Diplomarbeit

Ultrasound-detected structural and inflammatory changes associated with hand osteoarthritis in an elderly population: Results of the Bruneck study

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Graz, am 23.01.2018 *Nina Gasperi eh*

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Zusammenfassung

Hintergrund:

Die Arthrose ist die weltweit häufigste Gelenkserkrankung. Sie stellt eine erhebliche sozioökonomische Belastung dar und hat einen starken negativen Einfluss auf die Lebensqualität der betroffenen Personen. Die Arthrose der großen Gelenke wie zum Beispiel des Knies und der Hüfte ist relativ gut erforscht; zur Arthrose der Hände hingegen ist nur wenig wissenschaftliche Literatur verfügbar. Zur Diagnosestellung einer Arthrose wird das Nativröntgen nach wie vor als häufigste bildgebende Methode eingesetzt. Frühere Studien weisen darauf hin, dass der muskuloskeletale Ultraschall es ermöglicht, arthrotische Gelenkveränderungen bereits in frühen Stadien sichtbar zu machen und gewinnt deshalb zunehmend an Bedeutung. Nur wenige Studien haben sich bisher sich mit der Prävalenz von arthrotischen Veränderungen in der Allgemeinbevölkerung beschäftigt; man geht aber davon aus, dass diese sehr hoch ist.

Zielsetzung:

Das Ziel dieser Arbeit ist die Prävalenzerhebung der Fingerpolyarthrose (FPA) in der Kohorte der Bruneck Studie, einer prospektiven Untersuchung welche in den 90er Jahren an 1000 gesunden Brunecker BürgerInnen gestartet wurde. Mit Hilfe des Ultraschalls sollen die entzündlichen und strukturellen Veränderungen an den Händen von ProbandInnen mit FPA und gesunden ProbandInnen beurteilt werden. Des Weiteren werden mögliche Korrelationen zwischen Ultraschallveränderungen und Funktionseinschränkung ermittelt.

Methoden:

Von den ursprünglich 1000 Gesunden, welche in die Bruneck Studie eingeschlossen wurden, konnten für die Untersuchungen 2016 noch insgesamt 353 Personen rekrutiert werden, von denen 22 aufgrund unvollständiger Daten ausgeschlossen wurden. Die ProbandInnen wurden klinisch hinsichtlich knöcherner Schwellung, Weichteilschwellung und Druckschmerz untersucht. Die Diagnose der Fingerpolyarthrose wurde anhand der ACR-Kriterien (1) gestellt, da Röntgenuntersuchungen nicht verfügbar waren. Es wurden verschiedene klinische Scores (SF-SACRAH, FIHOA, HAQ) zur Ermittlung der Handfunktion erhoben. Mit Hilfe des Ultraschalls wurden das Handgelenk und die kleinen Fingergelenke

untersucht. Folgende Veränderungen wurden evaluiert: Osteophyten, Synovialhypertrophie/Erguss, Erosion, und Power Doppler. Die Prävalenz, die Stärke der Ausprägung und die Lokalisation der Veränderungen wurden ermittelt. Es wurden zudem Vergleiche zwischen Gruppen von ProbandInnen mit Fingerpolyarthrose (Gruppe A) und Gesunden, welche keine Schmerzen oder Weichteilschwellungen aufwiesen (Gruppe B), durchgeführt. In einer Subanalyse wurde zudem eine Gruppe von Personen untersucht, welche außerdem keine knöcherne Schwellung aufwies (Gruppe B1).

Ergebnisse:

In dieser Studie erfüllten 98 Personen (26.9%) die ACR Kriterien für die FPA. Bei den untersuchte ProbandInnen zeigte sich eine sehr hohe Prävalenz arthrotischer Ultraschallveränderungen. Dies galt sowohl für ProbandInnen mit erfüllten Kriterien einer FPA als auch für gesunde ProbandInnen. 100% der Personen aus Gruppe A, 99% der Personen aus Gruppe B und 97% der Personen aus Gruppe B1 hatten zumindest eine US-Veränderung. Von den vier untersuchten Ultraschallveränderungen waren Osteophyten und Veränderungen der Synovia in allen Gruppen am häufigsten nachweisbar. In Gruppe A wiesen 100% der Personen zumindest einen Osteophyten und 93% der Personen zumindest eine Synoviale Hypertrophy/Erguss auf. In Gruppe B und Gruppe B1 zeigte sich auch eine hohe Prävalenz dieser Veränderungen (Gruppe B: 99%, 63%) (Gruppe B1: 94%, 41%). Das am häufigsten betroffene Gelenk war das DIP2, wohingegen das MCP4 am seltensten betroffen war. 82.6% der untersuchten DIP2 Gelenke wies zumindest eine US-Veränderung auf. Die an den Händen der gesunden ProbandInnen nachgewiesenen Ultraschallveränderungen waren signifikant weniger stark ausgeprägt als die Veränderungen in PatientInnen mit erfüllten ACR-Kriterien. In den ProbandInnen mit FPA konnte außerdem ein signifikanter Zusammenhang von Osteophyten und synovialen Veränderungen mit einer Beeinträchtigung der Handfunktion nachgewiesen werden.

Schlussfolgerung:

Die Prävalenz der FPA ist in dieser Studie mit 26.9% etwas höher als in vergleichbaren früheren Studien. Sowohl bei Personen mit FPA als auch bei gesunden Personen waren arthrotische Ultraschallveränderungen sehr häufig nachweisbar. Osteophyten und synoviale Veränderungen waren am häufigsten, Erosionen und erhöhter Power Doppler

Signale seltener darstellbar. Die Ergebnisse dieser Studie könnten darauf hinweisen, dass der muskuloskeletale Ultraschall eine geeignete Untersuchungsmethode für die Detektion von arthrotischen Veränderungen der Gelenke ist, noch bevor PatientInnen klinische Symptome entwickeln und die Diagnose einer Arthrose gestellt werden kann. Um zu ermitteln, ob es sich bei den Ultraschallveränderungen um frühe Zeichen einer Handarthrose handelt oder ob diese Veränderungen im Alter physiologisch sind, sind weitere Evaluierungen notwendig. Diese werden voraussichtlich in einer weiteren Follow-Up-Untersuchung im Rahmen der Bruneck Studie in 5 Jahren erhoben werden.

Abstract

Background:

Osteoarthritis is the most common joint disease worldwide. It has a major socio-economic impact and a negative effect on the quality of life of affected patients. While OA of the knee and the hip is relatively well studied, not much data about hand OA are available. Conventional radiography (CR) is the golden standard imaging tool to diagnose OA but Ultrasound (US) is increasingly used in early stages of OA. Only a few previous studies evaluated the prevalence of US signs of OA. These studies demonstrated that certain OA signs are quite common among healthy people.

Objectives:

The aim of this study was to investigate the prevalence of hand OA in the cohort of the Bruneck study. This study originally included 1,000 subjects who were recruited from the official population register in 1990 for the baseline evaluation by random sampling.

Furthermore, the prevalence of structural and inflammatory US signs of OA in the joints of the hands was investigated in subjects with hand OA and in healthy subjects. The preferential location of these changes was determined. We also analyzed possible correlations of abnormal US findings with functional impairment.

Methods:

353 of the originally 1,000 subjects of the Bruneck study attended the study visit that took place between April and May 2016. 22 individuals were excluded due to incomplete data, leaving 331 subjects for further analysis. The participants were clinically evaluated for the presence of bony enlargements, soft tissue swelling and tenderness of the hand joints.

The ACR criteria (1) were used for the diagnosis of hand OA in this study, hand x-ray was not available. Three clinical scores (SF-SACRAH, FIHOA, HAQ) were used to assess functional impairment of the hands. Ultrasound was performed at transverse and longitudinal planes of the plantar side of the wrists, and the palmar and dorsal side of hand joints. The following US criteria were assessed: osteophytes, synovial hypertrophy/effusion (SH/E), erosion and Power-Doppler (PD) abnormalities. A semi-quantitative grading system was used, with a range from 0 to 3. We defined 2 groups according to the presence or absence of hand OA: group A were subjects fulfilling the

ACR criteria for hand OA. Group B were healthy individuals, i.e. they did not report any hand pain, aching, tenderness or soft tissue swelling. We further defined a subgroup of group B which were patients without any bony enlargements (group B.1). The prevalence, frequency, severity and location of the different US sings were investigated for all groups.

Results:

In this study, 98 subjects (26.9%) fulfilled the ACR criteria for hand OA. The prevalence of abnormal US findings associated with OA was high in all investigated groups. 100% of the subjects of group A, 99% of the subjects of group B and 97% of the subjects of group B1 presented at least one US abnormality. Osteophytes and synovial changes were the most common abnormalities. In group A, 100% of the subjects showed at least one osteophyte and 93% showed at least one SH/E. A high prevalence of these changes was also found in group B (99% and 63%, respectively) and in group B1 (94% and 41%, respectively). The most commonly affected joint was the DIP2, while the MCP4 seemed to be rarely affected. 82.6% of the examined DIP2s showed at least one US abnormality. US changes in healthy subjects were less prominent as compared to subjects fulfilling the ACR criteria. Osteophytes and synovial inflammation correlated with functional impairment.

Conclusions:

The prevalence of hand OA was slightly higher in the present compared to previous studies. US abnormalities suggestive of OA were common in all investigated groups Overall, osteophytes and SH/E were more common than erosions and Power Doppler abnormalities. Our results suggest that US might be a method which enables detection of osteoarthritic changes before patients develop symptoms characteristic for OA. A follow-up clinical and US examination as part of the Bruneck study is scheduled in 5 years' time and will shed light on the question whether US findings of OA precede clinically overt OA or whether these findings could be considered normal.

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Glossar und Abkürzungen

ACR	American College of Rheumatology
ARRIMUS	Austrian Rheumatology-Radiology Initiative for Musculoskeletal Ultrasound
BMI	Body Mass Index
CMC	Carpometacarpal joint
CR	Conventional Radiography
CS	Chondroitin Sulfate
DIP	Distal Interphalangeal Joints
EULAR	European League Against Rheumatism
FIHOA	Functional Index for Hand Osteoarthritis
FPA	Fingerpolyarthrose
GDF5	Growth Differentiation Factor 5 Gene
GRD	Gross Domestic Product
HAQ	Health Assessment Questionnaire
IL-1	Interleukin 1
iNOS	Nitric Oxide Synthase
IR	Incident Rate
JSN	Joint Space Narrowing
K&L scale	Kellgren and Lawrence Scale
MCP	Metacarpophalangeal joint
MRI	Magnetic Resonance Imaging
MSUS	Musculoskeletal Ultrasound
MTP	Metatarsophalangeal Joints
NO	Nitric Oxide
NSAIDs	Nonsteroidal Anti-inflammatory Drugs
OA	Osteoarthritis
OARSI	Osteoarthritis Research Society International
OMERACT	Outcome Measures in Rheumatology
OR	Odds Ratio
PANLAR	Pan-American League of Associations for Rheumatology
PD	Power Doppler

PIP	Proximal Interphalangeal Joints
RA	Rheumatoid Arthritis
RCT	
(SF-)SACRAH	(Short-form-) Score for the Assessment and Quantitation of Chronic Rheumatic Affections of the Hands)
SH	Synovial Hypertrophy
SH/E	Synovial Hypertrophy and/or Effusion
TNF	Tumor Necrosis Factor
US	Ultrasound
VAS	Visual Analog Scale
VV	Verbruggen–Veys anatomical phase score

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1 Introduction

1.1 Osteoarthritis

1.1.1 Definition

Osteoarthritis (OA) is a complex, chronic, multifactorial disease including systemic and mechanical features. (2) It affects different intra-articular tissues of most peripheral synovial joints (mostly hip, knee, hands and/or spine) and results in the typical global joint involvement. (3,4)

OA is associated with changes and loss of articular cartilage, dysregulation of local turnover and repairing processes, increased thickness and sclerosis of the subchondral bone, outgrowth of osteophytes at the joint margins and changes of periarticular structures. Even though cartilage is poorly innervated its abnormalities lead to clinical symptoms such as pain. (1,4–6)

OA worsens progressively with time and synovitis in episodic courses can lead to exacerbation of pain and swelling. (4)

1.1.2 Prevalence and Incidence

Osteoarthritis is one of the most common rheumatic disorders (3) and the most prevalent joint disorder worldwide. (7) Prevalence of radiographic OA is variable, depending on the selection criteria, criteria for diagnosis and variation of the interpretation of radiographic results. (8,9)

A Croatian study aiming at the determination of the prevalence of radiographic OA in an urban Caucasian population aged 52-74 years showed that the hip was the most frequent site of OA in men with a prevalence of 27.3% whereas distal interphalangeal joints preponderated in women with a frequency of 43.5%. Knee OA was rarest in men (4.3%) as well as in women (9.9%). Polyarticular or generalized OA (three or more affected joint groups) was found in 10.8% of all women and in 5.9% of men. (9) A Swedish study pointed out that the prevalence of knee OA was 25.4% in a cohort of adults of age 56-85 years. (10)

The incident rate (IR) of knee and hip OA increases rapidly between the ages of 50 and 75 years and decreases in the oldest people, both in women and men. Hand OA in women peaks at an age of 60-64 years. (11)
Table 1 shows the IR of hand, hip and knee OA in men and women aged 40 years or older in a Southern European/Mediterranean nation (Catalonia). (11)

Incident Rates (/1000 person-years)	**female**	**male**	**overall**
hand OA	3.5	1.3	2.4
knee OA	8.3	4.6	6.5
hip OA	2.4	1.7	2.1

Table 1: Incident rates of OA in a Southern European/Mediterranean nation (Catalonia). (11)

1.1.3 Impact

OA is a major public health concern. In a study from 1990, OA was rated as one of the top 15 leading causes of disease burden in Australia (12). OA was on eighth place of the list of non-fatal burden of disease worldwide and its prevalence rate is believed to increase due to an aging population. Furthermore, OA contributed significantly to the causes of disability burden in Australian women (responsible for 5.7% of the total years of life lost to disability) and to a lesser extent in Australian men (3.9%). (13) Because OA can severely limit patients' activity, particularly walking, it has a great effect on participation in social activities and quality of life (14) and it was shown that patients with multi-site, hip or knee OA have a greater risk of developing symptoms of depression than patients without OA. (15)
Symptomatic knee and hip OA is the most common reason for joint replacement surgery (16). A review of cost-of-illness factors estimated the social cost of OA to be between 0.25% and 0.50% of a country's Gross Domestic Product (GDP). (17)

1.1.4 Etiology

Risk factors of OA can be divided into two groups: personal risk factors and joint associated risk factors.

Personal risk factors

Age: Many studies have documented a significant correlation between age and OA. (14,18) Age is the most important risk factor for OA (9) but it was pointed out that this is true only up to a certain age. Risk of hip and knee OA has a peak around 75 - 80 years with a decrease in risk in older people. The risk for hand OA was found to be highest after the menopause age, which is typically between 55 - 60 years. (11)

Gender: Female sex is associated with a significantly higher risk of knee, hip and hand OA in general, but it seems, that the extent of risk of female sex depends on age: women have the highest risk to develop OA after the age of 50 years (19), the climacteric period, where hand OA rates are 3.5 times higher in females than in males. (11) This suggests an association between OA and female hormones. The exact contribution of hormonal changes to cartilage destruction, however, remains unclear. (20) The difference in prevalence of OA between women and men could also be explained by other factors such as lower volume of cartilage, higher rates of bone loss or lack of muscle strength in the former compared to the latter. (14)

BMI/Obesity: Previous studies identified obesity as a risk factor for OA (7,18) and a systematic review pointed out that a 5-unit increase of the BMI leads to an increase of the risk for Knee OA of 35%. The effect of increased BMI on OA risk seems to be much higher in women than in men (21) and it is also a stronger risk factor for OA in lower limbs, especially the knee, which seems to be obvious because of the increased load at this site. (7) However, since a weak but significant association between obesity and hand OA has also been described (22), the effect of weight on the development and progression of OA may not only be biomechanical, but there may also be metabolic systemic effects on non-weight-bearing joints. (6,14)

Serum Lipid Levels: A recent 11-year follow-up study with the aim of evaluating the association between hyperlipidemia and the development of hand OA could not show a significant correlation between total or LDL cholesterol and radiographic hand OA. However, high HDL-c levels appeared to have some protective effect against hand OA, while higher triglyceride levels seemed to increase the risk for the disease. (23)

History of OA: A history of previous hand OA is associated with a higher risk of both hip and knee OA, a history of knee OA correlates with an increased risk of hip OA and vice versa. This correlation was found to be independent of age, gender and BMI. (11)

Other personal risk factors: Several studies suggested that diet may play a role in OA as higher intake of antioxidants, e.g. Vitamin C, has been demonstrated to positively influence the progression of OA. (24) A higher education level and higher weekly amount of moderate activity are other protective factors. (18) Furthermore, genetic factors and family history of OA have an enormous impact on the development of OA: the growth differentiation factor 5 gene (GDF5), for example, plays a substantial role in the etiology and pathogenesis of OA, and a polymorphism within GDF5 was associated with a higher severity of the disease. (2,6)

Joint associated risk factors.

Injuries: Joint injuries strongly increase the risk for OA (10): anatomic abnormalities as a result of an injury, and therefore a disrupted integrity of the joint, or tears of protective ligamentous and fibrocartilaginous structures increase the vulnerability of the joint. (6) This is best studied in the knee which is one of the most frequently injured joints. (14)

Abnormal alignment: Malalignment has also been studied best in the knee. (6) For example, varus alignment of the knee significantly increases the risk of OA-incidence, while varus and valgus alignment both worsen the progression of already established knee OA. (25) This is caused by an increased stress on a focal area of cartilage, which leads to cartilage loss. (6)

Exercise/Use of joint: Moderate daily physical activity is considered a protective factor against OA, especially endurance and running sports. In contrast, performing high-

impact or power sports such as soccer or rugby or practicing any sport on a high level seems to be associated with a higher OA risk. Workers which perform repetitive movements like miners (knees and spine) or farmers (hip) are more likely to develop OA. (10,26)

1.1.5 Clinical Presentation

OA symptoms vary between joints. In general, pain is among the most common complaints of patients. In the early stages of the disease it is mostly movement-related whereas in more advanced stages, pain may also occur at rest. Another characteristic symptom is stiffness after inactivity. Morning stiffness can also be present but has a lower intensity and shorter duration as compared to patients with inflammatory arthropathies. Joints affected by OA may present hard bony enlargements with or without soft tissue swelling, tenderness, diminished range of motion and crepitation. (16)

Further joint specific symptoms are shown in Table 2.

Joint-specific OA	**Specific symptoms**
Knee OA	Insidious onset of pain Gelling Limited range of motion Walking-difficulties Varus deformity
Hip OA	Groin pain Thigh, buttock or knee pain Limited range of motion
Spine OA	Pain in the neck and occiput Radiation down the arm Weakness Paresthesia
Hand OA	Involvement of second and third DIP is particularly common Bony enlargement of the DIPs (Heberden's node) Bony enlargement of the PIPs (Bouchard's node) Enlargement are often more pronounced in the dominant hand Acute phase of inflammation with symptomatic relief afterwards Deformity Pain at the base of the thumb

Table 2: Joint specific OA symptoms. (4,6,16)

1.1.6 Relevant Anatomy of the hand joints

Knowledge of the joint anatomy is an essential prerequisite for understanding the pathophysiology, symptoms and therapy of hand OA. The joints of the hand are synovial joints, also called diarthroses, which means that the articulating bones are surrounded by a fibrous capsule. The capsule is blended with the periosteum and consists of an outer fibrous layer and an inner serous synovial membrane. The joint surfaces are covered with hyaline cartilage (cartilago articularis) and the joint cavity is filled with synovial fluid, which is secreted by the synovial membrane (figure 2). Hyaline cartilage and synovial fluid are important factors for the reduction of friction between the joint surfaces during movement. (27) Synovial fluid is furthermore essential for the nourishment of the joint. It contains hyaluranon which is essential for the lubrication. The viscosity of the synovial fluid varies with temperature, which is why stiffness often increases with cold temperatures. The joint is stabilized by ligaments that are integrated in the outer fibrous layer of the capsule. (28)

Essential features of the joints are ensuring a stable connection between the connected bones, transferring power, distributing load correctly and, most importantly, providing the full range of motion pain-free. To guarantee the latter, the joint surfaces requires to be covered with intact hyaline cartilage so the surfaces can slide friction-free. (29)

1.1.7 Pathogenesis

Although the word osteoarthritis derives from the greek words osteon (bone) and arthron (joint), the structure which is typically affected first is the cartilage. (29) During the course of the disease several other joint tissues are affected.

The primary defect in OA is the thinning of hyaline cartilage, caused by enzymatic processes breaking down proteoglycans and collagen fibers into fragments within the extracellular matrix.

The enzymes stromelysin and matrix metalloproteinases are markedly elevated in the extracellular matrix of the articular cartilage in patients with OA. They interfere with the assembly of proteoglycans which consequently lose their ability to regulate the movement of water and synovial fluid in- and outside the cartilage. This causes the

cartilage to absorb too much fluid which leads to an inability of coping with the stress of weight bearing.

The content of proteoglycane furthermore decreases with age (30) and in addition to that, protective factors such as muscle strength also decrease with age. Previously injured joints or joints with abnormal alignment also present an increased vulnerability compared to normal joints and are less capable to deal with stress. (31)

OA was once believed to be a non-inflammatory joint disease, but it was shown that in the course of the disease several inflammatory pathways are upregulated. (32) Inflammatory cytokines, particularly Interleukin 1 (IL-1) and tumor necrosis factor alpha (TNFα), play major roles in the initiation and progression of OA by decreasing collagen synthesis and increasing (other) inflammatory mediators such as inducible nitric oxide synthase (iNOS) and NO. NO subsequently leads to cartilage degradation by stimulating apoptosis in chondrocytes. (33)

Thinning and partial absence of cartilage leave the subchondral bone unprotected. This results in sclerosis and formation of cysts and osteophytes by endochondral ossification, particularly at the site of tension at joint margins. Osteophytes are believed to stabilize the joint. (31) The new formations alter the bone contour and joint anatomy. Simultaneous thickening of the joint capsule can result in adherence to the deformed underlying bone limiting the movement of the joint. (30)

1.1.8 Diagnosis and evaluation of hand OA

A 2008 evidence-based recommendation was published by the *European League Against Rheumatism (*EULAR) stating that hand OA cannot be diagnosed using a single feature. According to these recommendations, a combination of several features is required to establish OA diagnosis including history of risk factors, clinical findings and imaging. (34)

1.1.8.1 Clinical Findings and assessment of hand OA

Clinical OA is often described as a combination of symptoms including pain, stiffness and other symptoms as well as radiographic signs of OA. (32) The diagnosis can be made by clinical assessment alone and other imaging can be reserved for ruling out

alternative diagnoses or for confirming the diagnosis in unclear cases. (35) In this context it is important to note that symptomatic OA can appear before any radiographic changes are found. (32) It is recommended to assess functional impairment, and a number of validated instruments such as the SACRAH or the FIHOA are available for its assessment. (34)

ACR criteria

The American College of Rheumatology (ACR) suggested criteria for the classification of hand OA which are depicted in table 3. In their classification, the following ten joints are evaluated: the second and third DIP, the second and third PIP, and the first CMC joints of both hands. (1)

Hand pain, aching, or stiffness
And
3 or 4 of the following features:
Hard tissue enlargement of 2 or more of 10 selected joints
Hard tissue enlargement of 2 or more DIP joints.
Fewer than three swollen MCP joints
Deformity of at least 1 of 10 selected hand joints

Table 3: Classification criteria for hand OA developed by the American College of Rheumatology (ACR). (1)

SACRAH

Rheumatoid Arthritis (RA) and OA are the leading rheumatologic causes of function impairment of the hands. (36) Therefore, the *Score for the Assessment and Quantitation of Chronic Rheumatic Affections of the Hands* (SACRAH) was developed to measure the functional impact on the hands in patients with OA or RA. The original questionnaire consisted of 23 questions regarding three categories of symptoms: hand function, stiffness and pain.

Using a visual analogue scale (VAS) (range from ‘0mm’ to ‘100mm’), the score can be used to monitor therapy and to measure hand involvement. (37)

A short form of the SACRAH (SF-SACRAH) was developed for the clinical daily routine. It consists of 5 questions and was also found to be reliable and sensitive for the detection of changes concerning functional impairment of the hands. (36)

FIHOA

Another score to measure function of hands in OA-patients was developed in 1995. The Functional Index for Hand OsteoArthritis (FIHOA) consists of 10 questions about daily activities such as cutting with a knife, buttoning, shaking hands and writing. It uses a 4-point Likert-scale (0 = possible without difficulty, 3 = not possible) with a total score ranging from 0-30. A lower score reflects a better hand function. (38)

1.1.8.2 Imaging of OA

Imaging has become increasingly important for diagnosis, prognosis and follow-up of OA, as well as for understanding risk factors and progression of the disease. (39,40) It is more and more used in clinical practice as well as in research which could possibly lead to an increment of health costs. The European League Against Rheumatism (EULAR) has therefore developed in 2017 evidence-based recommendations for the use of imaging in symptomatic peripheral joints in OA. Regarding diagnosis, it was stated that if OA shows its typical presentation, imaging is not required in order to make a diagnosis even though it is applied for diagnostic purposes in many studies. When the presentation is atypical, Ultrasound (US) can be used to confirm the diagnosis or to look for additional or alternative diagnoses. For monitoring, EULAR found imaging not to be necessary to follow-up patients unless there is a rapid worsening of symptoms or a change in clinical characteristics. Radiography should be the first imaging technique used in OA whereas other techniques should be reserved for unclear cases (41)

Radiography

It is very common to use conventional radiography to define OA. It has been considered the reference technique in clinical studies (42) and due to its high feasibility and low costs it has become the imaging method of choice in clinical practice.

However, there is a considerable discordance among radiographic changes, clinical symptoms and the degree of disability. (29) A positive but varying association between Conventional Radiography (CR) findings and pain has been observed. Besides, the association between CR findings and impairment of hand function is variable ranging from no association to a moderate association. (43)

The direct visualization of hyaline cartilage and other soft tissues is restricted with conventional radiography, and minimal cartilage changes occurring in early stages of the disease are difficult to identify(4)

Evaluation of radiographic hand OA

Common features of hand OA in radiography

Pathological features assessed by radiography include changes of the subchondral bone, bone remodeling and attrition such as erosion, osteophytes, sclerosis and cysts. (4,29) Since hyaline cartilage cannot be depicted directly, the loss of cartilage is indirectly measured by joint space narrowing. Erosions which often occur in the central part of the joint could falsify assessment of JSN by increasing the joint space width. (44)

Scoring systems

The most commonly used criteria for radiographic evaluation are the *Kellgren and the Lawrence criteria (*K&L scale) which classify the severity of OA by the assessment of osteophytes, joint space narrowing, sclerosis and cysts using five grades (0-4). Grades 2 or higher represent a definite radiographic diagnosis of OA. (14,44) It has been criticized that the grading system has been described differently in several studies and that the grading is different depending on the examined joint. Additionally, an over-emphasis of osteophytes has been criticized using the K&L scale. A joint presenting joint space narrowing or a sclerotic joint can only be diagnosed with OA, if osteophytes are also present.

Alternative scoring systems are the *Osteoarthritis Research Society International* (OARSI) *atlas,* which enables assessment of individual radiographic features on semi-quantitative scales (such as grading of osteophytes, joint space width) rather than a global score (44,45), and the *Verbruggen–Veys anatomical phase score,* which consists of five phases representing the evolution of hand OA. (46) A recent publication compared the reliability and sensitivity of the OARSI, the VV score and the K&L-score reporting similar results for all scores. (47)

MRI

Up to now, MRI has been considered to be the most reliable and precise imaging technique for OA and due to its high sensitivity to detect cartilage, synovial and bony changes, it has become an important tool for research. (39)

The *Outcome Measures in Rheumatology* (OMERACT) and the *Osteoarthritis Magnetic Resonance Scoring System* (HOAMRIS) are common scoring systems. They grade synovitis, erosive damage, cysts, osteophytes, cartilage space loss, malalignment, and bone marrow lesions. A good to very good intra- and interreader reliability has been reported for the HOAMRIS. (48) MRI was shown to be able to detect twice as many joints with erosion and osteophytes than CR. (49) It can visualize all joint structures, hence the joint can be evaluated as a whole organ and changes can be detected much earlier than with CR. However, routine clinical use of MRI is rare due to its high costs and limited availability. (39)

Ultrasound

See Chapter 2

1.1.9 Therapy

There is no cure for OA, therapy aims to minimize symptoms and improve quality of life.

A few recommendations for therapy of hand OA are available such as the *Pan-American League of Associations for Rheumatology* (PANLAR) recommendations from 2016. They are based on a consensus of clinical experts suggesting to individualize therapy depending of several factors such as location, severity and type of OA, presence of inflammation as well as level of pain/disability. A combination of pharmacological and non-pharmacological therapy has been proposed. (50) The 2008 EULAR recommendations for management of hand OA are evidence based and also suggest that therapy should consist of pharmacological and non-pharmacological interventions and should be individualized considering various factors. (51) Furthermore, the ACR published guidelines in 2012, endorsing the use of nonpharmacological and pharmacological therapies in OA of the hand, hip and knee. (52)

1.1.9.1 Pharmacological Therapy

Paracetamol

Paracetamol (up to 4 grams per day) is recommended as first-line analgesic for hand OA in combination with topical therapy. It should be preferred over oral NSAIDs because of its superior safety profile especially as a long-term therapy. (53) Evidence on the efficacy of paracetamol in hand OA is weak and the recommendation is based on the extrapolation of its known positive effect in knee and hip OA. (54)

Systemic Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

NSAIDs are the cornerstone in OA therapy, but they are known to cause gastrointestinal and cardiovascular complications in the long term. For instance, the risk of getting an upper GI complication including peptic ulcer perforation, obstruction, and bleeding is 3 to 5 times higher in patients treated with oral NSAIDs compared to individuals without this treatment. (55)

Oral NSAIDS have an analgesic and an anti-inflammatory effect and should be prescribed at the lowest effective dose for the shortest time possible, if response to paracetamol and topical analgesics are not adequate. The side effects which are particularly relevant for older patients with several comorbidities should be considered. If properly prescribed, NSAIDs can provide a satisfying and secure treatment. (54) It has been observed in clinical trials that NSAIDs have a better effect on pain reduction than placebo. Oral NSAIDs further improved functional impairment and grip strength. (56)

Topical NSAIDs

Topical NSAIDs are indicated as an early treatment in mild to moderate OA. (56)

The efficacy of this treatment has been investigated in a few studies: *Simon et al.* found that topical diclofenac was more effective for improvements of pain, function and overall health in patients with knee OA than placebo. Oral diclofenac did not show a better effect than topical diclofenac but topical NSAIDS are considered to be safer since there are no known gastrointestinal and cardiovascular side effects. (57) Local adverse events such as skin rushes, dry skin or paresthesia may occasionally occur with topical NSAIDs-therapy. (58) According to the ACR recommendations for the treatment of hand OA, topical NSAIDs should be preferred over oral NSAIDs in patients over the age of 75 years especially when OA pain is limited to a few joints, due to the superior safety profile of local therapy. (52,59,60)

Topical Capsaicin

Capsaicin is an alkaloid extracted from the chili pepper. Applied topically, it alleviates pain by desensitizing epidermal nerve fibers and causing reversible nerve degeneration. (60)

Topical Capsaicin treatment appeared to be effective in reducing pain according to a study published 2014 in form of an abstract.(61) Capsaicin, however, may be associated with severe local adverse effects, such as itching, pricking, burning sensation and eye irritation. Nerve degeneration does not occur immediately but develops over time. Patients may therefore experience severe pain during early treatment. A study found 82% reduction of nerve fibers in skin biopsies after daily treatment with topical capsaicin over three weeks. In re-biopsies conducted 6 weeks after treatment, a dermal re-innervation of 83% was found. Sensibility returned to a normal value except for the sensation of cold, which remained impaired at least until the end of the study, which was 6 weeks after the last application. (62) Topical capsaicin is recommended by various guidelines including the ACR, the EULAR and the PANLAR – recommendations, even though there are doubts concerning the restitution of nerve function to normal after cessation of therapy. (60)

Systemic Chondroitin Sulfate

Chondroitin sulfate (CS) is recommended for pain relief and functional improvement by PANLAR. Because of its low toxicity and possible benefit, CS is also recommended by EULAR even though it has been acknowledged that the effect may be small and that it is unclear which patients are suitable for such a treatment. (51) CS may be effective in symptom alleviation including pain, function impairment and loss of grip strength. It also decreases erosive radiographic progression. (63) (54) The ACR does not recommend treatment with CS. (50,52)

1.1.9.2 Non-pharmacological Therapy

Most recommendations suggest education concerning disease course, self-management and the principles of joint protection, for example on how to avoid adverse mechanical factors. Education should go along with an exercise training aimed at improve both range of motion and muscle strength. Exercises should be done with low intensity in phases of no inflammation and are believed to increase pinch and grip-strength.

Education and exercise are helpful, but have a very small effect in relieving pain and increasing range of motion and strength. (51,54,64)

Splints are mostly used for OA of the first CMC joint and are supposed to stabilize, immobilize and protect this joint. (54) Splints may lead to a reduction of inflammation and to a decrement of pain. Furthermore, when used in the initial phases of the disease, splints may reduce the development of deformities. Splints should be custom-made. Randomized controlled trials (RCTs) showed a reduction of hand pain in patients using a splint compared to those not using it. (64)

The application of thermal agents is suggested by both the ACR and the EULAR. EULAR furthermore recommends heat application before exercises. Heat can be applied in form of paraffin wax or hot packs. It is considered an effective and safe way to relieve pain although it has not been formally studied in hand OA yet, but only in knee and hip OA. (51,52,54)

1.1.9.3 Surgical Therapy

In patients with severe pain or disability due to OA of first CMC joint, and if conservative treatments have failed, surgical treatment may be considered. Possible interventions are an arthroplasty with ligament reconstruction and tendon interposition, arthrodesis, trapeziectomia or total joint replacement. (50,51)

1.2 Ultrasound

1.2.1 Ultrasound in Rheumatology

Over the last years, musculoskeletal US (MSUS) has become a common tool in clinical practice of rheumatology all over the world. A 2008 survey assessed the presence of MSUS in rheumatologic training programs throughout the United States and found that 41% of the programs included MSUS. In 2017, this rate increased to 94%. (65) MSUS is a real time, highly dynamic imaging technique and can be used for diagnosis, follow-up and monitoring of rheumatic diseases as well as for guided invasive procedures such as needle aspiration and intraarticular injections. US has several benefits over other imaging tools, as it is radiation-free, cheap, broadly available, not stressing and well tolerated by the patients. It does not have any side effects or contraindications and it allows an immediate and direct correlation between imaging findings and clinical assessment improving the management of patients. The possibility to show and explain the patients directly the pathologies may also improve their compliance.

US is furthermore cost-efficient and the ongoing miniaturization of the machines and the easy portability allow the use of US in different clinical settings such as a bedside procedure. The optimization of imaging quality and Doppler sensibility further simplified the use of US. It also allows the comparison of the side of interest with the asymptomatic contralateral side. (66–68)

However, there exist some negative aspects of MSUS that should be mentioned. First of all, it is more time consuming compared to clinical examination alone. It requires a skilled operator and it is highly dependent on the operator's expertise. US has a long and steep learning curve. Even with experienced operators, findings may still be operator-dependent. (35,69) There is also a considerable dependence on the quality of equipment. Furthermore, the field of view is limited because pathologies inside the bone cannot be assessed. (68)

US is an appropriate imaging tool for a wide range of rheumatic and musculoskeletal conditions including inflammatory and degenerative diseases, crystal arthropathy, connective tissue diseases, vasculitis and regional pain syndromes. (67)

A selection of pathologies visible in patients with rheumatic diseases by US are presented in table 4:

- Effusions, synovitis, and bursitis
- Tendon pathology including tendinosis, tenosynovitis, and tendon tears
- Cartilaginous, osseous, or osteochondral lesions including cartilage damage, cysts, erosions, fractures
- Enthesopathy, encompassing pathologic changes at tendon, ligament, fascia, or joint capsule attachments
- Compression neuropathy
- Postoperative complications

Table 4: Abnormalities in rheumatologic diseases seen by US (68)

Two MSUS techniques are mainly used in rheumatology: the grey scale and Doppler [Color Doppler and Power Doppler (PD)]. Since MSUS is considerably operator dependent, standardization of the scanning procedures is very important to improve image quality. The first guidelines in this regard were published by EULAR in 2001 (70), an update has been released in August 2017:
Accordingly, high resolution linear transducers should be used with frequencies between 6 and 14 MHz for deep/intermediate structures and ≥15MHz for superficial structures. While examining a joint, the probe should be held perpendicular or parallel to the bony cortical surface for an optimal depiction of structures. A dynamic scanning technique should be carried out and musculoskeletal structures should be evaluated as they move slowly. The probe should be adjusted continuously to maintain the correct position. Compression with the probe can be used to distinguish compressible liquid collection from non-compressible tissues. No or very little compression is important while performing Doppler examinations of superficial structures not to compress small vessels. Ultrasound transmission gel should be applied generously. (67)

The *Austrian Rheumatology-Radiology Initiative for Musculoskeletal Ultrasound* (ARRIMUS) further recommended a structured documentation of pathological changes in two or more plains and the use of scoring systems to evaluate findings.

Regarding rheumatoid arthritis, CR is the golden standard imaging tool but US has become a commonly used imaging method for its diagnosis and for monitoring the efficacy of treatment. (68) Studies examining US as an imaging method for RA found

that US is more sensitive for detecting signs of articular damage than CR, especially in early RA. Sensitivity of US for the detection of bone erosion is comparable to MRI. (71,72) US was also found to be a sensitive technique to detect synovitis in RA patients when using MRI as a comparator. Furthermore, US was more sensitive to detect synovitis than clinical examination for large joints such as knee and shoulder. (73) Besides, , US is also indicated for the assessment of disease remission and as an outcome measure. (74)

1.2.2 Ultrasound for OA

1.2.2.1 Evaluation of sonographic hand OA

Common features of hand OA in ultrasound

US is useful to assess most OA signs including osteophytes, changes of the hyaline cartilage, synovial hypertrophy, vascularization and joint effusion. Changes of the subchondral bone such as cysts are not visible by US. (35) Indications for the use of US in OA joints are depicted in table 5.

Indications for the use of US in OA joints

- **Assessment of cartilage lesions**
- **Detection of osteophytes**
- **Detection of erosions**
- **Detection of joint effusion**
- **Detection of synovial hypertrophy**
- **Differentiation between active and inactive synovitis (Doppler modalities)**
- **Assessment of periarticular soft tissue abnormalities in OA (bursitis)**
- **Evaluation of mucous cysts (hand OA)**
- **Execution of US guided procedures (aspiration of joint and periarticular effusion, injections, biopsies)**
- **Monitoring of** OA **disease progression from early to late stages**
- **Follow-up of the response to local and systemic therapies**

Table 5: Indications and clinical applications of US in OA. (75)

Synovitis has become an important subject of research in OA since it is present in about 10% of hand joints affected by OA and could be a valuable prognostic factor for structural outcomes. (76) A study from 2016 for example demonstrated that ultrasound detected inflammatory signs predicted progression of JSN and osteophytes. Even low grade synovitis increased significantly the risk of radiographic progression. US could therefore help to identify patients with OA at a high risk of disease progression. (77)
A wide range of osteoarthritic cartilage abnormalities can be seen using US like loss of the echogenic texture, irregularities of the margins and cartilage thinning. (3) To assess the cartilage of PIP and DIP joints with US, a maximal flexion of fingers is necessary in order to keep the probe perpendicular to the cartilage surface. A maximal flexion of fingers, however, is often not possible for patients with severe OA. MCP joints are easily accessible for US and since they are often affected by OA, as well, it has been proposed to assess the cartilage of MCP joints and to extrapolate the results to the other finger joints. (78)

Scoring systems

In 2008, a group of experts in ultrasound proposed a preliminary scoring system for synovial hypertrophy and effusion (considered as one feature: synovitis), osteophytes and PD abnormalities in OA. It was suggested to score 15 joints including the first carpometacarpal joint, MCP 1–5, PIP 1–5, and DIP 2–5. Erosions, JSN and cartilage changes were not considered. According to this score, synovitis, osteophytes and PD abnormalities are graded dichotomously as being present or absent (0-1) or semi-quantitatively from 0 to 3 (0=absent, 1=mild, 2=moderate, 3=severe changes). A reliability exercise conducted by this group demonstrated a moderate intra- and interobserver reliability, which was best for osteophytes. Reliability was better in patients with lower level of pathology. (79) Mathiessen *et al.* published an ultrasound scoring system (also with gradings ranging from 0-3) for osteophytes in 2012. This system yielded a high sensitivity and specificity for the individual grades compared to MRI, with better results in joints with severe osteophytes (80).

In 2016, the OMERACT ultrasonography group published a semi-quantitative scoring system for osteophytes and cartilage abnormalities with grades ranging from 0 to 3. For cartilage scoring only a fair interobserver reliability was found and therefore the semi-quantitative evaluation was not recommended. Instead, it was suggested to evaluate the

presence or absence of cartilage damage dichotomously (0/1), which revealed a very good reliability. The authors concluded that the poor reliability of the semiquantitative scoring could have been caused by different beam angles and because the cartilage is not uniformly damaged.

The scoring system for osteophytes showed excellent reliability. An ultrasound atlas was developed by Mathiessen *et al.* which can be used as a reference. (78,80)

1.2.2.2 Comparison of ultrasound to other imaging methods

One of the most important advantages of US in the evaluation of osteoarthritic joints over x-ray is the ability of the former to depict synovial abnormalities such as hypertrophy, increased vascularity and effusion.

US performed also better or at least equally well for depicting OA at knees when compared to MRI. (81) An advantage of US over MRI for the assessment of OA is the possibility to conduct dynamic examinations, for example at a weight-bearing joint. (82) Another study compared the assessment of osteophytes in hands by US, MRI and CR, reporting that US detected more osteophytes than CR. The higher sensitivity of US could in part be explained by the fact that CR can only depict osteophytes if they are tangentially to the x-ray beam while US is a multiplanar imaging method. A good accordance between osteophytes detected by MRI and US was found even though US was only performed at the dorsal side of the joints while MRI also depicted osteophytes at other parts of the joints. Osteophytes, however, occur more often at the dorsal side of joints (83), the assessment of this part of the joint might therefore be sufficient in clinical practice. (80)

1.2.3 Purpose of this research

There is little literature available on the prevalence of imaging changes indicating OA in the general population. A few previous studies reported that certain OA signs are quite common among healthy people. For instance, Padovano *et al.* examined the prevalence of synovial inflammatory findings and showed that 88% of healthy individuals had at least one US change compatible with synovitis (SH, SE or PD). (84) Mathiessen *et al.* found osteophytes in 28% of joints without radiographic OA and bony enlargement. (85) US is believed to be more sensitive for the detection of osteophytes than CR and furthermore, it is able to depict synovial abnormalities. (81)

To the best of our knowledge, this is the first study evaluating systematically the prevalence of different signs suggestive of OA (Osteophytes, Synovial Hypertrophy/Effusion, Erosion and PD abnormalities) using US in a large random population.

1.2.4 Aim of this research

The aim of this study was to investigate the prevalence of hand OA in the population of the Bruneck study. It originally included 1,000 subjects who were recruited by random sampeling from the official population register in 1990. Furthermore, the prevalence of structural and inflammatory US signs of OA in the joints of the hands was investigated in subjects with hand OA and in healthy subjects. The preferential location of these changes was determined. We also analyzed possible correlations of abnormal US findings with functional impairment

2 Methods

Study

The Bruneck study is a prospective population-based study conducted in the hospital of Bruneck in northern Italy. The original purpose of the study was the evaluation of the prevalence, risk factors and pathogenesis of artheroslerotic changes of the carotids. The baseline examination took place in 1990, follow-up examinations were scheduled every 5 years. (86) Since the beginning of the study, the topics under investigation have been expanded continuously.

In May 2016, a rheumatologic visit including an ultrasound and clinical examination of the hands was included in the study protocol. The Bruneck study was reviewed and approved by the responsible local ethics committee. All subjects had an oral briefing with a medical doctor before their clinical examinations and gave their written informed consent.

Study subjects

All study subjects are inhabitants of the city of Bruneck and were recruited for the base-line -evaluation in 1990 from the official population register by random sampling. A stratification for age and sex was performed with 125 individuals per sex and decade of age (5^{th} to 8^{th} decade). Of the 1000 subjects originally included in 1990, a total of 353 subjects appeared to the study visits taking place between April and May 2016. 22 individuals were excluded due to incomplete data, leaving 331 subjects for further analysis.

We defined 2 groups according to the presence or absence of hand OA: group A were patients with a clinical diagnosis of hand OA and fulfilment of the ACR criteria for hand OA. (1) Group B were healthy individuals, i.e. they did not report any hand pain, aching, tenderness or soft tissue swelling. We further defined a subgroup of group B which were patients without bony enlargements (group B.1).

Medical history and clinical examination:

Medical history and clinical examination was conducted by a medical student (N.G), who was specifically trained in the assessment of hand OA by an experienced rheumatologist (C.D.). Medical history concerning pain at hands, knees, hips and spine,

joint replacement surgery and the items of the ACR classifications criteria for OA were obtained. The ACR criteria for hand OA were assessed for all participants. (1)
Clinical examination was performed at wrists, CMCs, MCPs, PIPs and DIPs evaluating for the presence of soft tissue swelling, bony enlargements and tenderness. These parameters were coded as binary variables (present / non present) and assessed for each examined joint.

Clinical scores

All study participants were asked to complete the SF-SACHRA (36), the Health Assessment Questionnaire (HAQ) (87) and the Functional Index for Hand Osteoarthritis (FIHOA). (38)
The SF-SACRAH consists of five questions using a 10-point Likert-scale (0= best, 10= worst) for each of the questions. Three questions address activities of daily live ("locking/unlocking a door", "fastening/unfastening a zip", and "turning pages of a newspaper"), one question is related to morning stiffness and one question is to evaluate pain in the hands.
The FIHOA consists of ten questions assessing the hand function during daily activities such as cutting with a knife, buttoning, shakings hands and writing. It uses a 4-point Likert scale (0=possible without difficulty, 3=not possible).
The HAQ consists of 19 questions concerning the following activities: dressing and grooming, arising, eating, walking, hygiene, reach, grip, sex and other everyday activities. Patients indicate difficulties in performing these activities on a 4-point Likert scale where 0 = "possible without any difficulties" and 3 = "not possible". (87)

Ultrasound examination

US evaluation was performed by two rheumatologists experienced in musculoskeletal sonography [C.De. (8 years of experience), A.Ad. (5 years of experience)]. The sonographers were unaware of clinical results. The participants were in a sitting position opposite of the examiner with the hands resting on a horizontal examination table in a darkened room. The hands were held in a neutral position, the duration of each examination was ~20 minutes. US was performed at transverse and longitudinal planes of the dorsal side of the wrists and the palmar and dorsal sides of the following joints: CMC, MCP1-5, PIP1-5, DIP2-5. We used a GE Logic E ultrasound device.

The following abnormalities were assessed by B-mode US: erosions, osteophytes, synovial hypertrophy and/or effusion (SH/E). In addition, Power Doppler (PD) sonography was conducted. An ultrasound case report form was developed using a semi-quantitative grading system for SH/E and PD (0 = no change, 1 = mild change, 2 = moderate change, 3 = severe change). Erosions were graded from 0 to 3 with 0 = no change, 1 = cortical break 0-1mm, 2 = cortical break 1.1-2mm; 3 = cortical break >2mm.

The OMERACT score (78) was used for assessing osteophytes, defining osteophytes as cortical protrusion and grading them semiquantitavely (0 = none, 1 = minor., 2 = moderate, 3 = major size of osteophytes). The ultrasound atlas of osteophytes developed by Mathiessen *et al*. was used as a reference (Fig. 4). (80)

A global ultrasound sum score was calculated for each group by summing all semiquantitative scores of all four US abnormalities investigated.

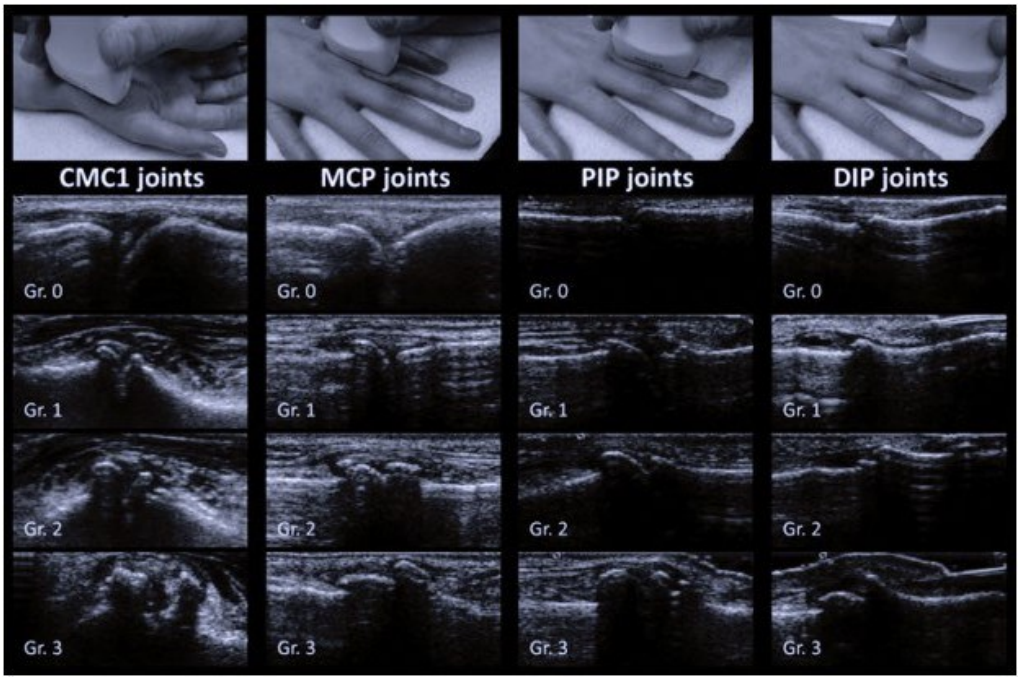

Figure 1: Ultrasound atlas of osteophytes. Osteophytes graded from 0 to 3 are depicted for the different joints of the hand (CMC, MCP, PIP, DIPS). The distal part of the joint is oriented on the right. (80) Used with the kind permission of BMJ Publishing Group Ltd.

Statistical analysis

All statistical analyses were done using R [R Core Team (2016). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria URL: https://www.r-project.org/]

Descriptive statistics were used to summarize the data. Differences between groups regarding demographic and clinical parameters were analyzed using Fisher's exact test for binary parameters and the two-sided Student's T test for unpaired samples for continuous parameters. Possible associations between US findings and the three different clinical scores (SF-SACHRA, FIHOA and HAQ) were assessed using spearman's rank correlation test. Fisher's exact test was used to compare the prevalence of US changes between groups. Pearson's chi-squared test was used to compare the proportion of patients with different grades of US changes between groups.

3 Results

Complete data sets were available in 331 participants. Of these 167 (50.5%) were men and 164 (49.5%) were women. The mean age of the total study population was 75.7±7.2 years (range 65-99).

Eighty-nine individuals (26.9%) fulfilled the ACR criteria of hand OA (group A) and 208 individuals (62.8%) were in the healthy control group B. Subgroup B.1 (individuals without bony swelling) consisted of 32 subjects. 34 subjects did not meet the inclusion criteria for any group. The make-up of the study population is depicted in figure 5.

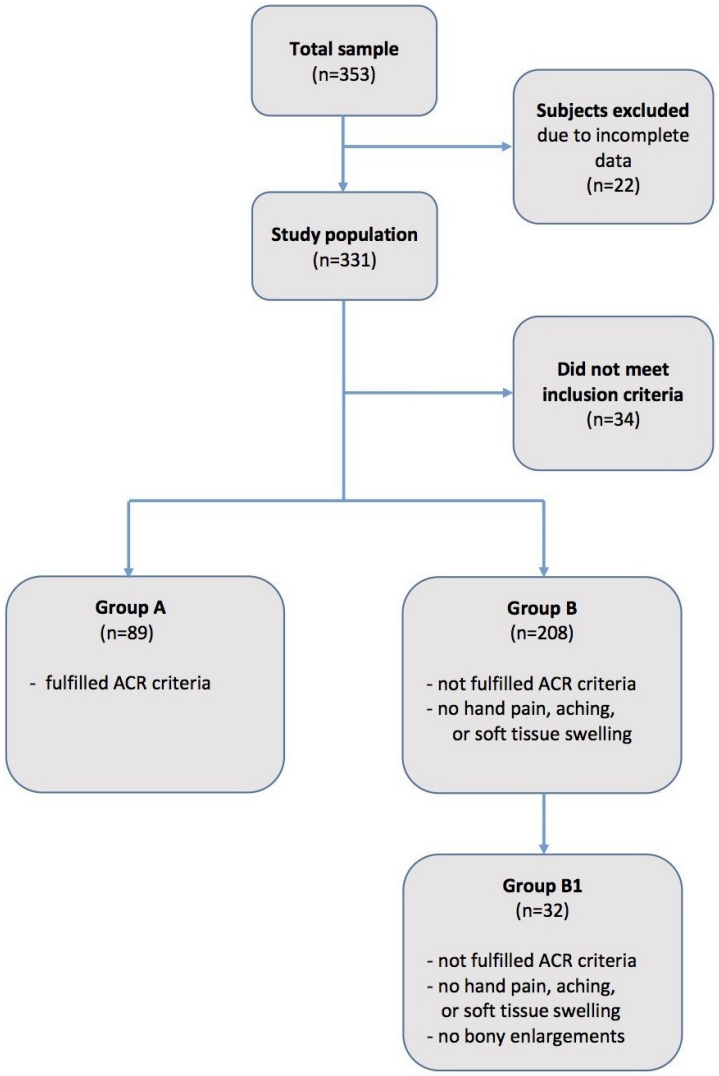

Figure 2: Flowchart of the study population.

3.1 Demographic data

The prevalence of hand OA was 26.9%. Demographic data including sex, age, type of work and medical history are depicted in table 6. There were more women in group A (64%) than in group B (41%). Subjects in group A appeared to be older compared to the subjects in group B; however, the difference was not statistically significant. Both prevalence of morning stiffness and duration of morning stiffness in minutes were significantly higher in group A when compared to group B. In group A morning stiffness was present in 41 % of the subjects and the indicated mean duration of the stiffness was 6.8 ± 11.8 minutes. In group B only 3% of the subjects complained about morning stiffness with a mean duration of 0.36 ± 2.6 minutes. Medical treatment for osteoporosis was significantly more frequent in group A when compared to group B. There was no significant difference in type of work (white collar/blue collar), the presence of a joint replacement and the prevalence of hip, knee or spinal pain between the two groups.

	Group A	Group B	P
Age (years), mean (SD)	76.91 ± 6.89	75.27 ± 7.26	0.07
Female, n (%)	57 (64%)	86 (41%)	p<0.001
Former blue collar worker, n (%)	45 (79%)	83 (68%)	0.16
Any joint replacement (yes)	14 (16%)	19 (9%)	0.11
Bony enlargement (yes)	88 (99%)	176 (85%)	p<0.001
Tendon insertion pain (yes)	45 (51%)	58 (28%)	p<0.001
Hip pain (yes)	13 (15%)	17 (8%)	0.1
Knee pain (yes)	28 (31%)	42 (20%)	0.05
Spinal pain (yes)	34 (38%)	76 (37%)	0.79
Treatment for osteoporosis (yes)	37 (42%)	45 (22%)	p<0.001
Morning stiffness in hands (yes)	35 (41%)	6 (3%)	p<0.001
Duration of morning stiffness in minutes (mean ± SD)	6.82 ± 22.83	0.36 ± 2.6	0.01

Table 6: Demographic and clinical data for group A and group B. Comparisons between groups A and B were done using the Fisher's exact test for binary variables (gender, occupation, joint prosthesis, bony enlargements, tendon insertion pain, hip pain, knee pain, spinal pain, treatment for osteoporosis and the presence of morning stiffness). For continuous variables (Age and duration of morning stiffness) sudent's T-test was performed. Abbreviations: p p-value, SD standard deviation

3.2 US findings

3.2.1 Frequency and severity of US findings at population level

3.2.1.1 Frequency of abnormal US findings

Almost all study subjects (229, 99%) showed at least one US abnormality. Most of these changes were osteophytes, which were found in 99% of the participants. At least one joint with SH/E was observed in 73% of the study population whereas erosions and PD abnormalities were less frequent (14% and 18 %, respectively).

All 89 study subjects in **group A** showed at least one abnormal US finding (Table 7). Osteophytes were the most frequently observed abnormality occurring in 100% of subjects in group A, followed by SH/E and PD, which were observed in at least one joint in 93% and 33% of subjects, respectively. Erosions were the least frequent finding as only 17% of the examined subjects in group A showed at least 1 joint with ≥1 erosion.

In **group B,** 99% of the study subjects showed at least one abnormal US finding which is comparable to group A. Ninety-nine percent of the 208 subjects in group B had at least one osteophyte, 63% presented with at least one abnormal SH/E finding and 12% of the examined subjects had at least one erosion or one PD finding. Group B had significantly less SH/E and PD abnormalities compared to group A ($p<0.001$).

In **group B.1,** the prevalence of abnormal US findings was still very high with 97% of the subjects presenting with at least one abnormal US finding in any of the investigated joints. Ninty-four percent of the 32 subjects in group B.1 had at least one osteophyte, 41% presented with at least one SH/E finding. Also, group B1 had significantly less

SH/E and PD abnormalities compared to group A (p<0.001). None of the 32 subjects showed erosions in any of the investigated joints and only one subject was PD positive (Table 7).

US changes	Group A	Group B	p-value (A vs. B)	GroupB1	p-value (A vs. B1)
All US abnormalities	89 (100%)	205 (99%)	1.0	31 (97%)	0.27
Osteophytes	89 (100%)	24 (99%)	0.56	30 (94%)	0.07
SH/E	83 (93%)	132 (63%)	<0.001	13 (41%)	<0.001
Power-Doppler	29 (33%)	24 (12%)	<0.001	1 (3%)	<0.001
Erosion	15 (17%)	24 (12%)	0.26	0 (%)	0.01

Table 7: Percentage of subjects with at least 1 US change.

3.2.1.2 Severity of abnormal US findings

In order to investigate the severity of changes, a total US score was calculated for each subject by summing all semiquantitative scores of all four US abnormalities investigated (erosion, osteophytes, synovial hypertrophy and/or effusion, PD). The highest total US score was seen in Group A (39.4, range 2-175) compared to group B (17.8, 0-97) and group B.1 (8.8, 0-48).

Next, we investigated the number of individuals with grade 1, 2 or grade 3 findings for each US abnormality. Almost half of the subjects in group A (47.2%) had at least one grade 3 osteophyte compared to 21.1% and 6.2% of subjects in group B and B.1, respectively. These differences were statistically significant (p<0.001). Concerning SH/E, the majority of subjects in all groups had only grade 1 findings (31.2-49.9%) whereas more severe SH/E was less common. In group A for example, only 12.4% of the subjects had at least one grade 3 SH/E as compared to 2.9% and 3.1% of subjects in group B and B.1, respectively. These differences were statistically significant (p<0.001). The vast majority of subjects in all groups did have any erosions or PD abnormalities, particularly grade 2 and grade 3 abnormalities were rare. In group A, 10.1% of the subjects had at least one grade 2 erosion and 18% had at least one grade 2

PD abnormality compared to 5.8% and 5.3 % of subjects in group B, respectively. In group B1, no subject presented with an erosion and only 1 subject (3.1%) had a grade 2 PD abnormality.

The complete results for all groups and US abnormalities are listed in table 8

		Osteophytes	SH/E	Erosion	PD
Group A	none	0 (0%)	6 (6.7%)	74 (83.1%)	60 (67.4%)
	At least 1x1	15 (16.9%)	44 (49.4%)	4 (4.5%)	11 (12.4%)
	At least 1x2	32 (36%)	28 (31.5%)	9 (10.1%)	16 (18%)
	At least 1x3	42 (47.2%)	11 (12.4%)	2 (2.2%)	2 (2.2%)
Group B	none	3 (1.4%)	76 (36.5%)	184 (88.5%)	184 (88.5%)
	At least 1x1	78 (37.5%)	86 (41.3%)	11 (5.3%)	13 (6.2%)
	At least 1x2	83 (39.9%)	40 (19.2%)	12 (5.8%)	11 (5.3%)
	At least 1x3	44 (21.2%)	6 (2.9%)	1 (0.5%)	0 (0%)
p-value	(A vs B)	<0.001	<0.001	0.28	<0.001
Group B1	none	2 (6.2%)	19 (59.4%)	32 (100%)	31 (96.9%)
	At least 1x1	20 (62.5%)	10 (31.2%)	0 (0%)	0 (0%)
	At least 1x2	8 (25%)	2 (6.2%)	0 (0%)	1 (3.1%)
	At least 1x3	2 (6.2%)	1 (3.1%)	0 (0%)	0 (0%)
p-value	(A vs B1)	<0.001	<0.001	0.10	0.01

Table 8: Number of subjects with at least one abnormal US finding for four different US abnormalities. For each group (A, B and B.1) the number of subjects with at least one abnormal US finding graded as 1, 2 or 3 are depicted. The number of subjects with no abnormal findings are also shown ("none").

3.2.2 Frequency of US findings at joint level

The prevalence of abnormal US findings in the different joint groups (DIPs, PIPs, MCPs, wrists), were compared for each group separately. 98.9% of subjects in **group A** had at least one abnormality in the DIP joints. PIP (93.3%) and MCP (82.0%) joints

were also frequently affected. At wrists, only 23.6% of the subjects showed one or more abnormalities, however, only SH/E and PD were scored at this site (Table 9).

The most frequently affected individual joint was the DIP2 (82.6% of the examined DIP2 presented with at least one US finding) as detailed in table 10.

In g**roup B,** PIPs were most frequently affected, 87% of subjects showed US abnormalities at this level, whereas DIPs and MCPs showed US changes less frequently (81.7% and 79.8% of the subjects, respectively). At wrists, 13.9% of the subjects had at least one US abnormality (Table 10). DIP2 was the most commonly affected individual joint (48.3%) (see Table 10).

In **group B.1**, 78.1% of the subjects showed at least one US abnormality at PIPs, 71.9% at MCPs and 62.5% at DIP joints (Table 9).

MCP4 and 5 were the least commonly affected joints in all groups (Table 10).

		≥1US change	**Osteo-phyte**	**SH/E**	**Erosion**	**PD**	**SH/E +PD**
Group A	wrists	21 (23.6%)	N/A	21 (23.6%)	N/A	4 (4.5%)	4 (4.5%)
	MCPs	73 (82%)	69 (77.5%)	46 (51.7%)	10 (11.2%)	9 (10.1%)	9 (10.1%)
	PIPs	83 (93.3%)	83 (93.3%)	63 (70.8%)	0 (0%)	12 (13.5%)	12 (13.%)
	DIPs	88 (98.9%)	88 (98.9%)	40 (44.9%)	2 (2.2%)	5 (5.6%)	5 (5.6%)
Group B	wrists	29 (13.9%)	N/A	27 (13%)	N/A	6 (2.9%)	4 (1.9%)
	MCPs	166 (79.8%)	153 (73.6%)	69 (33.2%)	19 (9.1%)	12 (5.8%)	11 (5.3%)
	PIPs	181 (87%)	173 (83.2%)	75 (36.1%)	5 (2.4%)	5 (2.4%)	3 (1.4%)
	DIPs	170 (81.7%)	166 (79.8%)	52 (25%)	2 (1%)	2 (1%)	1 (0.5%)
Group B1	wrists	3 (9.4%)	N/A	3 (9.4%)	N/A	0 (0%)	0 (0%)
	MCPs	23 (71.9%)	22 (68.8%)	8 (25%)	0 (0%)	1 (3.1%)	1 (3.1%)
	PIPs	25 (78.1%)	23 (71.9%)	6 (18.8%)	0 (0%)	1 (3.1%)	1 (3.1%)
	DIPs	20 (62.5%)	19 (59.4%)	3 (9.4%)	0 (0%)	0 (0%)	0 (0%)

Table 9: US findings at a joint group level. The number of study subjects with one or more US abnormalities in each joint group (wrists, MPCs, PIPs, DIPs) is depicted. The percentage of subjects with at least one US finding for the different US changes (Osteophytes, SH/E, Erosion, PD, SH/E+PD) is also shown.

Group A		Group B		Group B1	
DIP2	147 (82.6%)	**DIP2**	201 (48.3%)	**PIP1**	29 (45.3%)
DIP5	132 (74.2%)	**CMC**	192 (46.2%)	**MCP2**	27 (42.2%)
DIP3	131 (73.6%)	**DIP5**	183 (44%)	**DIP2**	22 (34.4%)
CMC	122 (68.5%)	**PIP1**	182 (43.8%)	**DIP5**	19 (29.7%)
PIP1	116 (65.2%)	**MCP2**	175 (42.1%)	**CMC**	17 (26.6%)
DIP4	94 (52.8%)	**DIP3**	155 (37.3%)	**DIP3**	14 (21.9%)
PIP3	93 (52.2%)	**PIP5**	126 (30.3%)	**PIP5**	13 (20.3%)
PIP5	93 (52.2%)	**PIP2**	123 (29.6%)	**MCP1**	12 (18.8%)
PIP2	91 (51.1%)	**PIP3**	123 (29.6%)	**PIP3**	11 (17.2%)
MCP2	90 (50.6%)	**MCP1**	121 (29.1%)	**MCP3**	8 (12.5%)
PIP4	82 (46.1%)	**DIP4**	117 (28.1%)	**PIP2**	8 (12.5%)
MCP1	70 (39.3%)	**MCP3**	102 (24.5%)	**DIP4**	8 (12.5%)
MCP3	61 (34.3%)	**PIP4**	96 (23.1%)	**PIP4**	6 (9.4%)
MCP5	41 (23%)	**MCP5**	63 (15.1%)	**MCP4**	4 (6.2%)
MCP4	24 (13.5%)	**MCP4**	38 (9.1%)	**MCP5**	4 (6.2%)

Table 10: Frequency of affection on a joint level. The percentage of the examined joints showing at least one US abnormality is depicted. The joints are listed according to the frequency of affection.

Osteophytes were the most frequent abnormality in all joints. In **group A,** osteophytes were most prevalent at the DIPs where 98.9% of subjects showed at least one osteophyte (Table 9). The DIP2 was the most commonly affected joint (82.6% of all examined DIP2s), followed by DIP3 (72.5%), DIP5 (71.3%) and the 1st CMC joint (67.4%) (Table 11). In **group B**, osteophytes were more common at PIPs (83.2%) than at DIPs (79.8%) (Table 9). However, when calculating the prevalence of osteophytes for each joint separately, the DIP2 was again the most commonly affected site (47.6%) followed by the 1st CMC (44%), the PIP1 (42.5%) and the DIP5 (42.1%) (Table 11). In **group B.1,** the PIPs were the most frequently affected joint group (in 71.8% of the subjects). The PIP1 joint yielded the highest prevalence of osteophytes (42.4%), followed by the MCP2 (37.5%) and the DIP2 (32.8%) (Table 11).

SH/E were predominantly found at PIPs as 70.8% of subjects in group A and 33.2% in group B showed a t least one joint with SH/E at this site. In group B.1, the MCPs were

the most frequently affected site where 25% of the subjects showed SH/E (Table 9). On a single joint level, the PIP1 was the most frequently affected site in group A (30.9% of the joints showed abnormalities), whereas in group B and group B.1, the MCP2 most commonly yielded SH/E (12% and 10.9%, respectively, Table 11).

Erosions and abnormal PD findings were significantly less frequent. In group A, erosions were most frequently observed at the MCP 2 (3.9%), MCP5 (1.7%) and 1st CMC (2.8%). PD abnormalities were predominantly found at 1st CMC (9.6%) and MCP2 (5.1%). In group B, these findings were very rare. Erosions were again most frequently found at the MCP2 and MCP5, and positive PD was most often found at 1st CMCs and MCPs (1.9% each). In group B1 there were no erosions and only two joints with abnormal PD findings (Table 11).

Synovial inflammation as defined by SH/E and PD positive findings was most commonly found at PIP joints (in 13.5% of the study subjects), whereas it was less frequent at wrists (4.5 of the subjects) and DIPs (5.6%) in group A. In group B, synovial inflammation was often seen at MCP joints and 1st CMCs (Table 9 and 11).

		Osteophytes	SH/E	Erosion	PD
Group A	CMC	120 (67.4%)	36 (20.2%)	5 (2.8%)	17 (9.6%)
	MCP1	61 (34.3%)	20 (11.2%)	1 (0.1%)	1 (0,6%)
	MCP2	79 (44.4%)	39 (21.9%)	7 (3.9%)	9 (5.1%)
	MCP3	46 (25.8%)	24 (13.5%)	1 (0.6%)	2 (1.1%)
	MCP4	13 (7.3%)	13 (7.3%)	1 (0,6%)	0 (0%)
	MCP5	31 (17.4%)	13 (7,3%)	3 (1,7%)	1 (0,6%)
	PIP1	109 (61.2%)	55 (30.9%)	0 (0%)	2 (1,1%)
	PIP2	87 (48.9%)	36 (20.2%)	0 (0%)	2 (1,1%)
	PIP3	80 (44.9%)	49 (27.5%)	0 (0%)	6 (3.4%)
	PIP4	70 (39.3%)	44 (24./%)	0 (0%)	4 (2,2%)
	PIP5	87 (48.9%)	38 (21.3%)	0 (0%)	4 (2,2%)
	DIP2	147 (82.6%)	30 (16.9%)	1 (0,6%)	2 (1,1%)
	DIP3	129 (72.5%)	36 (20.2%)	1 (0,6%)	3 (1,7%)
	DIP4	91 (51.1%)	25 (14%)	0 (0%)	1 (0,6%)
	DIP5	127 (71.3%)	19 (0.7%)	0 (0%)	0 (0%)
Group B	CMC	183 (44%)	26 (6.2%)	2 (0.5%)	8 (1.9%)
	MCP1	109 (26.2%)	19 (4.6%)	4 (1%)	4 (1%)
	MCP2	149 (35.8%)	50 (12%)	17 (4.1%)	8 (1.9%)
	MCP3	87 (20.9%)	29 (7%)	2 (0.5%)	5 (1.2%)
	MCP4	20 (4.8%)	20 (4.8%)	1 (0.2%)	2 (0.5%)
	MCP5	49 (11.8%)	17 (4.1%)	6 (1.4%)	1 (0.2%)
	PIP1	177 (42.5%)	45 (10.8%)	0 (0%)	2 (0.5%)
	PIP2	114 (27.4%)	28 (6.7%)	1 (0.2%)	0 (0%)
	PIP3	106 (25.5%)	45 (10.8%)	0 (0%)	2 (0.5%)
	PIP4	77 (18.5%)	34 (8.2%)	3 (0.7%)	2 (0.5%)
	PIP5	117 (28.1%)	26 (6.2%)	2 (0.5%)	2 (0.5%)
	DIP2	198 (47.6%)	30 (7.2%)	1 (0.2%)	1 (0.2%)
	DIP3	152 (36.5%)	34 (8.2%)	1 (0.2%)	1 (0.2%)
	DIP4	106 (25.5%)	27 (6.5%)	1 (0.2%)	0 (0%)
	DIP5	175 (42.1%)	27 (6.5%)	0 (0%)	0 (0%)

		Osteophytes	SH/E	Erosion	PD
Group B1	CMC	17 (26.6%)	1 (1.6%)	0 (0%)	0 (0%)
	MCP1	10 (15.6%)	2 (3.1%)	0 (0%)	0 (0%)
	MCP2	24 (37.5%)	7 (10.9%)	0 (0%)	1 (1.6%)
	MCP3	6 (9.4%)	2 (3.1%)	0 (0%)	0 (0%)
	MCP4	2 (3.1%)	2 (3.1%)	0 (0%)	0 (0%)
	MCP5	3 (4.7%)	3 (4.7%)	0 (0%)	0 (0%)
	PIP1	27 (42.2%)	3 (4.7%)	0 (0%)	0 (0%)
	PIP2	6 (9.4%)	2 (3.1%)	0 (0%)	0 (0%)
	PIP3	7 (10.9%)	5 (7.8%)	0 (0%)	1 (1.6%)
	PIP4	4 (6.2%)	2 (3.1%)	0 (0%)	0 (0%)
	PIP5	12 (18.8%)	2 (3.15)	0 (0%)	0 (0%)
	DIP2	21 (32.8%)	1 (1.6%)	0 (0%)	0 (0%)
	DIP3	14 (21.9%)	0 (0%)	0 (0%)	0 (0%)
	DIP4	7 (10.9%)	1 (1.6%)	0 (0%)	0 (0%)
	DIP5	19 (29.7%)	1 (1.6%)	0 (0%)	0 (0%)

Table 11: US findings at the joint level. The number and percentage of examined joints showing at least one US finding is depicted for Osteophytes, SH/E, Erosion and PD

3.3 Correlations between clinical signs and US findings

In order to investigate possible associations of US findings with functional impairment in patient with hand osteoarthritis (group A), correlation analyses were conducted.
There was a significant positive correlation between the SF-SACHRA and total osteophyte and SH/E scores ($corr_{coeff} = 0.46$, $p < 0.001$) and $corr_{coeff} = 0.27$, $p=0.036$, respectively). Also, the FIHOA score correlated with the total osteophyte ($corr_{coeff} = 0.39$, $p = 0.0028$) and PD score ($corr_{coeff} = 0.4$, $p < 0.001$).

There was a significant correlation between the US osteophyte score and the number of bony enlargements as assessed by clinical examination in all groups. Interestingly, this appeared to be more pronounced in group B ($corr_{coeff} = 0.52$, $p < 0.001$) as compared to group A ($corr_{coeff} = 0.39$, $p < 0.001$).

4 Discussion

4.1 Prevalence of hand OA

The prevalence of hand OA differs greatly in the literature. (9,88) Since the diagnosis of OA cannot be made using a single feature but is based on a combination of several factors including history, clinical symptoms and imaging, the prevalence varies according to the selected diagnostic criteria. In this study a subject was considered to suffer from hand OA if the ACR criteria for hand OA were fulfilled. 89 out of 331 study subjects fulfilled these criteria and the prevalence of hand OA was 26.9%. This is slightly higher compared to a similar study published by Mannoni *et al*. where subjects were recruited from an Italian community dwelling for older people, 19.9% of the study subjects met the ACR criteria. (89)

4.2 Demographic Data

Clinical and demographic data were compared between subjects suffering from hand OA (group A) and „healthy“ subjects (group B). Not surprisingly, group A consisted of significantly more women than group B ($p < 0.001$) which is in agreement with previous data showing that female sex is a risk factor for hand OA. (11) In group A, the mean age was slightly higher (76.91 years) as compared to group B (75.27 years) but the difference was not statistically significant. Earlier studies demonstrated that the incident-rate of hand OA peaks at age 60-64 but that it does not increase constantly beyond that age. This is especially true for women. (11)

Comparing the type of occupation (blue collar/white collar), no difference was found between groups A and B even though occupations that require repetitive hands movements (e.g. farmer) are a known risk factor for OA. (32) However, it is important to mention that a substantial part of the study subjects (131 out of 331) did not state their former occupation but indicated their actual status which was mostly “homekeeper” or “retiree”. These study subjects were not included in the evaluations.
The duration of morning stiffness in group A was comparable to that of the medical literature. It has been reported that the mean duration of morning stiffness in patients

with hand OA usually lasts a few minutes and almost always less than 30 minutes (29). Nevertheless, the mean duration of morning stiffness in earlier studies was between 8 and 44.0 minutes. (90–92)

4.3 US findings

4.3.1 Frequency and severity of abnormal US findings

There is very little literature available on the prevalence of imaging changes indicating OA in the general population. We observed that almost everyone (99%) of our elderly study subjects had at least one US finding compatible with OA. This result is in accordance with the high prevalence of osteophytes reported by Kodama *et al*. in a study of Japanese elderly people (mean age: 65.6±13.0 years) using x-ray and a modified K&L scale. Ninety percent of individuals presented with more than one osteophyte grade 2 or higher. (93) However, the comparability between the Japanese study and our investigation is limited due to the facts that different imaging techniques were used and that in our study, also small osteophytes (grade 1) were assessed. Furthermore, it has to be considered that US is known to be more sensitive in the assessment of osteophytes than CR. This is because with CR, osteophytes can only be depicted if they are located tangentially to the beam while US is a multiplanar imaging method. CR misses more easily osteophytes at the palmar and dorsal side of the joints. (83,94)

Apart from osteophytes, we also observed a high prevalence of SH/E not only in patients with hand OA but also in healthy subjects. To our knowledge, there is only one similar other study that investigated the prevalence of synovitis in healthy subjects. Padovano *et al.* reported that 88% of healthy individuals presented with at least one US change compatible with synovitis (SH, SE or PD), the most common location being the MTP joints. (84) Since bony enlargements were not an exclusion-criteria of this study, we believe that this population corresponds to our group B, where 63% of the subjects presented with SH/E and 12% with PD even if the mean age in Padovano's study was significantly lower (35.5 years) than in our cohort. Both studies, however, confirm the observation that signs of synovitis are quite common in healthy subjects.

In the subgroup of healthy subjects without bony enlargements (**group B.1**) there was still a high prevalence (97%) of abnormal US findings. Similar to the results in the other two groups, osteophytes and SH/E were the most common US abnormalities.

Whether US findings of OA precede clinically overt OA is unclear so far. A recent study examined joints with no radiographic OA and no bony enlargement with ultrasound. In 28% of those joints osteophytes could be detected by US and those joints were more likely to present with radiographic and clinical OA (bony enlargements) after 5 years. (85)

Alternatively, and taking into account that the greatest part of the changes was of grade 1, it could be concluded that US changes grade 1 can still be considered as normal. This was also proposed by Millot *et al.* regarding synovial changes in a healthy population (95) and by Padovano *et al.* where the greatest part of changes in healthy subject was of grade 1. In the latter study, however, the examiner was aware of the fact that only healthy subjects were included and this could have biased the examiners toward a lower grading of changes. (84) In our study, the ultrasound examiner was blinded to the clinical diagnosis.

4.3.2 Location of US changes

In patients with hand OA (**group A**), DIPs yielded most frequently US signs of OA, particularly osteophytes, whereas in healthy subjects, PIPs were most commonly affected.

Jonsson *et al.* observed in a previous study in randomly selected individuals from the elderly general population and using a photographic method to diagnose and grade hand osteoarthritis, that the DIP2 was the most commonly affected joint followed by DIP3 and PIP3 (96). This is in accordance to our findings.

4.4 Correlation between clinical signs and US findings

In patients with hand OA (**group A**), higher total scores of osteophytes correlated with a higher SH-SACRAH as well as with a higher FIHOA score. Additionally, the SF-SACRAH correlated with the total score of SH/E and the FIHOA with the total score of PD. Our study is the first to show that US findings including osteophytes and synovitis in hand joints correlate with function impairment in patients with hand OA. In previous studies, osteophytes and synovitis were significantly associated with joint pain but the association with functional impairment was not significant. (97,98)

Clinically detected bony enlargements are often used as a marker for OA since they are believed to reflect osteophytic changes at these joints. However, Cicuttini *et al.* found a poor agreement between Heberden's nodes and radiologically detected osteophytes at the same joint. (99) In our study, there was a moderate correlation between total US verified osteophytes and bony enlargements in all groups; however, we did not investigate whether these bony enlargements and osteophytes occurred at the same joint.

Interestingly, 94% of the subjects in group B.1 presented with at least one osteophyte although none of them had clinical bony enlargements. This indicates that osteophytes can be detected by US even before bony enlargements are clinically palpable. This assumption is supported by a previous study showing that US detected osteophytes in healthy subjects predicted the development of clinical bony enlargement at the same joint 5 years later. (85)

5 Conclusion

In this study, the investigated prevalence of hand OA was slightly higher compared to similar studies. The prevalence of abnormal US findings was high, not only in patients with hand OA but also in asymptomatic individuals. Osteophytes and synovial proliferation and/or effusion were more common than erosions and PD abnormalities. Our results suggest that US might be valuable for the detection of osteoarthritic changes before patients develop clinical symptoms of OA. Low-grade US findings, however, might also be considered as normal as long as they are not associated with pain or functional impairment.

A follow up clinical and US examination as part of the Bruneck study is scheduled in 5 years and will shed light on the question whether specific US abnormalities will be linked with future development of clinical OA.

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