 1 SD and 2.5 SD below normal BMD. Osteopenia is a reduction in bone mass due to imbalance between bone resorption and formation, favoring resorption, resulting in demineralization and leading to osteoporosis (Wactawski-Wende et al. 1996). The risk factors for osteoporosis can be divided into non-modifiable and modifiable risk factors. The non-modifiable risk factors include sex, age, early menopause, thin or small

body frame, race, and heredity. Lack of calcium intake, lack of exercise, smoking, and alcohol consumption are the modifiable risk factors. Peak adult bone mass is reached at about the age of 35 years for cortical bone and a little earlier for trabecular bone. Bone mass subsequently declines with ageing. This is an universal phenomenon, occurring in both sexes and in all races. Women have less bone mass than men. With ageing this difference becomes more pronounced (Hardanti et al. 2011).

The association between osteoporosis and oral bone disease was found already in 1960 (Groen et al. 1960). Osteoporosis can affect all craniofacial and oral structures (Aggarwal et al. 2012). Osteoporosis is reported to cause bone loss in the alveolar processes of the maxilla and the mandible, which provide bony framework for tooth anchorage (Wactawski-Wende et al. 2005).

Some researchers have investigated whether dental radiographs could play a role in the detection of individuals with osteoporosis (Nackaerts et al. 2008). Bone mass in the jaw might be related to that of other skeletal sites in which osteoporosis was a significant problem (Kim et al. 2004, Hua et al. 2009). The association between systemic osteoporosis and oral health remains controversial (Makker et al. 2012) while studies in this area are limited. Therefore, the relationship between systemic osteoporosis and oral health is still a complex problem of great interest for a large number of researchers and clinicians. Some epidemiological studies found that non-osteoporotic women´s mandibular bone mass was not affected by age but was significantly associated with skeletal bone mass at the spine and wrist. The trabecular pattern was a highly significant predictor of future skeletal fracture risk (Jeffcoat et al. 2000, Jonasson et al. 2011).

Biochemical markers of bone turnover can be used to predict individual bone loss and therefore, they may help to alert patients to the risk of pathologies in the TMJ (Vlasiadis et al. 2008). Thus, studies which evaluate the above mentioned contributing factors to define relationship between TMJ pain and several bone characteristics and ADL in population are justified.

4.4. TMJ arthroscopy

Although some patients with TMJ disorders are successfully treated by nonsurgical means or by arthrocenthesis, there is still a group of patients who do not respond to these procedures and for whom an arthroscopic surgery is necessary. Arthroscopy is an important diagnostic and therapeutic modality in the treatment of TMJ disorders being an alternative to arthrotomy (“open” TMJ surgery). It can be very effective in eliminating symptoms as pain and mandibular dysfunction, increasing the mandibular range of motion for approximately 80% of patients, as well as acute and chronic “closed lock” due to osteoarthritis and adhesive capsulitis, where nonsurgical treatment has been unsuccessful. (Barkin et al. 2000, Ohnuki et al. 2003, Gonzalez-Garcia et al. 2008).

Arthroscopy is a technique for direct visual inspection of internal joint structures, including biopsy and other surgical procedures performed under visual

control, giving a possibility to diagnose degenerative changes in TMJ earlier than other techniques (Holmlund et al. 2001, Herb et al. 2006). The progress in the research and applications of TMJ arthroscopy in joint disease has led to the acceptance of small operative procedures as a safe, minimally invasive means to effectively treat a number of intra-articular and degenerative TMJ problems (McCain 1992, Holmlund et al. 1996, 2001, Thomas et al. 2012).

Arthroscopy was first described by Takagi in 1939. Onishi in 1970 was the first to perform arthroscopy of the human TMJ and the first results were published by him in 1975 (Onishi 1975, 1980). Murakami and colleagues (1984) described the scientific and clinical considerations of TMJ arthroscopy.

It has been shown that during arthroscopy several inflammatory and pain mediators causing destructive changes, foreign bodies as grains of chondromatosis are washed out elicitating joint sounds (Sakamoto et al. 2000, Shibuya et al. 2002, González-Pérez et al. 2011). Arthroscopic examinations of the TMJ have generally been confined to the superior joint space. Superior joint compartment adhesions and disc immobility can be treated during arthroscopic procedure, leading to resolution of symptoms and return of joint function (Ohnuki et al. 2003, Sanroman 2004, Politi et al. 2007, Tozoglu et al. 2011).
Inferolateral approaches to the inferior joint space have been described but routine puncture of the lower compartment is avoided, because in this case only the posterior non-functional parts of the disk and condyle are visualized, and there is always at least some risk of damaging the lateral disk attachment (Kumar et al. 2012).

Indications for arthroscopy are radiographic bone changes in the TMJ, characteristic of osteoarthritis with disc displacement or deformity, and non effectiveness of conservative treatment with NSAIDs, intraoral splints or arthrocenthesis. In practice, the decision to operate and the choice of the method seems to be a matter of the individual surgeon´s, training, experience, and attitude toward the surgical management of TMJ disorders. Involvement of the TMJ in patients with rheumatoid arthritis or other connective tissue diseases is rather common and arthroscopy with simultaneous biopsy is indicated in these situations. Posttraumatic complaints may also be an indication for arthroscopy (Thomas et al. 2012).

Contraindications to arthroscopy are similar to those for other elective procedures such as any medical condition that places the patient at an increased risk from general anesthesia or the surgical procedure itself. Local contraindications include skin or ear infections, possible tumour seating, and severe or advanced fibrous ankylosis resulting in severe limitations and movement of the condyle. Surely arthroscopy is contraindicated in the case of acute arthritis (Kumar et al. 2012).Emotional instability, obesity that prevents the joints from being palpated adequately are also considered contraindications.

All cases for arthroscopy are usually classified as advanced Wilkes (1989) stages IV and V, and in rare cases, stage III.

The Wilkes stages are as follows:

I. Early stage
   a. Clinical: No significant mechanical symptoms other than opening reciprocal clicking; no pain or limitation of motion
   b. Radiologic: Slight forward displacement, good anatomic contour of the disc, negative tomograms, no bone structure changes
   c. Pathoanatomy: Excellent anatomic form; slight anterior displacement, passive incoordination demonstrable

II. Early intermediate stage
   a. Clinical: One or more episodes of pain: beginning major mechanical problems consisting of mid-to-late opening loud clicking; transient catching and locking
   b. Radiologic: Slight forward displacement; beginning disc deformity, slight thickening of posterior edge; negative tomograms, no bone structure changes
   c. Pathoanatomy: Anterior disc displacement; early disc deformity; good central articulating area

III. Intermediate stage
   a. Clinical: Multiple episodes of pain; major mechanical symptoms consisting of locking (intermittent or fully closed): restriction of motion, function difficulties
   b. Radiologic: Anterior disc displacement with significant deformity or prolapse of disc (increased thickening of posterior edge), negative tomograms, no bone structure changes
   c. Pathoanatomy: Marked anatomic disc deformity with anterior displacement; no hard tissue changes

IV. Late intermediate stage
   a. Clinical: Slight increase in severity over intermediate stage
   b. Radiologic: Increase in severity over intermediate stage; positive tomograms showing early-to-moderate degenerative changes – flattening of eminence, deformation of condylar head, erosions, sclerosis
   c. Pathoanatomy: Increase in severity over intermediate stage; hard tissue degenerative remodelling of both bearing surfaces (osteophyts), multiple adhesions in anterior and posterior recesses; no perforation of disk or attachments

V. Late stage
   a. Clinical: Characterized by crepitus; variable and episodic pain; chronic restriction of motion and difficulty with function
   b. Radiologic: Disc or attachment perforation, filling defects, gross anatomic deformity of disc and hard tissues, positive tomograms with essentially degenerative arthritic changes
   c. Pathoanatomy: Degenerative changes of disc and hard tissues; perforation of posterior attachment; multiple adhesions, osteophyts, flattening of condyle and eminence, subcortical cyst formation.

5. AIMS OF THE STUDY

The general goal of this thesis was to investigate radiographic changes in the TMJ, to explore the associations of TMJ pain/discomfort with daily activities, to find out the role of bone markers and select effective treatment modalities.

Specific aims:

1. To find whether there are any associations between TMJ pain/discomfort and biochemical markers of bone turnover on the activities of daily living.
2. To compare radiographic changes in the TMJ with the lumbar spine and femoral neck BMD and to find whether there is any relationship between TMJ radiographic changes, between the level of 25(OH)D and the number of missing teeth.
3. To estimate and analyse the findings in the upper joint compartment by arthroscopic treatment in patients with TMJ internal derangements.
4. To evaluate the longer-term success rates of arthroscopic surgery of TMJ disorders.

6. MATERIAL AND METHODS

6.1. Study Subjects

Population-based cohort studies (*I-II*) were conducted in Väike-Maarja municipality, Estonia, in 2006. Study subjects were randomly selected from the registers of general practitioners in the region. Initially an invitation letter was sent to subjects and of those 103 responded to participate in our study. A total group of randomly selected participants (n = 103) consisting of 61 females and 42 males (aged 26–70 years) were invited. Of those invited, 95 (92%) persons took part in the study. Eight persons from 103 were not agreed to participate in the radiographic investigation. No inclusion/exclusion criteria were applied. An informed consent was obtained from all the subjects who participated.
(Table 1).

Table 1. Demographic data of population-based cohort (n=95)

	Age (years)	Gender (%)	TMJ pain episodes (%)
	median		
Female	54	58	54
Male	55	37	29

TMJ pain episodes = percentage of patients having current or present pain episodes in the TMJ

All participants underwent radiographic investigation (OPTG), venous blood sampling. The subjects were asked to evaluate the influence of the TMJ pain/ discomfort.

6.2. Study patients

Study *III* included 29 patients (25 females and 4 males), age 18-69 years (median 37). The patients were referred from medical practitioners and dentists to the Maxillofacial Department of Tartu University Hospital between 2000 to 2007.

Indications for arthroscopy were radiographic bone changes in the TMJ, characteristic of osteoarthritis, and non effectiveness of arthrocentesis (5 patients), intraoral splints (2 patients) or conservative treatment (22 patients) with NSAIDs mainly Clotam® (Acidum tolphenamicum) and Arcoxia ® (Etoricoxib) prescribed by general practitioners or dentists before referring these patients to our institution for consultation. All patients included in the study failed to respond to at least 6-12 months of preoperative conservative treatment. The duration of complaints ranged from 1 to 4 years. Six patients had a bilateral procedure and 23 had a unilateral procedure. There were done 19 (55.8%) right joints and 16 (44.2%) left joint arthroscopies. The preoperative diagnosis of these patients was osteoarthritis in 26 cases, rheumatoid arthritis with involvement of the TMJ in two cases and one pseudogout case. The postoperative follow-up period of 29 patients was 6 months. After a median of 5 years they were asked to attend check-up. Only 18 of these patients came for reexamination. This group consisted of 4 men and 14 women.

Study *I* and Study *II* were approved by the Ethics Committee at the Faculty of Medicine, University of Tartu (protocol No.140/18, 2005). Study *III* was approved by the Ethics Committee at the Faculty of Medicine, University of Tartu (protocol No. 94/3, 2000). All participants gave their informed consent before the start of the study.

6.3. Assessment of pain. The Activities of Daily Living scale, VAS

In Study *I* all participans were asked to evaluate the influence of pain/ discomfort in the TMJ on daily activities. A rating scale based on methods introduced in medical and behavioural science and modified by List and Helkimo was used (1995). The questions of the scale were translated into Estonian from English by one of the authors (Voog et al. 2003a). A modification of the rating scale was used where one of the questions (number 10) in the original scale was excluded since it proved inadequate. The scale ranged from 0 (activity without any pain/discomfort in the TMJ) to 10 (activity impossible due to pain/discomfort in the TMJ). The persons were asked to mark the number that best

described their present ability to perform each activity considering their pain/ discomfort from the TMJ. The questions in English were: "If you feel pain/ discomfort in the area of the TMJ are you able to:

1 socialize with family and close friends? (ADL 1)
2 perform daily work? (ADL 2)
3 perform daily household chores (preparing meals, cleaning, taking care of small children)? (ADL 3)
4 sit in a company or participate in other social activities (e.g. parties)? (ADL 4)
5 exercise (walk, bicycle, jogging, etc)? (ADL 5)
6 perform hobbies (read, fish, knit, play an instrument)? (ADL 6)
7 sleep at night? (ADL 7)
8 concentrate? (ADL 8)
9 eat (chew, swallow)? (ADL 9)
10 talk (laugh, sing)? (ADL 10)
11 yawn, open mouth wide? (ADL 11)
12 how much does the pain/discomfort affect your daily activities? (ADL 12)

In Study *III* the scores for the preoperative and postopertive maximal interincisal opening (MIO) and VAS for pain were compared. MIO was measured as a distance between upper and lower incisial edges by using 100 mm ruler. Joint pain/discomfort was assessed with 100 mm visual analogue scale with the end points marked as „no pain" and „worst pain ever experienced". The absence of pain was scored as 0. If pain was present the patient was asked to select a field from 1 mm to 100 mm.

TMJ clinical involvement was characterized by the following symptoms as pain (both at rest, and upon chewing), tenderness to palpation of the joint, sounds (crepitation, clicking), closed lock, intermittent lock, and restricted mandibular mobility e.g. difficulty in opening the mouth and stiffness in the morning, were observed. The symptom related factors obtained by using the questionnaire were documented.

6.4. Blood sampling

In Studies *I-II* venous blood samples were obtained on the same day as the clinical and radiographic examinations were performed. Quantitative changes in bone turnover were assessed by measurement of serum biochemical markers as follows: 25(OH)D, CTX-1 and P1NP.All samples were taken in the morning (after an overnight fast) between 8 a.m. and noon using pre-cooled tubes. Serum was separated and the samples were stored at –20°C until analysis.

6.5. Analysis of bone markers

All samples were analysed simultaneously in duplicate to minimize inter-assay variations. The analyses were performed at the United Laboratories of the University of Tartu Hospital.

The 25(OH)D level (collected from January to March) in the serum was measured by radioimmunosorbent assay produced by DiaSorin (Stillwater, Minnesota, USA). The intra and inter-assay CVs were 4.1% and 5.7% respectively. For group discrimination, we used 25 nmol/L as the critical value for deficiency and 50 nmol/L as the cut-off value for insufficiency. The 75 nmol/L was considered to be the optimal 25(OH)D level (Chopin et al 2008).

P1NP was determined by the Elecsys 1010/2010 total P1NP serum kit (Roche Diagnostics, Mannheim, Germany), which employs the electrochemiluminescence immunoassay (ECLIA) technique. The reference range of the bone formation marker P1NP for premenopausal women is 15.1-58.6 ng/ml, for postmenopausal women 16.3-73.9 ng/ml and for men aged 51 to 70 years, < 36.4 ng/ml.

The CTX-1 was determined by Elecsys 1010/2010 β-CrossLaps/serum kit (Roche Diagnostics, Mannheim, Germany) whose sensitivity of the assay is 0.01 ng/ml. The mean (SD) and mean +2SD figures are: for premenopausal women, 0.025-0.573 ng/mL; for postmenopausal women, 0.104-1.008 ng/mL; for men aged 31 to 51 years, 0.016-0.584 ng/mL; for men aged 51 to 71 years 0.096-0.704 ng/mL; and for men older than 71 years, 0.066-0.854 ng/mL.

6.6. Radiographic examination

In Study *I-II* bilateral TMJ images were obtained with the orthopantomograph apparatus CRAEX 3 (Soredex orion corporation LTD, Finland) by half-open mouth. The OPTGs were evaluated for presence of radiographic signs of bone structural changes as erosions, flattening and osteophytes of the condyle and temporal bone. Erosion in condyles on the radiographs was scored according to Helenius et al. (2004) as follows: score 1 – very slight erosion; score 2 – erosion on top of the condyle; score 3 – half of the condyle is eroded; score 4 – the condyle is totally eroded. Flattening and osteophytes were evaluated visually in OPTG (flattening – a flat bony contour deviating from the convex form, osteophyte – a marginal bony outgrowth). For statistical analysis the total sum of radiographic changes was used (left and right TMJ together). The presence of dental removable prosthesis and occluding pair of teeth were taken into account. Root remnants and third molars were excluded.

All OPTGs were examined by three independent investigators (one radiologist, one mafillofacial surgeon and dentist) without knowledge of the patient's laboratory or clinical data. Thirty percent of OPTGs were randomly selected for reexaminig (every third OPTG) independently on two occasions three months apart on separate forms for intraobserver error assessment.

In the patient group (Study *III*) the radiographic changes of the TMJ were evaluated by using OPTG and CT SOMATOM (CRAEX 3, Soredex orion corporation LTD, Finland; AR HP Spiral; Siemens, Erlangen, Germany). All CTs were performed by closed and open mouth. All CT scans were examined by the same radiologists without knowledge of the patient's data. The criteria for osteoarthritis diagnosis were structural bone changes as erosion, flattening, sclerosis, subchondral pseudocysts, the width of space (Figures 3, 4).

Fig.3. Osteoarthritis of the TMJ. Signs of erosion on the surface of the condyles in a coronal view of the CT. An irregular outline of the condyles is evident. The bone structure of the both glenoid fossa is normal.

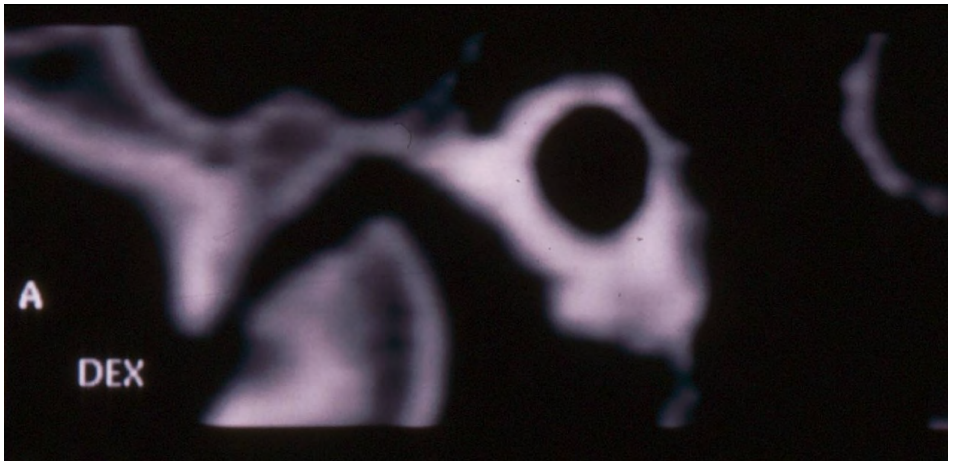

Fig.4. Sagittal view of the CT from the left temporomandibular joint. Sign of flattening of the condyle.

The CT sections were evaluated for presence of radiographic signs of bone changes within three regions (lateral, central and medial) of the mandibular and temporal part (eminence) of the TMJ. The recording of the signs was made in the axial, coronal and sagittal views. The radiographic signs had to be visible in at least two different slices in each of the regions to be recorded. The changes

are defined as follows: erosion – a local area with decreased density of the cortical joint surface including or not including adjacent subcortical bone, sclerosis – a local area with increased density of the cortical bony joint surface that may extend into the subcortical bone, subchondral pseudocyst – a well defined, local area of bone rarefication underneath an intact cortical outlining of the joint surface, flattening – a flat bony contour deviating from the convex form, osteophyte – a marginal bony outgrowth. The grade of the total changes of the TMJ can be evaluated according to the scoring system developed by Rohlin & Petersson (1989) as well.

All cases were classified as advanced Wilkes (1989) stages. All CT scans were examined by the same radiologists without knowledge of the patient's laboratory or clinical data.

6.7. Bone mineral density measurement

All participants from Studies *I–II* underwent BMD measurement. Bone mineral density of the lumbar spine (LT score) and femur (FT score) were measured at each centre by DXA with a densitometer (GE-Lunar Progidy, Madison, Massachusetts, USA) at the lumbar spine (L2 to L4) in the anterior-posterior view and at the left hip (femoral neck; Lewiecki et al. 2008). BMD was expressed in grams of bone mineral per square centimeter (g/cm^2), as the number of SD from the mean of healthy age- and sex-matched people, the Z-score, and as the number of SD from the mean of healthy, young sex-matched people, the T-score. The values were obtained from the Lunars combined European/US reference population (Lunar 1998).

T-score was used for analysis based on the World Health Organization (WHO) criteria. The universally accepted WHO criteria for assessing BMD contrast individual T-scores to peak BMD in healthy adult control populations. In this scheme, "osteoporosis" refers arbitrarily to T-values below –2.5, "osteopenia" to values between –1.0 and –2.5, and "normal" to values above –1.0 (Whyte 2005).

The subjects were allocated into two groups; group one had normal bone mineral density values and group two had abnormal bone mineral density values.

6.8. Arthroscopic surgery of the temporomandibular joint

From November 2000 to December 2007 twenty nine patients, 25 female and 4 male, underwent TMJ arthroscopy. A total of 35 joints were operated. The stage of disease was classified according to Wilkes (1989). Bilateral cases were classified by the worse joints. Fourteen of the 29 patients were classified according to Wilkes as stage IV, and 15 were classified as stage V of osteoarthritis at the time of surgery.

Arthroscopy (arthroscope KARL STORZ GmbH&Co.KG) was performed under nasotracheal general anaesthesia, marking line and puncture points on the skin surface. The puncture site was located by manipulating the mandible anterio-inferiorly. For distension of the superior compartement, 1% lidocain solution (B Braun Melsungen AG, Melsungen, Germany) 2.0 ml was inserted. Through the small skin incision 0.75–1.0 cm from the tragus, a puncture into the posterior recess was made with a trocar (obturator inserted). From the first skin incision ~ 0,75 cm in the anterolateral direction another skin incision was made for the outflow cannula inserted into the upper joint anterior recess. Following insertion of the trocar (diameter 1.8 mm, length 4 cm) into the joint space, the blunt obturator was removed and a Forward-Oblique Telescope 30º (HOPKINS®), diameter 1.9 mm, length 6.5 cm, fiber optic light transmission incorporated, was inserted. The superior surface of the disc, articular fossa, and the internal aspects of the posterior and medial capsule were examined. The upper joint compartment was examined from the posterior pouch *via* the intermediate zone to the anterior pouch. The upper compartment was swept clear under constant irrigation with an isotonic saline solution. After diagnostic arthroscopy was completed, forceps, a palpation hook or a blunt probe were used to cut fibres and adhesions, facilitating repositioning of the disc. During the arthroscopy a sweeping procedure between the disc and fossa released the adhesions and fibrillations, increasing the mobility of the joint. Release of the adhesions and fibrillations of the superior suface of the disc and shaving the surface of articular fossa in the upper joint compartment were performed with the aid of a blunt obturator or a hook and with grasping forceps, scissors or a double-edged knife. The surgical procedure was completed by irrigating the joint space to remove small tissue fragments. Arthroscopic lysis and lavage included also a lateral release of the upper joint compartment, performed with the aid of a blunt obturator or a hook.Thus the locked disc could be mobilized sufficiently.

All patients received an intravenous prophylactic antibiotics dose at the beginning of the procedure.

6.9. Statistical analysis

For the descriptive statistics of the variables, median and IQR were used. The variables were tested for differences between the groups with the Mann-Whitney U-test. The significance of the correlations was tested by Spearman rank correlation coefficient (r_s). A significance level of less than 0.05 was considered significant. In Study *III* statistics were performed using the WINKS SDA Software (Texasoft, Cedar Hill, TX).

7. RESULTS

7.1. The associations of TMJ pain and bone characteristics on the activities of daily living (Paper I)

The influence of TMJ pain/discomfort on daily living activities in this study was found to vary between the activities and the gender. TMJ clinical involvement (pain/discomfort) in the healthy population was 47%.

Highly significant correlations were found between female gender and the following activities of daily living: social life (ADL 1; p=0.015), performing daily work (ADL 2; p=0.024), performing daily household chores (ADL 3; p=0.021), exercising (ADL 5; p=0.003), performing hobbies (ADL 6; p=0.023) and yawning, opening the mouth wide (ADL 11; p=0.009).

A statistically significant difference between the ADL data and the bone status was found (Figure 1, Paper I). Correlations between ADL data and the serum levels of background factors (CTX-1, P1NP and 25(OH)D) are presented in Table 2, Paper I.

The median levels of the bone characteristics are given in Table 2.

Table 2. Serum level of 25(OH)D and bone markers of population-based cohort (n=95)

Gender	25(OH)D		P1NP		CTX-1	
	median	IQR	median	IQR	median	IQR
Female	58.5	22.3	40.0	24.5	0.3	0.2
Male	54.5	23.3	24.5	22.2	0.3	0.2

25(OH)D – Vitamin D in nmol/L, P1NP – Procollagen-1N-collagen in ng/L, CTX-1 – C-telopeptide of type I collagen in ng/ml, IQR – interquartile range

The women had lower 25(OH)D level compared to the men (p=0.04). Lowering of 25(OH)D correlated negatively with activities of daily living such as social life with family (ADL 1; $r_s = –0.26$, p=0.017), other social activities (ADL 4; $r_s = –0.32$, p=0.002), exercising (ADL 5; $r_s = –0.21$, p=0.047), performing hobbies (ADL 6; $r_s = –0.30$, p=0.005), concentrating (ADL 8; $r_s = –0.31$, p=0.004), eating (ADL 9; $r_s = –0.22$, p=0.041), how much the pain/discomfort affects daily activities (ADL 12; $r_s = –0.26$, p=0.017).

The median value of TMJ pain was 76.9% for the women (IQR 5) and 53.2% for the men (IQR 4.2; Table 3, Paper I). The women were more affected by pain/discomfort in the TMJ.

The correlation between TMJ pain/discomfort and ADL was found in all ADL questions. The impact of TMJ pain/discomfort was the greatest on eating (ADL 9) in 68 % of the men and 77% of the women and smallest on performing

daily household chores (ADL 3) in 37% of the men and in 61% of the women.

The age was not significantly correlated to any ADL question.

Subjects with more TMJ pain/discomfort experienced a significant negative impact on activities of daily living.

7.2. Relationship between temporomandibular joint radiographic changes and bone mineral density (Paper II)

In this study we found that subjects with a lower LT score had significantly less occluding pairs of teeth ($p=0.018$; Figure 2, Paper II) and had a removable prosthesis in more cases ($p=0.008$; Table 3, Paper II).

Subjects with a removable prosthesis had lower values of LT score and FT score. Subjects with a lower LT score had also a significantly lower FT score ($p<0.001$; Figure 3, Paper II).

Radiographic changes as erosions, flattenings and osteophytes in the TMJ correlated negatively with P1NP ($r_s=–0.217$, $p=0.041$). CTX-1 correlated positively with P1NP ($r_s=–0.6449$, $p<0.001$) and negatively with 25(OH)D ($r_s= –0.207$, $p=0.042$).

The total sum of radiographic changes in the TMJ was observed in 57% of the participants. Erosions occurred in 80 %, flattening occurred in 37 % and osteophytes occurred in 5% of the participants (Figure 4, Paper II).

Out of 95 participants, 42 % had abnormally low values of LT score. Among them osteoporosis was observed in 10.4 % and osteopenia in 31.6 %.

7.3. Long-term evaluation of arthroscopic surgery with lysis and lavage of temporomandibular joint disorders (Studies III, IV)

Fibrous adherences within the superior joint space were present in all 29 cases, fibrillations in 22 cases (76%). Of the radiographic changes, erosions were the most frequent findings in 69% of the cases. Arthroscopic findings were as follows: irregularities of joint surfaces, foldings and synovitis (hyperaemia of the inner wall), localising also in the posterior part of the disc, intra-articular fibrous adhesions, intracapsular adhesions, fibrillations of superior surface of the disc and arthrotic lesions of temporal cartilage, foreign bodies, chondromatosis (Table 3).

Table 3. Clinical, radiographic and arthroscopic findings in patients who underwent arthroscopy (N=29)

Signs and symptoms	sum	% abn	Radiographic findings	sum	% abn	Arthroscopic findings	sum	% abn
Pain	25	86	Flattening	10	34	Adhesions	29	100
Hypomobility	23	79	Bone cyst / Subchondral pseudocycts	9	31	Chondromatosis	5	17
Closed lock	5	17	Erosions	20	69	Fibrillations	22	76
Intermittent lock	5	17	Reduced space	10	34	Synovitis	9	31
Deviation	4	14	Sclerosis	8	27	Eburneation of fossa	15	52
			Hypomobility of condyle	4	14	Displaced disc	23	23
			Osteophytes	5	17			

Sum – total number of patients with findings; % abn = percentage of individuals with abnormal findings

We found no significant differences between the results of follow-up when comparing the shorter follow-up time results (6 months) and longer-term results (5 years). Median preoperative VAS score was 71 mm, six months after arthroscopy it was 27 mm and five years after treatment 20 mm. Median preoperative MIO was 32 mm, six months after treatment it was 41 mm and five years after treatment, 42 mm (Figures 5,6, Paper III). Duration of symptoms was positively correlated with age (r_s=0.57, p<0.001).

The MIO five years after arthroscopy was negatively correlated with VAS five years after arthroscopy (r_s=–0.38, p=0.040). The VAS five years after arthroscopy was in turn positively correlated with VAS six months after arthroscopy (r_s=0.38, p=0.040), closed lock (r_s=0.43, p=0.018) and clinical diagnosis (r_s=0.35, p=0.050).

Assessment of the symptoms reported by the patients as well as the objective signs noted on clinical examination confirmed resolution of pain at movement and increased vertical opening of the mouth. The patients achieved a significant relief of symptoms in most cases: excellent jaw function, painless MIO (more than 40 mm) and free excursive movements.

There were two complications: damage to the superficial branches of the facial nerve resulting in paraesthesia in the preauricular region. These symptoms disappeared during one month.

8. DISCUSSION

In this thesis we have studied the population-based group of subjects to describe the impact of TMJ pain/discomfort on ADL in relation to BMD. This was the first attempt to characterize TMJ complaints in Estonia in connection with skeletal bone health. The overview of the TMJ arthroscopy in group of arthritic patients gave additional information about reasons and treatment of pain and dysfunction in disease.

The study demonstrates that TMJ pain/discomfort has a significant negative impact on activities of daily living. We found that TMJ clinical involvement in the healthy population was 47%, which is comparable with the corresponding finding from other studies (Rutkiewicz et. al 2006).Especially disturbed were eating, yawning, opening the mouth wide, performing daily work and sleeping at night also. It was found that a relatively high median pain level influenced the performance of daily work in these subjects.

In our study the median value of TMJ pain in the male as well as in the female group was relatively high considering that the study sample consisted of voluntary participants. It shows a relatively high prevalence of TMJ problems in a population based investigation. Our findings show that middle-aged women have more TMJ complaints than middle-aged men. The above results are consistent with the findings of other studies which also concluded that the incidence of chronic craniofacial pain conditions among women is 1.5 to 2 times higher than among men (Unell et al. 2006). Some authors believe that women are more concerned with health and thus seek treatment more frequently (Pereira et al. 2009). Some researchers have found that women are generally also more affected by pain (Dao et al. 2000). With regard to biological factors, quantitative as well as qualitative differences in endogenous pain inhibitory systems have been implicated, as well as an influence of gonadal hormones. According to some studies, presence of female reproductive hormones enhances pain response, while other studies suggest that these hormones decrease pain response. These contradictory findings could be explained if hormones act differently in peripheral tissues and at different levels of the nervous system (LeResche 2007). It has been established that hormonal factors play also a role in TMJ pain conditions. Such association has been found in several studies (Dao et al. 1998, Gunson et al. 2012, Rezaii et al. 2012).

Comparing the different sexes we found highly significant correlations between female gender in following activities of daily living: social life, performing daily work, performing daily household chores, exercising, performing hobbies and yawning and opening the mouth wide. The same correlations in male were less significant. Psychosocial factors such as sex role beliefs, pain coping strategies, and pain related expectancies may also contribute to differences between the sexes (Dworkin et al. 2002, Guarda-Nardini et al. 2012).

Pain is a personal experience and the most reliable information about pain can be obtained from the patient. Use of an ADL questionnaire is a very convenient method for pain assessment. As this questionnaire is very simple and

easy, to handle and it can be recommended for future clinical trials in patients with TMJ disorders (Murakami et al. 2000, Undt 2006 a). However, patient questionnaires cannot replace further consideration of the patient´s medical history and performing of physical examination, laboratory investigations or other tests. Patient questionnaires must be interpreted by the physician for correct patient management similarly to laboratory tests and other quantitative data (Hansson et al. 1992, Sokka et al. 2003).

Only a few systematic reviews have addressed to daily activities or quality of life in relation to management of TMJ disorders. We concluded that use of specific questionnaires is justified for assessment of the character of TMJ pain.
Age was not significantly correlated to any of the ADL questions. This could be explained by the relatively high median age of the study subjects (55 years). It has been reported that changes in the TMJ due to remodeling or arthrosis mainly appear after the age of 45 (Öberg et al. 1971). It is generally accepted that quality of life is negatively affected by social and economical conditions by chronic pain and disturbed sleep. The relatively high involvement of TMJ by pain in subjects of our study could also be by social and economic conditions in Estonia.

Associations between TMJ pain/discomfort with Vitamin D on with the activities of daily living was evident. Subjects with lower 25(OH)D values experienced difficulties in performing physical exercises, engaging hobbies, they have problems with eating, participating in static social gatherings or other social activities. The social life of these persons was disrupted to a considerable degree.

We found that the women had a significantly lower 25 (OH)D level compared to the men. However, some studies have not found any relationship between low 25(OH)D levels and the gender (Bolek-Berquist et al. 2009). The above difference between the sexes can be explained by the fact that men work more out of doors in summer and experience longer exposure to UV light. Also men have different sunbathing habits than women. Finally, the fat tissue is the physiological depot for vitamin D suggesting that the obese have an increased storage capacity of 25(OH)D, which concerns women more (Gallagher et al. 1996, Wortsman et al. 2000). Estonia's population is at high risk for D-hypovitaminosis. It has been demonstrated that 25(OH)D levels are low all year round in Estonia (Kull et al. 2009). It was found that for optimal physical performance, 25(OH)D concentrations of 100 nmol/L appear to be more advantageous, and vitamin D supplementation should be maintained at this level (Ross and al. 2011, Toffanello et al. 2012). The 25(OH)D concentration above 125 nmol/L should raise concern among clinicians about its potential adverse effect, particularly on extra skeletal outcomes.

Several findings show that the association between vitamin D and physical performance has remained controversial. Some studies found a significant association between low serum vitamin D concentration and physical performance (Bischoff-Ferrari et al. 2004c, Gerdhem et al. 2005, Houston et al. 2007, Kwon et al. 2007, Boxer et al. 2008). However, some other studies focused specifi-

cally on the association of vitamin D with muscle strength, muscle power and muscle contraction speed and due to that the association was not found (Annweiler and al. 2009a, 2009b, 2009d). Generally, adequate vitamin D level is based on parathyroid hormone levels, but not on physical performance outcomes (Annweiler et al. 2009d). Not much clinical research has focused on the specific effects of vitamin D deficiency on jaw pain. Vitamin D deficiency can result in a predisposition to TMJ disorders and musculoskeletal pain. People with vitamin D deficiency may develop a disease characterized by unmineralized osteoid leading to bone pain (Abdel-Fattah 1992). Based on our results, low 25(OH)D level can predict TMJ bone destruction and additional vitamin D consumption might be suggested to avoid TMJ dysfunction. This study demonstrated that pain/discomfort originating from the TMJ is influenced by the biochemical markers of bone turnover. Similar results were found by Wang (2007). More focus has been placed on the role of biochemical mediators in the development and progression of TMJ pain and dysfunction and the identification of biochemical markers of TMJ disease (Voog et al. 2003b, 2004a, 2004b, Israel et al. 2006). The P1NP level depends on many factors, such as diet, level of physical activity, season, etc. Subjects with normal P1NP levels are physically and socially more active. Low P1NP values may predict various bone diseases (Milam 2000). According to our data, P1NP level remained in the reference range. A statistically significant difference was found between eating and P1NP level.

The total sum of radiographic changes in the TMJ was observed in 57% of the study participants. These findings suggest that decreased levels of P1NP may influence bone formation in the TMJ by causing radiographic signs such as erosions, flattening and osteophytes.

The CTX-1 correlated positively with P1NP and negatively with 25(OH)D. It has been found that subjects with an increased level of bone metabolism markers have a low level of 25(OH)D. We found that subjects with increased levels of P1NP and CTX-1 have less TMJ pain/discomfort. Several studies have reported relationship between biochemical markers and mandibular cortical bone (Vlasiadis et al. 2007). In the current population based randomly selected study *(I–II),* we demonstrated a significant correlation of low BMD with radiographic changes, as well as with occluding pairs of teeth. Subjects with lower BMD values had less occluding pairs of teeth and more of removable prostheses. Increased rates of BMD are associated with greater risk of tooth loss (Kribbs 1990, Makker et al. 2012). This is in accordance with a study performed by Sato et al. 1998 who found that bite force and number of residual teeth were significantly correlated with BMD of the trabecular mandibular condyle. Zlataric et al. (2002) demonstrated that the patients with severe erosion of the cortex had significantly lower BMD values.

According to our study, radiographic changes in the TMJ seem to be related to BMD. These findings support the importance of the functional loading and dental state for the mandibular condyle. The TMJ radiographic changes were negatively correlated with P1NP which has proved to be a sensitive marker of

bone formation. The P1NP was correlated with CTX-1 which is currently considered one of the most sensitive markers of bone resorption. The correlation between these two markers is probably due to equal shift / balance in normal bone metabolism where osteoblasts are acting simultaneously with osteoclasts.

Based on our data, high level of CTX-1 correlated with low level of 25 (OH)D. According to Abdel-Fattah (1992), low 25(OH)D level can also predict TMJ destruction.

Osteoporosis has been linked to the loss of teeth, while calcium and vitamin D supplements can bolster bone density in the jaws (Dietrich et al. 2004). Low skeletal bone mineral density induces changes in mandibular bone structure and bone mass. This situation can generate dental- and periodontal disease and can result in the loss of teeth and temporomandibular joint bone. Lofman et al. in 2005 and Khatoonabad et al. in 2011 reported that the biochemical markers of bone turnover were related to current bone mass and provide information about future bone loss. Biomarkers have the potential to provide an early warning of the initiation of breakdown of the articular matrix, which in future could lead to earlier treatment to prevent joint destruction that leads to disability (Kraus et al. 2011) The markers of joint tissue metabolism have opened up novel possibilities for earlier diagnosis of radiographic changes in joints and of OA. (Garnero et al. 2002, Kumm et al. 2012). Typically TMJ radiographic changes develop slowly and progressively. The evaluation of biomarkers earlier, in the molecular stage, before there have developed radiographic changes resulting in pain/discomfort can improve the treatment.

Several techniques are used to image the TMJ: panoramic radiography, plain radiography, conventional and computed tomography, digital volume tomography or cone-beam computed tomography, arthrography and MRI. Therefore, use of OPTGs could be useful as a simple screening method to estimate bone structure changes in the TMJ as well as to provide valuable information about the quality of the jaw bone such as joint space narrowing, osteophytes, subchondral sclerosis and subchondral cysts (Aggarwal et al. 2012).

The CT is generally accepted as the most useful technique to reveal minute small details and more accurately depict TMJ osseous changes. It was found TMJ CT changed or modified the diagnosis in 65% of the judgments and influenced treatment recommendations in 40%. These changes were substantive for 21% of the diagnoses and 22% of the treatment plans (Rriberto-Rotta et al. 2011). The benefits of the CT images information is very important for patients´ final diagnosis. The CT imaging must improve treatment planning and prognosis. However, the current gold standard for diagnosing OA and its progression and other TMDs are still plain radiography and arthroscopy.

Arthroscopic lysis and lavage has been an effective treatment for TMJ disorders refractory to nonsurgical treatments (Holmlund et al. 2001, Ohnuki et al 2003, Sanroman 2004, Politi et al. 2007). Arthroscopic lysis and lavage have proved to be effective in 84% of patients in the case of osteoarthritis of the TMJ (Dimitroulis 2005). Our long-term study consisted of mainly patients of osteoarthritis. We found that lysis and lavage improved translation of the joint and

decreased or eliminated pain. Lysis of adhesions and joint lavage are the most commonly performed TMJ arthroscopic surgical procedures to relieve painful hypomobility. The objectives of these techniques are to eliminate restrictions on the disc and the lateral capsule, to wash out microscopic debris resulting from the breakdown of the articular surfaces, to irrigate the joint and to stimulate the normal lubricating properties of the synovial membrane (Nitzan et al. 1994).

Adhesions may cause retention of the disc in its anteriorly displaced position, which may explain the failing response to conservative treatment.

A number of arthroscopic findings as fibrous adherences mainly between the disc and the fossa, fibrillations with „crab meat"appearance, mild granulations, irregularities of the condylar surface, foreign bodies, increased vascularisation are to be found. We observed synovitis in the upper joint space of the TMJ during arthroscopy and this inflamed synovium may cause pain. Alterations in the constituents of the synovial fluid affect lubrication of the joint causing stickness and decreased mobility. In our study, pain and hypomobility were part of a wide spectrum of symptoms appearing in the context of chronic dysfunction of the TMJ. Some authors have reported that the major symptom is the closed lock phenomenon (Davis et al. 1991). Among arthroscopic findings fibrillation has proved to be the most common accounting for 76% of cases (Dimitroulis 2002). In our study closed lock was found in 17.2 % and fibrillations in 75.8 % of the cases.

Politi and Piecuch (2000) performed long-term evaluation following temporomandibular joint arthroscopic surgery with lysis and lavage 2 to 10.8 years after treatment and Murakami et al. (2000) analysed long-term results covering 10 years. On the basis of assessment of the symptoms reported by the patients as well as of the objective signs noted on clinical examination confirmed resolution of pain on movement and increased vertical opening.

In our study a significant maintained decrease in VAS score was achieved after 6 month and also after 5 year follow-up. A significant and maintained improvement in MIO was also observed over the same period of time. Our results are comparable to those reported in other papers (Sorel and Piecuch 2000, Smolka and Iizuka 2005). The advantages of arthroscopic surgery and lavage, compared with open joint surgery, according to the Jaw Pain and Function Questionnaire, are that arthroscopic surgery is less invasive, is associated with lower morbidity and and requires a shorter hospital stay (Undt et al. 2006b).

No statistical differences were observed between arthroscopic lysis and lavage and operative arthroscopy in relation to postoperative pain or MIO at any stage of the follow-up period (Gonzalez-Garcia et al. 2008). Limitation in condylar movement probably originates from changes in the upper compartment, which restricts the sliding motion of the disc. During this procedure several inflammatory mediators available in the synovial fluid as prostaglandins (Murakami et al 1998), cytokines (Kardel et al. 2003, Voog et al. 2003b, 2004a) and serotonin as pain mediator (Voog et al. 2004b) etc. are washed out.

It is also important to use adjunctive therapy postoperatively to obtain maximum success with arthroscopic surgery, e.g. physical therapy especially in the

case of haemorrage, as it may prolong healing time. A pressure dressing during the first couple of hours after the operation is recommended. The long-term, 5 year outcome of TMJ arthroscopic lysis and lavage was considered to be acceptable and effective. This treatment offers favourable long-term stable results with regard to increasing MIO and reducing pain and dysfunction. Intra- and postoperative complications for arthroscopy are rare. Bleeding may occur from branches of the temporal vein during puncture or from damage to the middle ear. Extravasation of the irrigation fluid into the surrounding tissues may sometimes occur due to leakage of the irrigating fluid into the surrounding tissues, caused by accidental perforation of the TMJ capsule. There were two complications within this study: damage to the superficial branches of the facial nerve resulting in paraesthesia in the preauricular region. These symptoms disappeared during one month.

Based on our results, we can conclude that arthroscopy is a highly effective, minimally invasive and safe surgical technique for the treatment of intra-articular TMJ pathology, especially OA. A multidimensional understanding of the TMJ pathology improves its diagnosis and treatment.

Limitation of the study

Some limitations of the studies should be noted. If all the patients treated had taken part in the long-term reexamination we could evaluate success rates more thoroughly. In our opinion these did not affect generally the results obtained.

9. CONCLUSIONS

Pain/discomfort in TMJ has a significant negative influence on activities of daily living and is related to the biochemical markers of bone turnover and 25(OH)D level. Several functions of daily activities such as eating, swallowing, exercising and social life are the most disturbed ones.

TMJ radiographic changes and teeth loss seem to be related to the low levels of BMD and 25(OH)D.

Fibrillations and fibrous adhesions are the most usual pathological signs of arthroscopic findings in patients with internal derangement of the TMJ.
Arthroscopic releasing of these restrictive bands improves joint mobility and contributes to reducing pain level.

The results of TMJ arthroscopy offered favourable long-term stable results with regard to increasing maximal interincisal opening and reducing pain and dysfunction.

10. SUMMARY IN ESTONIAN

Temporomandibulaarliigese piltdiagnostika seos valu ja luumarkeritega. Artroskoopilise ravi kaugtulemused.

Sissejuhatus

Enamlevinud temporomandibulaarliigese (TML) haiguste sümptomiteks on valu, palpatoorne hellus, liigese helid, samuti raskused suu avamisel ja üldine liigutuste piiratus. Temporomandibulaarliigese häired halvendavad patsientide igapäevaelu toiminguid nagu rääkimine, söömine ja sotsiaalne tegevus. Personaalselt hinnatud igapäevase eluga toimetuleku küsimustiku e. ADL (activities of daily living) väärtused mängivad tähtsat rolli TML haiguste ennetamises ja tõenduspõhises ravis.

TML radioloogilised nähud (erosioonid, lamenemine ja osteofüüdid) on hästi hinnatavad ortopantomogrammil (OPTG). Samuti saab OPTG abil hinnata okludeeruvaid hambapaare, alveolaarluu resorptsiooni, alalõualuu tihedust, korteksi paksust ja laiust ja võrrelda seda üldise luutihedusega, et seeläbi ennetada osteoporoosi. Enam detailsemat infot mineraliseerunud luustruktuuridest saab kasutades kompuutertomograafiat (KT).

Prokollageen tüüp I N-terminaalne propeptiid (P1NP) ja C-terminaalne telopeptiid (CTX-1) on ühed tundlikumad luuainevahetuse biokeemilised markerid. Samuti on D vitamiinil tähtis roll luu ainevahetuses omades seoseid mitmete igapäevase elutegevuste aktiivsustega.

Antud uurimuses analüüsiti TML haiguste artroskoopilise kirurgia ravitulemusi. On antud põhjalik ülevaade TML artroskoopiast, selle vajadusest ja tulemustest. Kuna Eestis ei ole epidemioloogilisi uuringuid alalõualiigese kahjustuste haaratuse kohta seni läbi viidud, siis antud töö lisab oma panuse TML valu ning luu ainevahetuses osalevate markerite ja elukvaliteedi hindamiseks..

Põhieesmärk

Töö põhiliseks eesmärgiks oli uurida alalõualuuliigese radioloogilisi muutusi, selgitada välja antud piirkonna valu seoseid igapäevaelu toimetulekuga, tuua välja luumarkerite roll ning valida efektiivne ravimeetod.

Uuringu eesmärgid

1. Selgitada välja seosed TML valu/ebamugavustunde, luu biokeemiliste markerite ja igapäevaelu toimingute vahel.
2. Võrrelda seoseid luutiheduse ja TML radioloogiliste muutuste vahel, kirjeldada seoseid hammaskonna seisundi, TML radioloogiliste muutuste ja 25(OH)D vahel.
3. Hinnata ja analüüsida TML patoloogiatega patsientidel alalõualuuliigese ülemise kambri artroskoopilisi leide.
4. Hinnata artroskoopiajärgseid kaugtulemusi TML patoloogia korral.

Uuritavad ja meetodid

Uuritavaid valiti juhuslikkuse printsiibil Väike-Maarja (Eesti) perearstide nimistustest 2006 aastal. Grupp koosnes 103 vabatahtlikust (61 naist ja 42 meest) vanuses 26–70 aastat. Uuritavatele saadeti teavitus uuringu kohta ning lõplikuks uurimuses osalevateks vabatahtlike arvuks kujunes 95 (92%), kaheksa inimest 103-st ei andnud nõusolekut radioloogiliseks uuringuks. Töös kasutasime List ja Helkimo poolt modifitseetitud ADL küsimustikku. Kõik osalejad täitsid küsimustiku, mille skaalal 10 väärtust: 0 – valu/ebamugavustunnet TML ei ole, 10 – tugev valu/ebamugavustunne. Kõigile vabatahtlikele teostati ortopantomogramm (OPTG, CRAEX 3, Soredex orion corporation LTD, Finland), millel hinnati alalõualuuliigestes olevaid radioloogilisi muutusi: erosioone (Helenius jt.2004) ja visuaalselt osteofüüte ja alalõualuuliigese pea lamenemist. Hinnati okludeeruvate hambapaaride arvu. Kõik OPTG uuringud olid analüüsitud 3 uurija poolt (üks radioloog, üks näo-lõualuude kirurg ja üks hambaarst). Kolmekümnel protsendil uuritavatest hinnati 3 kuu möödudes uuesti OPTG. Täiendav uuring teostati samade hindajate poolt juhuvaliku alusel (valiti iga kolmas OPTG) ilma täiendava infota eelmise hindamisprotokolli tulemuste kohta.

Kõigil vabatahtlikel teostati kogu luustiku Dexa uuring luutiheduse määramiseks (GE-Lunar Progidy, Madison, Massachusetts, USA). Luutihedust mõõdeti nimmelülide L2–L4 ja reieluupea piirkonnast (LT score, FT score) ning kogu keha keskmine luu mineraalne tihedus teisaldati analüüsimiseks standardiseeritud ühikutele (g/cm²).

Uuringutega sama päeva hommikul: määrati vereseerumis 25(OH)D) tase (jaanuar – märts, DiaSorin kit,Stillwater, Minnesota, USA), P1NP tase (Elecsys 1010/2010 total P1NP serum kit, Roche Diagnostics, Mannheim, Germany) ja CTX-1 tase (Elecsys 1010/2010 β-CrossLaps/serum kit, Roche Diagnostics, Mannheim, Germany).

Teine uuringurühm koosnes 29 patsiendist (25 naist ja 4 meest, keskmise vanusega 37.5 a), kes olid suunatud Tartu Ülikooli Kliinikumi näo-ja lõualuukirurgia osakonda. Nendel oli diagnoositud TML patoloogia OPTG (CRAEX 3, Soredex orion corporation LTD, Finland) ja kompuutertomograafia (AR HP Spiral; Siemens, Erlangen, Germany) ja kliinilise pildi alusel. Radioloogilistel uuringutel hinnati erosioone, lamenemist, skleroosi, subkondraalseid pseudotsüste ja liigesepilu ning muutusi, mis tekivad osteoartriidi puhul (Rohlin ja Petersson 1989). Preoperatiivne diagnoos oli 26-l patsiendil osteoartriit, 2-l reumatoidartriit ja ühel juhul pseudopodagra.

TML haiguse staadiumite klassifitseerimisel kasutati Wilkes´e klassifikatsiooni: 14-l patsiendil Wilkes´e IV staadium ja 15-l Wilkes´e V staadium (Wilkes 1978, 1989).

Artroskoopia näidustusteks olid radioloogilised muutused TML-is (osteoartriit), kui artrotsentees ei osutunud efektiivseks (5 patsienti), oklusiooniteraapia mitteefektiivsus (2 patsienti) ning kui konservatiivne ravi ei andnud tulemusi (22 patsienti). Artroskoopia sai teostatud ajavahemikus 2000–2007 a. Tartu Ülikooli Kliinikumis näo-ja lõualuukirurgia osakonnas (november 2000 a. – detsember 2007 a.). Kuuel patsiendil sai teostatud kahepoolne artroskoopia ja 23

patsiendil ühepoolne (paremal 19 (55.8%), vasakul 16 (44.2%). Artroskoopia käigus vabastati liited, silendati liigese pinnad, uhuti välja koeosised ja põletikumediaatorid. Enne protseduuri said kõik patsientid antibiootikumi profülaktilises doosis.

Postoperatiivseid tulemusi hinnati 6 kuu ja 5 aasta möödudes. Hinnati suu maksimaalset avamist e. *maximal interincisal opening* (MIO) ja valu tugevust valu skaalal e *visual analogue scale* (VAS) enne ja pärast ravi, subjektiivseid sümptomeid ning radioloogilisi muutusi.

Viie aasta möödudes kutsuti patsiendid korduvale uuringule, kuhu tuli 18 patsienti (4 meest ja 14 naist), kellel viidi läbi uus kliiniline läbivaatus.

Statistiliseks analüüsiks kasutati Mann-Whitney U-testi, Spearmani korrelatsiooni (rs), kasutades vabavara WINKS SDA Software (Texasoft, Cedar, Hill, TX). Statistiliselt peeti oluliseks $p< 0.05$.

Tulemused

1. Populatsiooni uuringus osales 57 naist (keskmine vanus 54 a.) ja 37 meest (keskmine vanus 55 a.). Neljakümne seitsmel protsendil vabatahtlikest esinesid kaebused TML piirkonnas (valu, krepitatsioonid, suuavamise piiratus). Statistiliselt oluline erinevus ilmnes naistel järgnevate igapäevaelu toimetuleku tegevuste vahel: seltskonnas viibimine (ADL 1; p=0.015), igapäevaste tööde sooritamine (ADL 2; p=0.024), kodutööde sooritamine (ADL 3; p=0.021), sportimine (ADL 5; p=0.003), hobide harrastamine (ADL 6; p=0.023), haigutamine, suu maksimaalne avamine (ADL 11; p=0.009). Meestel väljendusid antud seosed nõrgemini. Statistiliselt kõige olulisem seos ilmnes ADL 9 (valu/ebamugavustunne söömisel) luumarkeritega CTX-1 (p=0.02) ja P1NP (p=0.04) vahel.

Naistel oli 25(OH)D tase madalam võrreldes meestega (p=0.04). 25(OH)D tase oli seotud enamiku ADL küsimustega (p=0.02). Madala 25(OH)D taseme korral oli häiritud söömine (p=0.04), hobide harrastamine (p=0.005), sportimine (p=0.04), seltsimine (p=0.017), konsentreerumine (p=0.004) ja üldine igapäevategevus (p=0.017). ADL kõik küsimused omasid seost TML valu/ebamugavustundega. Märgatav erinevus esines meeste ja naiste vahel. Naistel esineb tunduvalt rohkem kaebusi TML liigese piirkonnas, seetõttu hindasid nad oma igapäevast eluga toimetulekut halvemaks kui mehed. Naised vastasid positiivselt 76.9% juhul, mehed 53.2% juhul. Vanus ei omanud seost ADL küsimustiku vastustega.

2. Madala luutihedusega (LT score) uuritavatel oli vähem okludeerivaid hambapaare (p=0.018) ning seetõttu rohkem eemaldatavaid proteese (p=0.008).

Uuritavatel, kellel oli madalam LT skoor oli märkimisväärselt madalam ka FT skoor ($p<0.001$). Selgus, et TML radioloogilised muutused on seotud madala P1NP tasemega ($rs=–0.217$, p=0.041). CTX-1 korreleerus positiivselt P1NP-ga ($rs=–0.6449$, $p<0.001$) ja negatiivselt 25(OH)D-ga ($rs=–0.207$, p=0.042) .

TML radioloogilisi muutusi oli avastatud 57% uuritavatest kokku. Erosioone esines neist 80%, liigesepähiku lamenemist 35% ja osteofüüte 5% uuringus osalevatest vabatahtlikest. 42% vabatahtlikest oli avastatud luu mineraalainete tiheduse häire. Osteoporoos leiti 10.4% osalejatest, osteopeenia 31.6% .

3. Sagedasemad artroskoopia leiud olid fibrillatsioonid liigese ülemises kambris (76% juhtudest), liigespindade ebatasasused, sünoviit, liigese- ja kapslisisesed adhesioonid, kondromatoos. Radioloogilistel uuringutel sagedasemad leiud olid erosioonid (69% juhtudest).

Statistiliselt oluline korrelatsioon oli VAS-i (preoperatiivne) ja TML artroskoopiliste leidude vahel ($r=0.49$, $p=0.006$). Vanus omas positiivset korrelatsiooni TML haiguste tekkimisega ($r=0.57$, $p<0.001$).

4. Postoperatiivselt VAS-i näitajad vähenesid nii 6 kuu kui 5 aasta möödudes ($r=0.38$; $p=0.040$). Preoperatiivselt keskmine VAS oli 71 mm, 6 kuud pärast artroskoopiat 27 mm ja 5 aastat hiljem 20 mm. Postoperatiivselt MIO näitajad paranesid nii 6 kuud ($r=0.56$, $p<0.01$) kui ka 5 aastat hiljem ($r=0.58$, $p<0.001$). Preoperatiivne keskmine MIO oli 32 mm, 6 kuud pärast ravi 41 mm ja 5 aastat hiljem 42 mm.

Järeldused:

1. Valu/ebamugavustunne alalõualuuliigeses on seotud luutihedusega ja madala 25(OH)D tasemega. TML valu korral on suu avamine piiratud ja on söömine häiritud. Madal mineraalainete sisaldus lõualuudes omab tähtsust elukvaliteedi hindamisel ja sotsiaalsel heaolul.
2. Uuringu analüüsi põhjal võib öelda, et radioloogilised muutused alalõualuuliigeses ja okludeeruvate hammaste arv on tihedalt seotud madala luutihedusega ja 25(OH)D madala tasemega.
3. TML artroskoopilistest leidudest esinesid sagedamini fibrillatsioonid ja adhesioonid. Artroskoopiline kirurgia võimaldab vabastada ja eemaldada patoloogilised koeosised, parandades seega liigese liikuvust ning likvideerida valu.
4. TML haiguste artroskoopilise ravi kaugtulemuste analüüs andis tunnistust kliiniliste näitajate normaliseerumises (väheneb valu, paranes suu avamine ja alalõualiigese funktsioon).

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Education and employment

1984–1992	Abja-Paluoja Elementary School
1992–1995	Viljandi Russian Gymnasium
1995–2000	Undergraduate student, Department of Stomatology, Faculty of Medicine, University of Tartu
2000–2001	Intern, Department of Stomatology,Faculty of Medicine, University of Tartu
2001–2006	Resident in the field of oral-and maxillofacial surgery, Department of Stomatology, Faculty of Medicine, University of Tartu
2006–2013	PhD Student, Department of Stomatology, Faculty of Medicine, University of Tartu
2006–	Maxillofacial surgeon in Tartu University Hospital, Clinic of Stomatology
2004–	Maxillofacial surgeon, Dr.Aino Rull Dentistry
2011–	Maxillofacial surgeon, “Stigma”private clinic

Membership in professional societies

2007–	European Association for Oral and Maxillofacial Surgey
2003–	Estonian Association for Oral and Maxillofacial Surgery
2002–	Baltic Association for Maxillofacial and Plastic Surgery

Scientific work

The major areas of research include the TMJ problems, I am especially interested in modern TMJ diagnostic methods and surgical treatment. The main directions of research include the influence of TMJ pathology/pain on activities of daily living in relation to biochemical markers of bone turnover and 25(OH)D level.

Four of my articles have been published internationally and I am also a co-author of one chapter: “Temporomandibular joint arthroscopy versus arthrotomy” in the book “Regional Arthroscopy” 2013. I have given presentations at several leading conferences in the field.

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Haridus- ja ametikäik

1984–1992	Abja-Paluoja Põhikool
1992–1995	Viljandi vene Gümnaasium
1995–2000	Tartu Ülikooli arstiteaduskond, stomatoloogia eriala
2000–2001	Internatuuri läbimine.Tartu Ülikooli arstiteaduskond, stomatoloogia eriala
2001–2006	Arst-resident näo-ja lõualuukirurgia erialal, SA Tartu Ülikooli Kliinikum, Stomatoloogia kliinik
2006–2013	Doktorant, Tartu Ülikooli Stomatoloogia kliinik
2006–	Näo-ja lõualuukirurg, SA Tartu Ülikooli Kliinikumi Stomatoloogia kliinik
2004–	Suu-näo-ja lõualuukirurg, Dr.Aino Rulli Hambaravis Viljandis
2011–	Suu-näo-ja lõualuukirurg, ”Stigma” erakliinik.

Ühiskondlik tegevus

2007–	Euroopa Näo-Lõualuukirurgide assotsiatsioon
2003–	Eesti Suu-ja Näo-Lõualuukirurgia Selts
2002–	Balti Näo-Lõualuu-ja Plastikakirurgide Assotsiatsioon

Teaduslik tegevus

Peamiseks uurimisvaldkonnaks on alalõualiigesega seonduvad probleemid, eriline huvi on alalõualiigesehaiguste kaasaegne diagnostikameetodika ning kirurgilise ravi aspektid. Peamisteks uurimissuundadeks on alalõualuuliigese patoloogia/valu korral mõju igapäevaeluga toimetulekule, seos luuainevahetuse biokeemiliste markerite- ja D-vitamiiniga.

On ilmunud 4 rahvusvahelist publikatsiooni ja olen raamatu „Regional Arthroscopy“ 2013 peatüki ”Temporomandibular joint arthroscopy versus arthrotomy” kaasautor. Poster-ja suuliste ettekannetega olen esinenud mitmetel eriala juhtivatel teaduskonverentsidel.

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