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**EVALUATION OF PROSTHESES IN
SHOULDER ARTHROPLASTY:
METHODS FOR ASSESSMENT OF
OUTCOME**

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Evaluation of prostheses in shoulder arthroplasty: Methods for assessment of outcome

THESIS FOR DOCTORAL DEGREE (Ph.D)

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To Madeleine, Elsa, Georg and Irma;

“After climbing a great hill, one only finds that there are many more hills to climb.”
— Nelson Mandela

ABSTRACT

Today, the shoulder joint is the third most commonly replaced joint after the hip and knee joints and the incidence is increasing. In Sweden, 1863 primary Shoulder Arthroplasties and 195 revisions were performed in 2017. The most common diagnoses are Osteoarthritis and irreparable tears of the rotator cuff, with or without arthropathy, often referred to as cuff tear arthropathy.

Different Shoulder Arthroplasty (SA) concepts include anatomical total shoulder arthroplasty (TSA), hemiarthroplasty (HSA) and reversed shoulder arthroplasty, but also humeral head resurfacing (HHR) and stemless arthroplasties. All concepts offer pain relief, improvement of function and in quality of life for the different diagnoses. Unfortunately, there are sometimes complications after SA. They involve periprosthetic joint infection, humeral and glenoid fractures, stress shielding, loosening of the glenoid and humeral component but also glenoid erosion and cuff rupture. Some of these complications are most common within 1 year after operation, some after several years, both may lead to a revision. This, together with the fact that new designs of implants and methods of fixation of SA continues to develop, stresses the importance of continuous monitoring of implant survival and follow-up.

The overall aim of this thesis was to describe clinical examples of different methods to assess the outcome after Shoulder Arthroplasty. The most common methods are clinical examination, radiographic assessment, Patient Reported Outcome Measure (PROM), National Joint registries, where revisions are an important outcome, but also Clinical Trials. All of these methods are used in one or more of the 4 papers in this thesis and shows the complexity of the topic and the practical work.

In paper I we used Radio Stereometric Analysis (RSA) in an experimental set-up and concluded that marker-free RSA can be used for a humeral head resurfacing arthroplasty. In paper II we used data from the Swedish Shoulder Arthroplasty Registry (SSAR) with PROM and revisions to conclude that age is the only factor that affects revision when comparing HSA and HHR. Paper III is a long-time follow-up of a Randomized controlled study where we used radiological assessment, PROM and revisions. The conclusion was that both TSA and HSA develop severe radiological changes 10 year after primary operation. Paper IV is a prospective RSA cohort study where we also evaluated PROM and revisions. The conclusion is that HHR seems to obtain a secure fixation in the humerus, after an initial migration. But also that the prostheses shows continuous glenoid wear.

The main conclusion of this thesis is that patient's operated with SA needs continuous monitoring and several methods may be used to evaluate the outcome.

SAMMANFATTNING (SUMMARY IN SWEDISH)

Idag är glenohumeral-leden (axelleden) den tredje vanligaste leden som opereras med protes efter höft- och knäleden och förekomsten ökar. I Sverige utfördes 1863 primära axelprotesoperationer och 195 revisioner under 2017. De vanligaste diagnoserna är artros och irreparabla skador på rotatorkuffen, med eller utan artropati, ofta kallad cuffartropati.

Det finns olika typer av axelproteser: Totalplastik, hemiplastik och omvänd totalplastik, men också ytersättning och stamlös protes. Alla olika typer av axelproteser ger minskad smärta samt förbättring av funktion och livskvalitet för respektive diagnos. Tyvärr förekommer komplikationer efter operation med axelprotes. De innefattar infektion kring protesen, frakturer, benförlust kring protesen s.k. ”stress shielding”, lossning av glenoid- och/eller humeruskomponenten men även glenoiderosion och cuffruptur. Vissa av dessa komplikationer inträffar oftast inom ett år efter operationen, andra efter flera år, men båda kan leda till omoperation, s.k. revision. Detta, samt det faktum att nya modeller av implantat och fixationsmetoder av axelproteser fortsätter att utvecklas, ökar vikten av kontinuerlig uppföljning av implantatens överlevnad och eventuella komplikationer.

Det övergripande målet med denna avhandling var att beskriva olika sätt att utvärdera och mäta resultatet efter axelprotesoperation. De vanligaste metoderna är klinisk undersökning, radiologisk uppföljning, patientrapporterade utfallsmått (PROM), Nationella kvalitetsregister, där revisioner är ett viktigt mått, men också via kliniska studier. Alla dessa metoder används i ett eller flera av de fyra delarbetena i denna avhandling och visar på komplexiteten i detta ämne.

I delarbete I använde vi Radio Stereometrisk Analys (RSA) i en metodstudie där slutsatsen blev att s.k. marker-free RSA kan användas för ytersättande axelproteser. I delarbete II använde vi data från Svenska axelregistret med PROM och revisioner och drog slutsatsen att patientens ålder vid operation är den enda faktorn som påverkar risken för revision när man jämför ytersättande och s.k. stammad hemiplastik. Delarbete III är en långtidsuppföljning av en randomiserad klinisk studie där vi också använde röntgen, PROM och kontrollerade eventuella revisioner. Slutsatsen blev att både totalplastik och hemiplastik utvecklar kraftiga förändringar på röntgen 10 år efter operation. Delarbete IV är en prospektiv RSA-studie av en kohort med patienter där vi också mätte PROM och revisioner. Slutsatsen blev att ytersättande axelproteser växer fast men visar tecken på nötning (erosion) in i glenoiden (ledpannan).

Sammanfattningsvis så är huvudslutsatsen av denna avhandling att patienter som opereras med axelplastik behöver följas upp kontinuerligt, att många olika metoder kan användas för att utvärdera resultatet men att vilka metoder som är bäst inte är klarlagt.

LIST OF SCIENTIFIC PAPERS

- I. Measurement of migration of a humeral head resurfacing prosthesis using radiostereometry without implant marking.
Olof Sköldenberg, Magnus Ödquist
Acta Orthopaedica, 82:2, 193-197, DOI: 10.3109/17453674.2011.566133

- II. Lower age increases the risk of revision for stemmed and resurfacing shoulder hemi arthroplasty.
Magnus Ödquist, Kristofer Hallberg, Hans Rahme, Björn Salomonsson & Aldana Rosso
Acta Orthopaedica, 89:1, 3-9, DOI: 10.1080/17453674.2017.1411081

- III. Hemi- versus Total Shoulder Arthroplasty in patients with Rheumatoid Arthritis: A 22 year follow-up of implant survival with a 10 year systematic radiological assessment of a prospective randomized controlled study.
Magnus Ödquist, Carina Grönhagen, Hassan Abbaszadegan, Ulf Lillkrona and Björn Salomonsson
Manuscript

- IV. Glenoid Wear and migration pattern of a humeral head resurfacing implant. A prospective study using Radio Stereometric Analysis.
Magnus Ödquist, Olof Sköldenberg, Hassan Abbaszadegan and Björn Salomonsson
Manuscript

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LIST OF ABBREVIATIONS

CSS	Constant Shoulder Score
CT	Computed Tomography
HHR	Humeral Head Resurfacing Arthroplasty
HSA	Hemi Shoulder Arthroplasty
NARA	Nordic Arthroplasty Register Association
OA	Osteoarthritis
POA	Primary Osteoarthritis
PROM	Patient Reported Outcome Measures
RA	Rheumatoid Arthritis
RCT	Randomized Clinical Trial
RLL	Radio Lucent Lines
SA	Shoulder Arthroplasty
SASA	Stemless Anatomical Shoulder Arthroplasty
SOA	Secondary Osteoarthritis
SSAR	Swedish Shoulder Arthroplasty Register
TSA	Total Shoulder Arthroplasty
RSA	Radio Stereometric Analysis
RTSA	Reversed Total Shoulder Arthroplasty
WOOS	Western Ontario Osteoarthritis of the Shoulder Index

INTRODUCTION

History and background

The first shoulder arthroplasty (SA) was made of metal and implanted by Jules Emilé Péan in 1893, in a patient suffering from tuberculosis in the proximal humerus. The implant had to be removed after 2 years. Péan was inspired by Themistocles Gluck who at least 3 years earlier had presented a design of a SA made of Ivory (1).

The modern use of SA started with Charles Neer who in the 1950's began to use a hemi shoulder arthroplasty (HSA) for the treatment of fractures of the proximal humerus. Motivated by the positive results of this treatment he expanded the use of HSA to osteoarthritis (OA) and elective procedures in the 1970's. Later on he added a glenoid component made of polyethylene to create the TSA (2). Since then, there has been a continuous development and in the early 1990's the concept of anatomical reconstruction of the proximal humerus where introduced (3).

In the earlier years of SA, the main indications were fractures and RA, but today the most common diagnoses are osteoarthritis (OA) and irreparable tears of the rotator cuff, with or without arthropathy, often referred to as cuff tear arthropathy (4, 5). SA is still used for fractures of the proximal humerus, rheumatoid and inflammatory arthritis, avascular necrosis of the humeral head but these indications are less frequent. For patients with a degenerative diagnosis who have a failed conservative management with residual disabling pain and limitation of shoulder function, SA is used as treatment.

Today, the shoulder joint is the third most commonly replaced joint after the hip and knee joints (6) and the rate is increasing. In Sweden, 1863 primary Shoulder Arthroplasties and 195 revisions were performed in 2017 (7). The average incidence in Sweden is 9.1/100 000 per year (8).

Different Concepts of Shoulder Arthroplasty

The most commonly used different SA concepts includes anatomical total shoulder arthroplasty (TSA), hemi shoulder arthroplasty (HSA) and reversed total shoulder arthroplasty (RTSA), but also humeral head resurfacing (HHR) and stemless anatomical arthroplasty (SASA).

Total Shoulder Arthroplasty

An anatomical total shoulder arthroplasty consists of a stemmed metal humeral component and a shallow polyethylene glenoid component. **(Figure 1)** The humeral component can either be uncemented or cemented, but the polyethylene glenoid component is usually cemented into place (9). TSA requires an intact rotator cuff because the resultant anatomic joint replacement relies on native soft-tissue structures for mobility, stability and longevity. A TSA also requires adequate glenoid bone stock to allow anatomic placement of the glenoid prosthetic component. OA and inflammatory arthritis are the main indications for TSA. The goal of anatomic total shoulder arthroplasty is anatomic glenohumeral joint replacement that addresses pathologic conditions involving both sides of the joint (10). TSA shows good results with significant improvements in scores for function and pain (11).



Figure 1: Total Shoulder Arthroplasty Left shoulder. Take special note on the mark in the Glenoid. A Hemi Shoulder Arthroplasty only consists of the component on the humeral side. (Courtesy of B. Salomonsson)

Hemi Shoulder Arthroplasty

The hemi shoulder arthroplasty consists of a stemmed metal humeral component (**Figure 1**) or a HHR (9). (**Figure 2**) In HSA, the entire humeral head is removed followed by placement of an intramedullary stem into the proximal aspect of the humerus whereas HHR consists of reaming the proximal portion of the humeral head and fitting a metal-alloy cap over the remainder of the head (12). The outcome for HSA and HHR because of OA are reported to be good but inferior to TSA (5, 9, 13).



Figure 2: Humeral resurfacing Arthroplasty right shoulder. (By Magnus Ödquist)

Reversed Total Shoulder Arthroplasty

Reverse shoulder arthroplasty (RTSA) is a semi-constrained type of SA where the native center of rotation is transferred medially and distally compared to the native one. This allows restoration of deltoid tension and thus abduction and elevation of the arm by the isolated deltoid contraction, without rotator cuff action. (14). RTSA usually consists of four implants a humeral component, with a polyethylene insert, the glenosphere which attaches to the baseplate which in turn is attached to the glenoid (15). The indications for this type of implant are irreparable tears of the rotator cuff, with or without cuff tear arthropathy. But it is also used for the treatment of fractures in the elderly population because of the risk of impaired healing of the tubercles or limited preconditions for rehabilitation. It has also become very useful in revision for anatomical arthroplasties or failed fracture healing.



Figure 3: Reversed Total Shoulder Arthroplasty left shoulder. (Courtesy of B. Salomonsson)

Stemless Anatomical Shoulder Arthroplasty

Anatomic stemless shoulder arthroplasty (SASA) refers to implant designs with metaphyseal fixation using a standard humeral neck cut, and excluding humeral head resurfacing techniques (**Figure 4**). Stemless implants differ from resurfacing implants because resurfacing implants require reaming of the articular surface but do not involve osteotomy of the humeral neck. Recently the interest in stemless but also short-stemmed implants has increased substantially (16).



Figure 4: Stemless Shoulder Arthroplasty left shoulder. (Courtesy of B. Salomonsson)

Results and Complications after Shoulder Arthroplasty

Results

TSA offers reliable pain relief, improvement in function and quality of life for OA patients. TSA also provides long term survival, and satisfaction rates of up to 95% (17) . Patients who receive a HSA also shows improvement but compared to TSA the clinical outcome is inferior and HSA have higher revision rates (18-22). Reliable results can also be achieved with RTSA (23) and HHR (24).

General complications

Periprosthetic joint infection after SA is a rare but serious complication with an incidence of 0.98% in the US (25). Periprosthetic humeral and glenoid fractures have a prevalence of 1.0% and are observed after all types of SA (26). Stress shielding means that any joint implant inserted into the medulla of a long bone changes the distribution of load in the adjacent bone, and may subsequently cause resorption of bone (27). Stress shielding is a predisposing risk factor for postoperative periprosthetic humeral fractures.

Humeral component loosening has a prevalence of less than 1% (28). Radiological diagnosis of humeral component loosening is based on analysis of periprosthetic humeral radiolucent lines (RLL). The fixation surface of the humeral component is divided into 8 zones according to Sperling, and it is considered “at risk” when a radiolucent 2-mm-wide line or greater is present in three or more of the eight zones (29). Also may heterotopic bone formation appear after SA and develops early after surgery but is often low grade and does not significantly affect the function (30).

Specific complications

For **RTSA**, instability with complete dislocation is the most common complication, but also scapular notching (repetitive contact during adduction between the humeral component and the inferior scapular neck) (31) and fractures of the scapular spine and acromion, usually caused by excessive tension of the deltoid muscle per-operatively (32).

For **TSA**, glenoid component loosening is the most common complication (28) and its origin is multifactorial. Rotator cuff deficiency causes superior migration of the humeral component. This generates superior tipping of the glenoid component, called “rocking horse” phenomena. Malposition of the glenoid component is also a cause of loosening. The fixation of the glenoid component can be divided into 5 zones according to Amstutz (33). Radiologically, glenoid loosening is defined as glenoid component migration, tilt, or shift or as a complete RLL more than 1.5 mm thick. The correlation between glenoid component loosening and RLL is debated. Incomplete periprosthetic radiolucent lines or radiolucent lines less than 1.5 mm thick are commonly seen. Asymptomatic radiolucent lines occur at a rate of 7.3% per year after primary shoulder replacement (34, 35). Rotator cuff tears account for 9.0% of all complications after TSA (28). That complication is a serious concern since the TSA cannot perform their biomechanical function without rotator cuff integrity. Risk factors for rotator cuff tears after SA are oversized prosthesis, malrotation of the humeral component, multiple surgeries and aggressive physiotherapy involving external rotation during the early postoperative period, and tendon compromise in humeral lengthening (4). Subscapularis insufficiency is the most common rotator cuff abnormality after TSA and it is responsible for anterior instability (36).

For **HSA** and **HHR**, Progressive wear of the native glenoid is the most common complication. Replacement of the humeral head modifies biomechanical constraints on the glenoid, leading to the long-term development of osteoarthritic remodeling. The radiological diagnosis will be made on the standard radiographs, showing a progressive narrowing of the glenohumeral space but also posterior glenoid wear.

Different methods to evaluate the outcome after Shoulder Arthroplasty

New implants for SA are expected to be equivalent or superior to existing implants regarding clinical outcomes, complications, and survival of the implant. Still, new designs of implants and methods of fixation are only required to provide data on the safety of the material, not clinical efficacy, before they are released on to the market (37). Possible solutions to this could be to use the IDEAL framework which describes a pathway for generating and analyzing data of surgical innovation, or the Orthopaedic Data Evaluation Panel (ODEP) which rates implants based on evidence (38, 39). There are unfortunately examples of clinical disasters as with the hip resurfacing arthroplasty with metal on metal bearings (40). Also in a recent study by Craig et al, they conclude that the life-time risk of revision is much higher for younger patients than previously considered (41). Altogether this highlights the importance of continuous monitoring of implant survival and follow-up as well as establishes reasons for revision but also the stepwise introduction of new orthopedic innovations (42, 43).

Clinical examination

The patient who have received a SA is usually scheduled for a follow-up with the operating surgeon or sometimes, (as often within research studies), the patient will see another doctor or if applicable, a physiotherapist. This clinical follow-up is could be combined with different scores or Patient Reported Outcome Measures (PROM).

Plain radiographs

From the diagnosis of the pathology in the shoulder to the long-term follow-up of the implant, standard radiographs (x-ray) is the basis of evaluation for SA (4). It is also easy available, have a low cost and is reproducible (26). Most of the common types of failure, including component loosening, glenoid wear, bone loss, periprosthetic fractures or instability, can be diagnosed with standard radiographs. Standard plain X-rays with true anterior-posterior view and a lateral view are obtained after any SA procedure (44). It allows verification of the correct positioning of the implants and provides reference images for future follow-up and monitoring (45).

Computed tomography

Computed tomography (CT) is a complement to standard radiographs in preoperative planning of SA. CT is useful for demonstration of the extent of osteoarthritis, the amount of bone available for fixation in the glenoid and the glenoid version (4). The latter cannot be determined accurately on standard axillary radiographs, either preoperatively or postoperatively (46). The widely used modified Walch classification system for the description of glenoid morphology is based on CT reconstructions (47). Patient-specific instrumentation (PSI) is today sometimes used for TSA. It offers increased accuracy in the placement of the glenoid component and the preparation and pre-operative planning is based on CT. CT can also be used together with a

specific software program as an alternative to Radio Stereometric Analysis (RSA) in evaluating orthopedic implants (48).

Radio Stereometric Analysis

Radio Stereometric analysis (RSA) (49) is the gold standard for measuring micro motion of orthopedic implants (50). With RSA, it is possible to get highly accurate three-dimensional measurements from calibrated stereo radiographs. By making measurements over time, implant migration can be quantified and loosening predicted with high sensitivity (51). The method requires the insertion of tantalum markers into the skeleton and the implant to create 2 rigid bodies, called segments. Instead of implant marking the marker-less method may be used (52). The migration of the implant segment in relation to the skeleton segment for translation and rotation around the x-, y-, and z-axes (the 6 degrees of freedom) is then calculated. A review from 2017 concluded that RSA is a highly precise method for measurement of early migration of orthopedic implants in the upper limb (53).

Other imaging methods

Magnetic resonance imaging (MR) and ultrasound are mainly used for imaging of the rotator cuff tendons before and after surgery (26). Bone mineral density (BMD) can be measured with dual energy X-ray absorptiometry (DXA) around HHR (54). If the BMD is reduced around the humeral prosthesis this may be caused by stress shielding (55-57).

Patient Reported Outcome Measures

When a patient reports on their own health status directly without interpretation from a surgeon or other medical professional, this is known as a patient reported outcome measures (PROM) (58). Patients scheduled for SA often have reduced shoulder function and activities of daily living pre-operatively (59). A patient-derived questionnaire can provide a high level of agreement with surgeon assessments of outcome after SA (60, 61). Together with more objective measurements such as x-ray, it gives a broader understanding of the outcome after SA. PROM after orthopedic surgery is used by many joint registries. There are several shoulder outcome scores (62) even though not all of them are relevant for the outcome after SA. There are differences in which scoring systems is mostly used between Western Europe and USA (63). The PROMs listed below are the one used in this current thesis why they are described separately.

Constant shoulder Score

Constant and Murley published their original article in 1987 (64). The Constant Shoulder Score (CSS) has become the most widely used shoulder evaluation instrument in Europe (62). The scoring system combines physical examination tests (65 points) with subjective evaluations by the patients (35 points). The maximum 100 points represents a normal shoulder.

Western Ontario Osteoarthritis of the Shoulder Index

The Western Ontario Osteoarthritis of the Shoulder Index (WOOS) is a patient-reported, disease-specific questionnaire for the measurement of quality of life in patients with osteoarthritis (65). The WOOS results can be combined to a single score representing the percentage of a healthy shoulder from 0% to 100 %.

EuroQol five dimensions

The EuroQol five dimensions (EQ-5D) is a standardized instrument that measures health outcomes of a wide range of health conditions and treatments (66). It is often used also for outcome measurement after surgical interventions of the upper extremity and has a good reliability and validity (67). There are two parts to the EQ-5D: the descriptive system and the visual analog scale (VAS). The result is usually combined to a single index ranking from – 0.54 (worse than death when below zero) to 1 (best imaginable health state).

Revisions

A revision after a SA can be defined as either removal, exchange, or addition of an implant component (68) and reasons for revision in a hierarchy according to the Nordic Arthroplasty Register Association (NARA): Infection, periprosthetic fracture, luxation and instability, loosening, rotator cuff problems, and then all other reasons including pain. The last group other also includes glenoid erosion, overstuffing of the joint and malposition of the implant (8). It is important to remember that when using revision and implant survival as the only outcome measurements it will not capture patients with underperforming SA who declines a revision surgery (69). Some of these patients will go through a re-operation such as arthroscopy. Reasons for re-operation can be stiffness, pain, tears of the rotator cuff, and suspect infection (70) (71)

National Joint registries

National joint registries are important for monitoring of surgical outcomes (72) and the main purpose is to collect information on patients, procedures and implants (73). The results from a nationwide registry may be generalized to the single shoulder surgeon as well as to the patient, regardless of comorbidity, age, and severity of disease that lead to a SA (20). The Swedish Hip Register is a good example of the importance of collecting and analyzing data on revisions and other complications and then, based on the collected information, be able to improve the results (74). This is also true for the Australian Orthopedic Association National Joint Replacement Registry (75). The Swedish Shoulder Arthroplasty Registry (SSAR) was established in 1999 by The Swedish Shoulder and Elbow Society (76). It collects data from primary shoulder arthroplasties and revisions performed in Swedish hospitals. Besides the PROM with WOOS and EQ-5D, the registry also uses a Satisfaction Level (SL). SL is collected as an ordinal Likert scale. “How satisfied are you with the shoulder after the operation?” and it offers 5 possible alternatives from very disappointed to very satisfied.

Clinical Trials

One definition of a clinical trial is that the participants receive specific treatments according to a research plan created by the investigators (77). In an observational study, investigators assess outcomes in groups of participants according to a research plan or protocol. Participants may receive interventions (for example a SA) or procedures.

Cohort studies are a type of observational studies, these are either looking back over patient records to see what has happened to them, often called retrospective studies, or following a group of people over time to see what will happen to them, called prospective study.

An experimental study is when researchers deliberately influence the course of events and investigate the effects of an intervention or treatment on a carefully selected population of subjects.

A randomized clinical trial (RCT) is considered the best design of a study in order to investigate the effect of surgical procedures with implants. They use inclusion and exclusion criteria in order to make the study population as homogeneous as possible. (78).

A systematic review is a critical assessment and evaluation of existing research. It may help us understand what we already know about a treatment, but also find any gaps in the existing research and suggest future studies.

OVERALL AIM OF THE THESIS

The overall aim of this thesis was to describe clinical examples of different methods to assess the outcome after Shoulder Arthroplasty.

AIMS OF THE STUDIES

Paper I

The aim was to validate the marker-free RSA method by determining the accuracy and precision when used on HHR.

Paper II

The primary aim was to identify risk factors for revision in elective primary HHR and HSA for OA, and to compare PROM results from SSAR. The secondary was aim to investigate the performance of SHA comparing revision risk and patient satisfaction for patients suffering from POA and SOA.

Paper II

The primary aim was to evaluate the radiological and clinical outcome for patients with RA, treated with TSA or HSA, at a minimum of 10 years after surgery. The secondary aim was to check the revision rate more than 22 years after surgery.

Paper IV

The primary aim was to evaluate the fixation of the Copeland HHR on the proximal humerus and to analyze the migration pattern and glenoid wear up to 2 years with RSA. The secondary aim was to correlate the RSA results with the clinical outcome and revisions until 5 years after surgery.

METHODS

Ethics

Paper I did not involve humans or animals. Paper II-IV was all approved by the Stockholm regional Ethics Committee of the Karolinska Institute. The Danderyd Hospital radiation protection review board approved the radiographic examinations in Paper III and IV.

Paper I

A methodological in vitro study with the purpose to validate marker-free RSA for HHR.

Experimental set-up:

We used the Copeland humeral head resurfacing prosthesis (79) (Zimmer-Biomet, Warsaw, IN) in 3 sizes (3, 5, and 6). The manufacturer had marked each HHR with 3 tantalum markers at the outer periphery and the distal tip of the implant. The prostheses were implanted in a humeral phantom (Sawbones; Sawbones Europe, Malmö, Sweden) and in addition, 6 tantalum markers (1.0 mm) were placed in the sawbone to serve as the reference segment for the RSA analysis. The phantom was then placed above a uniplanar calibration cage (Uniplanar digital 43; RSA Biomedical AB, Umeå, Sweden). Digital radiographs (Bucky Diagnostic; Philips, Eindhoven, the Netherlands) were then taken using 1 fixed and 1 mobile X-ray source. The exposure was set to 125 kV and 2.5 mAs. The radiographs were saved in a standard Dicom file format (resolution 254 dpi) and uploaded to a workstation. UmRSA 6.0 computer software (RSA Biomedical AB) was used for all measurements and migration analyses. We performed the following procedure to measure the migration of the implant in relation to the sawbone:

1. The phantom was placed above the calibration cage at the point of intersection of the central x-rays.
2. One set of radiographs were taken (position 1, series 1).
3. The calibration cage, the X-ray tubes, and the phantom were repositioned.
4. One set of radiographs were taken (position 1, series 2).
5. The prosthesis was tilted and rotated by 0.5–1.0 degrees in relation to the sawbone to simulate migration of the implant.

Steps 1 to 5 were then repeated 5 times, giving us position 2, series 1 and 2, position 3, series 1 and 2, and so on. The markers in the sawbone formed the 3-D reference segment and were not altered between exposures. **(Figure 5)**

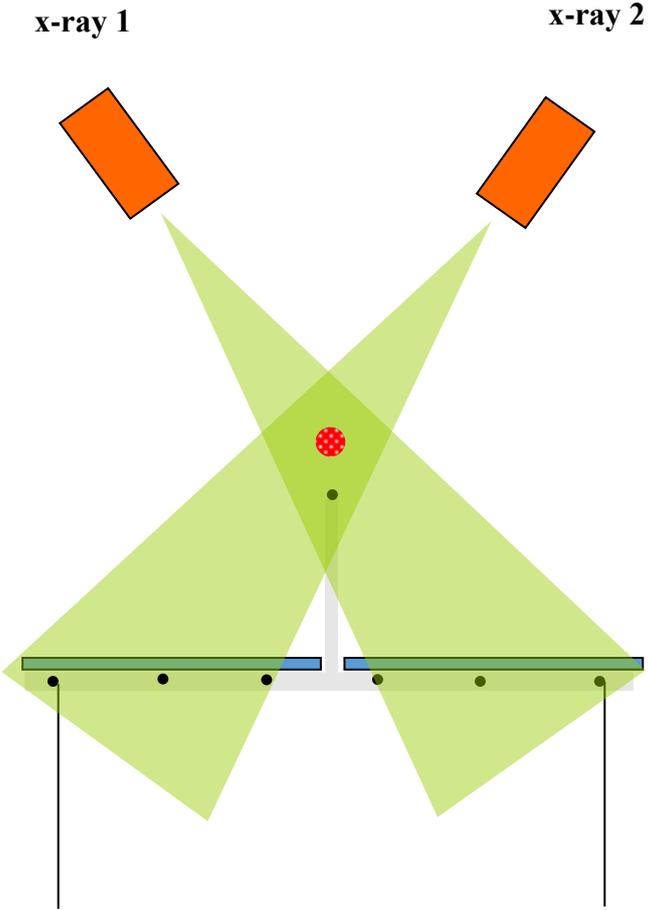


Figure 5: Set-up for RSA examination X-ray tubes, calibration cage and phantom. (Courtesy of Olof Sköldenberg)

Standard RSA

For standard RSA, the 3 tantalum markers on the prosthesis were first measured to obtain the prosthesis segment. (**Figure 6**)

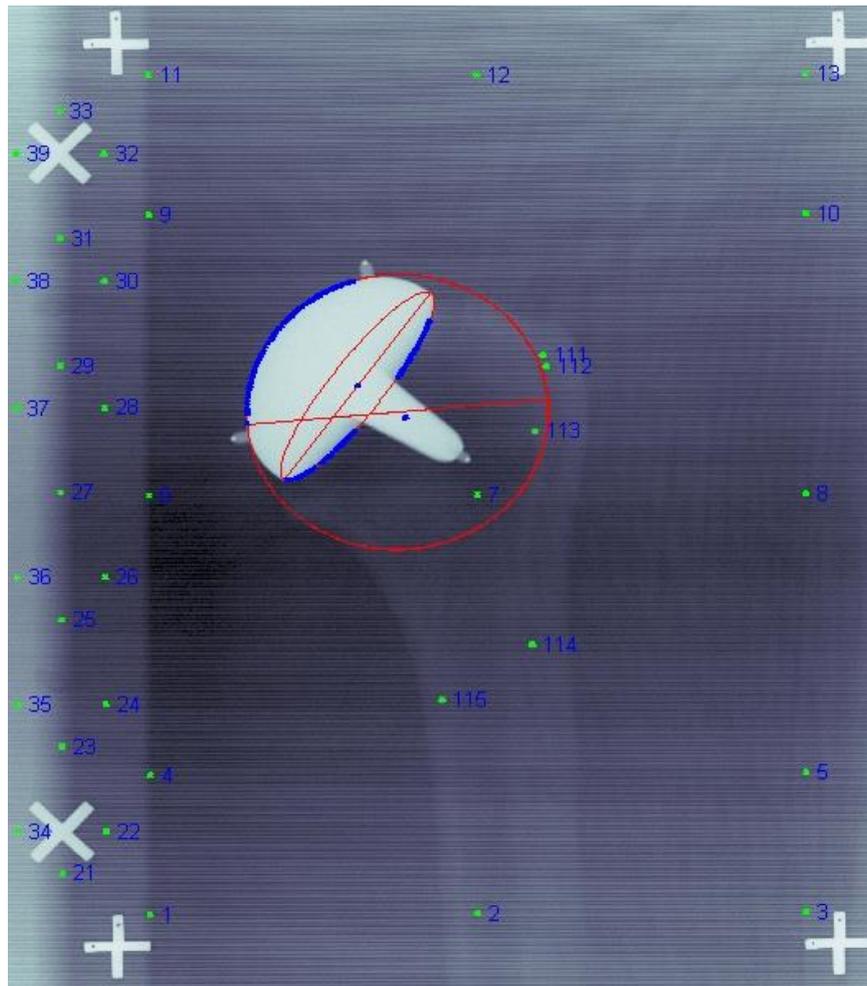


Figure 6: Sawbone model used in Paper I, note the tantalum beads on the Humeral Head Resurfacing Arthroplasty.
(By Magnus Ödquist)

Marker-less RSA

The Copeland prosthesis is a hemisphere at its outer periphery, but the sides are tapered and slope inward towards the opening of the circle. We used a goniometer to place points on 75 degrees of the contour of the hemisphere (**Figure 6**) and then placed points on the opening circle of the prosthesis according to the method of the software. The software then automatically detected the boundaries of the prosthesis and calculated a prosthesis segment. The marker-less algorithm corresponds to a generalized hemisphere. The hemisphere's opening circle does not have to occur at the "equator" or have the same radius as the outer shell. The algorithm creates a prosthesis segment by adding points to the top of the hemisphere ("north pole"), the bottom of the hemisphere ("south pole"), the most anterior and posterior point of the opening circle, and the center of the hemisphere (80).

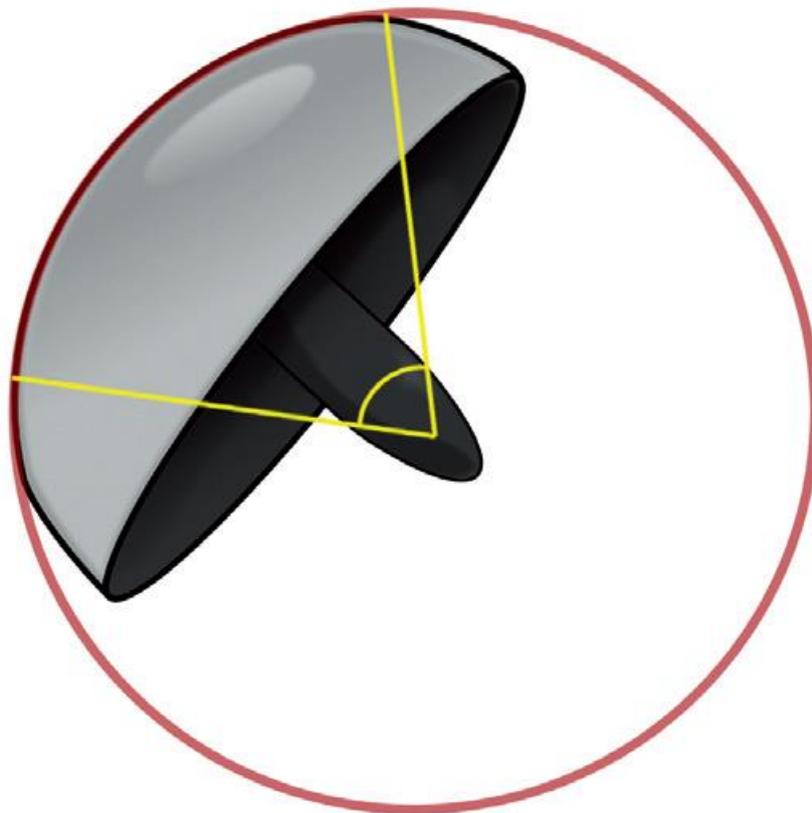


Figure 6: Marker-less RSA. A schematic HHR showing the outer hemisphere and the inward slope of the rim. The red line describes a perfect circle. The yellow sector shows the 75 degrees on the hemisphere where points for marker-less RSA are placed. (Courtesy of Olof Sköldenberg)

Precision

Precision—also called reproducibility—is the degree to which repeated measurements under unchanged conditions show the same results, and it refers to random errors. To calculate the precision of both RSA methods, the double measurements (series 1 and 2) taken at each of the 6 positions were analyzed for migration. The difference between the double measurements was then calculated. Since no migration of the implant in relation to the sawbone occurred, this difference represents the precision of the methods. Having used 3 different sizes of the prosthesis, we therefore had 18 double sets of radiographs on which to calculate precision.

Accuracy

Accuracy is defined as the closeness of a true value (in this study, by standard RSA) to the most probable value, which has been derived from a series of measurements (in this study, by marker-less RSA). Accuracy includes both random and systematic errors. The accuracy of standard RSA was assumed to be perfect; i.e., standard RSA measures the true migration of the implant (50, 81). In order to calculate the accuracy of the marker-less RSA, the migration between 2 phantom positions was measured with both standard RSA and marker-less RSA. Ideally, this would be zero since both methods measured the same migration. To generate independent measurements, this was calculated pairwise for positions 1–2, 3–4, and 5–6. As 3 different sizes of the prosthesis were measured, we had 9 different sets of migration analysis performed to determine accuracy.

Statistics

We defined the precision for standard and marker-less RSA as 2.11 SD (17 degrees of freedom) of the difference between the double examinations (*dprec*). We defined the accuracy for marker-less RSA as 2.26 root mean square (RMS) (9 degrees of freedom) of *daccur*. (RMS, a measure of the magnitude of varying quantity, since the difference between the two methods could be both positive and negative). We used SPSS statistical software version 17.0 for Windows.

Paper II

An observational registry study from the SSAR. Currently all units that perform shoulder arthroplasties report to the SSAR, and more than 80% of the shoulder arthroplasties in Sweden are registered. We analyzed all elective primary hemi shoulder arthroplasties, both HSA and HHR as well as cemented and uncemented, reported within SSAR from January 1, 1999 to December 31, 2009 for the diagnoses primary osteoarthritis (POA) and secondary osteoarthritis (SOA). In the SSAR, secondary OA is defined as sequelae after trauma, dislocations, or other injuries to the joint, as well as late sequelae after infection in the joint. 950 shoulders were diagnosed with POA and 190 with SOA. Previous surgery to the shoulder was in many cases reported parallel to the diagnosis of POA, depending on the type of procedure. Patients with non-union after fracture or cuff deficiencies were excluded from the analysis. Implants not considered to be stemmed, nor of the resurfacing type, were also excluded from the study, e.g. short-stemmed implants or implants with bipolar heads. Finally, 198 surgeries with incomplete information were also excluded from the study. **(Figure 7)**

All hemi shoulder arthroplasties were analyzed for risk factors for revision and after 5 years Patient Reported Outcome Measures (PROM). Revision was defined as removal, exchange, or addition of an implant component. Causes for revision were categorized by a hierarchy according to NARA, where the last group “other” includes glenoid erosion, overstuffing of the joint and malposition of the implant (8) The PROM used were WOOS, EQ-5D and patient satisfaction level (SL) which SSAR sends out to all patients 5 years after surgery.

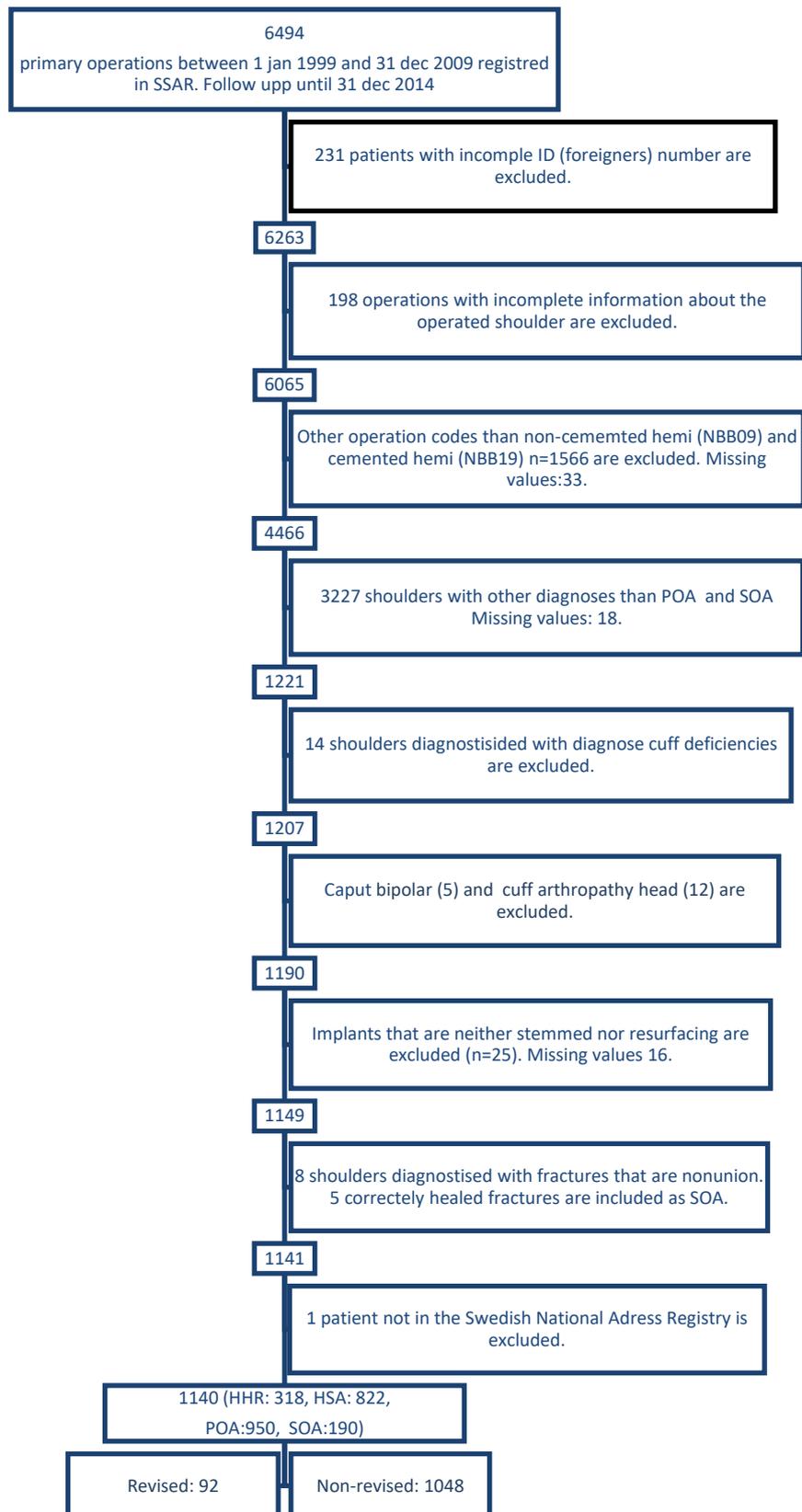


Figure 7: Data included and analyzed in Paper II.

Statistics

The survival times for the implant were analyzed using a Cox regression model. Since there are some patients who were operated bilaterally (142 bilateral implants, 7 revised) the correlation of the data is incorporated in the model by modifying the variance–covariance matrix and the standard errors using a cluster term to allow for intragroup correlation. Earlier studies performed on revision risk of knee prostheses show that there are negligible consequences of analyzing bilateral observations as independent in the survival model, as long as the revision rate for bilateral patients is low (82). In the shoulders we observed a low bilateral revision rate and the correlation in implant survival for bilateral patients may be lower than in the knee case, thus we believe that the cluster correction in the variance–covariance matrix is sufficient to handle the intragroup correlation in the model. Furthermore, 277 patients (26%) died during the follow-up period and 5 patients (0.5%) were lost to follow-up. These patients were censored in the analysis. We assumed that the censoring is independent; meaning that, after adjusting for covariates, the risk for revision for the censored patients is similar to the risk for revision for patients who remain in follow-up with the same covariates. The objective of the analysis is to investigate whether the risk of revision depends on the implant type by using a simple model. We controlled for potential confounding factors recorded in the SSAR: sex, diagnosis (POA or SOA), and age at the primary operation, and operation year. The operation year is used as proxy for the learning effect. We also tested for interaction effects between age and implant, implant and diagnosis, and diagnosis and age. We retained only the statistically significant terms in the model in order to obtain smaller standard errors for the remaining estimates. The proportional hazard assumption was tested using the Schoenfeld residuals. The overall fit of the model was assessed visually using the Cox–Snell residuals. Differences in PROM values between implant type and diagnosis were assessed using the Kruskal–Wallis test and chi-square test. In this case, only 1 operation was considered for the bilateral cases. The analysis was performed using the software Stata version IC/13.1 for Windows, (StataCorp LP, College Station, TX USA). A p-value of 0.05 or less was considered statistically significant for all the analyses presented in this work.

Paper III

A long-time follow-up of a prospective, randomized controlled trial.

The original study

The patients in the original study were included between November 1st 1991 and January 31st 1997. Evaluation was performed pre-op, during the post-op period and after one, two and five years respectively. The indication for surgery was severe RA of the shoulder with pain, not responding to non-surgical treatment, and correlating radiological changes. All RA-patients with this indication referred to the orthopedic department at Danderyd Hospital were eligible for inclusion. The presence of disease-modifying anti-rheumatic drugs (DMARD) at the time of surgery was collected. As conventional DMARD at the time of the study we considered Auranofin, Hydroxychloroquine, Sulfasalazinum, Penicillaminium, Ciclosporinium, Leflunomide, Minocycline, Methotrexatum and Azathioprinum. Randomization was performed per-operatively after surgical exposure and evaluation of the glenoid. If the bone quality was deemed sufficient for fixation of a glenoid component, then the patient was randomized between receiving a TSA or HSA. Two patients were lost after inclusion, leaving 48 shoulders in 41 patients (36 women and 5 men) remaining in the study. For 18 shoulders in the original study the glenoid bone quality was too poor and thus they were not randomized but otherwise followed the study protocol, all 18 receiving a HSA. Randomization between HSA and TSA was done in the remaining 30 shoulders. 14 shoulders were randomized to HSA and 16 to TSA. During the surgical procedure it was not possible to obtain an adequate fixation of the glenoid component in 4 of the 16 shoulders randomized to TSA. Therefore also these 4 received a HSA instead of the randomized TSA procedure. 48 shoulders were operated with either TSA (n=12) or HSA (n=36). The aim in the original study was to follow the patients regularly until 5 years. **(Figure 8)**

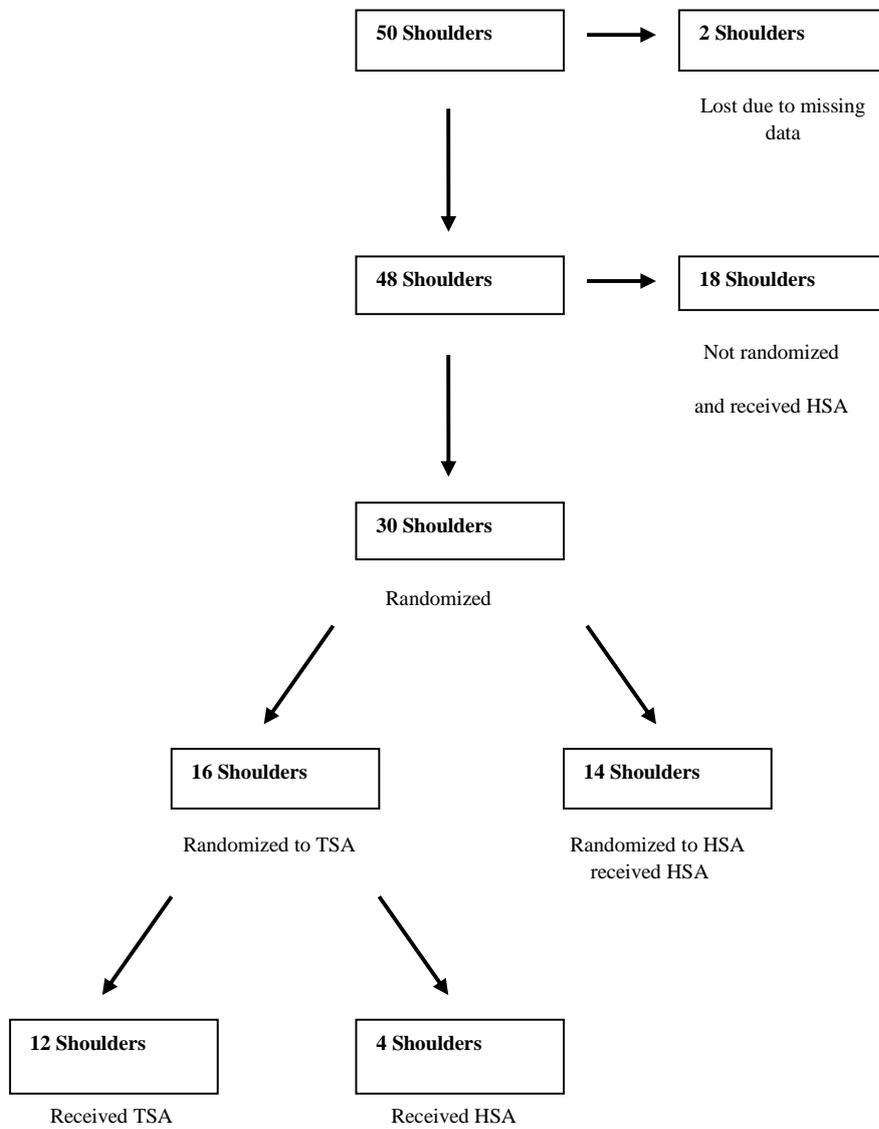


Figure 8: Flowchart over inclusion and randomization between HSA and TSA in the study. (By Magnus Ödquist)

The current study

The inclusion criteria in this current follow-up were patients that had participated in the original study above, and that agreed to participate in the follow-up. The follow up consisted of a radiographic examination, a functional assessment including shoulder specific scores, CSS, WOOS and EQ-5D, the latter performed by one physiotherapist and one independent Orthopedic surgeon. We also checked for any additional revision reported to SSAR through our local clinical data up till minimum 22 years after surgery. All data was collected following a strict protocol.

Clinical outcomes

Initially the CSS were used and the measurements for the study and the CSS score were all conducted by the same experienced physiotherapist. At the 10 year follow-up the EQ-5D and WOOS were added. WOOS and EQ-5D questionnaires were both developed during the period of the original study, thus they were only available for the 10 year follow-up.

Radiological evaluation

The evaluation included standard radiographs in two projections, anteroposterior and trans axillary lateral view. Two independent experienced shoulder surgeons analyzed the radiographs in consensus. They were classified according to Larsen from 0 to 5 (83). Postoperative radiographs and from the follow-ups at 2, 5 and 10 years were analyzed but only 5 and 10 years data is presented here.

The humeral component for superior migration (SM) in mm, medialization of the humerus (MH) in mm, subsidence (SS) in mm and the tilt of the humeral component (TH) in degrees were measured on plain radiographs. The radiographs were also assessed for rotator cuff rupture, which was considered to be present if the value of SM at follow-up was negative or totally erased compared to the immediate post-operative value.

The glenoid wear (GW) in mm, medial migration of the humeral head into the glenoid (MG) in mm were analyzed for HSA. The tilt of the glenoid component (TG) for TSA was measured in degrees (**Figure 9**).

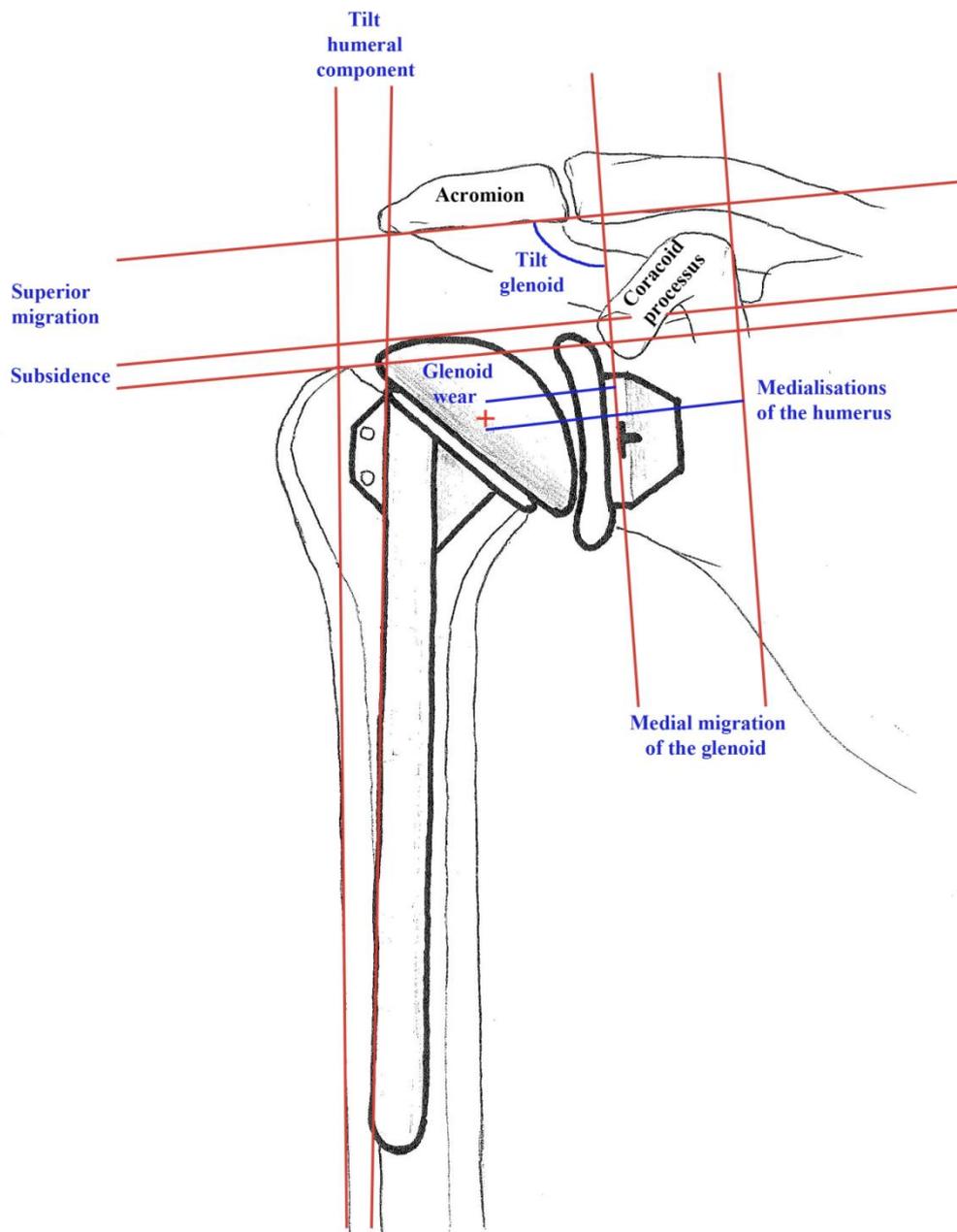


Figure 9: Radiological assessment of the implants. (Courtesy of Anton Borgström)

The cement-bone, or component-bone interface, was divided into radiographic zones for measurement of radiolucent lines (RLL) in mm around the components (**Figure 10**). 8 zones for the humeral component according to Sperling (29) and 5 zones for the glenoid component according to Amstutz (33) were used. The humeral component was defined radiographically “at risk” for loosening when RLL was 2 mm or more in width in 3 or more zones according to Sanchez-Sotelo (84). Each zone around the glenoid component was scored according to Nagels (85). The glenoid component was defined as loose when the grade was four or higher, around the component spanning the whole cement-bone interface, or when there was an apparent change in the component position. In the current study we only present the radiographic assessment results for the dichotomous variables of yes or no for; Superior migration, Cuff rupture and Glenoid deficiency and glenoid loosening for TSA. The glenoid medial migration is also reported in mm.

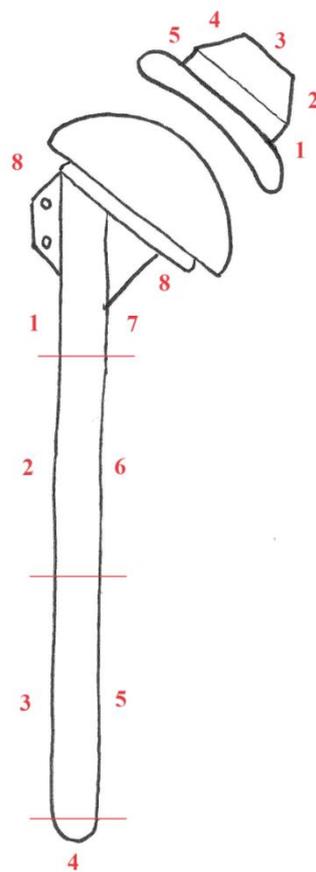


Figure 10: Radiographic zones for measurement of radiolucent lines around the implant according to Sperling (Humerus) and Amstutz (Glenoid). (Courtesy of Anton Borgström)

Revisions

Revision was defined as removal, exchange or addition of an implant component. Causes for revision were categorized by a hierarchy where the last group “other” includes glenoid erosion, overstuffing of the joint and malposition of the implant according to NARA. We made a search in SSAR for any additional revision reported at Danderyd hospital. This is possible since all clinics that report to SSAR have access to its own local clinical data in the registry.

Statistics

Continuous variables were presented as mean and standard deviation (SD) or median and range. Categorical variables and baseline characteristics were presented as total number. Wilcoxon rank sum, Pearson Chi Square test and Spearman’s rank test were used. $P < 0.05$ was considered as statistical significant in all statistical analyses. For statistical analyses we used JMP 14 (SAS Institute Inc, Cary, North Carolina, USA).

Paper IV

This prospective cohort study was performed between 2009 and 2016 at Danderyd hospital, Stockholm, Sweden with patients recruited between 2009 and 2010. All patients referred to the orthopedic department at Danderyd Hospital for OA in the shoulder, were eligible for the study. We included patients aged 50-85 years old, with primary or secondary osteoarthritis of the shoulder not responding to conservative treatment. We excluded severely ill patients not suited for surgery, those with severe destruction of the glenoid surface or cuff tear arthropathy, and patients not able to follow the study protocol. All patients gave informed consent prior to any study-specific visits and were followed postoperatively by research nurses at regular follow-up visits. (Figure 11) All data were collected in a patient specific case report form.

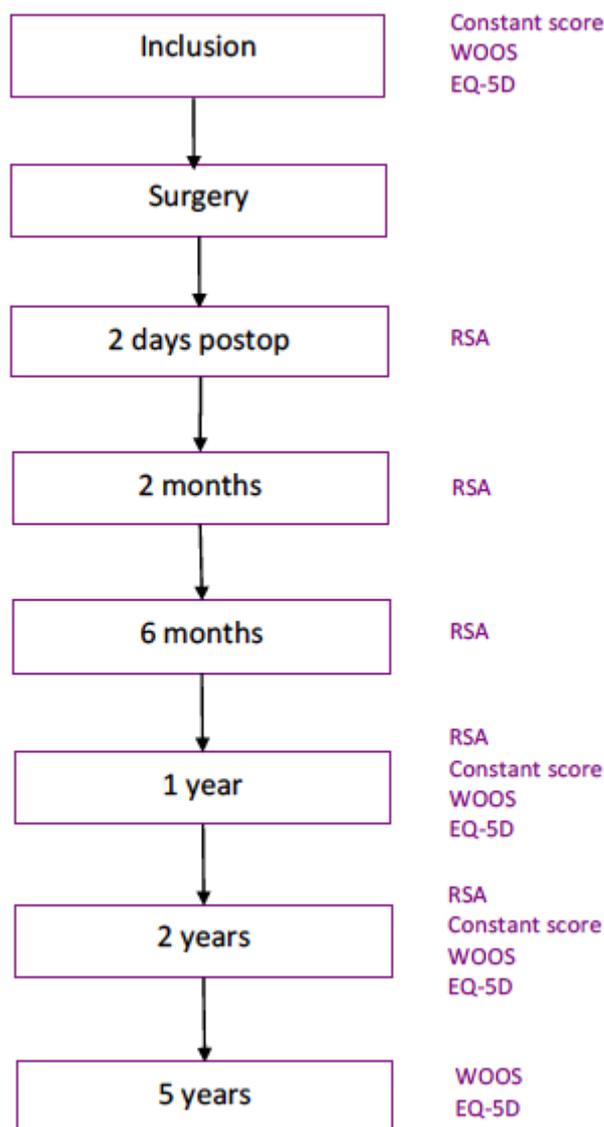


Figure 11: Study visits and data collection. RSA=Radio Stereometric Analysis, WOOS=Western Ontario Osteoarthritis of the Shoulder Index, EQ-5D=EuroQol five dimension 3L. (By Magnus Ödquist)

We used a standard deltopectoral approach. 1.0 mm Tantalum markers were inserted with a “bead-gun” and were placed in the proximal humerus, the coracoid and around the glenoid. **(Figure 12)** All patients received the same implant, Copeland Humeral Resurfacing Head (Zimmer-Biomet Inc. Warsaw IN USA). Learning curve for the implants was not included in this study. Three surgeons performed all procedures (HA, MÖ, BS). Post-operatively the arm was placed in a double sling for 6 weeks and the patients were allowed to elevate the arm forward. All patients were instructed by an experienced physiotherapist post-operatively.

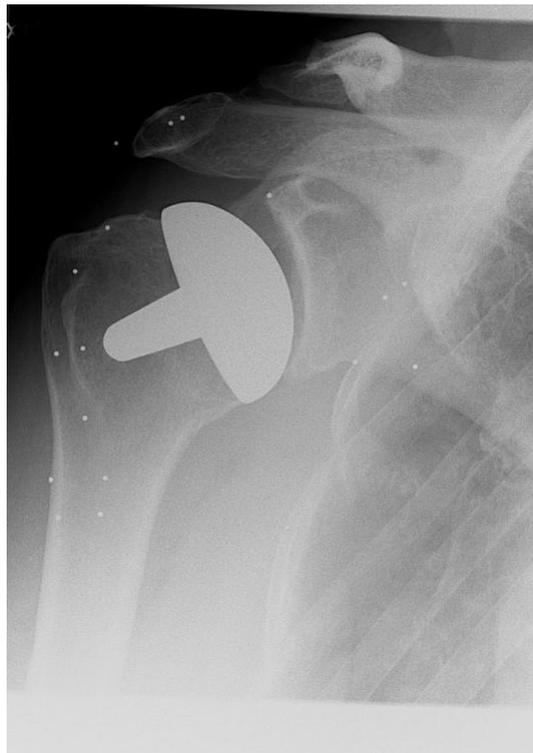


Figure 12: Humeral Head Resurfacing Arthroplasty right shoulder. Tantalum beads inserted in the proximal humerus, the coracoid and around the glenoid. (By Magnus Ödquist)

Outcomes:

The main outcomes were the total migration (the combined 3D vector of x-, y- and z-translation) of the HHR in relation to the proximal humerus and the glenoid, measured with RSA at 2 years. The secondary outcomes were functional outcome measured with CSS and patient reported outcome scores PROM where we used WOOS and EQ-5D. We also correlated the total migration and glenoid wear to the 5 year WOOS, EQ-5D and revisions collected through the clinics access to the SSAR. Revisions were defined according to NARA.

Radio Stereometric Analysis

For the RSA follow-ups we used digital calibrated radiographs, a uniplanar calibration cage (Uniplanar digital 43; RSA Biomedical AB), and analyzed all data using the UmRSA software (RSA Biomedical AB, Umeå. The 1.0 tantalum markers implanted during surgery was used as reference for the measurements. The examinations were performed with the patient in a supine position and with the operated arm in a shoulder immobilizer.

Based on one of our earlier studies (52), marker-free RSA can be used for HHR implants. The method is not precise enough to measure rotations, thus only translations are used in this study as a proxy for the overall migration of the implants. The translations of the calculated center of gravity of the HHR in relation to either the proximal humerus segment or the glenoid segment was calculated at each follow-up visit and compared with the immediate postoperative measurements. For the glenoid wear, the 2-month RSA examination was used as a reference examination to exclude the distention of immediate postoperative intra-articular joint effusion.

At the 1 year follow-up we performed double examinations 10 min apart on all patients with complete repositioning of the X-ray tubes and the calibration cage. We calculated the precision as the 99% CI (SD 2.7) of the difference between the examinations and found it to be between 0.14 and 0.33 mm for migration of the HHR in relation to the proximal humerus and 0.62 to 0.92 mm for glenoid wear. The mean error of rigid body fitting was used to evaluate the stability of the markers over time and, per recommendations from the RSA guidelines, we excluded examinations in which this value was >0.3 mm as this indicates migration of the markers.

Sample size

A power calculation with the assumption that with 90 % power and a p-value of <0.05 using total migration of the implant as outcome, showed that 13 patients must be included to detect a translation of the HHR in relation to the humerus and to detect any medial migration into the glenoid. This calculation assumed a precision of the RSA method for total migration of 0.3 mm with an SD of 0.3 and was derived from a previous publication from our group (52). The RSA method is complicated with an expected technical loss of at least 20% of the examinations and we therefore planned to include approximately 25 patients in the study.

RESULTS

Paper I

- The precision was good for translations when either of the RSA methods was used.
- For rotations, the precision was better for standard RSA (0.05–0.33°) compared to (0.62–1.73°) for marker-less RSA.
- The accuracy of marker-less RSA was 0.47 mm, 0.39 mm, and 0.22 mm for x-, y-, and z-translation. The accuracy was 1.56°, 1.10°, and 0.92° for x-, y-, and z-rotation.

Paper II

- 1140 primary procedures were included of which 142 were bilateral. 318 (28%) HHR and 822 (72%) HSA.
- 8% (76/950) prostheses because of POA and 8% (16/190) prosthesis because of SOA were revised. (**Figure 7**)
- Age at primary surgery was the main factor that influenced the risk of revision, lower age increased the risk (if a patient is 1 year older, he or she has an approximately 6% lower risk of revision surgery than the younger) and was the explanation for the difference between HSA and HHR. (**Figure 13**)
- HSA and HHR had similar outcomes measured by PROM, but the POA group had higher scores than the SOA group with a clinically relevant difference of 10% in WOOS.

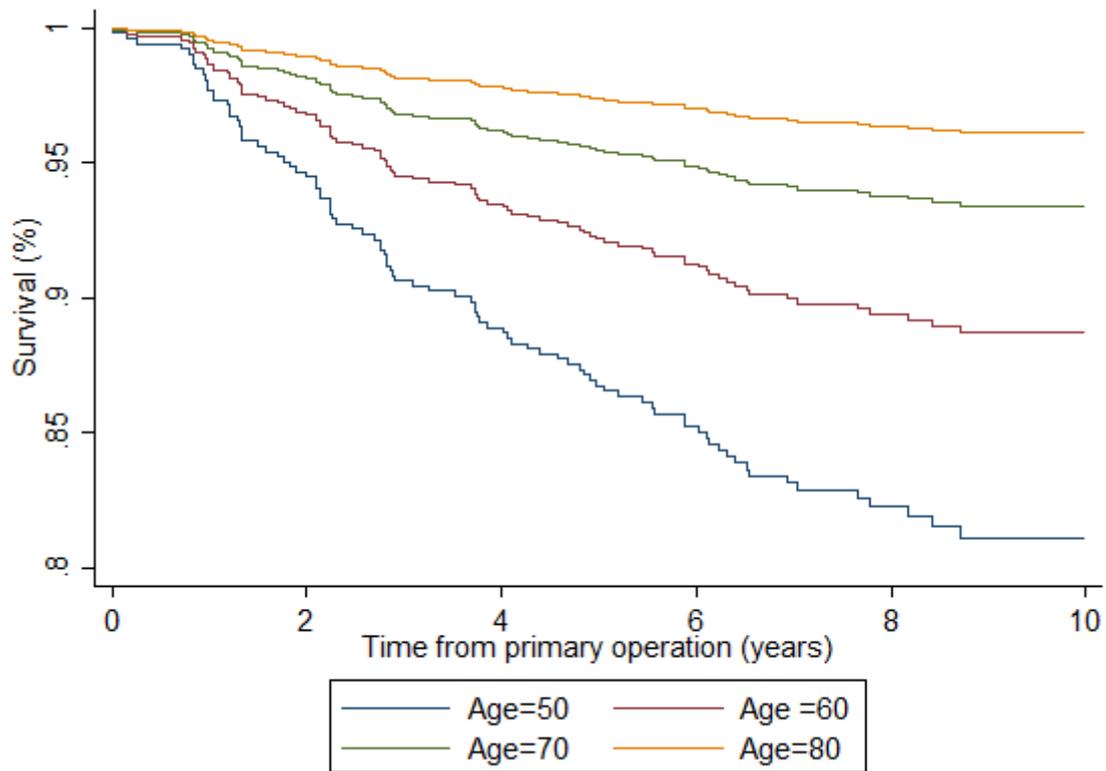


Figure 13: Survival curves for different median ages and results from the Cox model. Only age has a significant effect for revision (no statistically significant effect from diagnoses, implant and gender).

Paper III

- 33 shoulders participated in the 10 year follow-up (**Figure 14**). All of the 31 shoulders that had an x-ray had radiological changes.
- For TSA (n=10), 6 glenoid components were loose, 3 had radiolucent lines and one was unchanged. For HSA (n=21) all had glenoid erosion. (**Figure 15 and 16**).
- The mean CSS in the TSA group were 47 and for HSA 32 (p=0.03). WOOS for TSA was 69%, and 48% for HSA (p=0.019).
- Six shoulders (12%) had been revised within 22 years, four TSA and two HSA.

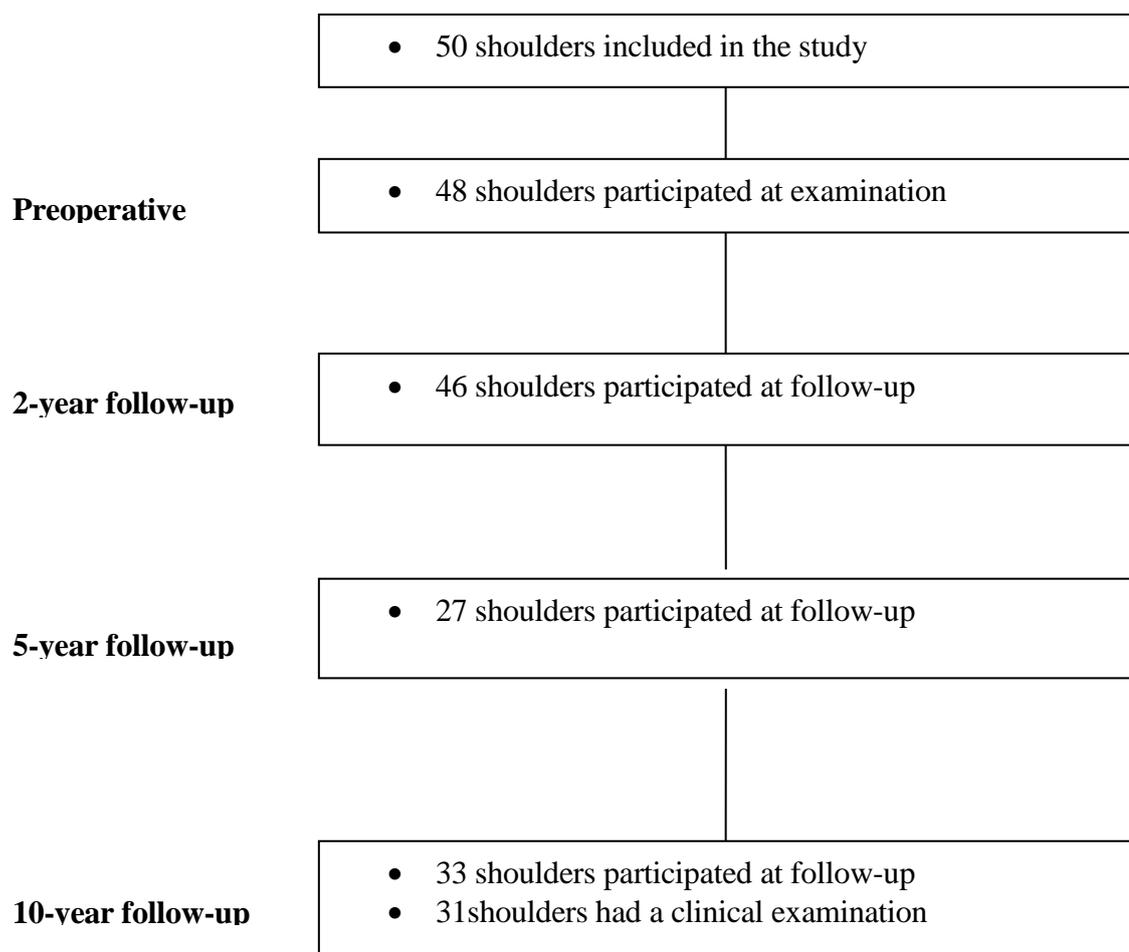


Figure 14: Participation and collected data from follow-ups in Paper III



Figure 15: Total Shoulder Arthroplasty left shoulder at 10 year follow-up with major disruption of the glenoid component. (By Magnus Ödquist)



Figure 16: Hemi Shoulder Arthroplasty right shoulder at 10 year follow-up with severe glenoid erosion (By Magnus Ödquist)

Paper IV

- 21 patients were enrolled (mean age 64, male:female 11:10) in the study (**Figure 17**)
- After an initial migration at two months the implants were stable in relation to the humerus with no statistically significant difference between the 2-month and the 2-year value ($p=0.23$).
- The Glenoid Wear continued to increase during the study period with an initial migration of mean 2.3 mm and at 2 years 3.5 mm with a statistically difference between the 6-month and 2-year value ($p=0.046$). (**Figure 18**)
- The WOOS, EQ-5D and CSS all improved at 2 years compared to the preoperative values. We found a weak correlation between glenoid wear at 2 years and the WOOS score at 2 and 5 years, but it did not reach statistical significance.
- There were 4 re-operations and 3 revisions within 5 years after the primary operation, all due to pain.

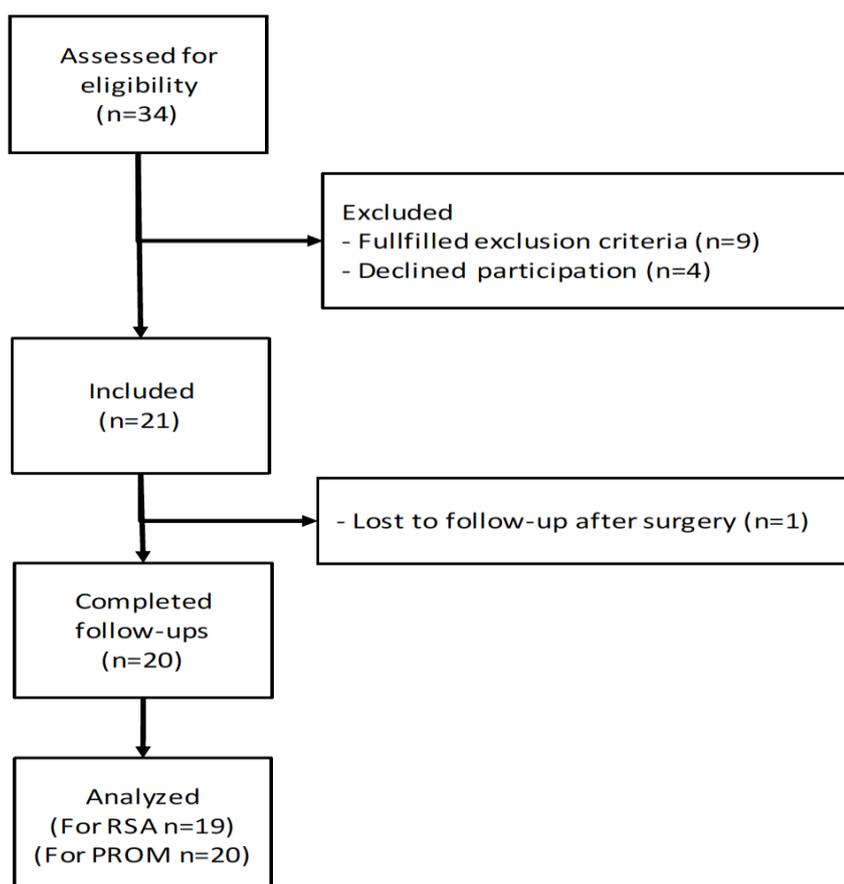


Figure 17: Flowchart of patients in Paper IV. (By Magnus Ödquist)

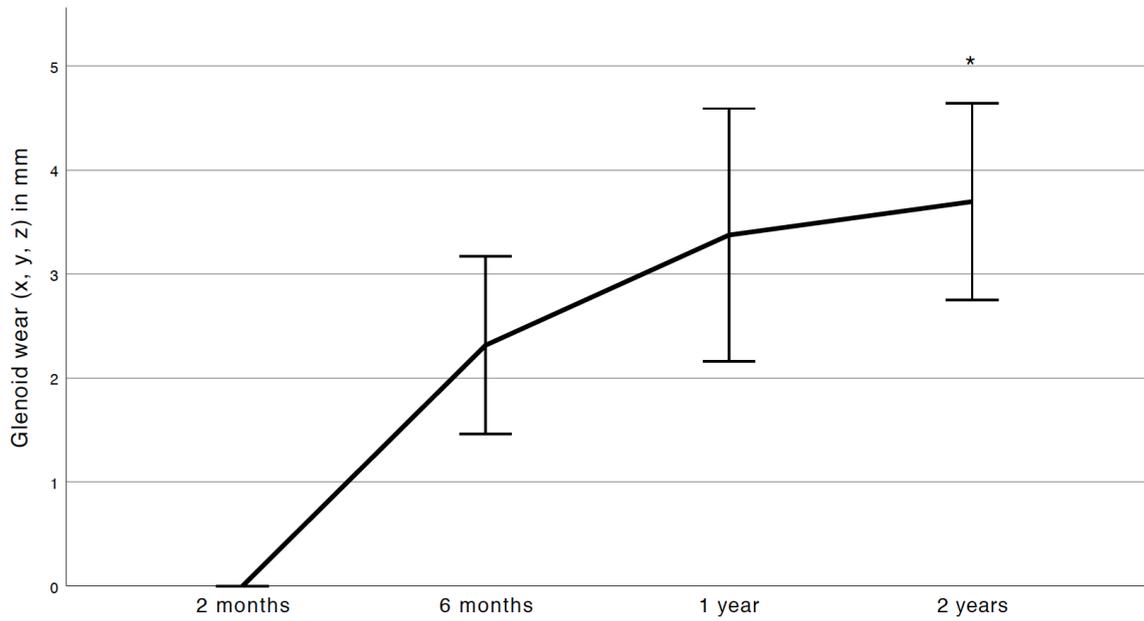


Figure 18: Line chart of the mean (and 95% CI) of wear of the resurfacing head into the glenoid. The 2 months postoperative RSA examination is used as baseline. The asterix (*) indicates statistical significance compared to the 6 months value with the Student's T-test at $p \leq 0.05$. (By Magnus Ödquist)

GENERAL DISCUSSION

Paper I

We found the accuracy to be good for translations, but slightly less so for rotation along the x-axis (flexion/extension) and y-axis (anteversion/retroversion). This has been well documented by the authors who first described the method (80). High-precision measurements of a humeral head resurfacing prosthesis using RSA have not been reported previously, but loosening evident on plain radiographs has been described as subsidence or as increasing inclination angle of the implant (13, 86). For marker-less RSA, this would correspond to y-translation and z-rotation of the implant. There are advantages in using marker-free RSA systems when performing clinical trials involving hemispherical implants. Most importantly, the problem of marker occlusion is solved for prosthesis markers. However, bone markers are still necessary and they should be placed carefully to prevent occlusion by the implant. In standard RSA studies of acetabular cups, the loss of relevant patient data due to marker occlusion is typically 20–25% (87, 88). In studies using marker-free systems, one can presumably expect a lesser amount of data loss. The marking of implants is costly, time-consuming, and can often because of approval issues, only be arranged with the cooperation of the manufacturer. Marker-free software systems thus provide the possibility for industry-independent studies to be done at a lower cost.

Paper II

The main findings were that age at primary surgery was the main factor influencing the risk of revision: we found that a lower age increased the risk of revision. The revision rates in our study are in accordance with earlier publications (89-91). We also found that HSA and HHR had similar outcomes measured by PROM. There was a clinically relevant difference between POA and SOA regarding shoulder functionality (a difference of 10% in WOOS). The group with POA had higher scores than the SOA group. The most commonly given reason for revision in all groups was “Pain and other”. This may include a number of different reasons such as unidentified low-grade infection (92), and unspecified pain due to overstuffing or glenoid erosion. Similar to our results, a revision rate of 25% in HSA have been reported at long-term follow-up of mean 17 years, with a mean age of 51 years at index surgery for the revised shoulders, and with deterioration of the result over time (93). Similar to our study, a higher risk for a revision and for an unsatisfactory result in the younger population has also been demonstrated and in addition a less good result in secondary osteoarthritis has been reported (94, 95). In a report from the Danish Shoulder Arthroplasty Registry on 1,209 shoulder arthroplasties, there were no differences in failure rates between HSA and HHR, or between types of osteoarthritis (POA or SOA), the latter a finding that is contrary to our study (20). This Danish study had a shorter follow up compared with our minimum 5 years, which might be a possible reason for differences between the results.

Paper III

Clinical outcome

The results from the EQ-5D suggest that RA patients as a whole has a limited quality of life and this could probably be due to the long duration, and often painful disease of multiple joints. There are very few long-term studies evaluating treatment of shoulders in RA patients with the WOOS score. The WOOS score in our present study showed higher scores in TSA compared to HSA, 64% of a healthy shoulder for TSA and 53% in the HSA group but was not significant between the two treatments. The results are similar with the results in the SSAR (7). In our study a difference in outcome was only detected in the TSA group. The mean developments of CSS over time seem to conform to the development of mean active elevation. The HSA group improved their mean CSS but did not achieve a statistically significant increase. In a mixed diagnosis group of 1174 shoulders, Pfahler et al found TSA to be superior to HSA in measures of CSS, their follow-up of 3 and 5 years showed improvement in both TSA and HSA, but at 5 years TSA showed a slight decrease and HSA seemed to be equal or slightly better, compared to 3-years follow-up (96). Similar results were found in 105 RA shoulders in a study made by Trail et al. (97). Their findings are also similar to those of our present study, although we saw this decrease for TSA between 5 and 10 years after operation. Results of our present study also suggest that HSA improves during the first 2 to 5 years, and then remains on the same level. It is important though, to keep in mind that the study by Pfahler et al. contains shoulders with many different diagnoses (such as osteoarthritis, fracture and osteonecrosis) and is not totally comparable to our population of RA patients.

Radiographic findings

There are studies that show association between loosening and pain but also studies that show no correlation (98, 99). In a larger study of 303 consecutive Shoulder Arthroplasties made by Barlow, (100), they concluded that both HSA and TSA provides pain relief and improved motion in patients with RA. Also that there is a high rate of component lucency, but component revision is uncommon. The surgical procedure in that study was performed from the late 1976 to the early 1991 while makes the patients and the treatment comparable to our present study. The results from that study are in line with ours.

Revisions:

TSA is considered superior to HSA in providing pain-relief and function of the osteoarthritic shoulder, also having a lower risk for revision in patients with RA in the shoulder (19, 101). We found 14% revisions (6/44 shoulders) 25% (4/12) for TSA and 6% (2/32) for HSA during the 22-years follow-up.

The strengths of our present study are the initial randomization procedure with a structured protocol, the length of follow-up, and the use of same physiotherapist to perform all the clinical assessments at the follow-up. Another strength is that the two surgeons who performed the operations together were not the same as the ones who conducted the follow-up, or examined the radiographs. The radiographs were taken in the same angle and position, but with the individual difference in anatomy and if the patient was relaxed or not, the angles of both the arms were not standardized, and the difference in image quality could have impacted the radiographic assessment between the examinations.

The weakness of our study is the lack of continuity of the PROM outcome with use of different layout of the forms for the CSS score. Small changes and updates of the forms used in this study have made the comparison between the different follow-ups less reliable. The fact that not all included patients could be treated as they were randomized is also a weakness, but it also reflects the reality of the clinical setting at that time. The small study sample is a weakness. Betts et al. followed 58 shoulders in 49 patients over a mean of 19.8 years and at their last follow-up, 14 shoulders in 12 patients were still alive (102). In our study, 32 shoulders of 48 attended a 10-years follow up. In the TSA group, every patient survived to the 10-year follow-up. To our knowledge, no other randomized studies on TSA and HSA have reported results of a follow up of more than 10 years. We could have used radiology specialists to analyze the radiographs independently, in order to get a more reproducible and exact examination of the radiographs. On the other hand, the orthopedic surgeons now involved had experience to assess the radiographs and they were familiar to the evaluation of RA shoulders. Also, the classifications were standardized and consisted of simple measurements of distances. The 10 year follow-up were conducted quite some time ago but we believe that it would have been unethical not to finish reporting the results of this study and additionally we included values for revision up till 22 years after surgery.

Paper IV:

The main findings of our study was that the implant fixation in the humerus can be considered as adequate, that all patients with a hemi HHR developed glenoid wear (GW) and that implant loosening was not a clinical problem in this study.

We have also shown that with RSA it is possible to study implant migration in the shoulder using a marker-free algorithm, this has also been shown by Mechlenburg (103). But our results also show that RSA is a reliable method to measure GW caused by HHR, and in addition also the direction of the GW. The most common way to measure glenoid wear is by plain radiographs (104, 105) but also Computed Tomography (CT) (106) or multichannel CT (MCCT) (107, 108). In a study by Parsons et al, used a Microscribe 3-DX digitizing device were used with a reported precision of 0.23 mm (109).

GW was detectable in all patients and in 37% (7/19) patients it was more than 5 mm. This is similar to what previous studies have found (110-112). The prevailing direction of the glenoid wear was posterior and superior, indicating that the HHR may cause an asymmetrical glenoid wear over time which might influence both the clinical outcome and the surgical demands if revision becomes indicated.

In a retrospective study by Al-Hadithy they reviewed 53 Copeland HHR at a mean follow-up of 4.2 years and concluded that Copeland HHR can provide functional results similar to modular stemmed prostheses (24). Rasmussen et al showed a mean WOOS score of 67 one year after surgery (20). Our clinical results were similar to these two studies.

19% (4/21) of the patients were revised within 5 years after the primary operation due to painful GW. In a study by Rasmussen et al. from the Danish Shoulder Arthroplasty Registry they found that 7.5 % of HHR needed revision until 5 years after operation (91). Soudy et al had 17% revisions after 56 months of which 9.5% where due to glenoid wear (113).

In a systematic review and meta-analysis from Bryant et al they concluded that in short-term follow-up of two years, total shoulder arthroplasty provides more consistent improvement in function than hemiarthroplasty for patients with primary osteoarthritis of the shoulder (19). However TSA may also have disadvantages. These include a more complex and technically demanding procedure, increased blood loss, operating room time and increased costs. Another concern with TSA is glenoid component loosening (114) which may lead to decreased function. The weaknesses of this study of implant fixation and glenoid wear is that we only had 21 patients which was not enough to show a significant correlation between glenoid wear, and clinical outcomes such as pain. The study is not randomized, lack of a control group and has a short follow-up time. Also we cannot show rotations of the implant with marker-free RSA. The strengths of our study is that with the precision of the used RSA method we were able to show that glenoid wear is a reality for all patients operated with a hemi HHR.

And it is also a strength that we could show that it is possible to use marker-free RSA to study both implant fixation and glenoid wear in a clinical study of shoulder HHR.

General Discussion:

In a study by Sims et al they found that in 46 studies, that met the inclusion criteria and were registered on ClinicalTrials.gov, 383 different outcome measures were used (115). They concluded that there is a need to develop a core outcome set for SA. A core outcome set has now been developed by an international consensus group (43). In an earlier study by the same author they made a proposal on how to report complications (116). The most common way for the orthopedic surgeon to gain knowledge about any complication or the general result after SA is through clinical examination of the patient. When it is performed in closed connection to the surgery it is usually the treating orthopedic surgeon who sees the patient. For research purposes, or in follow-up after longer periods of time after the primary operation, the investigator may be another orthopedic surgeon or a physiotherapist. The strengths of the latter are that any bias between the operating surgeon and the patient is minimized.

This thesis has used different methods for assessment and evaluation of the result after SA. The methods discussed here are used in one or more of the 4 papers and show the complexity of the topic and the practical work. In paper I we used RSA in an experimental set-up. In paper II we used data from the Swedish Shoulder Arthroplasty Registry (SSAR) with PROM and revisions, which we also used in Paper III. That study is a long-time follow-up of an RCT where we also used radiographic assessment and clinical examination. Paper IV is a prospective RSA cohort study where we also checked for PROM and revisions.

Radiological assessment:

The follow-up, both the regular scheduled after an elective SA, but also in studies is very often combined with a radiographic evaluation. Plain radiographs are easy to obtain and gives information about possible complications such as signs of loosening, superior migration and glenoid wear. There are also several classifications based on findings on x-rays, in Paper III we used the Larsen classification for RA when assessing the pre-operative x-rays (83). We also made simple measurements of distances from the x-rays, for example superior migration. Since the majority of the shoulders had severe radiological changes the measurements were judged to reflect the true values. In the opposite case, where only small changes are present, a minimal change of the position of the shoulder could alter the measurement in mm which may lead to a low precision. We also evaluated the x-rays for signs of loosening after dividing the humeral and glenoid component in zones according to Sperling and Amstutz respectively (29, 33, 84). In general, the weaknesses of plain radiographs and CT are that even if we obtain information about the implant it does not provide information about the patient's opinion of the outcome. CT provides more information than plain radiographs but is more expensive and exposes the patient to higher radiation. The CT is usually the second line of radiological investigation if

plain radiographs are normal or inconclusive. For RSA, the method is the gold standard for evaluating migration of orthopedic implants and in an ideal setting all implants should be part of a RSA study (51). In Paper I we found that marker-free RSA can be used for HHR. The accuracy was good for translations but slightly less so for rotation. With this limitation the marker-free method by-passes the problem with implant marking. Still, RSA is expensive, especially compared to plain radiographs and CT, also time-consuming and it is almost exclusively used in scientific studies. In Paper IV we used marker-less RSA and were able to measure the glenoid erosion with precision after HHR.

Patient Reported Outcome Measures:

The assessment of a treatment from healthcare professionals, like orthopedic surgeons, and patients own self-assessment by PROM, are not always consistent (117, 118). In a study from Nilsson et al, they stated that for planned interventions aiming to restore functional ability, for example hip replacement surgery, the outcome cannot only be assessed from X-ray images. Self-assessments by patients, of whether they can move freely and without pain or not, are also needed (119). In an attempt to address this, we used both PROM (WOOS, CSS, EQ-5D) and radiologic evaluation in paper III and IV. In Paper III all patients had radiological changes at 10-year follow-up, the majority severe changes, but only 12% were revised until 22 years after the primary operation. WOOS at 10 year follow-up for TSA was 69% and 48% for HSA which is a possible explanation of why relatively few are revised.

Constant shoulder Score

In a study by Conboy et al, they found the CSS easy to use, with low inter- and intra-observer errors, but imprecise in repeated measurements (120). In another study Johansson and Adolfsson concluded that standardized strength test in the Constant-Murley shoulder assessment is reliable in young subjects with healthy shoulders, independent of technique or whether calculated with mean or maximum values (121). In Paper III and IV we used CSS and the same experienced physiotherapists performed the physical tests of the CSS.

Western Ontario Osteoarthritis of the Shoulder Index

The WOOS has been translated and validated, among many other countries, for Sweden and Denmark (122, 123). It is also used by the Nordic arthroplasty registries, and the SSAR also collects pre-operative scores. We used WOOS in Paper II, III and IV. Regarding Paper III WOOS did not exist when the original study started, and therefore no pre-operative values were available. Rasmussen et al, states that differences in preoperative shoulder function may influence the differences in WOOS score at follow-up (20). Paper II is a registry-based study where we used WOOS from the SSAR.

EuroQol five dimensions

The EQ-5D is supposed to be relevant to patients across the spectrum of health care. The instrument was motivated in part by health economics considerations in order to assist healthcare decision-makers on the cost-effectiveness of different treatments (124)

In a review from Grobet et al, about the use of EQ-5D for orthopedic disorders in the upper extremity, they concluded that it is mostly used to assess quality of life in patients with shoulder disorders that had gone through a surgical procedure (67). Paper II shows no differences in EQ-5D, regardless implant type and diagnosis but a clinically relevant difference in WOOS of >10% between POA and SOA. This illustrates the importance to use more than one PROM in clinical studies. In paper III the results from the EQ-5D suggest that RA patients as a whole has a limited quality of life and this could probably be due to the long duration, and often painful disease of multiple joints.

Revisions:

In a large study by Fevang et al from the Norwegian Arthroplasty register, they found 6% revisions after 5 years and 8 % after 10 years for HSA and HHR. They did not find any difference between HHR and HSA. But they also stated that there was no information about any patients suffering from pain that, for some reason, were not revised. On the other hand, the use of revision or implant survival as outcome factors does, however, allow comparison of results for subgroups of patients with different diagnosis and types of implants (89). This is applicable on Paper II where we found that the risk of revision for HSA and HHR is similar when adjusted for age and does not depend on primary diagnosis or sex. A lower age increased the risk of revision.

National Joint registries

In a study from De Steiger et al, from the Australian Orthopedic Association National Joint Replacement Registry they describe a method to report prostheses with a higher than expected rate of revision, referred to as “outlier” prostheses. Their conclusion was that Arthroplasty registries are good at identifying outliers, and they can determine multiple factors that affect outcome and furthermore that international collaboration between registries will continue to play a major role in this work (75). In 2014 a collaboration of common registry analyses between the national registries in Denmark, Norway, and Sweden started as part of the Nordic Arthroplasty Register Association (NARA) (125). The possible advantages of NARA are the high number of cases with increased statistical strength to compare arthroplasty types and arthroplasty brands for different diagnoses concerning revision rates and reasons for revision. By using identical variables and related values it is also possible to compare results between the participating countries. Among the limitations are the reduced number of variables compared with the national registries and the lack of a common patient-reported outcome measure (8) .

Paper II is a registry study from the SSAR where the strengths are the high number of patients and a minimum of 5-year follow-up time. We also conclude that the possibilities to draw generalized conclusions are an important effect of a nationwide registry data analysis. However, a limitation was the 70% response rate on PROM at 5 years. We do not have information additional to the data within the registry, or on the non-responders to the PROM questionnaires. These are weaknesses that come with a registry-based study.

Clinical Trials

To be conclusive a RCT need to be well designed and with sufficient power. Some of the challenges in performing a large RCT lie in recruiting a sufficient number of patients and to find the economic resources for the study and its administration. If the study design is to lean, and without enough margins, it may suffer from loss of follow-up. That may reduce the reliability and the possibility to make general conclusions from the data obtained from the RCT (20, 78). In paper III we made a long time follow-up of a prospective RCT. In the original study 48 shoulders were randomized between TSA and HSA, but because of technical difficulties during surgery only 12/48 actually received a TSA. This illustrates some of the difficulties with RCT. Recently there has been an increased interest in registry-based randomized clinical trials. Nyberg et al, states in the Swedish guidelines for registry based RCT that it is possible to combine some of the critical attributes of a RCT with the practical features of a large-scale clinical registry (126).

Summary

This thesis has showed and highlighted different methods how to measure, evaluate and assess the outcome after SA. The results in Paper II-IV show that there is a need for continuous assessment after SA. Therefore all SA should be monitored post-operatively with regular follow-ups but is not clear at which time intervals. The follow-up should include a clinical visit combined with a disease specific PROM, and if any suspicion of implant related complications the patient should be scheduled for x-ray. Some of these suggestions are already taken care of if the operating clinic is reporting to a SA register. Still, the follow-up through the SSAR are made every 5th year were a WOOS questionnaire are sent out to all patients in the register. And the SSAR does not take any action according to the result of the WOOS. Thus, several challenges left to be solved.

IMPLICATIONS FOR FUTURE RESEARCH:

The results from paper I showed that marker-less RSA are an accurate method to describe the migration of a humeral head resurfacing prosthesis. We then used the method in paper IV and it has also been used by others (103).

From paper II we consider it would be of special interest to further study the impact of age on PROM and revision rate for all types of shoulder implants and to continue with register-based comparisons between HSA and TSA.

Based on our findings in paper III, ROM, function and quality of life the TSA seems to be superior to the HSA, but is still unclear which of the two methods that provides the best pain relief and strength preservation in a longer perspective. The results also raise the question which the most efficient way to monitor the patients after operation would be in order to .

In paper IV we had 21 patients which were not enough to show a possible significant correlation between pain and glenoid wear. We suggest future studies that take that into consideration.

MAIN CONCLUSIONS OF THIS THESIS

- The main conclusion of this thesis is that patients operated with SA needs continuous monitoring and several methods may be used to evaluate the outcome.
- That marker-free RSA can be used for HHR and is a simple and accurate alternative to standard RSA to describe the migration of the implant.
- That the risk of revision for HSA and HHR is similar when adjusted for age and does not depend on primary diagnosis or sex. A lower age at primary operation increases the risk of revision.
- Patients with RA operated with TSA or HSA develop severe radiological changes within 10 years after joint replacement for RA shoulder problems.
- The Copeland HHR arthroplasty seems to obtain a secure fixation in the humerus, after an initial migration. But also that the prostheses shows continuous glenoid wear. GW may lead to revision to a TSA.

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