

Long-term development of temporomandibular disorders in rheumatoid arthritis

Anna Kallenberg

Department of Stomatognathic Physiology
Institute of Odontology
Sahlgrenska Academy at the University of Gothenburg



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rheumatoid arthritis

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anna.kallenberg@odontologi.gu.se

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To my daughters: Hedvig, Dagmar and Karin

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Department of Stomatognathic Physiology, Institute of Odontology
Sahlgrenska Academy at the University of Gothenburg
Gothenburg, Sweden

ABSTRACT. Inflammatory joint diseases can affect the temporomandibular joint (TMJ) but there has been uncertainty to what extent. Most common are rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PS). Especially RA can cause a handicapping situation both generally and in the TMJ, which can cause difficulties in coping with ordinary life situations. The knowledge about long-term development in the TMJ and the relation of disease activity is not clearly documented. The aim of the first two studies was to compare RA, AS and PS with healthy controls without general joint or skin disease with respect to radiographic changes in the TMJ, subjective symptoms and clinical findings in the masticatory system. Panoramic images were performed to examine both TMJ condyles. Deviation in shape and changes of cortical outlines were recorded. Subjective symptoms and clinical and radiological findings were significantly more frequent in the disease groups than in the control groups. Pain, morning stiffness and reduced mouth opening capacity were most frequent and in RA followed by PA and AS. Signs and findings were mainly caused by the general disease and they were more common in RA than in PA and AS. In study 3, the aim was to investigate if RA patients differ from patients with temporomandibular disorders (TMD) and without general inflammatory joint disease (C group) regarding subjective symptoms, general well-being and self-rated physical health. The results showed that the RA group had fewer symptoms than the C group and they rated their mental well-being as normal while the C group showed higher tension, stress and muscle activity. In self-rated discomfort, the RA group reported as high results concerning TMJ and general joint pain, but not in general.

The aim of Study 4 and Study 5 was to investigate the long term development (15 years) of the RA group concerning subjective symptoms, clinical findings, general well-being, radiological changes, alveolar approximal bone loss (ABL) and medical data. The RA group reported no changes on subjective symptoms and discomfort while the well-being had deteriorated. There was a significant increase in muscle and neck tenderness, reduced vertical overbite and reduced number of teeth. There was significant radiological impairment in the TMJ and ABL in the RA group. The disease activity stayed on a medium level, indicating a generally stable situation for these patients, although the temporomandibular system had degraded. In spite of the degradation, the RA patients seemed capable of handling problems from this system. The C group was stable which indicates a good prognosis after 15 years regarding the temporomandibular system, while their opinion of their physical health had degraded. They were not affected in the TMJ and ABL in the long term in this study.

Keywords: Rheumatoid arthritis, Psoriatic arthritis, ankylosing spondylitis, temporomandibular joint diseases, temporomandibular disorders, long-term evaluation, orthopantomography, approximal bone loss, Health Assessment Questionnaire - HAQ, quality of life questionnaires, laboratory data, DAS 44, Ritchie's articular index, CRP.

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SAMMANFATTNING PÅ SVENSKA

Långtidsutveckling i käkssystemet hos patienter med reumatoid artrit

Avhandlingsarbetet innehåller två delar: 1. Tre olika inflammatoriska ledsjudomar jämfördes inbördes samt mot en kontrollgrupp(C) utan känd ledsjukdom och var patienter på en tandvårdsmottagning. Ledsjukdomarna var reumatoid artrit(RA), psoriasisartrit(PA) och ankyloserande spondylit(AS). Subjektiva symptom och kliniska och röntgenologiska fynd från käkssystemet registrerades. Röntgenförändringar i käklederna sågs i 66% av RA-gruppen, 38% av PA-gruppen, 30% AS-gruppen samt 12% i C-gruppen. Av reumatikerna uppvisar RA-gruppen fler och svårare besvär och fynd men har mindre muskelömheter än alla de andra grupperna. Resultaten visar att reumatikergruppen överlag uppvisar fler symptom samt fler och svårare förändringar i käkleder och tuggmuskler än kontrollgruppen och dessa härrör från den generella ledsjukdomen. 2: Jämförelse mellan en reumatikergrupp(RA) och en grupp patienter med bettfysiologiska besvär och utan ledsjukdom avseende subjektiva besvär, mental självuppskattning och bedömning av fysisk hälsa. Man fann att RA-gruppen hade färre besvär, normalt välbefinnande samt värre fysiska besvär än C-gruppen.

Efter 15 år gjordes uppföljning av dessa två grupper avseende utveckling av ovanstående variabler, kliniska fynd från käkssystemet samt bedömning av förändringar i käklederna och käkbensförlust samt eventuell koppling till generell sjukdomsaktivitet. Resultaten visar att i RA-gruppen sker efter 15 år ingen subjektiv förändring och endast tendenser till klinisk försämring i käkssystemet. Det försämrade allmänna välbefinnandet kan förklaras av den kroniska sjukdomen och den stabila fysiska uppfattningen visar på anpassning till situationen. Röntgenologiskt ses tydliga försämringar i käklederna och ökning av antal tänder med käkbensförlust. Ingen tydlig korrelation kunde ses med den generella sjukdomsaktiviteten, som kvarstod på medium nivå och de rapporterade fynden i ett långtidsperspektiv.

C-gruppen har förbättrats vilket bekräftar god långtids prognos avseende käkssystemet, trots gruppens uppfattning att de mentalt mår sämre och den fysiska uppfattning är oförändrad

LIST OF PAPERS

- I. Wenneberg B, Könönen M, Kallenberg A.
Radiographic changes in the temporomandibular joint of patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis.
J Craniomandib Disord 1990; 4:35-9.
- II. Könönen M, Wenneberg B, Kallenberg A.
Craniomandibular disorders in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis.
Acta Odontol Scand 1992; 50:281-7.
- III. Kallenberg A, Wenneberg B, Carlsson GE, Ahlmén M.
Reported symptoms from the masticatory system and general well-being in rheumatoid arthritis.
J Oral Rehabil. 1997; 24:342-9.
- IV. Kallenberg A, Ahlmén M, Wenneberg B.
Long-term development of signs and symptoms from the temporomandibular system in rheumatoid arthritis. A 15-year follow-up.
Submitted to J Orofac Pain 2013
- V. Kallenberg A, Ahlmén M, Wenneberg B.
The temporomandibular joint and alveolar bone level in rheumatoid arthritis. A 15 year follow-up.
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ABBREVIATIONS

ABL	Alveolar approximal bone loss
ADL	Activities of Daily Living
AI	Anamnestic Index (Helkimo)
ARA	American Rheumatoid Association
AS	Ankylosing Spondylitis
ASA	Acetyl Salicylic Acid
BSS	Body Symptom Scale
C	Control Group
CMD	CranioMandibularDisorders
CRP	Complement Reactive Protein
CT	Computer Tomography
DAS	Disease Activity Score
DI	Clinical Dysfunction Index (Helkimo)
DMARD	Disease-modifying antirheumatic drug
ESR	Estimated Sedimentation Rate
HAQ	Health Assessment Questionnaire
IP	Intercuspid Position
MACL	Mood Adjective Check List
MED	Medication
MTX	Metotrexate
PA	Psoriatic Arthritis

OA	Osteoarthritis
RA	Rheumatoid Arthritis
RAI	Ritchie's Articular Index
RDC/TMD	Research Diagnostic Criteria for Temporomandibular Disorders
RI	Radiological Index (temporomandibular joint)
SBU	Swedish Council on Health Technology Assessment
SCB	Swedish Statistical Database
SJC	Swollen Joint Count
TMD	Temporomandibular Disorders
TMJ	Temporomandibular Joint

1 INTRODUCTION

1.1 Papers 1 and 2.

The temporomandibular joint (TMJ) may be affected by several inflammatory joint diseases (G. Carlsson, 1979). Involvement of the TMJ has been shown a variation in percentage; rheumatoid arthritis (RA) from 2-98% (Franks, 1969; Syrjanen, 1985; Uotila, 1964), in psoriatic arthritis (PA) from 31-63% (Kononen, 1987; Lundberg & Ericson, 1967; Rasmussen & Bakke, 1982) and in ankylosing spondylitis from 4-32% (Maes & Dihlmann, 1968; Resnick, 1974; Wenneberg, Hollender, & Kopp, 1983). The different results depend on definitions, differences in population, type of examinations and joint involvement criteria. RA seems to affect the TMJ more frequently than PA and AS (Franks, 1969; Resnick, 1974; Syrjanen, 1985). By the time of this study, no controlled studies comparing these diseases concerning involvement in the TMJ had been published. The aim of Papers 1 and 2 were, therefore, to compare RA, PA and AS with each other and with a control group with regard to subjective, clinical and radiological symptoms.

1.2 Paper 3.

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease with a main feature also including the temporomandibular joint. Over the last years, involvement of the temporomandibular joint and masticatory system in RA has shown to be about 30 – 50% depending on differences in the type of examination (Tegelberg 1987; Bayar et al 2002; Puchner et al 2004). The progress of the disease varies and is related to many different factors (Aman et al., 2000). Since most previous studies have shown large variations in figures, it seemed important for future studies to include other relevant factors when judging the involvement of RA in the masticatory system including the TMJ. Paper 3 is a study on investigating subjective symptoms from the TMJ and the masticatory system and the general well-being and physical comfort/health (Ahlmen, Bengtsson, Sullivan, & Bjelle, 1990; Aman et al., 2000; L. O. Persson & Sjoberg, 1987; Sjoberg, Svensson, & Persson, 1979; Sullivan, Ahlmen, Bjelle, & Karlsson, 1993) in

patients with RA to a group of patients with temporomandibular disorders (TMD).

1.3 Paper 4

The influence on the TMJ from activity from rheumatic arthritis and the inflammatory processes has been well-documented (Tegelberg A, Nordahl S et al 2001, Kopp S, 2001, Appelgren et al 1995, Voog 2004, Bayar et 2002) from different aspects.

The need for knowledge on the development and progression of RA and also the validation of the criteria for assessment of the disease has been an important topic for many years. The suppression of the inflammation is the goal when treating patients with RA. Since it is a chronic disease, it is important to know the outcome in the long-term on the TMJ. The manifestation of RA can be various and the treatment results vary due to different reasons.

It is also important to know the possibility of remission and response to treatment. Both the EULAR and ACR criteria are in use ((Prevoe et al., 1996; A. M. van Gestel et al., 1996) and they have constructed methods for measuring disease activity. It is important to include parameters that show several aspects of the disease. The Disease Activity Score (DAS) is one of the most used and shows good validity (Prevoe et al., 1996; Svensson, Schaufelberger, Teleman, & Theander, 2000; A. van Gestel & van Riel, 1996). It combines the Ritchie articular index (RAI), number of swollen joints (SJC), ESR or CRP. General Health measured by VAS can also be used in the calculation. Several studies have shown that CRP is an alternative to ESR (Kushner, 1991; Mallya et al., 1982; Skogh, Gustafsson, Kjellberg, & Husberg, 2003; van Leeuwen et al., 1993; Wolfe, 1997a, 1997b). There have been no studies on DAS and the correlation to the TMJ in RA, which would be a more complete way of estimating the consequences of RA in the TMJ. There are few long-term studies on the progress of RA in the TMJ and its correlation to the medical/general status. The study design varies; the groups are relatively small, the correlation to general disease is not always clearly investigated, there are no control-groups without general disease and they report different treatment outcome. Tegelberg et al 1996 (Tegelberg & Kopp, 1996), studied effects of physical training after three years in rheumatoid arthritis and ankylosing spondylitis and

found a positive effect on TMD, although the degree of inflammation had increased. Wenneberg, B et al 1991 (Wenneberg, Kopp, & Grondahl, 1991) reports an improvement on subjective, clinical and radiological findings on steroid intra articular injection after eight years in patients with TMJ arthritis. Vallon et al, 2002 (Vallon, Akerman, Nilner, & Petersson, 2002) studied the long-term effect of steroid and nonsteroid intra articular injection in RA after 12 years. The results showed a slight and slow impairment in both groups. The general status was not evaluated.

1.4 Paper 5

The frequent inflammatory involvement of the temporomandibular joint (TMJ) in rheumatoid Arthritis (RA) has been well-documented (Akerman, Jonsson, Kopp, Petersson, & Rohlin, 1991; Ardic et al., 2006; Bayar et al., 2002; Bracco et al., 2010; Kallenberg, Wenneberg, Carlsson, & Ahlmen, 1997; Nordahl, Alstergren, Eliasson, & Kopp, 2001) (Kallenberg A., 2013). Since RA is a chronic disease, it is important to know the long-term outcome radiologically in the TMJ and in regard to the dental situation. However, knowledge in this field is limited since there are few long-term studies on the progression of RA in the TMJ and its correlation to the medical/general status. The study design varies since the groups are relatively small, the correlation to general disease is not always clearly investigated, and there are no control groups without general disease. Studies have registered the outcome of different treatments in the long-term. (Tegelberg & Kopp, 1996; Vallon et al., 2002; Wenneberg et al., 1991) Voog et al, 2003, 2004 (Voog et al., 2003, 2004) studied radiological findings from the TMJ in RA and PA (psoriatic arthritis) in relation to different inflammatory markers and the progress after 25-46 months. She found a correlation between these variables, although the progression was minor as a group, but larger as progression in individuals. Documentation regarding the long-term progression of RA in the temporomandibular system is insufficient and requires a thorough and extensive investigation. To evaluate the TMJ radiologically, computer tomography and MRI are regarded to be more accurate methods than panoramic radiography.

In panoramics, it is difficult to determine a correct form where there are also distortions making it not as exact as other radiological methods. (Ahmad et al., 2009; Crow, Parks, Campbell, Stucki, & Daggy, 2005; Dahlstrom & Lindvall, 1996; Epstein, Caldwell, & Black, 2001; Fallon, Fritz, & Laskin, 2006; Honey et al., 2007; Masood, Katz, Hardman, Glaros, & Spencer, 2002; Mawani et al., 2005; Molander, 1996; Ruf & Pancherz, 1995; Sato, Fujii, Takada, & Yamada, 1990; sbu, 2004; Schmitter et al., 2006; Winocur, Reiter, Krichmer, & Kaffe, 2010). It is considered as having an acceptable reliability, but registering a negative finding does not exclude disease (Dahlstrom & Lindvall, 1996). However, it is accurate when studying gross changes in the TMJ. In determining the dental/alveolar bone status, panoramics can also be useful and is sometimes the first choice (Winocur et al., 2010). Estimating alveolar approximal bone loss (ABL) is possible with both intraoral and panoramic radiography according to the SBU (Swedish Council on Health Technology Assessment). There is an underestimation of the ABL-status (sbu, 2004) and Akesson (Akesson, Hakansson, & Rohlin, 1992) describes that the underestimation of bone loss in panoramics ranges from 13-23% and in bitewings from 11-23%. Molander (Molander, Ahlqwist, & Grondahl, 1995) concludes that panoramics are useful but not alone in limited regions. Persson (R. E. Persson et al., 2003) et al found that panoramic radiography may in parts substitute intraoral radiographs to evaluate bone level. (Akesson et al., 1992; Molander, 1996; Molander et al., 1995; R. E. Persson et al., 2003; sbu, 2004)

Knowledge regarding the effects from inflammatory diseases is not fully known concerning the effect on dental alveolar bone loss (ABL) and RA. The similarities in the pathogenesis and possible common underlying inflammatory response in both periodontitis and RA have been discussed for several years. Many studies show correlations between RA and periodontal disease but there is uncertainty concerning the connection between the two diseases. (Ribeiro, Leao, & Novaes, 2005) (Biyikoglu et al., 2009; Demmer, Molitor, Jacobs, & Michalowicz, 2011; Mirrieles et al., 2010)

Pain is one of the major symptoms in rheumatoid arthritis and causes different negative consequences on daily activities. Fatigue and stiffness also affects the patients. Different methods have been created

to examine these aspects. One of the most reliable is the Health Assessment Questionnaire (HAQ) (Bruce & Fries, 2003). The reliability between HAQ and the severity of the disease and progression is good. (Bessa-Nogueira, Vasconcelos, Duarte, Goes, & Bezerra, 2008; Bruce & Fries, 2004; Bruce & Fries, 2005; Wiles et al., 2000)

2 AIM

- To compare rheumatoid arthritis (RA), psoriatic arthritis (PA) and ankylosing spondylitis (AS) and control subjects with regard to subjective, clinical and radiological symptoms in the masticatory system. (Paper 1 and Paper 2).
- To compare an RA group and a control group with temporomandibular disorders without any diagnosis regarding subjective symptoms in the masticatory system, self-rating physical health, self-rated mental well-being and to study the correlation between subjective masticatory symptoms and general well-being (Paper 3).
- To study the long-term development of RA in the TMJ and masticatory system and the progression of the general disease and compare the findings with a control-group (C) with temporomandibular disorders without any diagnosis of general joint disease (Paper 4).
- To study the long-term development of a group of RA patients concerning differences regarding radiological findings in the TMJ and concerning approximal alveolar bone loss (Paper 5).

3 PATIENTS AND METHODS

3.1 Paper 1 and Paper 2

The patient groups in Paper 1 and Paper 2 are the same. The C group is also the same in the two first papers, but in Paper 1, they are in higher numbers than in Paper 2. (See Table 1)

The RA group comprised 61 subjects with rheumatoid arthritis, according to the ARA criteria (definite and classical). (Ropes, Bennett, Cobb, Jacox, & Jessar, 1958). They were randomly selected from among patients attending the polyclinic at the Department of Rheumatology at the University Hospital of Gothenburg, Sweden. Their median age was 58 years (range 24 -80), where 12 % were males and 88% females. The RA group has been described previously (Kallenberg et al., 1997).

The PA group comprised 61 subjects with psoriatic arthritis, according to the criteria of Moll and Wright (Moll & Wright, 1973) (13), randomly selected from subjects referred from various parts of Finland to the Psoriasis Center in Helsinki for rehabilitation. Their median age was 51 years (range 25-72), where 61% were males and 39% females. The PA group has been described earlier (Kononen, 1986).

The AS group comprised 61 subjects with ankylosing spondylitis, according to the Rome criteria (Kellgren, 1963). They were randomly selected from the Ankylosing Spondylitis Patient's Association in Gothenburg and/or attended the Department of Rheumatology at the University Hospital of Gothenburg, Sweden. Their median age was 43 years (range 25-72), where 72% were males and 38% females. The AS group has been described in detail earlier (Kononen, 1986)

The C group comprised 61 (Paper 1) or 77 (Paper 2) subjects with no known inflammatory joint or skin disease. This group was randomly selected from subjects attending the Dental Clinics, University of Helsinki, for restorative dental treatment. Their median age was 51 years (range 21-72), where 66% were males and 34% females. Details regarding the C group have been given earlier (Kononen, 1986).

Table 1. Distribution of the subjects by gender and group in Paper 1 and Paper 2. C1 represents Paper 1 and C2 represents Paper 2.

	RA	PA	AS	C1	C2
Men	7	37	46	51	37
Women	54	24	15	26	24
Total	61	61	61	77	61

Paper 1: Radiographic Examination:

Orthopantomography was used to examine the condyles of the TMJs of subjects in all groups. Radiographs were made with the teeth in the incisal position, i.e. with the mandible slightly protruded. If the condyles had not been accurately imaged, another radiograph was made with the mouth maximally opened. Radiographic signs of deviation in shape (flattening, osteophytes, loss of condylar head); changes of cortical outline (erosions and sclerosis); and subcortical cysts were recorded.

A radiographic index modified after that of Wenneberg (Wenneberg et al, 1983) was constructed. The right and left condyles were scored separately. The radiographic signs were scored as 1 point when local and as 2 when extensive. Accordingly, a total score from 0 to 24 points was established for each subject. Before interpretation of the radiographs, the radiographic signs used were defined and discussed by the three examiners. The radiographs were read in random order by the examiners independently and without reference to provenance. The findings were compared and, in cases of disagreement in interpretation, discussed until the examiners achieved full agreement in their interpretations.

Paper 2. Subjective symptoms from the masticatory system were assessed by questionnaire. The same questionnaire was used in both Sweden and Finland. Questions were posed concerning stiffness/tiredness in the jaws, sounds from the TMJ, difficulties in

wide mouth opening, pain in the face/jaws, headaches, pain in the face/jaws on opening wide and /or chewing and TMJ locking/luxation. The anamnestic dysfunction index (Ai) was determined (Helkimo, 1974).

Clinical examination.

Clinical findings from the masticatory function system were recorded by routine examination procedures (Carlsson & Helkimo 1972; Krogh-Poulsen & Olsson 1969) The examination included palpation of the masticatory muscles and the TMJ, maximal mouth opening capacity, pain on mandibular movements and TMJ sounds. The occlusion was examined for interferences between the retruded position (RP) and intercuspal position (IP) causing lateral displacement of the mandible > 0.5 mm as measured in the incisal region. The sagittal and vertical distance between RP and IP was measured to the nearest millimeter. Interferences of the mediotrusion side within 3 mm of IP, as measured in the incisal region, were also recorded.

The severity of the clinical signs was estimated by the clinical dysfunction index (Di) of Helkimo (Helkimo, 1974).

3.2 Paper 3

RA group

The patients in this group attended the outpatient clinic of the Department of Rheumatology at the Sahlgrenska University Hospital, Gothenburg and were investigated in a consecutive order as they attended the unit for medical treatment. All patients had a diagnosis of definite or classical RA (Ropes et al, 1958) and were subjected to a thorough medical, psychological and social examination by the staff at the hospital, including physician, nurse, physiotherapist, social worker, etc (Ahlmén, 1990). Eighty-seven patients (8 men and 79 women) were clinically examined, comprising a questionnaire, a clinical stomatognathic examination and extraoral and intraoral photographs.

Radiographic examinations included orthopantomograms and cephalometric radiographs. Six of the patients were later excluded because of other diagnoses than RA (two with juvenile chronic arthritis; one with ankylosing spondylitis; one with psoriatic arthritis; one had an uncertain diagnosis; and one was excluded due to lack of interest in the investigation). After exclusion, 81 patients remained (74 women and 7 men), with a mean age of 56.1 years (range 22-80 years) in the RA group (Table 2). This group received conservative dental treatment by different dentists in the Gothenburg area and had no previous treatment due to TMD.

C group

The comparison group originally comprised 49 consecutive patients referred to the Department of Stomatognathic Physiology in Gothenburg for the diagnosis and treatment of TMD. These patients had no history of general joint symptoms, were matched to the RA patients according to gender and age and underwent the same examinations as the RA group including the medical, odontological and psychological examination by the same dentist, physician and nurse, etc. If the medical examination revealed signs of joint disease, the patient was excluded. Eight of the patients in group C were later excluded. One because of unmatchable age; one due to lack of interest; three with former joint diseases revealed at the medical examination; and three not wanting to attend the medical examination. The remaining 41 patients (35 women and 6 men) had a mean age of 51.1 years (range 22-76 years) and comprised the C group. The patients in this group received their conservative dental treatment in the Gothenburg area regularly and had not received any treatment for TMD during the previous three years. (Table 2)

Table 2. Age and gender distribution of the individuals with rheumatoid arthritis (RA group) and those with temporomandibular disorders but without general joint symptoms (C group).

	Age groups						Total
	21 -30	31 -40	41 -50	51-60	61 -70	71 -80	
RA							
Males	0	3	0	0	2	1	7
Females	1	10	11	21	27	4	74
C							
Males	1	1	1	1	2	0	6
Females	2	6	9	8	6	4	35

Assessment of subjective symptoms in head and face and general well-being.:

Twenty-eight multiple-choice questions were used in determining subjective symptoms from the masticatory system. The questions included symptoms and conditions in the masticatory system (e.g. severity, frequency and duration of pain and dysfunction, impaired chewing ability, joint sounds, etc.); general joint symptoms (pain, stiffness, duration, relation to symptoms from the TMJ, medication); dental status; dental treatment; and the need for stomatognathic treatment. If the patients had difficulties in understanding any of the questions, the examiner gave a short explanation. Apart from general information about the purpose of the questionnaire, the examiner only gave neutral and uniform explanations when necessary. Data from this questionnaire was also used to calculate the anamnestic dysfunction index according to Helkimo (1974). The severity of the subjective symptoms in the masticatory system was determined by the patients according to a 5 point scale (1 = no or minimal discomfort, 2 = slight discomfort, 3 = moderate discomfort, 4 = severe discomfort, 5 = very severe discomfort).

All patients responded to questions concerning general morning

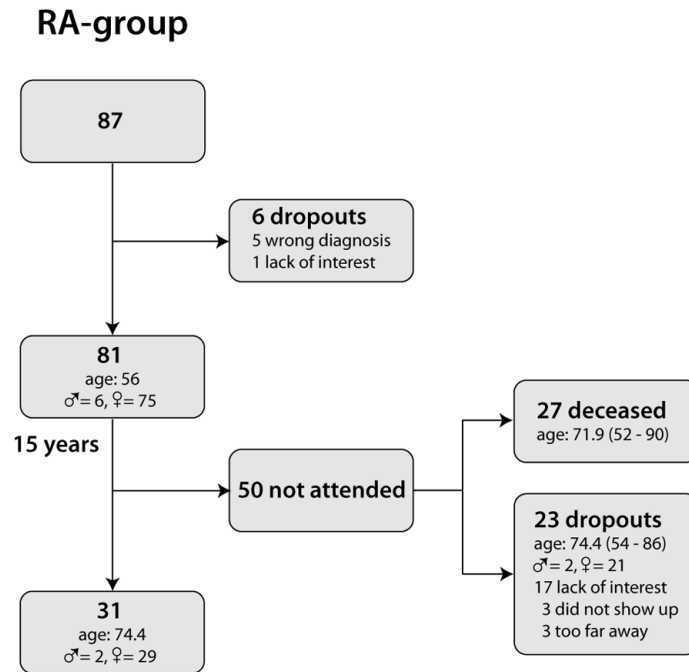
stiffness, pain at rest and motion, and ability to carry out daily activities. They also answered 48 questions included in a Body Symptom Scale (BSS), (Sjoberg, Svensson & Persson, 1979; Persson & Sjoberg, 1987; Ahlmen, 1990), which is a questionnaire regarding the patient's own opinion of his or her physical health, e.g. concerning headaches, joint problems and joint pain, sleeping disturbances, tiredness, sweating, etc. The BSS is divided into three subgroups each giving a score ranging between 1 and 4. A higher score indicates less discomfort. They answered 72 questions in the Mood Adjective Check List (MACL), (Sjoberg et al., 1979); Augustinsson, Sullivan & Sullivan, 1986; Persson & Sjoberg, 1987; Ahlmén, 1990). The MACL questionnaire concerns the patient's own opinion of her/his mental well-being. It is divided into six subgroups: 1. *pleasantness/unpleasantness*; 2. *activation/deactivation*; 3. *calmness/tension*; 4. *extroversion/introversion*; 5. *positive/negative social orientation*; and 6. *confidence/lack of confidence*. In each subgroup, a score ranging from 1 to 4 was assigned to each patient. A higher score indicates a more positive emotional state. These questions were asked in a random order to achieve as adequate answers as possible. An overall MACL score was also determined (range 1-4). The questionnaires were designed for computer analysis as in earlier investigations (Oden & Wedel, 1975; Wenneberg & Kopp, 1982).

3.3 Paper 4

The RA group from Paper 3 was examined after 15 years. 31 patients (38%) attended the examinations. Twenty-seven patients (32%) were deceased and 23 patients (30%) did not participate due to various reasons. The majority of the dropouts answered they did not wish to participate (n=17). Others were too sick or handicapped. Three did not show up. Some now lived too far away (see Fig 1).

The C group from Paper 3 was also examined after 15 years. At the follow-up, 18 patients (44%) attended the investigation. Twenty-one (51%) did not attend the follow-up. The reasons were mostly not wishing to due to lack of interest and/or being healthy in the temporomandibular system. Three were sick, one had moved, three did not show up or could not be reached. Two patients (5%) were

deceased. (Fig 1). Informed consent was obtained from all subjects participating in the study.



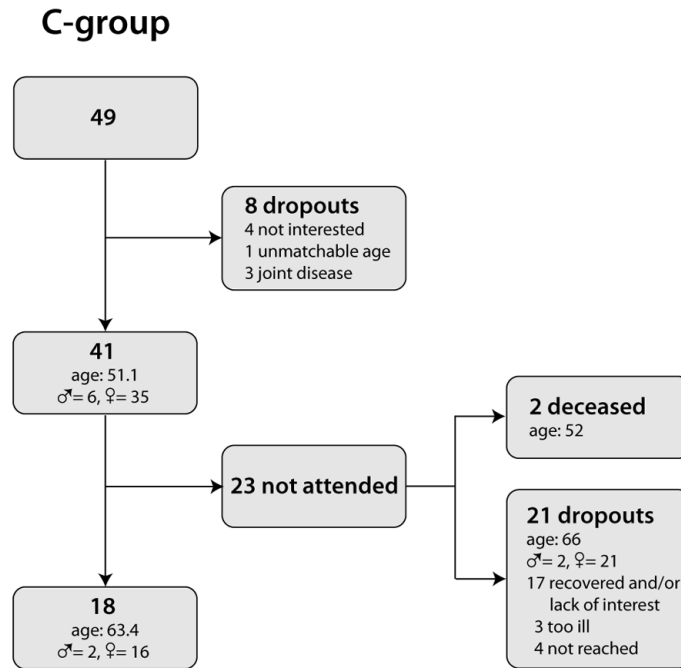


Figure 1. Number of patients in the RA group and C group at Examinations 1 and 2, number of drop-outs and reasons for not attending.

Subjective and clinical examinations

The RDC/TMD criteria (Dworkin et al., 2002) were not used because it did not exist at the first examination and it does not allow quantitative comparisons, which was the scope. All patients received the same questionnaire consisting of 28 multiple-choice questions concerning subjective symptoms from the masticatory system described in paper 3. (Helkimo, 1974) (Kallenberg et al., 1997). The subjective symptoms were also recorded and calculated according to Helkimo's Anamnestic Index (Ai 0 – II) (Helkimo, 1974). The Helkimo's Index was used to allow comparison at both examinations.

The clinical examination from the masticatory system was performed by routine examination procedures (Helkimo, 1974) and is described in Paper 2. All the clinical signs were quantified in the Helkimo's (1974) Dysfunction Index (Di 0 – III) (Helkimo, 1974). The same examiner performed all clinical examinations on both occasions.

Medical examination. The same rheumatologist performed the investigations on both occasions. In this article, the following variables are reported: CRP (C-reactive protein). CRP is registered from ≥ 4 since a level above 4 is considered abnormal. Ritchie's Articular Index (RAI) measuring the number of joints tender on palpation (max 78 points). SJC (swollen joint count) – the number of swollen joints. A 44 joint count was used. DAS (disease activity score) – a validated index that measures disease activity in RA and is a combined index. DAS 44 was used which is calculated on 44 joints (original DAS). Using DAS, several thresholds have been developed for evaluating the disease activity, that is, remission <1.6 , low <2.4 , high disease activity >3.7 (Lerndal & Svensson, 2000). SJC and DAS were not measured in the C group because if they had raised levels in CRP and RAI, they were excluded. If this was not the case and the CRP was still high due to e.g. an infection, the "C patient" could still attend.

Physical discomfort and general well-being. All patients also answered 48 questions included in a Body Symptom Scale (BSS) (Ahlmen et al., 1990; Kallenberg et al., 1997; L. O. Persson & Sjoberg, 1987; Sjoberg et al., 1979), which is a questionnaire regarding the patient's opinion of his/her physical health, described in Paper 3.

The MACL (Mood Adjective Check List, also called MOOD) comprised 72 questions concerning the patient's own opinion regarding their mental well-being (Ahlmen et al., 1990; Kallenberg et al., 1997; L. O. Persson & Sjoberg, 1987; Sjoberg et al., 1979; Sostmann, Reich, Grapentin, & Langer, 1990; Sullivan, Ahlmen, & Bjelle, 1990; Sullivan et al., 1993). The MACL is divided into six subgroups. It is also described in Paper 3.

3.4 Paper 5.

The RA group from Paper 3 was examined after 15 years. 31 patients (38%) attended the examinations. Twenty-seven patients (32%) were

deceased and 23 patients (30%) did not participate due to various reasons. The majority of the dropouts answered they did not wish to participate (n =17). (See paper 4) (Fig 1).

The C group from Paper 3 was also examined after 15 years. At the follow-up, 18 patients (44%) attended the investigation. Twenty-one (51%) did not attend the follow-up. Two patients (5%) were deceased. (See Fig 1). Informed consent was obtained from all subjects participating in the study.

Clinical examination.

The clinical examination from the masticatory system was recorded by routine examination procedures and is described in an earlier article 4. (Helkimo, 1974; Kallenberg A., 2013; Wenneberg, 1983). All the clinical signs were quantified in the Helkimo (1974).

Medical examination.

The medical examination comprised several parts which is described in previous articles (Kallenberg et al., 1997; Kallenberg A., 2013). In short, CRP, RAI, SJC and DAS were measured.

Also, the HAQ was registered and (Bruce & Fries, 2003, 2005) the Health Assessment Questionnaire (HAQ) (Eular 2000), comprises eight questions asking about the patient's ability to:

1. Dress and wash hair
2. Rise up from a chair and in and out of bed
3. Meals. Cut meat, raise a full glass to the mouth and do cooking
4. Walk outdoors on level ground and walk downstairs
5. Hygiene. Wash and wipe everywhere on the body
6. Range of motion. Lift a 2 kg bag of sugar from a highly situated shelf and bend down to the floor.
7. Grip: Open car doors, jars with screw lids and turn on the water tap.

8. Other activities: Shop, get in and out of a car and vacuum clean.

Each question has six alternatives with different points graded from 0-3 depending on the importance of the dysfunction: Without difficulties (0); with some problems (1); very difficult and/or using aids (2); help from someone (2) and, can't do at all (3). The maximum point is 24. The sum of the points is divided with the number of questions answered and a sum between 0.13 – 3.00 is created. A higher value means a more handicapping situation.

Medication present at Examination 2 The medication these patients were given were grouped into:

MED 1 Paracetamol

MED 2: ASA ; MED 1 and MED 2 were pooled into the same group = (MED 2)

MED 3: NSAID (i.e. anti-inflammatory drugs)

MED 4: Steroids (cortisone)

MED 5: DMARD (ie MTX, Embrel)

In MED 1 – MED 3, the patients reported yes (=1) or no (=0), while in MED 4 they reported 1 (older type), 2 (MTX), 3 (biological type) or 4 (several of the above mentioned). They have been added to either yes (=1) or no (=0). The results of medication are shown in the Discussion part 5.4

Radiographic examinations

Panoramic radiographs were taken by the orthopantomograph, Cranex Tome 001 x 1.3 at the Department of Oral Radiology, Faculty of Odontology, Gothenburg, according to their routine procedures. If the condyles were not accurately imaged, another radiograph was made with the jaw in maximal protrusion. The radiographic signs and interpretations were defined and discussed between the authors (AK, BW). All radiographs from both examinations and both groups (RA/C) were read blindly and thus the examiner did not know which radiograph belonged to which examination or group. The

temporomandibular joints and the marginal bone loss were reviewed by one and the same examiner on all occasions. Only the condyles were examined due to the risk of misinterpretation in the fossa – eminence area. Radiographic signs of deviation (flattening, osteophytes, and loss of condylar head), changes of cortical outline (erosions, sclerosis) and subcortical cysts were recorded. A radiographic index ad modum Wenneberg was used (Wenneberg, Kononen, & Kallenberg, 1990) (see paper 1). The right and left condyles were scored separately. The score was 1 point when the sign was local/mild and 2 points when the sign was extensive/severe. A total score between 0 to 24 points was thus given to each patient. The approximal alveolar bone loss (ABL) was measured on the pantomogram. The number of teeth with a larger bone loss than 2 mm measured from the enamel cement junction was counted. An adjusted ruler ad modum Björn (Björn H, 1969) was used to compensate for the magnification (1.3 x). Only approximal surfaces were counted due to insecurities to measure other surfaces. The total number of teeth was also registered.

4 RESULTS

4.1 Paper 1 and Paper 2

Radiographic findings.

The radiographic index (RI) showed significantly higher values in the disease groups (RA, PA and AS) compared to the C group ($p < 0.05$ and $p < 0.01$).

In all different specific radiographic parameters, except for osteophytes and sclerosis, the RA group showed significantly higher values ($p < 0.05$ and $p < 0.01$).

In the RA group, cortical erosions of the condyle was more frequent in women than in men ($p < 0.05$), while in the AS group, cortical erosions and flattening of the condyle were more frequent in men than in women ($p < 0.05$).

No significant difference between genders was found in the PA or C group regarding any radiographic sign.

Subcortical cysts ($p < 0.05$) in the RA group and cortical erosions in the PA group correlated negatively to age ($p < 0.05$).

No significant correlations between age and radiographic signs were found in the AS or C group. (See Table 3)

Table 3. Percentage distribution of radiographic changes in the mandibular condyle

Radiographic change	RA (n=61)	PA (n=61)	AS (n=61)	C (n=77)
Flattening	34†	23*	20*	8
Osteophytes	7	13†	3	1
Loss of condylar head	8*	2	6	0
Cortical erosions	56†	18†	18†	1
Cortical sclerosis	10	3	0	7
Subcortical cysts	13†	0	0	0

Subjective symptoms

The severity of subjective symptoms and the anamnestic index were significantly higher in all three disease groups than in the C group ($p < 0.05$ and $p < 0.01$). Fifty-one per cent in the RA and 53% in the PA group had an Ai II compared with 25% in the AS and C groups.

The RA group had significantly more symptoms on most of the parameters except on TMJ sounds/locking and pain in jaws on opening wide than in any of the other groups ($p < 0.05$ and 0.01). (Table 4.) Pain in the jaws on function was more common in the PA group (0.01), and as a whole, the disease groups had more significant symptoms than the control group. Of the disease groups, the AS group reported fewer symptoms than the others.

No significant correlations to age and gender were found in any of the four groups with regard to individual symptoms.

Table 4. Percentage distribution of symptoms from the masticatory system in the rheumatoid arthritis (RA), psoriatic arthritis (PA), ankylosing spondylitis (AS) and control (C) groups.

Symptoms	RA (n = 61)	PA (n = 61)	AS (n = 61)	C (n = 61)
Morning stiffness/tiredness in the jaws	20**	22**	15*	3
Sound from TMJ†	61	57	44	46
Difficulties in wide mouth opening	33**	17	20*	5
Pain in the face/jaws headache at rest	33**	20*	12	2
Pain in the face/jaws on opening wide and/or chewing	25*	43**	13	5
TMJ locking/luxation	7	17	5	13

Clinical findings

In general, higher frequencies of the clinical findings were seen in the RA, PA, and AS groups than in the C group. However, the RA group showed significantly less muscle tenderness than the PA, AS, and C

groups ($p < 0.01$). The maximal mouth opening capacity was significantly less in the three disease groups than in the C group ($p < 0.01$) where the RA group had the lowest values. The occlusal support was similar in all four groups. The vertical and sagittal distances between RP and IP were significantly greater in the three disease groups than in the C group. ($p < 0.01$).

The dysfunction index showed significantly higher values in the RA and PA groups than in the C group ($p < 0.01$) but not in the AS group.

4.2 Paper 3

Subjective symptoms.

No significant gender differences in the RA and C groups were seen for any of the variables investigated. The males and females were thus pooled in each group.

37% of the RA group and 63% of the C group had their symptoms more than twice a week.

Headaches were reported by 53% of the C patients and 40% of the RA patients. Twenty-three per cent of the RA group were symptom free, while none in the C group was without symptoms in the head and face according to the questionnaire used ($p < 0.05$). 37% of the RA group and 63% of the C group had their symptoms more than twice a week.

The C groups evaluated their subjective symptoms significantly worse than the RA group ($p < 0.01$). In the C group, there was significantly less symptoms with higher age ($p < 0.05$).

The anamnestic index, according to Helkimo, showed significantly higher values in AiII in the C group ($p < 0.05$).

A majority of the patients had their symptoms in the temporomandibular system more than 6 months in both groups. 65% of the RA group and 55% of the C group had a duration of more than one year.

28% of the RA group reported a relationship between the debut of TMJ symptoms and the onset within the general joint disease.

General well-being and Body Symptom Scale.

The RA group had significantly more discomfort in BSS 1 and 2, which is related to joint and muscle pain and dysfunction ($p < 0.01$) compared to the C group.

Concerning mental well-being in Overall-MOOD, there were no significant differences but the RA group had lower values in deactivation/activation ($p < 0.01$) while the C group reported lower values in calmness/tension ($p < 0.01$).

4.3 Paper 4 and Paper 5

The Dropouts

After 15 years, 23 patients (30%) in the RA group did not participate. All of these patients were particularly asked for the reason. ($n = 17$). Their mean age by the time of Examination 2 was 74.4 (54 – 86) years, so they were 12 years older than the group which did attend Examination 2, which may explain a reason for not attending. Twenty-seven RA patients (32%) were deceased. Their mean age at Examination 2 should have been 78 (56 – 95) years, which differs from the other “dropout group” ($p < 0.01$). The cause of death was, in 56% of the deceased, possibly related to the general disease. At the follow-up, there were only two men in each of the groups. Therefore, all individuals were pooled in the respective groups for the statistic analysis.

Subjective symptoms.

There was no significant reduction of discomfort concerning subjective evaluation of the symptoms within the RA group (Figure 2), while the C group showed significant improvement ($p < 0.01$) regarding the severity of their symptoms. Comparing the RA and C groups, there were reduced symptoms in the C group ($p < 0.01$) (Figure 1).

The patients' different subjective symptoms were described according to Helkimo's anamnestic index (Ai). (Figure2).

Regarding individual symptoms, the RA group showed no significant changes, but there were tendencies toward more difficulties with the

mouth opening capacity, mandibular movements and pain in the jaws. (See Table 1).

The C group reported no improvement, although some tendencies were found.

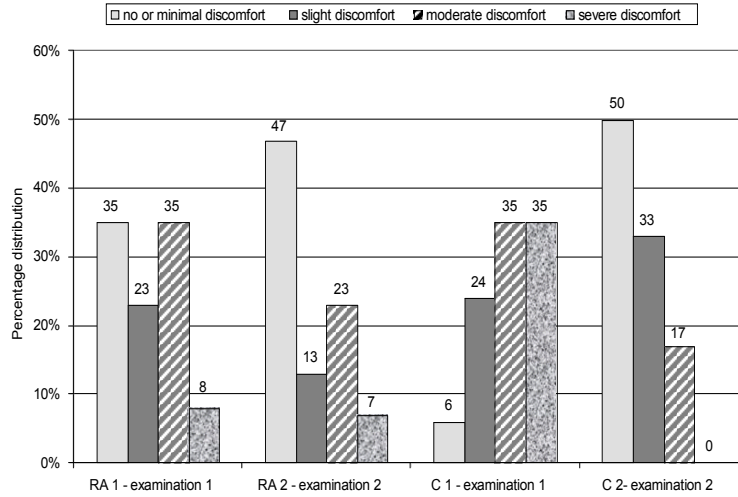


Figure 2. Percentage distribution and test of differences or reported evaluated subjective symptoms from the temporomandibular system in the RA and C groups at Examinations 1 and 2. (ns diff. between RA groups; $p < 0.01$ between C groups).

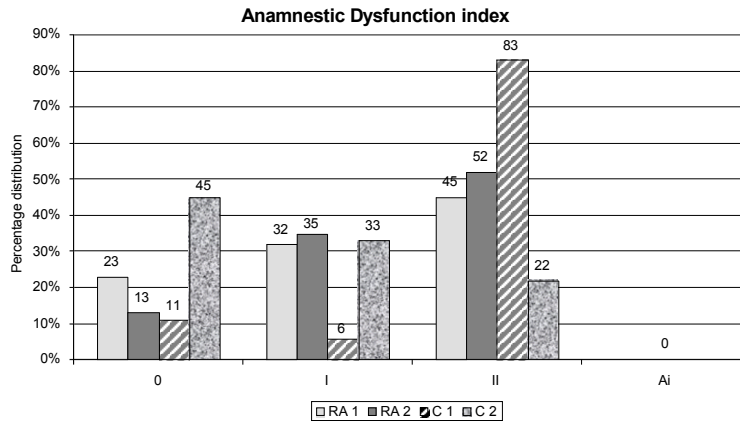


Figure 3. Percentage distribution and test of differences of reported symptoms (Ai) from the masticatory system in the RA and C groups at Examinations 1 and 2 according to Helkimo's dysfunction index (ns diff between RA groups; $p < 0.01$ between C groups).

Clinical findings

Neither the RA group nor the C group showed any changes between the two examinations according to Helkimo (Di). There were no significant differences between the RA and C groups **at the follow-up. Figure??**

Regarding individual clinical findings in the RA group at Examination 2, there were significantly more tender jaw and neck muscles ($p < 0.001$), while there were tendencies to more TMJ pain and pain on mandibular movements. Reduced vertical overbite ($p < 0.01$), reduced number of teeth ($p < 0.0001$) and increased number of occluding pairs of teeth ($p < 0.01$) were reported at Examination 2 (Table 2) in the RA group.

The C group showed reduced number of teeth ($p < 0.01$) between the two examinations.

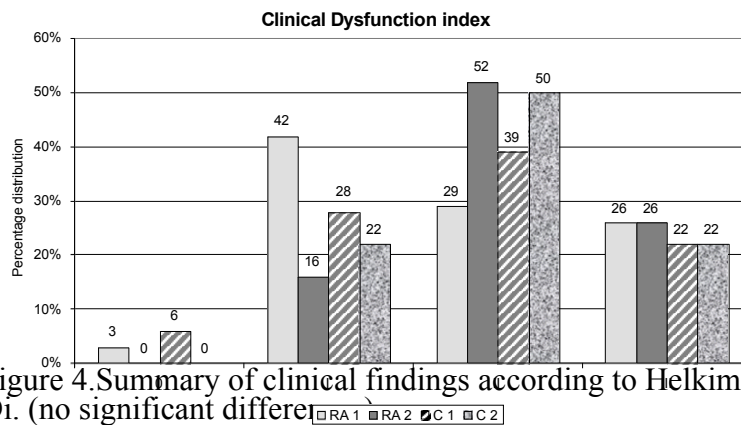


Figure 4. Summary of clinical findings according to Helkimo Di. (no significant differences between RA and C groups)

Table 5. Distribution of different clinical findings in the RA and C groups at the two examinations. It also shows tests of differences within and between the two groups. Percentage distribution and mean values and ranges are given. $p < 0.01 = **$, $p < 0.001$ or $p < 0.0001 = ***$

CLINICAL FINDING	GROUP			GROUP			p-value RA 1-C 1	p-value RA 2-C 2
	RA 1	RA 2	p-value RA 1-RA 2	C 1	C 2	p-value C 1-C 2		
Pain on palpation	36	52	$p < 0.05$	56	44	ns	ns	ns
Pain on palpation muscles	77	94	***	94	94	ns	ns	ns
Crepitation in the	77	90	ns	67	78	ns	ns	ns
Clicking in the TMJ	19	16	ns	61	28	$p < 0.05$	**	ns
Pain on movement	21	45	$p < 0.05$	28	56	ns	ns	ns
Pain on palpation	36	77	***	44	50	ns	ns	ns
Number of teeth	23	20	***	24	23	**	ns	ns
Number of occlusal	9	11	**	11	11	ns	ns	ns
Maximal mouth opening range	45 (34-57)	42 (35-59)	ns	45 (35-53)	47 (40-58)	ns	ns	ns
Vertical overbite range	4 (-3-+8)	3 (-1-+6)	$p < 0.01$ **	4 (1-10)	3 (0-6)	ns	ns	ns
Horizontal overjet range (in mm)	3 (1-11)	3 (0-6)	ns	3 (1-10)	4 (0-10)	ns	ns	ns
Sagittal distance range	1 (0-2)	1 (0-2)	ns	1 (0-3)	1 (0-2)	ns	ns	ns
Vertical distance range	1 (0-5)	1 (0-3)	ns	1 (0-3)	1 (0-2)	ns	ns	ns

ns = not significant $p < 0.05$ = tendency ** $p < 0.01$ *** $p < 0.001$

Medical Data.

All medical data was higher in the RA group than in the C group and the latter had normal values as could be expected. There were no significant differences between or within any of the groups. (Table 6)

Table 6. Distribution in CRP, Ritchie and SJC score.

GROUP	CRP	RITCHIE	SJC
	> 4	(0 - 78)	(0 - 44)
RA 1	19 (4 - 64)	10 (0 - 26)	13 (3 - 27)
	ns	ns	ns
RA 2	20 (4 - 81)	11 (0 - 26)	15 (3 - 28)
C 1	5 (4 - 14)	1 (0 - 10)	Missing data
	ns	ns	ns
C 2	4 (4 - 4)	1 (0 - 13)	1 (0 - 16)

ns = not significant p<0.05 = tendency **p<0.01 ***p<0.001

Table 7. DAS score and test of differences in the RA group (m=mean value)

Disease Activity core (DAS) in the RA group				
Level		DAS 1 n=29	DAS 2 n=31	p-value
High	> 3.7	10	17	
Medium	3.7 - 2.4	17	12	
Low	< 2.4	1	1	
Remission	< 1.6	1	1	
		m = 3.6	m = 3.7	ns

ns = not significant p<0.05 = tendency **p<0.01 ***p<0.001

m = mean value

General well-being (BSS and MACL).

The BSS-scale (the self-rated physical discomfort) is shown in Table 5. In the RA group, there were no differences between the examinations in any variable in BSS. In the C group, however, there were significantly lower values in all BSS between examinations indicating more discomfort. Between the RA and C groups, there were significantly lower values in the RA group in BSS1 and BSS 3 at both examinations, but no difference in BSS2 (Table 8).

Table 8. Self-rated discomfort in 31 RA and 18 C patients. (BSS) A higher score means less discomfort. The p-values show differences within the RA and C groups respectively and between the RA and C groups.

BSS scale	GROUP n=31			GROUP n=18				
	RA1 m	RA 2 m	RA 1-RA 2 p-value	C 1 m	C 2 m	C 1 C 2 p-value	RA 1-C 1 p-value	RA 2-C 2 p-value
BSS 1*	2.3	2.0	ns	3.4	2.7	**	****	***
BSS 2*	3.0	2.7	ns	3.4	2.6	**	ns	ns
BSS 3*	1.5	1.7	ns	3.5	2.4	***	****	***

m= mean, **=p<0.01, ***= p<0.001, ****= p<0.0001

In the RA group, there were significantly lower values in MACL 1, 2 and 7 ($p<0.01$) between Examinations 1 and 2 meaning generally more unpleasant mood and more passiveness (Table 6). In the C group, there was a significantly lower value in MACL 2 ($p<0.001$) also meaning a more mental passive situation. Between the RA and C groups at Examination 1, there were significantly lower values in the C group in MACL 3 ($p<0.001$). At Examination 2, there were significantly higher values in the C group MACL 6 ($p<0.01$), indicating better confidence in the C group (Table 9).

Table 9. Mood Adjective Check List (MACL). A higher score means a more positive emotional state. The results are given as x-means and SD.

The p-values show differences within the RA and C groups respectively.

	Normal values	RA GROUP n=31				C GROUP n=18			RA 1 - C 1 p-value	RA 2 - C 2 p-value
		RA 1 Mean (Range)	RA 2 Mean (Range)	RA 1 - RA 2 p-value	C 1 Mean (Range)	C 2 Mean (Range)	C 1 - C 2			
1*	3.38	3.4 (2.0-3.9)	3.0 (1.0-3.8)	**	3.1 (1.6-3.9)	3.1 (1.8-3.7)	ns	<0.05	ns	
2*	3.43	3.3 (2.0-3.9)	2.9 (1.7-3.8)	**	3.5 (2.0-3.9)	3.1 (1.9-3.9)	***	ns	ns	
3*	3.22	3.1 (1.5-4.0)	2.8 (1.5-4.0)	ns	2.3 (1.6-3.1)	2.7 (1.8-3.7)	(<0.05)	****	ns	
4*	3.06	3.1 (2.4-3.8)	2.8 (1.6-3.6)	(<0.05)	3.0 (1.9-4.0)	3.1 (2.5-3.7)	ns	ns	(<0.05)	
5*	3.64	3.6 (2.6-4.0)	3.4 (2.4-4.0)	ns	3.7 (2.5-4.9)	3.4 (2.7-4.0)	ns	ns	ns	
6*	3.07	3.1 (2.2-4.0)	2.8 (2.0-3.6)	($p<0.05$)	3.1 (2.3-4.0)	3.2 (2.7-4.0)	ns	ns	**	
7*	3.30	3.3 (2.6-3.8)	3.0 (1.7-3.6)	**	3.1 (2.3-3.5)	3.2 (2.3-3.8)	ns	(<0.05)	ns	

$p<0.05$ = tendency, **= $p<0.01$, ***= $p<0.001$

1* Pleasantness/unpleasantness 5* Positive/negative social orientation

2* Activation/deactivation

6* Confidence/lack of confidence

3* Calmness/tension

7* Overall mood

4* Extroversion/introversion

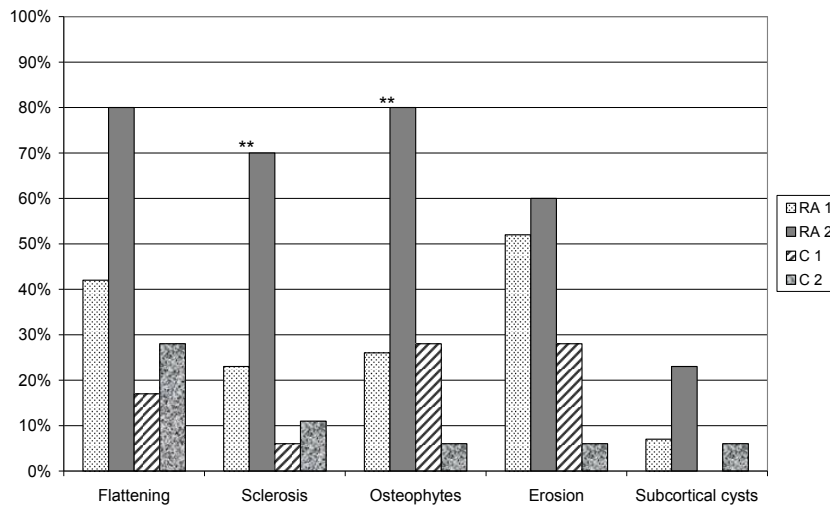
HAQ was only registered at Examination 2. There was a clear difference between the RA and C group, respectively ($p<0.0001$) as would be expected.

HAQ RA: $\bar{x} = 1.63$ (range 0.3 – 2.5), (SD=0.5) The HAQ-value runs between (0.13 -3.00)

Radiological findings

After 15 years, there were increased significant changes in the TMJ on the panoramic radiographs between the two investigations only in the RA group and on sclerosis and osteophytes ($p < 0.01$). The Radiographic Index also shows a significant degradation in the RA group ($p < 0.01$). See Figure and table:

Figure 5. Percentage distribution and test of differences of radiological changes in the mandibular condyles within the RA and C groups.



RA sign.	-	**	**	-	-
C sign.	-	-	-	-	- ** = $p < 0.01$

Regarding approximal bone loss (ABL) in the RA group, there was a significant increase in the number of teeth with a reduction of approximal bone height >2 mm from an average of 2.3 to 5.3 ($p<0.01$). No significant change could be registered in the C group. (See Table 9.)

Table 9. The radiological findings according to the radiographic index ad modum Wenneberg and test of differences within and between the two groups. A higher score means increased radiological change.

Radiographic Index (0-20 p)

GROUP	Mean	SD (range)	<i>p</i> -value
RA 1	2.5	2,5 (0 - 8)	$p<0.01^{**}$
RA 2	6.7	5,1 (0 - 16)	
C 1	1.2	1,7 (0 - 7)	ns
C 2	4.0	1,3 (0 - 4)	

Regarding approximal bone loss (ABL) in the RA group, there was a significant increase in the number of teeth with a reduction of approximal bone height >2 mm from an average of 2.3 to 5.3 ($p < 0.01$). No significant change could be registered in the C group. (See Table 3.)

Table 10. Distribution of approximal bone loss (ABL) recorded as number of teeth with > 2 mm loss measured from the enamel-cement junction within the two groups by panoramic radiographs. Test of differences, mean and range.

Approximal alveolar bone loss (ABL)			
Number of teeth with loss of alveolar bone height > 2 mm			
GROUP	Mean	SD (range) (diff)	p-value
RA 1	2.3	2,8 (0 - 10)	<0.01**
RA 2	5.2	5,3 (0 - 20) (2,9)	
C 1	3.0	4,7 (0 - 18)	ns
C 2	4.3	4,9 (0 - 17) (1,3)	

ns = not significant, $p < 0.05$ = tendency, ** = $p < 0.01$, *** = $p < 0.001$

The differences in medication after 15 years are shown in Table 11.

Regarding the medications, due to missing data, no statistical analyzes were made. Still, it is interesting to show the change between the examinations in the medical treatment. To what extent the new type of medication may have affected this study's results is difficult to say, but probably, improved results at the follow-up would have been shown.

Table 11. Percentage distribution of medication between the two examinations. The numbers within brackets are real numbers.

Medication	RA 1(81)	RA2(31)	C2(18)
Med1+2(ASA+paracetamol)	30	80(25)	28(5)
MED3(NSAID)	76	55(17)	17(3)
MED4(cortisone)	22	45(14)	--
MED5(Biol.type)	--	80(25)	--
Gold,penicillamine, chloroquine.	25	--	--
Cytotoxic drugs	4		

In the RA 2 group, 2 patients had one kind of medication, 6 had two kinds, 9 had three kinds and 8 had four kinds of medication.

5 DISCUSSION

5.1 Paper 1 and Paper 2.

The groups included in these studies should be commented on. The RA group was selected from a patient group seeking treatment at a rheumatology clinic, whereas the PA and AS groups were selected from patient organizations. (Syrjanen, 1985; Tegelberg, 1987; Tegelberg & Kopp, 1987b; Uotila, 1964; Wenneberg et al., 1990). Therefore, it can be expected that the RA group had a more severe disease level than the PA and AS groups and in unselected populations. The female/male ratio in this RA group is more skewed (7:1) than in unselected populations (3:1), which could be explained by random order. The ratio in PA and AS groups were similar to other studies (G. Carlsson, 1979; Wenneberg et al., 1990) (Kononen, 1987; Lundberg & Ericson, 1967; Rasmussen & Bakke, 1982; Resnick, 1974; Wenneberg, 1983; Wenneberg et al., 1983). The patient groups are not completely representative of the total spectrum of the diseases, but they still give us a picture of the engagement in the TMJ.

The questionnaires in assessing subjective symptoms and the methods for clinical examinations are well-documented and tested procedures. To reduce the observer variations and strengthen the validity results, the Helkimo's Dysfunction Index was used. (G. E. Carlsson, Egermark-Eriksson, & Magnusson, 1980; Helkimo, 1974; Kopp, 1976; Kopp & Wenneberg, 1983; Rieder, 1977; Wenneberg et al., 1983; Wenneberg & Kopp, 1982a, 1982b). (Garib & Qaradaxi, 2011)

Due to the limitations of the panoramic radiographic technique, only the condyles were evaluated (Petersson, 1976; Uotila, 1964). Later studies report that panoramics has its use, but its limitations should be considered (Dahlstrom & Lindvall, 1996; Fallon et al., 2006; Mawani et al., 2005; Molander, 1996).

Radiographic changes, according to the radiographic index, were found in 66% in the RA group, 38% in the PA, 30% in the AS group and 12% in the C group. Flattening and erosions of the condyle were reported significantly more often in the disease groups than in the C group. Erosions were reported in higher frequency in the RA group than in the other groups and especially in the women, which is in line

with the general disease. In the AS group, the findings were more frequent in men than in women, which reflects the severity and extension in men. Subcortical cysts were seen only in the RA group indicating a more severe inflammatory situation. Loss of condylar head was seen in all joint disease groups. All changes were significantly higher in the disease groups than in the C group, which had no known general joint disease. The C group's changes are probably due to osteoarthritis in the TMJ, which is in line with other studies. (Rasmussen, 1983). The changes found in the disease groups are therefore most likely due to the inflammatory joint disease and they are more common in the RA group which is in line with other studies but no comparison has been done before with all three joint diseases compared in the same study and with a control group. (Franks, 1969; Resnick, 1974; Syrjanen, 1985; Wenneberg et al., 1983)

The frequency of the subjective symptoms and clinical findings were mostly significantly higher in the disease groups than in the control group. Patients with RA reported more signs and symptoms than PA and AS. The findings are in line with other studies, but there are also reports on even higher symptoms and signs (Tegelberg, 1987; Tegelberg & Kopp, 1987b). Most common signs and symptoms were pain at rest and in function, morning stiffness with jaw dysfunction and difficulties in wide mouth opening and tenderness on palpation. There was significantly more crepitus in the RA and PA groups caused by structural changes in the TMJ, but not to that extent in the AS group which was a younger population. (Eriksson & Westesson, 1983; Kopp & Rockler, 1979; Oberg, Carlsson, & Fajers, 1971; Toller, 1973). Tenderness on palpation was not so common in the RA group as in the other disease groups, which might be explained by they attended medical care more often and had received anti-inflammatory medication. The occlusal differences and mediotrusion side interferences can be explained by the structural changes in the TMJ in the disease group and not in the C group.

The subjective symptoms, radiographic and clinical findings show that the general joint diseases RA, PA and AS also affect the temporomandibular system compared to a control group and RA in a higher frequency than the others. (Wenneberg et al., 1990) Most of the signs and symptoms originate from the general disease and the consequences from it which also has been reported in later studies (Kardel, Ulfgren, Reinholt, Hamada, & Holmlund, 2006).

5.2 Paper 3

The RA group in this study was comprised of outpatients attending medical treatment at the Department of Rheumatology at the Sahlgrenska University Hospital in Gothenburg. They were taken in a consecutive order, which may explain the skewed female/male ratio 74/7 compared to other studies (Allander, 1970; Kaarela, 1985; Tegelberg, 1987), but correspond better to samples from the Gothenburg area (Ahlmén et al., 1990). They can also be regarded as representative of RA patients except for the most severe cases.

The control group (C) comprised patients referred to the Department of Stomatognathic Physiology in Gothenburg for symptoms from the head and face and without any known general joint or skin disease. The frequency of symptoms was similar to patients with TMD in other reports and also the female overrepresentation, therefore, the C group can be considered representative of TMD patients (Agerberg & Helkimo, 1987; G. E. Carlsson, Kopp, & Wedel, 1982; Wedel, 1988).

The methods used for the assessment of symptoms from the temporomandibular system and general well-being have been used and evaluated before, whereby they were regarded as acceptable for use in this study. (Helkimo, 1974; Wedel, 1988) (Ahlmén et al., 1990)

As could be expected, all patients in the C group and about 75% of the RA group reported at least one temporomandibular symptom, while if you look at specific TMJ symptoms and mandibular movements, only about 50% of the RA group reported symptoms. Compared to the population studies, the RA group reported more pain and limitation on mandibular movements and function, tiredness in the jaws and crepitus (G. E. Carlsson, 1984; Mejersjö, 1984; Wedel, 1988). The fact that this RA group had fewer TMD symptoms than another Swedish RA group can be explained by the fact that the group in this study was not defined with TMD symptoms (Tegelberg & Kopp, 1987b).

Crepitus was more frequent in the RA group than in the C group. It indicates structural changes in the TMJ (Akerman et al., 1991; G. Carlsson, 1979) and Wenneberg et al 1990 verifies these results in radiographic examinations.

Only 5% of the RA group desired TMD treatment although they had symptoms from the temporomandibular system, which could be

explained by the reason that their general symptoms were of greater significance or they were not aware of the possibilities of TMD treatment. These figures differ from Aceves-Avila who compared a group of patients with RA, AS, OA and SLE with TMD, where RA (24%) was more frequent compared to AS (13%), OA (8%) OA and SLE (%) and where in total, 16% of the patients had requested treatment. Although the patients had severe impairment, they seemed to adapt to their situation. (Aceves-Avila, Chavez-Lopez, Chavira-Gonzalez, & Ramos-Remus, 2013).

There was great variation of the onset of TMJ involvement related to the course of the general disease, which can be explained that there is no typical time relationship between these.

The RA group reports more physical discomfort and general joint symptoms and less activity than the C group, as could be expected. Nevertheless, the RA group regard themselves as close to normal in mental well-being, while the C group reports more tension and anxiety, which is in line with other studies (Mejersjo, 1984; Wedel, 1988) and has also been discussed by other authors (Suvinen, Reade, Kempainen, Kononen, & Dworkin, 2005).

5.3 Paper 4 and Paper 5

These two studies are a 15 year follow-up based on the patient groups in Paper 3 and are described earlier. All the patients in the RA group and C group were invited to participate at the follow-up. There was a large Dropout especially in the RA group. All patients who could be reached were asked for their reason for not attending, which was mostly due to lack of interest and disability. Considering the length of this follow-up investigation is as long as 15 years, the number of patients who came to the follow-up is considered to be acceptable.

In the RA group, there were 31 (38%) patients who participated and 23 (30%) who did not attend. At Examination 2, the “non-attenders” would have been 12 years older than the RA group which attended. The follow-up RA group’s mean age was 47.9 (22-70) years at Examination 1, that is, the follow-up group was much younger at start and therefore might be in better condition than the Dropouts and may not have had the general joint disease for so long a time as the others.

When studying different temporomandibular variables, the Dropouts were in general on a more severe level at Examination 1. There were, however, no significant differences on the disease activity parameters between the RA group and the Dropouts at Examination 1.

Twenty-seven RA patients (32%) were deceased. Their mean age at Examination 2 would have been 71.9 (56 –95) years, which differs from the other “dropout group” ($p < 0.01$). The cause of death was, in 56%, possibly related to the general disease.

44% of the original C group attended Examination 2, two (5%) patients were deceased, while 21 did not wish to attend (Kallenberg A., 2013).

Some studies on dropouts in rheumatoid arthritis show that the dropouts can be associated with disability, other conditions and outcome (Darmawan, Rasker, & Nuralim, 2003) (Kauppi, Sokka, & Hannonen, 2005). The results in this study partly agree with these articles, but the level of inflammation as measured in this study is on the same level in all RA groups. The disability and handicapping situation may be the most likely factor for not attending, also in this study.

Subjective, clinical, medical and general well-being findings as well as radiological findings from the TMJ and approximal alveolar bone loss.

After 15 years, the RA group reported no significant differences on subjective symptoms at the $p < 0.01$ -level, but there was a tendency to increased subjective symptoms especially on pain and reduced mandibular movements. This could mean they have adapted to a

poorer situation and might not dare use the jaws as much as normal. Clinically, they reported increased pain on palpation of jaw muscles and neck, reduced vertical overbite, reduced number of teeth and increased occluding pair of teeth. There was also a tendency to reduced maximal mouth opening capacity, which might indicate increased pain and possible changes in the TMJ. Between RA 1 and RA 2, the Di II had increased from 28% to 52%, and 25% had Di III at both visits.

The RA group improved their occlusion but had fewer teeth at Examination 2, which could indicate they have had more extractions and more prosthodontic treatment. A possible cause could be difficulties with oral hygiene which lead to extraction due to periodontal and/or cariological complications. The reduced vertical over-bite might be related to changes in the TMJ. There was no correlation between age and occluding pairs of teeth in the RA group or in the C group.

None of the RA patients went into remission indicating the disease was still active at the follow-up. DAS 44 was used since it is the original DAS and was used at both examinations. The DAS score increased from 3.6 to 3.7 (ns) between Examinations 1 and 2. There were no correlations on $p < 0.01$ or less between the disease parameters and subjective or clinical parameters, although there were several tendencies. It is difficult to conclude to what extent a connection exists between the general disease and the findings in the TMJ.

Concerning the general well-being in the RA group, the emotional status had significantly decreased in over-all MOOD, activity and unpleasantness, but the temporomandibular system did not seem to be affected by the emotional degradation. Concerning BSS (self-rated discomfort), they were at a steady state but experienced more discomfort than the C group.

The C group in this study is a patient group, which means the results are representative of a patient group and not of an ordinary control group.

It is also relevant to study the long-term outcome in the C group. Several studies of follow-up design have been made (Mejersjo, 1984; Mejersjo & Carlsson, 1984) (Osterberg, Carlsson, Wedel, & Johansson, 1992), where the TMD patients had fluctuating symptoms. In the age group corresponding to this study, there are reports with

different results. This C group showed improvement or no changes after 15 years on several symptoms and findings, which indicates a positive long-term outcome on the TMD-diseases affecting this group and is in line with other studies. (Dworkin et al., 1990; Kononen & Nystrom, 1993; Magnusson, Egermark, & Carlsson, 2000).

Regarding the self-rated discomfort (BSS) in the long-term, the C group found themselves at a better physical status than the RA group, although within the group, they reported deterioration, while the RA group reported no change.

On MACL, the C group reported no change in over-all MOOD. The differences within and between the groups might be explained by the consequences of the chronic and handicapping disease in the RA group.

Radiographic examinations were performed by panoramic radiography making it possible to study both the temporomandibular joint and the dental and alveolar regions. The cause for using this method is presented earlier in Paper 5.

The changes in the TMJs are possibly on a more severe level than shown in panoramics. If a CT or MRI had been taken, more changes in both groups would have been reported since these methods are more accurate (Ahmad et al., 2009; Crow et al., 2005; Epstein et al., 2001; Fallon et al., 2006; Helenius et al., 2006; Masood et al., 2002; Mawani et al., 2005; Schmitter et al., 2006; Winocur et al., 2010), although concludes that panoramic radiography is useful when determining TMJ changes. (Helenius et al., 2005)

In this RA group, there were degradations in the TMJ both totally and in different variables, which is not the case to that degree in the C group. Some of the findings can be due to osteoarthritis which has a frequency of approximately 15-20% in the general population and remodelling of the TMJ in both groups.

ABL shows a significant increase in the RA group but not in the C group. According to the method used in this study, there is a risk for under diagnosis when registering the approximal bone loss, meaning the ABL might be higher than reported in this study.

This study's results are in line with several authors (Garib & Qaradaxi, 2011; Mercado, Marshall, Klestov, & Bartold, 2001; Rutger Persson, 2012), who report increased attachment and bone loss in RA patients.

The approximal bone loss had increased between the two examinations in the RA group, but no correlations were found to any disease parameter. In literature, there are some reports on correlations between CRP and TMJ dysfunction in RA patients (Nordahl et al., 2001) (Mercado et al., 2001) and on DAS28(Hiz, Ediz, Ozkan, & Bora, 2012). In this long-term study, there are however only tendencies between the disease parameters (except on CRP) and radiological findings, TMJ capacity and ABL.

Mercado et al (Mercado et al., 2001) found there is a connection between periodontitis and RA, although this is not a causal relationship, and he discusses underlying inflammatory responses.

Raised CRP levels, especially in patients with moderate or severe disease levels and higher levels of HAQ, were correlated to more severe periodontal condition. Ribeiro et al 2005 (Ribeiro et al., 2005) found that after periodontal treatment, HAQ and Estimated Sedimentation (ESR) were reduced in RA patients.

Nordahl et al (Nordahl et al., 2001) also found a correlation between raised CRP and progressive TMJ and overall changes in bone loss in RA patients who had been examined with an interval of at least 12 months between the examinations.

Garib 2011 (Garib & Qaradaxi, 2011) reported that patients with advanced RA are more likely to develop more periodontal and TMJ problems compared to patients with periodontitis but without RA and concludes a need to inform patients with RA to consult a dentist for treatment of periodontitis.

Demmer et al (Demmer et al., 2011) found associations between periodontal infections and RA, but the observations made it difficult to draw clear conclusions between the two diseases, meaning that periodontal infections do not represent a strong RA risk factor. There are RA biases that complicate the data.

Gordon et al 2001(Gordon, West, Jones, & Gibson, 2001) reports from a 10-year follow-up in RA patients that there was a significant general

degradation, although these patients had been on DMARD medication. (Gordon et al., 2001)

This RA group had fewer teeth which is in accordance with other authors, (Garib & Qaradaxi, 2011; Gleissner, Willershausen, Kaesser, & Bolten, 1998; Mercado et al., 2001) who have discussed the connection between the periodontal status and RA. (Demmer et al., 2011) SBU had also discussed treatment of periodontal disease and RA and there is no complete agreement concerning the results (sbu, 2004).

The patients in this study had improved occlusal stability, which can indicate more regular prosthodontic treatment. There is no information if this RA group had received periodontal treatment or not and to what extent. The reduction in vertical overbite can be caused by changes in the TMJ, which is in line with other reports in literature (Akerman, Kopp, Nilner, Petersson, & Rohlin, 1988; Kuroda, Kuroda, Tomita, & Tanaka, 2012; Saeed, McLeod, & Hensher, 2001; Tegelberg & Kopp, 1987a). The HAQ level is on a medium level meaning there is a possibility the patients can have handicapping problems with their oral hygiene due to the general disease. The medication does not seem to affect the TMJ on a significant level.

In this study, results are in several cases contradictory to other authors. Possible reasons can be speculated on i.e. patient group, choice of methods, small sample at the follow up, analysis. This study has been eager to report as full cover results as possible and the aim has been to show what happens with the temporomandibular system in the long term in this patient group considering this is a chronic disease that can affect the patients in a severe way.

In this study, the C group seems to be in a stable temporomandibular situation after 15 years, both clinically and radiologically. The minor decrease on the ABL in numbers can be explained due to normal reduction of alveolar bone (Hugoson et al., 1986; Norderyd, Hugoson, & Grusovin, 1999; Wennstrom, Serino, Lindhe, Eneroth, & Tollskog, 1993).

6 CONCLUSION

Of the rheumatic inflammatory diseases RA, PA and AS, there are higher frequencies of temporomandibular signs and findings and radiological findings than in a normal population and they are generated from the general disease. Among the diseases, RA has in general more findings from the TMJ than PA and AS.

When comparing RA patients with a group of TMD patients without general disease but with pain, the conclusion would be that the RA group had less subjective signs and reported almost normal general well-being but more physical discomfort than the C group.

In the long-term follow-up after 15 years, the RA group showed no changes subjectively or clinically in the temporomandibular system, although clinically, they had degraded. Their decreased mental well-being can be due to the chronic disease and the consequences from it, while the stable self-rated discomfort can be a result of adapting to their situation.

In general, the C group had improved which indicates a good prognosis for TMD patients after 15 years, even though their opinion of their physical health had degraded and the well-being was unchanged.

In the RA group, there was a significant radiological impairment in the TMJ, approximal bone loss and the number of teeth in the RA group that is not clearly correlated to the general disease activity level. In spite of the degradation, the patients seemed capable of handling problems from this system.

The disease activity stayed on a medium level, measured in this way in this study, indicating a generally stable situation for these patients, although the temporomandibular system and alveolar approximal bone loss had degraded.

7 FUTURE PERSPECTIVES

In the future, the most important factor in the long-term for the temporomandibular system seems to be that the general disease is under control and the patients receive care for their disease. Future studies are necessary to receive additional knowledge regarding the different possible connections between inflammatory joint diseases and the temporomandibular system and periodontal status.

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