Shoulder arthroplasty in Norway

Risk of revision and death

Randi Margrete Hole

Thesis for the degree of Philosophiae Doctor (PhD)
University of Bergen, Norway
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UNIVERSITY OF BERGEN

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“Fais de ta vie un rêve et d’un rêve une réalité”

(Le Petit Prince, Antoine de Saint-Exupéry, 1943).

Scientific environment

This study was initiated in 2019 while working as a consultant surgeon at the Department of Orthopaedic surgery, Haukeland University Hospital, Bergen. The study is based on data from the Norwegian Arthroplasty Register (NAR), Department of Orthopaedic Surgery, Haukeland University Hospital, Bergen, Norway.

The Norwegian Arthroplasty Register is financed by the Western Norway health authorities.

Main supervisor was Professor Ove Nord Furnes (UiB) and Co-supervisor was Professor Jan-Erik Gjertsen (UiB). Statistical support was given by biostatistician Anne Marie Fenstad at the Norwegian Arthroplasty Register.

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Contents

Abbreviations

ASA	American Society of Anaesthesiologists
CI	Confidence Interval
COR	Center Of Rotation
HA	Shoulder Hemiarthroplasty
HR	Hazard Ratio
IQR	Interquartile Range
IV	Instrumental Variable
LMWH	Low-Molecular-Weight Heparin
NAR	Norwegian Arthroplasty Register
NARA	Nordic Arthroplasty Register Association
NPR	Norwegian Patient Registry
NSA	Neck Shaft Angle
OA	Osteoarthritis
ODEP	Orthopaedic Data Evaluation Panel
PE	Pulmonary Embolism
PHF	Proximal Humerus Fracture
PROM	Patient-Reported Outcome Measure
RCT	Randomized Controlled Trial

RECORD	REporting of studies Conducted using Observational Routinely-collected health Data
ROM	Range Of Motion
RSA	Reverse Shoulder Arthroplasty
SA	Shoulder Arthroplasty
SD	Standard Deviation
SHR	Sub Hazard Ratio
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TSA	anatomic Total Shoulder Arthroplasty
VTE	Venous Thromboembolism

List of Publications

I. Randi M Hole, Anne Marie Fenstad, Jan-Erik Gjertsen, Stein A Lie, Ove N Furnes

Thromboprophylaxis in primary shoulder arthroplasty does not seem to prevent death: a report from the Norwegian Arthroplasty Register 2005-2018.

Acta Orthopaedica 2021 Aug;92(4):401-407. doi: 10.1080/17453674.2021.1906595. Epub 2021 Apr 6.

II. Randi M Hole, Anne Marie Fenstad, Jan-Erik Gjertsen, Geir Hallan, Ove N Furnes

The Delta III and Delta Xtend reverse shoulder arthroplasty. Risk of revision and failure mechanisms: a report on 3,650 cases from the Norwegian Arthroplasty Register 1994-2021

J Shoulder Elbow Surg. 2023 Dec 15:S1058-2746(23)00575-X. doi:10.1016/j.jse.2023.07.010

III. Randi M Hole, Anne Marie Fenstad, Jan-Erik Gjertsen, Geir Hallan, Ove N Furnes

Survival of and risk factors for revision of reverse shoulder arthroplasties: results of 5,494 arthroplasties with up to 15 years follow-up reported to the Norwegian Arthroplasty Register 2007-2022

Submitted

The publications will be referred to by their corresponding Roman numbers, Paper I, Paper II, and Paper III, as noted above.

Abstract

The number of shoulder arthroplasties performed each year in Norway is increasing. The Norwegian Arthroplasty Register (NAR) has collected data on shoulder arthroplasty surgery since 1994 and was one of the first nationwide registers including shoulder arthroplasties. The indications have changed, and implants and techniques are constantly evolving. Studies with long-term follow up of shoulder arthroplasties are sparse and decisions on which implant to use is often based on the surgeons' preferences. Based on data from the NAR we have investigated surgical factors and implants that could influence the mortality, implant survival, risk of revision and reasons for revisions in patients treated with shoulder arthroplasty.

In **paper I** we compared risk of death after shoulder arthroplasty with and without the use of thromboprophylaxis. Secondary endpoints were revision within 1 year and intraoperative complications. We found no significant difference in the risk of death with or without the use of thromboprophylaxis (HR = 1.1, CI 0.6–2.4). Revision and intraoperative complications were also similar in the two groups.

In **paper II** we reported 10- and 20-year survival rates and compared implant survival, risk of revision and reasons for revision for the contemporary Delta Xtend reverse shoulder arthroplasty (2007-2021) and the formerly used Delta III (1994-2010). We found increased risk of revision for the Delta III with uncemented humeral stem compared to the Delta Xtend with cemented stem (HR 2.9, CI 1.7-5.0). Glenoid loosening was the main cause of revision for the Delta III, while instability was the main cause for the Delta Xtend. Men and fracture sequelae as the reason for primary prosthesis had increased risk of revision.

In **paper III** we included reverse shoulder arthroplasties performed between 2007 and 2022 with the aim of comparing implant survival of different implant designs and brands. Secondary aims were to assess risk factors and reasons for revision in different RSA designs and brands, and with different indications for primary surgery. We found

that implant survival of all reverse shoulder arthroplasties was high with 5-year survival over 90% for all brands, and 10-year survival of 95% for Delta Xtend, which were the most frequently used brand. No difference in risk of revision between inlay and onlay design were found. Instability and deep infection were the most frequent causes of revision. Proximal humerus fractures operated with uncemented humeral stem had an increased risk of revision compared to cemented stems (HR 3.5, CI 1.6-7.3).

In conclusion, our findings did not indicate reduced mortality associated with thromboprophylaxis use, and the practice of giving all shoulder arthroplasty patients thromboprophylaxis as a routine should be reevaluated. Risk of glenoid loosening with reverse shoulder arthroplasty has declined, and risk of revision is lower for the contemporary Delta Xtend compared to the Delta III with uncemented stem. Implant survival after reverse shoulder arthroplasties in Norway is high, and even if revision due to instability is a concern, low risk of revision can be expected with the implants currently in use.

Sammendrag på norsk

Antall skulderproteseoperasjoner som utføres hvert år i Norge øker. Nasjonalt Register for Leddproteser (NAR) har samlet inn data på skulderproteser siden 1994. Dette var et av de første nasjonale registrene i verden som inkluderte skulderproteser. Kirurgene fyller etter hver skulderproteseoperasjon ut et skjema som sendes til registeret. Her registreres informasjon om pasient, årsak til operasjon, operasjonstype og protese. Et tilsvarende skjema fylles ut ved alle komplikasjoner som fører til at pasienten må opereres på nytt (revisjon). Dødsfall registrert i Norge kobles til registeret.

Siden 1994 er det registrert endringer i årsaker til skulderprotesekirurgi. Proteser og teknikker er i stadig utvikling. Det finnes få studier med langtids oppfølging av skulderproteser, og valg av protese kan ofte være basert på kirurgens preferanser. Denne avhandlingen består av tre artikler. Vi har i dem studert ulike kirurgiske faktorer som kan påvirke dødelighet, proteseoverlevelse, risiko for revisjon og årsaker til revisjon etter skulderprotesekirurgi i Norge.

I den første artikkelen fant vi ingen forskjell i risiko for død de første tre månedene etter skulderproteseoperasjon hos pasienter som fikk tromboseprofylakse sammenlignet med de som ikke fikk tromboseprofylakse. Vi fant heller ingen signifikante forskjeller i risiko for revisjon av protesen første året, eller i komplikasjoner under operasjonen. Resultatene våre peker i retning av at det ikke er grunnlag for rutinemessig bruk av tromboseprofylakse ved skulderprotesekirurgi.

I den andre artikkelen sammenlignet vi resultatene etter operasjon med den tidligere brukte Delta III (1994-2010) mot den moderne Delta Xtend protesen (2007-2021). Vi fant økt risiko for revisjon ved bruk av Delta III protesen med usementert protesestamme sammenlignet med Delta Xtend med sementert stamme. Løsning av glenoid komponenten var hovedårsaken til revisjon av Delta III, mens instabilitet var hovedårsaken til revisjon av Delta Xtend. Menn og pasienter med følgetilstand etter skulderbrudd som operasjonsårsak hadde økt risiko for revisjon av protesen.

Resultatene viser at det var mindre risiko for revisjon ved den moderne Delta Xtend protesen.

I den tredje artikkelen inkluderte vi reverserte skulderproteser (RSA) operert i perioden 2007-2022. Vi fant høy proteseoverlevelse for alle inkluderte protesemerker, med 5-års overlevelse på over 90%, og 95% 10-års overlevelse for Delta Xtend, som var den mest brukte protesen. Vi fant ingen forskjell i proteseoverlevelse for inlay og onlay proteser som var de to ulike protesedesign i studien. Vi observerte høyere risiko for revisjon blant pasienter som gjennomgikk skulderbruddsoperasjon med reversert protese, hvor protesestammen var usementert, sammenlignet med de som ble operert med reversert protese med sementert protesestamme. Studien viser at det er gode resultater med reverserte skulderproteser i Norge. Ved å velge proteser med dokumenterte langtidsresultater, kan man forvente lav risiko for komplikasjoner som nødvendiggjør ny operasjon. Ved skulderbrudd bør protesen festes med sement i overarmsbeinet.

Denne avhandlingen dokumenterer ny og viktig kunnskap om skulderproteser i Norge som kan hjelpe ortopedene når de skal vurdere pasienter for operasjon.

1. Introduction

1.1 Anatomy of the shoulder

The shoulder joint is both structurally and functionally complex as it is highly moveable at the cost of stability. The shoulder girdle consists of the clavicle, the scapula, and its connection to the proximal humerus (Figure 1). Four joints make up the shoulder girdle complex: the sternoclavicular joint which connects the upper limb to the axial skeleton, the acromioclavicular joint, the scapulothoracic joints, and the glenohumeral joint. The glenohumeral joint is a ball and socket-type synovial joint. It is formed by an articulation between the head of the humerus and the glenoid cavity of the scapula. The socket (glenoid) is flat and shallow. The rotator cuff connects the humerus to the scapula and is made up of the tendons of four muscles, the subscpapularis, the supraspinatus, the infraspinatus, and the teres minor. The rotator cuff tendons attach to the tuberosities of the humerus and act to compress the humeral head into the glenoid cavity to provide stability and rotate the joint. Several other muscles contribute to the complex anatomy of the shoulder girdle, including the deltoid, pectoralis major, pectoralis minor, biceps, trapezius, and serratus anterior. The insertion of the muscles contributes to the fracture patterns seen in the proximal humerus (1), and also presents challenges in surgery of the shoulder girdle. Degenerative changes in the glenohumeral joint are common, but typicaly less symptomatic compared to changes in weight-bearing joints such as the hip and knee (2).

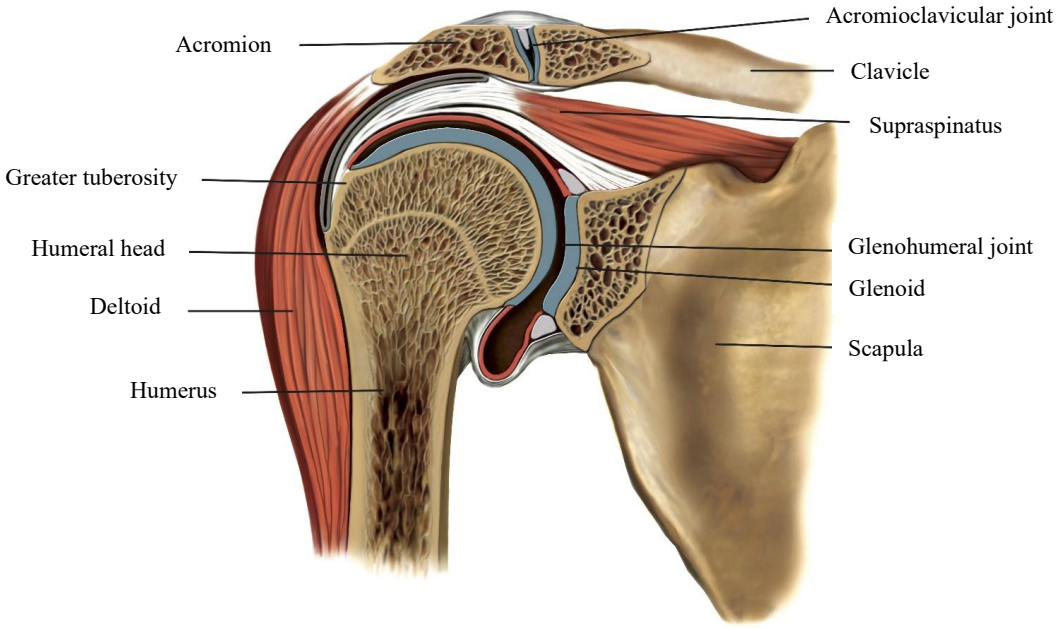


Figure 1. Anatomy of the shoulder. Anterior cross-sectional view of the shoulder joint. Illustration: Science Photo Library, with permission.

1.2 Historical review

The story of shoulder arthroplasty is a fascinating journey through innovation and refinement in medical technology.

Pioneers of shoulder arthroplasty

Jules Emile Péan (1830-1898) is credited with having performed the first total shoulder replacement in 1893, at the Hôpital International in Paris (Figure 2). This was likely the first metal joint prosthesis implanted in humans. He performed his shoulder replacement on a 37-year-old baker who was critically ill with tuberculosis of the proximal humerus and shoulder joint. The patient had refused amputation so Péan was left with the possibility of excising the infected tissue and implanting a prosthesis in a 2-staged procedure. He used a prosthesis designed by Dr J. Porter Michaels, a Parisian dentist. The stem was a platinum cylinder with two ridges and several holes for attachment of the periosteum and muscles. The head consisted of a ball of rubber hardened by boiling in paraffin (3). Péan stated in his original report that he used a prosthesis and the surgical technique inspired by his contemporary Themistocles Gluck. Gluck had described this a few years earlier, but his prosthesis was made of ivory and although he wrote about having inserted them in his article published in 1891, he did not describe any results or state definitively that the operations had been performed in humans (4). Péan's first attempt at shoulder prosthesis had excellent early postoperative result, but unfortunately the infection recurred, requiring removal of the prosthesis 2 years later (3).

Figure 2. Henri de Toulouse Lautrec, "Une opération par le Docteur Péan à l`Hôpital International", 1891. Lautrec`s cousin Dr Gabriel Tapié de Céleyran was one of Péan`s interns and Lautrec obtained permission to watch Péan operate. He produced some 80 drawings and sketches and 3 oil paintings from his year at the Parisian hospital. (Photo: Artcurial)

Evolution of the design and material

Since the early attempts various shoulder arthroplasty designs were introduced with varying results. Surgeons recognized the difficulty inherent in the development of a satisfactory prosthesis for the glenohumeral joint, the balancing of range of motion (ROM) and joint stability was difficult to obtain. Half a century followed without any reference to shoulder arthroplasty in the literature. In the 1950s several attempts were described using plastic prostheses. These were made of acrylic (Richard and Boron), polyamide (Macausland) or of polyethylene (Ross) (5, 6), and were mainly used to treat comminuted fractures of the proximal humerus. The plastic prostheses were eventually abandoned due to breakages, challenges with fixation and foreign body reactions (5, 6).

The introduction of the Neer I arthroplasty in 1953 by Charles Neer, marked the beginning of the modern era of shoulder arthroplasty. With his vitallium monoblock non-constrained hemiarthroplasty Neer stressed the importance of preservation of normal anatomy and tuberosity fixation and healing. Results were encouraging for fracture-dislocations, avascular necrosis, and osteoarthritis, but not in cases with a defective rotator cuff (7).

In the early 1970s both in the US (Kenmore) and in Germany (Engelbrecht) polyethylene glenoid components were developed to be combined with the Neer I prosthesis as a non-constrained prosthesis for patients with arthritis (6). Many designs for shoulder prosthesis appeared in the following years, but Neer showed the best results with his total shoulder prosthesis and paved the way for further developments (6). The significance of Charles Neer's contribution to the field of shoulder surgery cannot be overstated. Over the course of four decades his publications provided an increased understanding of the biomechanics of the shoulder and several implant designs (1, 7-9). Charles Neer continued to use his Neer II prosthesis until he retired in 1990.

With the second generation of non-constrained shoulder arthroplasties the concept of modularity was introduced. The humeral component consisted of two parts, a stem and a head, connected by a morse taper. With this concept prosthesis could better be adapted to the anatomy with different stem sizes, neck angles and head diameters. The Aequalis prosthesis developed by Walch and Boileau was one of the earlier prostheses of this kind (10).

In 1975 Zippel published a report describing a shell used to resurface the humeral head and articulating with a polyethylene glenoid component. Resurfacing total- and hemiarthroplasties became popular towards the end of the twentieth century and showed comparable results with those for stemmed prostheses (11).

In resurfacing arthroplasties, the approach to the glenoid is difficult. When the importance of placement of a glenoid component in arthritic patients was recognized, this was largely overcome with stemless implants where the head was resected, and fixation was only in the metaphysis. Humeral side complications and technical difficulties especially in posttraumatic arthritis and proximal humeral malunion could also be avoided. The stemless implants thus aimed to solve both the difficulties on the glenoid side and, at the same time, preserving humeral bone. TESS (12) was the first stemless implant designed in 2004 and this caused the decline of the use of resurfacing implants.

Originally the implants were made of Vitallium, a Chrome-Cobalt alloy. Molybdenum was added to the Vitallium alloy to increase its strength, improving the longevity of shoulder implants. By the 1980s, Titanium-Aluminum-Vanadium implants emerged (6). Today both alloys are extensively utilized.

1.3 Epidemiology

Studies from national arthroplasty registries have shown that there are large geographical variations in indications for shoulder arthroplasty and the use of different arthroplasty designs (13). Various implant designs have been developed over the past 30 years resulting in many available implants. Evolving knowledge, but also lack of systematic guidelines, surgeons' preference, local availability, and marketing strategies play a role in these variations (14).

When Lübekke et al reviewed data from several national joint registries in 2017 they found an incidence of 20 procedures /100 000 population in 2012, with large variations between the highest incidence of 34/100 000 in Germany and 5.6 /100 000 in the UK. An almost linear increase in procedure rates was seen in all included registries with no evidence of levelling off (13). Also, in the United States the incidence has increased (15, 16). A continuing increase is expected due to growing demand, increasing health care capacity, and/or expanding indications. (14, 17).

The implant designs have changed, and the use of the different implants for different diagnoses have also changed over the years (18-20). This change is partly evidence-based, but also influenced by the implant industry and marketing. Arthroplasty registry based studies have contributed greatly to identifying indications for revision and thereby, indirectly, categorical causes of failure. This post-marketing surveillance is one of the major goals of registries. A continuous independent surveillance of the quality and performance of the implants is necessary, and the registries have the possibility of analyzing large cohorts and discover complications that are rare and very difficult to detect in randomized trials or single center studies (21-23).

The Norwegian Arthroplasty Register (NAR) has collected data on shoulder arthroplasties (SA) since 1994 (24). All hospitals in Norway performing SAs report to the register. In the first 10 years of registration in Norway less than 200 SAs were reported each year. Since the start of the registration there has been a gradual increase

in the use of SAs in Norway, and by the end of 2022 the NAR has more than 12,000 primary SAs registered. In 2022 there were more than 1,000 primary SAs registered for the first time (Figure 3) (25). Fevang et al (26) reported on shoulder arthroplasties in the NAR from 1994-2005 and found that shoulder replacements were performed at 54 hospitals. On average 4 procedures were done per hospital per year, and only 2 hospitals reported more than 10 procedures annually. With the increased incidence the experience of the hospitals and surgeons have likely increased, and this may influence the results of surgery.

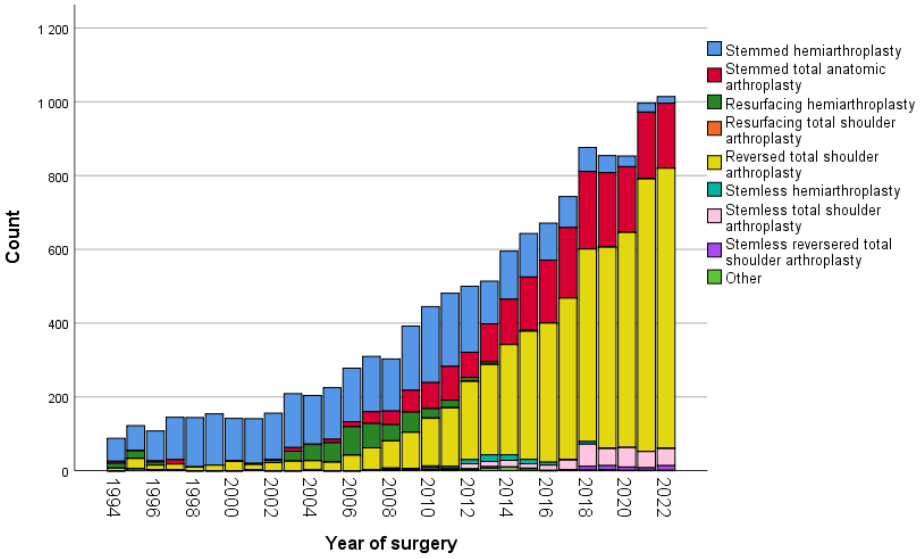


Figure 3. Primary shoulder arthroplasties reported to the Norwegian Arthroplasty Register (NAR) 1994-2022. From NAR, Annual report 2023

1.4 Shoulder arthroplasty design

Depending on the design the shoulder arthroplasties are classified as (Figure 4):

- **Anatomic shoulder arthroplasty**, where the implants resemble the normal shape of the shoulder bones. Anatomic shoulder arthroplasties can be divided into
    - Hemiarthroplasty (HA) – when only the humeral head is replaced.
    - Anatomic total shoulder arthroplasty (TSA) - when both the humeral head and the glenoid surface is replaced.
- **Reverse shoulder arthroplasty (RSA),** where both the humeral head and the glenoid surface are replaced, but the implants are reversed. In that way the ball is attached to the glenoid and the socket is attached to the humeral shaft.

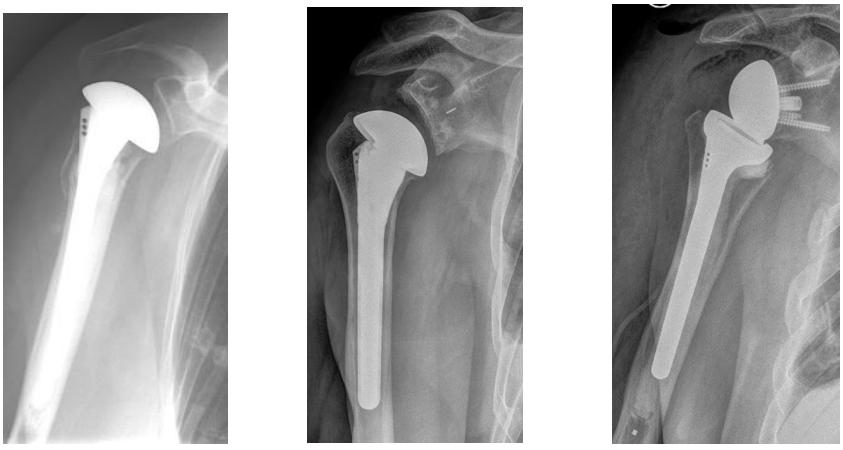


Figure 4 Shoulder arthroplasty designs. Left: Hemiarthroplasty with cemented humeral stem (no glenoid component). Middle: Total shoulder arthroplasty with uncemented humeral stem and cemented glenoid component (with radiopaque marker). Right: Reverse shoulder arthroplasty with cemented humeral stem and uncemented glenoid component with screws. Picture from local patients, with permission.

1.4.1 Anatomic shoulder arthroplasty

Anatomic shoulder arthroplasty can be divided into hemiarthroplasty (HA) or total arthroplasty (TSA) depending on whether a glenoid component is implanted. Initially, hemiarthroplasty was preferred due to technical difficulties in recreating the glenoid surface and concerns about glenoid component wear and loosening (26). However, over time, advancements in implant design, materials, and surgical techniques gradually improved the outcomes (27-29) and TSA is now generally preferred for most indications (28).Several studies have shown lower risk of revision, improved patient-reported outcome, and improved functional outcome when a glenoid component is used (30-35). TSA requires restoration of the normal shoulder construct with intact rotator cuff function and bony architecture. If those factors are uncorrectable, satisfactory results cannot be obtained. Early prosthesis failure caused by superior humeral head migration and glenoid loosening from eccentric loading occurs when the rotator cuff function is not intact. In this situation, reverse shoulder arthroplasty (RSA) could be an alternative option. Rotator cuff dysfunction, glenoid bone deformity, and preoperative stiffness are factors commonly related with poor clinical outcome in the litterature. These three factors independently can influence the outcome of TSA but sometimes coexist and also influence each other (36, 37).

1.4.2 Reverse shoulder arthroplasty

Although pain relief was reliably obtained with hemiarthroplasty, variable strength and function were seen in patients with deficient rotator cuff (7). The loss of the stabilizing effect of the rotator cuff led to superior migration of the humeral head. Neer explored new approaches for the challenging cases where the rotator cuff was torn, and the non-constrained prosthesis failed. In the early 1970s, Neer developed three variants of reverse prostheses, positioning the socket in the proximal humerus- and the prosthetic ball on the glenoid. However, he discontinued further development due to high failure rates (6, 38). Several reverse implant systems were designed and presented by different authors in the 1970s but were not very successful. Attempts to reproduce normal anatomy generated complications. Revision due to glenoid component loosening and

failure was the main problem, probably because the center of rotation in these prostheses was lateral to the scapula causing decreased shoulder mobility and increased torque forces. (6, 38).

The pioneering work of the French surgeon Paul Grammont led to the introduction of a new concept in reverse shoulder arthroplasty with his first reverse prosthesis in 1985 (the Trompette) (39). To improve the deltoid abductor component the center of rotation (COR) was medialized (39, 40). The design allowed for increased forces at the glenoid bone-implant interface and failure was seen due to loosening of the glenoid component. Changes in the glenoid component were made to address this concern. In 1991, the second generation of Grammont´s design (Delta III) medialized the center of rotation to the native glenoid surface and instead of cementing the glenosphere on the glenoid, the baseplate (metaglene) included a central press-fit peg and two divergent screws to resist the shear forces. The success of the design relies on the strength of the deltoid muscle. The deltoid strength was increased by moving the center of rotation distally and medially in comparison to the native glenohumeral articulation (Figure 5). The medialization of the component also decreased the mechanical torque at the glenoid component, avoiding glenoid loosening. The glenoid component articulates with a smaller humeral cup, almost horizontally positioned at a 155° angle. The results of the Delta III prosthesis have been extensively reported (41-43).

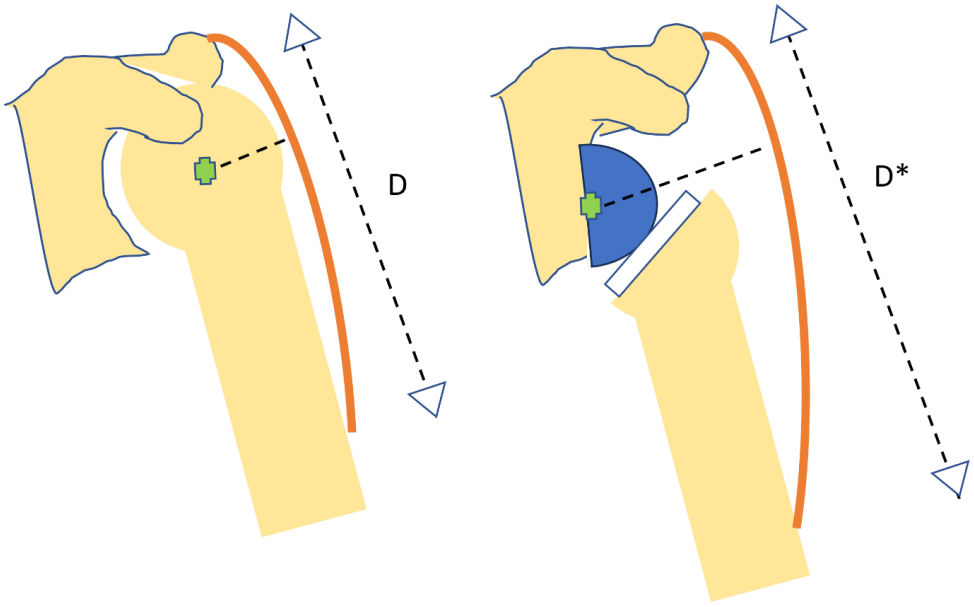


Figure 5. The mechanism of reverse shoulder arthroplasty. The normal ball-and-socket structure is reversed. By moving the COR (green cross) medially and distally the deltoid moment arm is increased (D →D). Adapted from Ingrassia, T., Nalbone, L., Nigrelli, V. et al. Biomechanical analysis of the humeral tray positioning in reverse shoulder arthroplasty design. Int J Interact Des Manuf* ***12****, 651–661 (2018) (44) with permission from Springer Nature.*

The Delta III was successful in restoring the range of motion in cuff-deficient patients, but still rotation often remained limited, and failure to restore sufficient tension in the deltoid could result in instability (42). Scapular notching was also a concern because it led to progressive bone loss of the scapular neck and subsequent loosening of the glenoid component (45). The Delta Xtend (DePuy Synthes) was introduced in 2006 as a successor to the Delta III. Several design changes were made to improve clinical results. The implant had less congruent humeral inserts to prevent polyethylene wear and improve range of motion (ROM) (Figure 6). The glenoid component was modified

to a smaller baseplate with a curved back surface and the possibility of an eccentric glenosphere to allow inferior overhang and thereby decrease the risk of notching (46, 47). The hydroxyapatite (HA) coating on the stem intended for uncemented fixation was the same on the Delta Xtend as on the Delta III, but the Delta Xtend has higher roughness underneath the coating. The Delta III had a modular stainless steel polished stem with (intended for uncemented fixation) or without HA coating (intended for cemented fixation). The Delta Xtend has two different stem options; the modular Delta Xtend stem is TiA6V grit blasted with HA coating, and the monobloc Delta Xtend stem is polished CoCr intended for cemented fixation. Glenoid components were also changed from stainless steel + HA for the metaglene (baseplate) and stainless steel for the glenosphere in Delta III to TiA6V+HA for the metaglene and CoCr for the glenosphere in Delta Xtend. Glenoid components are intended for uncemented fixation in both Delta III and Delta Xtend.

Fig 6. The Delta III reverse shoulder arthroplasty with cemented and uncemented stem (left) and the Delta Xtend reverse shoulder arthroplasty with cemented and uncemented stem (right). Glenoid components are shown with the uncemented stems. Both stems use the same glenoid component. All glenoid components are uncemented. (Reprinted with permission of Ortomedic As).

The Delta Xtend was supposed to solve some of the problems with the earlier Delta III prosthesis, but there are few reports in the literature on long term outcome comparing the two implants. Two papers have reported improved short-term clinical outcomes and survival for the Delta Xtend compared to the Delta III (48, 49). In addition, some retrospective case series with long-term outcomes have been published (50, 51).

When Flatow and Harrison wrote a review of reverse shoulder arthroplasties in 2011, their literature search in PubMed with the terms "reverse", "shoulder" and "arthroplasty" yielded 130 results (38). The same search at the end of December 2023 yields 3,489 results. This emphasizes the vast interest in the field and that this relatively new procedure has gained huge popularity. Today, reverse shoulder arthroplasty is a well-established procedure, continually evolving with ongoing refinements in implant designs and surgical techniques. Updated understanding of the biomechanics and associated complications, such as scapular notching, have led to changes in implant design and the recommended component positioning to improve ROM and at the same time maintaining the deltoid lever arm, and minimize joint reactive forces. It remains an essential option for pain relief and restoring function in patients with several challenging shoulder conditions, significantly improving their quality of life. Long-term results are, on the other hand, very sparse and as many new implants are constantly being introduced to the market, there is a need for continuous surveillance with long-term observational studies. The indications for RSA continue to expand from its initial use in cuff-deficient shoulder to indications such as from proximal humerus fracture, primary osteoarthritis, failed TSA and HA, irreparable massive rotator cuff ruptures and orthopaedic oncologic conditions. RSA was classically reserved for patients older than 70 years (42), but the age limit has gradually decreased as good clinical results have been reported (52). Many alterations and improvements have been made to the initial reverse arthroplasties, but the modern arthroplasties still rely on the same principles: 1) medialization of the center of rotation, 2) re-tensioning of the deltoid by distalizing the humerus, 3) a constant center of rotation leading to an inherently stable implant, and 4) a semi-constrained prosthesis with a larger arc of motion (42).

Until 2007, the exclusive reverse shoulder implant available in the Norwegian market was the Delta III (53). After this period, numerous brands of reverse shoulder arthroplasties have been introduced, each incorporating distinct design elements and implant features (54). These features encompass variations in neck-shaft angle (NSA), lateralization of glenoid component, and the choice between inlay- or onlay-design, all of which are intended to reduce the risk of revision and enhance surgical outcomes. However, the absence of long-term follow-up studies for these newer implants poses a limitation in assessing their efficacy over extended periods. The NAR provides a unique opportunity to assemble substantial patient cohorts and prospectively monitor them, facilitating the systematic registration of revisions and reoperations to contribute valuable insights into the performance of these contemporary implants.

Inlay versus onlay reverse shoulder arthroplasties

RSAs can be classified as either inlay (traditional Grammont) or onlay design depending on the position of the humeral tray (Figure 7).

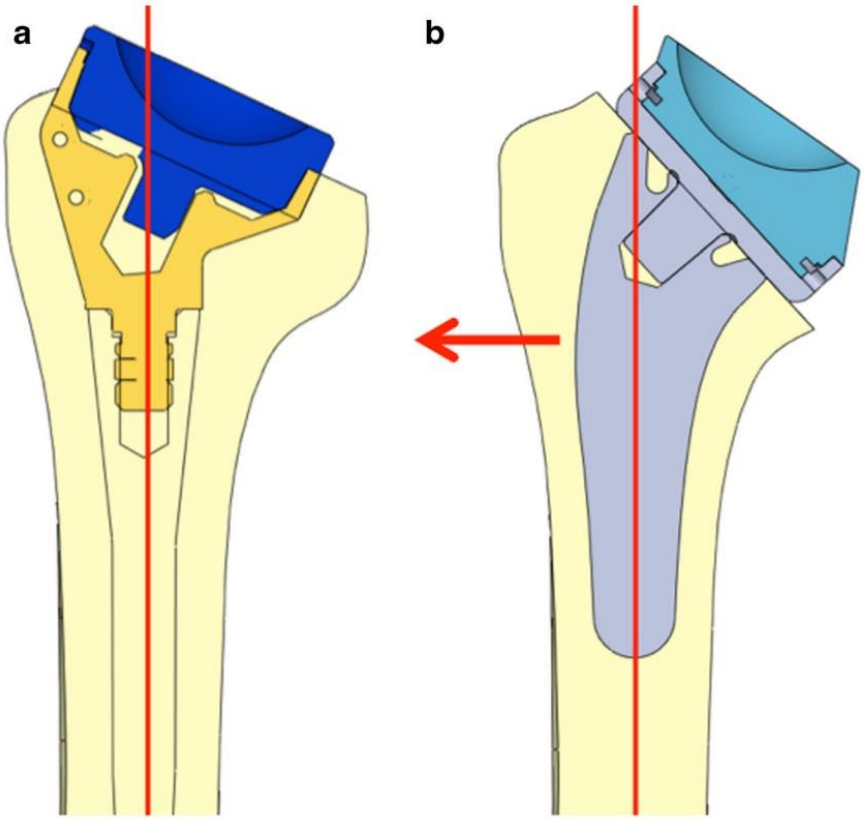


Figure 7. ***a.*** *Traditional inlay Grammont RSA with a straight stem and inlay humeral tray.* ***b****. Example of a design with curved stem and an onlay humeral tray. The red line passes through the center of the stem. Note that the center of the polyethylene is more medial with the curved stem which results in lateralization of the humerus (red arrow). From: Lädermann, A., Denard, P.J., Boileau, P. et al. Effect of humeral stem design on humeral position and range of motion in reverse shoulder arthroplasty International Orthopaedics (SICOT)* **39**, 2205–2213 (2015). *Reproduced with permission from Springer Nature.*

The inlay humeral stem is characterized by its placement within the intramedullary canal of the humerus, maintaining the patient`s native humeral anatomy to a greater extent (Figure 7a). This design potentially offers better stability and bone-implant interface. With the onlay design the humeral tray sits on the metaphysis at the level of the humeral neck cut (Figure 7b). The onlay system allows preservation of tuberosity bone stock, thus decreasing the risk of a greater tuberosity fracture. Onlay implant also increases lateralization and distalization of the humerus which increases the deltoid wrap. The increase in the deltoid lever arm can produce an increase in ROM. The increased tension in the deltoid may, however, contribute to scapular spine fractures and neurologic injuries (55, 56).

A systematic review and meta-analysis by Larose (57) found similar clinical improvements with the two designs. Less scapular notching but a higher rate of scapular spine fractures was reported for onlay implants. The risk of revision was not considered in the review.

In contrast to the traditional inlay designs where medialization of both glenoid and humeral components where achieved, most of the implants currently in use are designed with some lateralization (58). The traditional inlay/onlay design is now modified and much of the same effect as an onlay design can be achieved with lateralization of either the humeral or the glenoid component in an inlay prosthesis. However, although global lateralization theoratically has the same biomechanical effects, lateralization on the glenoid or humeral side may have different implications. Some implants lateralize almost exclusively on the glenoid side either with modifying the shape of the glenosphere, lateralizing the baseplate, or increasing the length of the scapular neck with a bone graft (59, 60). Glenoid lateralization is limited by glenoid bone erosion, inclination, or retroversion (61). Humeral side lateralization can be achieved by a curved stem, by onlay design compared to an inlay design (displacing the stem away from the glenosphere), or by altering the NSA. Humeral side lateralization has the advantage of a more anatomical position of the humerus, which

improves the tension of the remaining cuff, increased compressive forces on the joint and improved stability. Lateralizing on both humerus and glenoid bears the risk of excessive lateralization with joint overstuffing, polyethylene wear, nerve stretching, difficulty to reduce the joint, difficulty to repair the subscapularis and acromial impingement. The ideal amount of global lateralization remains unknown (58).

Biomechanical studies (62, 63) suggest that a lateralized COR and 135° NSA may be more important for clinical outcome than whether the humeral tray is inlay or onlay. Accordingly, the classification of inlay/onlay is not the only parameter describing the amount of lateralization of the arthroplasty (58).

All these different parameters that can be adjusted and individually tailored within each prosthesis brand can be compared in a register setting where large numbers of arthroplasties are reported. However, the register cannot assess how the surgeon has placed the implant, as pre- and postoperative x-rays are not available.

1.5 Indications for shoulder arthroplasty

There are several different conditions in the shoulder that may lead to an indication for shoulder arthroplasty. The most common will be described in detail in the following section.

Osteoarthritis

Osteoarthritis is one of the most common chronic health conditions (64). Osteoarthritis is a degenerative disease in which the cartilage in the joint break down over time. It is the most common type of arthritis and is more common in older people, usually affecting people over the age of 50 (65). Osteoarthritis leads to loss of cartilage, narrowing of the joint space and formation of bone spurs (Figure 8). The symptoms are pain, stiffness, and reduced shoulder function. Osteoarthritis can be primary or secondary to other joint injuries and diseases.

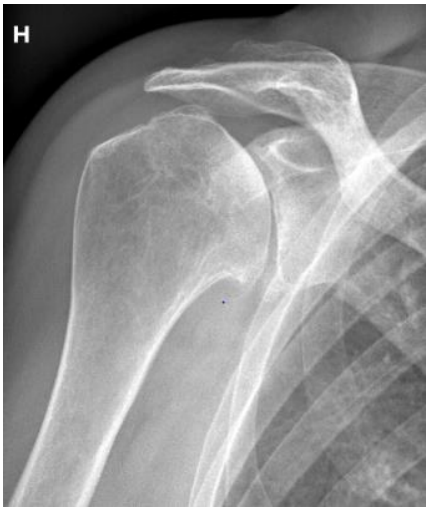


Figure 8. Frontal X-ray of right shoulder with signs of osteoarthritis: narrowing of joint space and formation of bone spurs (osteophytes). Picture from a local patient, with permission.

Acute proximal humerus fracture

Proximal humerus fractures (PHF) are the third most common fragility fractures in the elderly (66) with an incidence predicted to rise due to an aging population. As with most osteoporotic fractures, elderly females have the highest risk with female:male ratio of 2-3:1 (66, 67). Most proximal humerus fractures are simple and minimally displaced, and are best treated non-operatively, but up to 1/3 of fractures are thought to need surgery (68). Fracture dislocations nearly always require operative treatment, and the same may apply to high-energy PHFs or head-split fractures (Figure 9), but these are not covered by the Cochrane evidence (69). There is a lack of consensus on the optimal management of other PHFs and there is little high-level evidence to support the different operative methods, and even sparse evidence as to whether patients profit from operative treatment.

Randomized controlled trials have shown that there is no difference in functional outcome between non-operative treatment and locking plate or hemi-arthroplasty (HA) in the treatment of PHF. However, operative treatment has a significantly higher risk of complications and reoperations (69, 70). The ProFHER study (71, 72) evaluated clinical effectiveness and cost-effectiveness of surgical compared with non-surgical treatment of displaced fractures of the proximal humerus. The inclusion criteria was a displacement sufficient to be considered for surgical intervention by the treating surgeon. Fractures did not have to meet the displacement criteria of Neer with 1cm displacement or 45° of angulation of fracture parts (72). With a pragmatic parallel-group multicenter randomized trial design they found that surgical treatment did not result in better outcome for most patients with displaced fractures of the proximal humerus.

RSA is now the operative treatment of choice for the displaced proximal humerus fractures in the elderly, despite sparse high-level evidence to support this (73). The multicenter Delphi study included patients with displaced comminuted PHFs in patients 65-85 years and found superior results for reversed shoulder arthroplasty compared to plate fixation (74). The existing literature seems to discourage surgical intervention of PHF using locking plate or HA. However, there is a lack of randomized studies that have specifically compared RSA to non-operative treatment. Two ongoing studies aim to add to this knowledge: A Nordic randomised multicenter study (Deltacon) comparing RSA to non-operative treatment, and the ProFHER-2 study comparing RSA, HA and non-operative treatment (75).

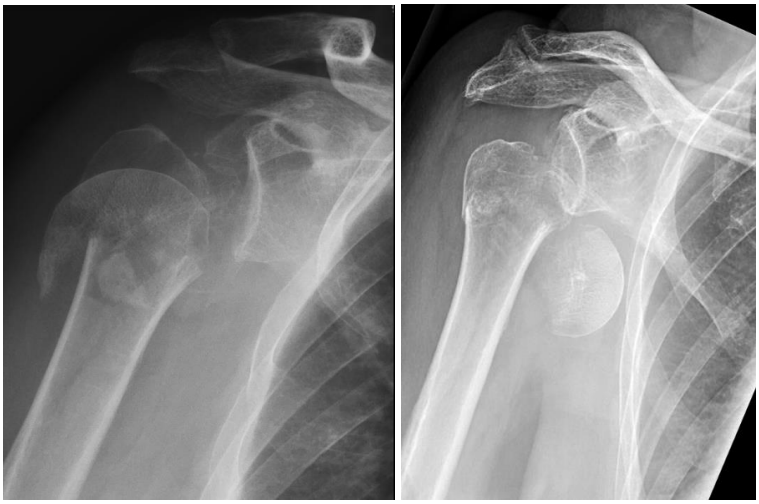


Figure 9. Frontal X-ray of right-sided displaced complex 4-part fracture of the proximal humerus (left) and fracture dislocation (right). Picture from local patients, with permission.

Fracture sequela

Treatment of complex humeral fractures or fracture-dislocations can be challenging. Late complications such as malunion, avascular necrosis, and nonunion are frequent and can lead to articular incongruens (76, 77) (Figure 10). Patients can be severely handicapped with considerable pain, stiffness, and functional impairment (77). Such complications can occur with initial non-operative treatment or when internal fixation was done initially. Stiff shoulders with altered anatomy, soft tissue damage and deltoid scarring can make shoulder arthroplasty a challenging procedure. Several studies have found unpredictable results and high risk of complications when arthroplasty surgery is done for fracture sequela compared to acute fractures (78-80).

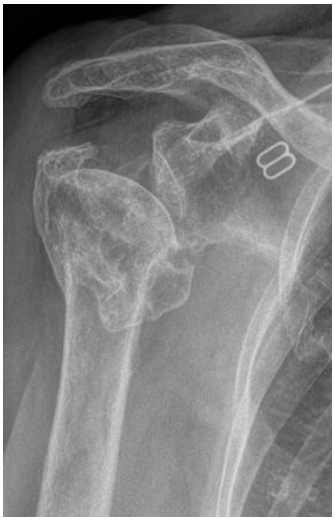


Figure 10. Sequela after proximal humerus fracture right shoulder. 3months after a 4-part proximal humerus fracture. Healing of fracture with valgus impaction of the head and displacement of the tubercles. Picture from a local patient, with permission.

Rotator cuff arthropathy

Rotator cuff arthropathy represents a spectrum of shoulder pathology characterized by rotator cuff insufficiency, superior migration of the humeral head, and arthritic changes of the glenohumeral joint. It was described in 1983 by Charles Neer et al (8). Rotator cuff arthropathy develops after a long-standing rotator cuff tendon tear. The balance in the shoulder is lost, and the head of the humerus can no longer be held in the glenoid socket. The head of the humerus moves upward and can eventually rub against the acromion and lead to acetabularization of the acromion (Figure 11). This causes pain and decreased range of motion. Rotator cuff tears can sometimes be balanced by the remaining muscles of the shoulder, and although many tears of the rotator cuff do not enlarge sufficiently to allow this condition to develop, large tears are more prone to end up with rotator cuff arthtropathy (81).

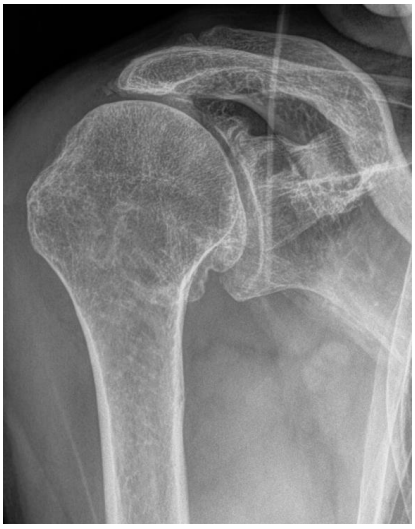


Figure 11. Chronic changes after a long-standing rotator cuff rupture, right shoulder. Superior migration of the humeral head with acetabularization of the acromion. Picture from a local patient, with permission.

Other indications

Several other indications may lead to the need for shoulder arthroplasty. Inflammatory arthritis as indication was common in the early years of the shoulder arthroplasty development, but has decreased considerably alongside the introduction of synthetic and biological disease-modifying anti-rheumatic drugs (82). Chronic glenohumeral joint instability is associated with development of premature osteoarthritis (83). Repeated subluxation and dislocation of the glenohumeral joint can lead to labral pathology and cartilage injuries that in turn leads to pain and reduced function (84). Hovelius et al found high incidence of arthropathy in his long-term follow up of shoulder dislocation (83). Rare indications for arthroplasty include avascular necrosis of the humeral head that can be primary or secondary, malignant tumours, glenoid dysplasia, and sequela after infections(85-87).

1.6 Implant fixation

Humeral stem fixation

Humeral stems come with smooth surfaces, requiring cement for fixation, or with surface enhancement like porous coating or calcium phosphate coating with hydroxyapatite to promote ingrowth, allowing for what´s known as press-fit fixation. There is an increasing shift toward the use of uncemented stems in total shoulder arthroplasty and in reverse shoulder arthroplasty (88). However, there is not sufficient literature to support this shift. Uncemented stems have the advantage of shorter operation time and lower cost (88). Use of bone cement comes with its set of risks, such as intraoperative hypotension, cement embolization, increased surgical time and cost of the procedure (89). Uncemented stems have been associated with early implant loosening (90) and periprosthetic fractures (88). More research with longer follow up is needed to assess the long-term impact of both fixation methods.

Glenoid component fixation

Glenoid component fixation is controversial, and several different designs have been proposed with a varying degree of success.

For TSA the cemented, pegged all-polyethylene glenoid is presently the gold standard. Metal-backed glenoid components and keeled all-polyethylen glenoid designs have shown inferior results (91).

For RSA the glenoid baseplate is usually uncemented and initial fixation is obtained by diverging screws. The number and orientation of screws vary between the different prosthetic designs.

1.7 Complications after shoulder arthroplasties

The epidemiology of failure mechanisms of shoulder arthroplasties (SAs) is changing with advancements in implants, technology, and surgical methods. A complication can be defined as an event that results in an adverse outcome for the patient, irrespective of

surgical revision. The complications can be implant specific or apply to shoulder arthroplasties in general. Several studies have reported more postoperative complications and higher revision rates following RSA than TSA (92, 93). According to a review by Bohsali the overall complication rate for SAs is trending downward (11% in 2017 compared with 14.7% in 2006) (94). The increased use of RSA combined with the higher revision rates compared to TSA warrants a close surveillance of the revision causes and revision rates.

The most frequent complications are described in more detail below.

Infection

Periprosthetic joint infection is a rare but serious complication of shoulder arthroplasties. It is however one of the most common reasons for revisions of painful, stiff, or loose shoulder arthroplasties (95). Incidence of revision due to infection is around 1%, but higher in males and with reverse shoulder arthroplasty where periprosthetic infection has been reported in up to 5 % of patients (93, 96, 97). The large subacromial dead space with formation of a hematoma can be a possible source of infection in RSA (96). When infection with cutibacterium acnes was described for shoulder surgery, it became evident that many of the patients with pain and stiffness as the only symptoms was in fact a low-virulent infection (98). The skin surrounding the shoulder has a unique microbiome. Cutibacterium acnes is a low-virulence bacteria found in the subcutaneous layer of the skin. During surgery in the shoulder area the c. acnes bacteria can be delivered into the surgical wound (99). Infection with c. acnes does not usually present with the classic infection signs of swelling, erythema and drainage (100). As a result, the clinical presentation of infection is often less obvious than prosthetic infections seen in other joints such as the hip and knee.

Dislocation and instability

Instability after shoulder arthroplasty can be associated with component-related factors such as malpositioning and incorrect sizing of the implant, as well as anatomic factors such as glenoid version, humeral subluxation, rotator cuff insufficiency, or a

combination of factors resulting in imbalanced or improperly tensioned soft tissues (101). Consistent and uniform definitions are lacking and the distinction between instability and dislocation in registry studies are not well defined. In this thesis dislocation and instability is considered together as one entity even if this means that complications grouped together may differ in nature. Recognition of which factor contributes to the instability is crucial before revision surgery. Revision surgery after instability of a shoulder prosthesis has a high risk of inferior results and re-revisions (101). The most reliable option in instability after a HA or TSA is revision to an RSA. Instability after an RSA is, however, much more challenging with limited options for revision (102).

Glenoid component loosening

Glenoid component loosening is among the most common complications for total shoulder arthroplasty (35, 103). Factors influencing implant loosening are numerous, and the recognition of these factors were probably the main reason for surgeons to be reluctant to prefer the total shoulder arthroplasties over hemiarthroplasties despite unsatisfactory clinical results of the latter. Keeled or pegged implant, all polyethylene or metal-back implant, polyethylene type, cemented or uncemented, cementing technique, glenoid exposure, reaming instrument, glenoid wear, glenoid retroversion, glenohumeral stability, and condition of the rotator cuff are all factors that can be of significance when considering glenoid implant loosening (104).

With RSA the glenoid component is also at risk of loosening. A systematic review by Shah et al (105) reviewed 113 studies with more than 8,000 arthroplasties for scapular notching and found 29.4% at a mean follow up of 3.5years. Medial notching of the scapula due to impingement between the polyethylene cup and the axillary border of the scapula can lead to erosion beneath the glenoid baseplate, polyethylene wear, and eventually loosening of the component. Although severe notching plays a role in glenoid baseplate stability, the effect of less severe notching on clinical outcomes is not clear. Studies of the early RSAs reported high rate of notching with 65 -74% of the cases (43, 106). To avoid or decrease the incidence of scapular notching several

technical modifications have been suggested. Focus on placement of the glenoid component low on the glenoid surface (107), larger glenosphere, tilting of the glenoid component, and lateral offset have decreased the scapular notching in later years (108). However, the best way to avoid scapular notching is still debatable (45, 109)

Periprosthetic fracture

Periprosthetic fracture is a universal complication for all kinds of arthroplasties (110). Due to the high number of hip and knee arthroplasties performed the vast majority of periprosthetic fractures occur with these surgeries, but as the incidence of shoulder arthroplasties are increasing, the number of complications is expected to increase (15). Intra- or postoperative fractures around the shoulder arthroplasty can lead to loosening and migration of the prosthesis.

Periprosthetic humeral and glenoid fractures demonstrated a prevalence of 1.0% in a large review (94), but with a wide range in different studies (111). The most common location of the fracture is the humerus and most of these events occurred intraoperatively (111). Fractures constitutes a significant part of all intraoperative complications (112). More fractures have been reported after RSA than TSA (94), and higher age seems to increase the risk (112). Scapular fractures are given more consideration in recent times as acromion and scapular spine fractures are seen after RSA. To avoid intraoperative glenoid fractures, it is advised to avoid over-reaming, and special care must be taken when a glenoid component is used in the non-arthritic shoulder (i.e. RSA after a proximal humerus fracture) (113). Intraoperative glenoid fractures during RSA can also occur with screw penetration of the glenoid vault. On the humeral side excessive reaming for uncemented stems should be avoided as it may increase the risk of fracture.

Postoperative fractures are most often attributed to traumatic events (114), and can be treated operatively or non-operatively. Humeral shaft fractures can be treated non-operatively with a fracture brace, or with open reduction and internal fixation if the stem is stable. Fractures distal to a well-fixed stem can be treated nonoperatively

similar to native humeral shaft fractures (115). If the implant is unstable revision surgery with long stem implants are recommended (111). A systematic review of the management of periprosthetic fractures of the humerus revealed lack of uniformity in classification and reporting of outcome (116).

Placing the humeral component more distally with subsequent arm lengthening in RSA can be another source of complication. Excessive lengthening can lead to elevated tension within the deltoid muscle, increasing the risk of stress fractures in the acromion (117). On the other hand, inadequate deltoid tensioning can lead to instability in the arthroplasty (118).

Venous thromboembolism

Controversies exist regarding thromboprophylaxis in orthopaedic surgery. A joint replacement increases the risk of thromboembolic events (119). The use of perioperative heparin significantly reduces the risk of deep vein thrombosis (DVT) and fatal pulmonary embolism (PE) in major orthopaedic surgery (120). Surgeons may be reluctant to use thromboprophylaxis due to the higher risk of bleeding- and wound complications that may lead to reoperation, prolonged hospital stay and increased hospital expenses (121, 122). The risk of deep infections due to haematoma formation may be a reason to avoid thromboprophylaxis (123). The competing risks of thrombotic and hemorrhagic complications are a major concern and the risk of bleeding must be weighted against the potential thrombotic events (124). Although these events may be less common in upper extremity surgery than in hip and knee arthroplasties (125), and reported in less than 0.1% in shoulder arthroplasty surgery (94), there is still no consensus on whether to use thromboprophylaxis as a standard in shoulder replacement surgery and recommendations are based on consensus in working groups or extrapolation of data from hip and knee arthroplasty studies. Thromboprophylaxis is recommended for all patients undergoing hip or knee arthroplasty (126), but there are no evidence-based guidelines specific to shoulder arthroplasty. The Norwegian national guidelines have no specific recommendations for thromboprophylaxis in shoulder arthroplasty surgery (127).

Key risk factors for venous thromboembolic events (VTEs) are advanced age, obesity, cancer, immobilization, genetic factors, hormonal therapies, previous VTE and surgery (especially major orthopaedic) (128). Common for all those risks are a disturbance of the normal physiologic state of the blood, the flow of blood or the vessel walls that will predispose for thrombosis, the Virchow`s triad (129). A combination of those will increase the overall risk. This implies that patients may have different risks of developing VTE depending on their comorbidity and type of surgery.

Deep venous thrombosis (DVT) and pulmonary embolism (PE) are considered a single clinical entity, VTE. The prevention and treatment of DVT and PE follow a common approach. Risk of death after VTE is higher than expected for the population (130), and especially PE seems to increase the risk of death for up to 3 months after onset (130).

Heparin prevents the formation or growth of blood clots by activating antithrombin, a blood protein that inhibits clotting factors such as thrombin (factor IIa) and factor Xa. Inactivating thrombin blocks the conversion of fibrinogen to fibrin which prevents the formation of clots and prolongs the clotting time of blood (131). Low molecular weight heparin (LMWH) showed a longer half-life than the high molecular weight fractions when studied in the 1970s, and this led to the development of LMWH for clinical use in the late 1970s (131). LMWH is preferred as thromboprophylaxis in major orthopaedic surgery as it has been proven to be safe and effective with convenient dosing. Heparins must, however, be administered intravenously (unfractionated heparin) or subcutaneously (LMWH) and this limits the use to temporary anticoagulation during and directly after hospital stays.

The NAR started collection of data on the use of thromboprophylaxis in 2005. Approximately 1/3 of shoulder arthroplasty patients reported to the registry had not received thromboprophylaxis and 2/3 of patients had received some form of thromboprophylaxis from 2005-2018 (132) (Figure 12). It is not known whether this distribution of thromboprophylactic medication is justified or not.

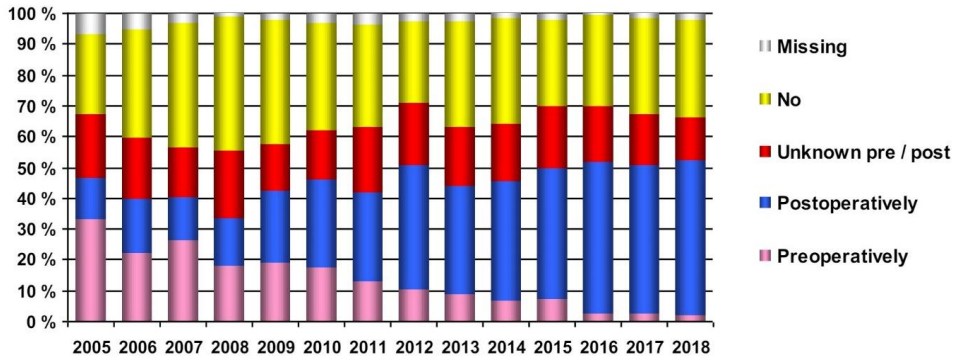


Figure 12. The distribution of thromboprophylaxis for shoulder arthroplasties in the Norwegian Arthroplasty Register 2005- 2018. Figure shows whether thromboprophylaxis is given or not, and the timing of distribution. Figure from the annual report of the Norwegian Arthroplasty Register, June 2019.

1.8 Outcome assessments

Revision

The success of an arthroplasty can be measured in different ways. The goal of surgery is good function, absence of pain, and a long-lasting result. Revision of the implant is an objective measure for failure, even if it gives no information about the patient`s function, level of pain or symptoms. Joint registries provide invaluable data on arthroplasties with revision as the endpoint. Component survivorship can be evaluated as the patients are followed from primary surgery through any subsequent revision and until death or migration in all the Scandinavian registries (133). Arthroplasty registry-based studies can contribute to identifying indications for revision and thereby, indirectly, categorical causes of failure. In all national joint registries survival of the implant is seen as the primary outcome, but definitions vary (134).

Surgeons' experience may influence and modify indications, techniques, outcomes, and complications over time. As surgeons' experience have increased with the increasing incidence of shoulder arthroplasties, the reluctancy to revise may also

become less, and revision may be done for causes that would earlier not be revised as options for revision are better, and surgical techniques are better. Revising an HA or a TSA may be done by conversion to an RSA with expected good outcome (135), while revising an RSA is generally considered more challenging.

Patient-Reported Outcome Measures

Revision as the endpoint by itself may not be the best parameter to judge whether the surgery is successful or not. Factors leading to the decision to revise are not fully understood (35). The implant survival rate does not provide information about patient's satisfaction, clinical outcome, and pain. The patient's opinion is important in a patient-centered approach to health care. Patients and surgeons may have different expectations and goals for the surgery and the outcome, and the patient`s perspective is important in considering whether the treatment was successful or not.

An important endpoint determining success or failure of a procedure is Patient-Reported Outcome Measures (PROM). Several different shoulder-specific PROMs exist, but there are still no consensus on the best score to evaluate the result after shoulder arthroplasty (136). Not all international registries collect PROM scores (134). PROM scores were only recently added to the NAR and are not evaluated in this thesis.

Clinical assessment

A clinical evaluation of the patient aims to assess range of motion (ROM), strength and function. Shoulder ROM must be assessed in different planes and can be expressed as absolute degrees of abduction, flexion, internal and external rotation or as points in a global shoulder scoring system (137, 138). Strength can be measured by using a spring balance or a dynamometer as described for the Constant-Murley score (139), but normal scores decrease with age and vary with sex, and scores should be adjusted for age and sex (140). The clinical assessment may be the gold standard, but is more work-demanding and expensive, and are not feasible in large studies.

2. Aims of the thesis

The overall objective of this thesis was to evaluate the results and identify surgical factors and implants associated with inferior results in patients receiving shoulder arthroplasty in Norway.

The specific aims of the three studies included were:

Paper I

- To evaluate whether use of thromboprofylaxis influences mortality after shoulder arthroplasty surgery.
- To evaluate whether use of thromboprophylaxis influences the risk of intraoperative bleeding complications, all-cause revision, and revision due to infection within 1 year.

Paper II

- To report 10- and 20-year implant survival, risk of revision, and reasons for revision for the Delta III and the Delta Xtend RSAs.

Paper III

- To report the survival of different RSA designs and brands, and factors associated with revision.
- To evaluate the reasons for revision in the different RSA designs and brands and with different indications for surgery.

3. Materials and methods

3.1 Collection of data

The Norwegian Arthroplasty Register (NAR) was established as a hip arthroplasty registry in 1987 (24) and started collecting data on arthroplasties in other joints, including shoulder, in 1994. The purpose of the NAR is to improve outcomes of joint replacement surgery by detecting poor prostheses, cements, and surgical procedures as early as possible. The register also provides important information on the implants and surgical procedures in use and on the patients in need of arthroplasties.

The collection of data in the NAR is performed as a prospective observational study. All hospitals in Norway performing SAs report to the register (26). Each patient must give written consent to be entered into the register. The main aim of the NAR is to identify inferior implants as early as possible. A detailed yearly report presenting the collected data is sent to all reporting hospitals and published online. Interactive results are presented on the following website: https://www.kvalitetsregistre.no/register/muskel-og-skjelett/nasjonalt-register-leddproteser. The registry also provides yearly hospital-specific results reported back to all participating hospitals, and in that way the NAR functions as a local and national quality registry. The NAR covers a population of approximately 5.5 million (2023), and the number of annually registered shoulder arthroplasties has increased from less than 200 annually in the first 10 years of registration to more than 1,000 in 2022. The NAR collects surgical data reported on a one-page paper form filled in by the surgeon immediately after the surgery (Appendix I). Data collected include name of operating hospital, date of operation, indication for surgery, type of surgery, implant details on product number level, type of fixation, laterality, duration of surgery and any intraoperative complications, as well as patient-related factors such as age, sex, and information on any former surgery in the shoulder. Since 2005 information also

includes details on chemical thromboprophylaxis (Figure 13) and comorbidity according to the ASA classification.

THROMBOPROPHYLAXIS
☐0 No ☐1 Yes First dose ☐1 Preoperative ☐2 Postoperative
Medication 1……...Dose on day of surgery……
Dose after surgery…..……for…..……days
Medication 2……... Dose after surgery…..……for…..……days
CONTINOUS THROMBOPROPHYLAXIS
☐0 No ☐1 Yes, type: ……..

Figure 13. Detail from the registration form (English translation) where surgeons indicate if the patient is given thromboprophylaxis or not, which medication is given, and whether the prophylaxis is started preoperatively or postoperatively. In addition, patients on continuous thromboprophylaxis are identified.

From 2019 a gradual transfer to electronic reporting was started. The electronic form gives the opportunity for more patient- and procedure-specific reporting, and several new variables specific to shoulder surgery were added to the registration. The Nordic Arthroplasty Register Association is a collaboration where data from the Nordic registries are merged to create a common dataset (133). When adding new variables to the electronic form in the NAR, a close collaboration with the NARA was important to make it feasible to merge more variables in the future. Most hospitals now report using electronic forms. All hospitals reporting electronically have the possibility to extract their own data at any time to facilitate local improvement in treatment.

The NAR uses the unique personal ID number given to each inhabitant in Norway and side of operation to link the primary shoulder arthroplasty to any subsequent implant revisions or other reoperations regardless of which hospital performed the primary operation. The quality of the registry relies on completeness of reporting. The registration completeness of shoulder arthroplasty in the NAR, using NPR data as reference, was 90.8% for primary SA and 84.6% for revisions in 2019-2020 (141).

Stickers from the implant packaging are attached to the registration form and punched into the NAR database by the registry staff to ensure correct registration of implants on a catalogue number level. In that way implants can be tracked on a very detailed level. Implant modifications are frequent and part of the innovation of products. Hence, it is important to identify the products accurately. All prosthesis components that are in use in Norway are pre-registered in the database, and unknown numbers are declined by the system to control for punching errors. When unknown prostheses are reported, the staff at the registry contact the manufacturer to collect information on new implants. The paper forms are archived at the registry and whenever there is uncertainty about the registration, the forms can be double checked. With the new electronic registration process, the implant barcodes are scanned and filed together with the registration form.

Information regarding deaths and emigrations was obtained from the Norwegian National Population Register.

3.2 Inclusion criteria

In **paper I** all patients operated with a shoulder arthroplasty in the period 2005-2018 were included regardless of the indication for the operation. All shoulder arthroplasty designs were included (HA, TSA, RSA, and others). We excluded patients where information on one or more of the variables of interest was missing (n=849). A total of 6,123 cases were included in the study.

In **paper II** all patients operated with Delta III or Delta Xtend reverse shoulder arthroplasty in the period 1994-2021 were included. All indications for operation were studied and 3,650 cases were included in the study.

In **paper III** all reverse shoulder arthroplasties reported in the period 2007-2022 were included. Several brands were introduced to the Norwegian market from 2007, and brands with more than 30 arthroplasties in the study period were included, excluding

42 arthroplasties. All indications for operation were included and 5,494 cases were included in the study.

3.3 Outcome measures

Since the start of the registration of shoulder arthroplasties in 1994 results have been published on the risk factors for revision (26), functional outcome (30, 31) and on the change in result over time (27). These early publications had a limited number of patients. There is a need for continuous surveillance and updated results from the later years as new implants have emerged and the techniques have changed.

Death

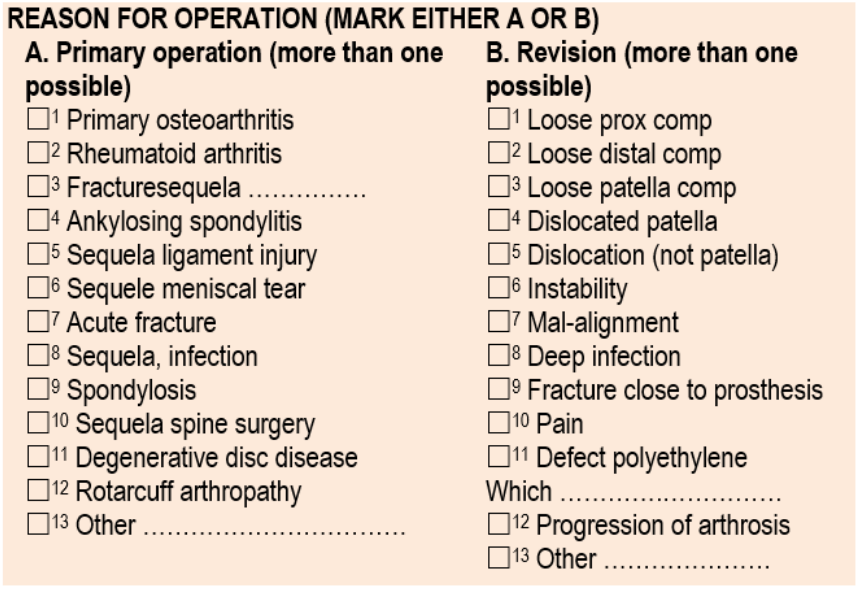
In **paper I** death in the first 90 days after surgery was defined as primary outcome, as deaths after this period were considered less likely to be related to the index procedure (142).

Risk of revision

Revision is a common outcome in arthroplasty registry research. A revision is defined as the insertion, exchange, or removal of any of the prosthesis components while a procedure without insertion, exchange or removal of components is registered as a reoperation. When registration started in 1994 only revisions were reported. Reoperations were added to the registration in 2011. Revisions and reoperations are reported to the NAR in the same way as primary operations. Each subsequent procedure is linked to the primary operation. The risk of revision may be influenced by several factors (patient specific, procedure specific, implant specific) and risk of revision is often investigated with proportional Hazard analyses where adjustments for relevant confounders can be done. The risk of revision was reported in **paper I**, **II** and **III**.

Reasons for revision

Reasons for revision were important secondary outcome measures in **all** three **papers**. When the surgeon reports a revision arthroplasty, a reason for revision must be reported. More than one reason for revision can be given in each case and the hierarchy developed by NARA was used in the analyses whenever more than one reason was given (133). The paper form used for the shoulder arthroplasties was a common form for all arthroplasties other than hip. The alternative reasons for revisions were thus not specific for shoulder arthroplasties, and specifications of "other" can be given in free text (Figure 14). All reports of "other" were evaluated and classified into shoulder-specific reasons whenever feasible. We identified the most common reasons for revision in shoulder arthroplasty, and these were included in the analyses of revision causes. Reasons that were seldom encountered were classified as "other".



REASON FOR OPERATION (MARK EITHER A OR B)

A. Primary operation (more than one possible)	**B. Revision (more than one possible)**
☐1 Primary osteoarthritis	☐1 Loose prox comp
☐2 Rheumatoid arthritis	☐2 Loose distal comp
☐3 Fracturesequela	☐3 Loose patella comp
☐4 Ankylosing spondylitis	☐4 Dislocated patella
☐5 Sequela ligament injury	☐5 Dislocation (not patella)
☐6 Sequele meniscal tear	☐6 Instability
☐7 Acute fracture	☐7 Mal-alignment
☐8 Sequela, infection	☐8 Deep infection
☐9 Spondylosis	☐9 Fracture close to prosthesis
☐10 Sequela spine surgery	☐10 Pain
☐11 Degenerative disc disease	☐11 Defect polyethylene
☐12 Rotarcuff arthropathy	Which .....
☐13 Other	☐12 Progression of arthrosis
	☐13 Other .....

Figure 14. Detail from the NAR registration form, updated in 2015, (English translation) where reasons for primary operation (A.) or revision (B.) is marked. Several reasons can be given for each operation.

3.4 Statistical analyses

All statistical analyses were performed using the package IBM SPSS version 24.0 (**Paper I**), 26.0.1.0 (**Paper II)**, 29.0 (**Paper III**), (IBM Corp, Armonk, NY, USA) and the statistical package R Version 4.0.0 (**Paper I**), 4.0.2 (**Paper II** and **III**) (R Foundation, Vienna, Austria) and Stata/SE 17.0 (**Paper II** and **III).**

In the descriptive statistics, continuous variables are presented as means, medians, and interquartile ranges. The median time of follow-up was estimated by the reverse Kaplan-Meier method. Categorical variables are presented as frequencies and percentages. Pearson`s chi square test was used for comparison of categorical variables.

Survival analysis is often used in registry studies to estimate the incidence of an outcome and study the prosthesis durability. Kaplan-Meier survival curves is the most used survival analysis. The analysis presents the proportion of patients who have not experienced the event (death or revision of the prosthesis) in relation to the time (22). In our studies, follow-up started on the day of the primary arthroplasty with censoring at the time of revision, death, emigration or end of the study.

In **paper I** bilateral cases were treated in the descriptive part as if they were independent, while the adjusted Hazard Ratios (HRs) were calculated using robust variance estimates to account for bilateral SAs. Calculation of the robust variance estimates follows the counting process formula of Andersen and Gill (143). In **paper I** we used adjusted Cox regression to compare the two subgroups, and in addition the causal effect of thromboprophylaxis was estimated using an instrumental variable (IV) approach. This analyzis follows the methods described by MacKenzie et al (144). The hospitals' annual propensity for using thrombosis prophylaxis was applied as instrument. Hence, the IV approach assumes that the hospital is related to the mortality only by thrombosis prophylaxis, and that the hospital is independent of unobserved covariates. Under these conditions the estimated HR can be interpreted as a causal HR of thrombosis prophylaxis on mortality.

In **paper II and III** implant survival with endpoint revision due to all causes was estimated by Kaplan-Meier analyses with censoring at the time of revision, death, emigration, or end of study. If a patient had sequential revisions, only the time to the first implant revision was included in the analyses. To investigate the risk of revision, we compared the different prostheses using Cox multiple regression analyses for each revision cause according to the NARA hierarchy adjusted for age, sex, and diagnosis. In **paper III** stem fixation and earlier surgery in the same shoulder were also adjusted for in the analyses. The proportional hazards assumption was evaluated graphically (145). In **paper II** the patients were divided into two groups, Delta III and Delta Xtend, and each group was further divided into subgroups with cemented or uncemented stem. All groups were compared in the Cox regression analyses. In **paper III** subanalyses were done for the different brands and for the different indications for surgery. Inlay and onlay designs were also compared. The results are presented for the entire period. In addition, in **paper II and III,** competing risk analyses were performed by calculating the subhazard ratios (SHRs) (146, 147) for each cause of revision. The Fine and Gray method is a regression model expressed as SHRs with the possibility to adjust for relevant covariates. The reason to present the SHRs was to calculate correct estimates for revision for each cause separately. The SHRs describe the relative effect of potential covariates on the subdistribution hazard function. The endpoint was revision due to a specific cause, with revision due to all other causes as the competing factor. If the patient died or emigrated, the follow-up time was censored (148).
In all papers statistical tests were two-sided, a 95% CI was calculated, and p-values below 0.05 were considered statistically significant.

3.5 Ethical approval

All papers used data from the NAR, which has concession from the Norwegian Data Inspectorate to collect patient data, based on a written consent from the patient (ref 24.1.2017: 16/01622-3/CDG), and comply by the Norwegian and EU data protection laws.

4. Results / Summary of papers

4.1 Paper I

Thromboprophylaxis in primary shoulder arthroplasty does not seem to prevent death: a report from the Norwegian Arthroplasty Register 2005-2018.

Hole RM, Fenstad AM, Gjertsen JE, Lie SA, Furnes ON. Acta Orthopaedica 2021 Aug;92(4):401-407

In this study, the use of thromboprophylaxis in shoulder replacement surgeries were investigated, aiming to discern its impact on early mortality, revisions within a year, and intraoperative complications. Examining data from 6,123 primary shoulder arthroplasties reported to the Norwegian Arthroplasty Register between 2005 and 2018, we employed Cox regression analyses, adjusting for age, sex, ASA score, diagnosis, implant type, fixation, surgery duration, and year of surgery.

Thromboprophylaxis was administered in 4,089 out of 6,123 surgeries. We found no significant difference in 90-day mortality between the groups with and without thromboprophylaxis (HR 1.1, CI 0.6–2.4) (Figure 15). Postoperative mortality risk increased with factors like older age (> 75), higher ASA class (≥ 3), and a diagnosis of fracture. Similarly, there was no notable variance in the risk of revision within one year between the two groups, and the occurrence of intraoperative bleeding was comparable (0.2% vs. 0.3%).

However, it is crucial to note our study lacked information regarding causes of death and their connection to thromboembolic events. Despite this limitation, our findings did not indicate any reduced mortality associated with thromboprophylaxis use. Consequently, the routine implementation of thromboprophylaxis in shoulder arthroplasty warrants reevaluation based on our observations.

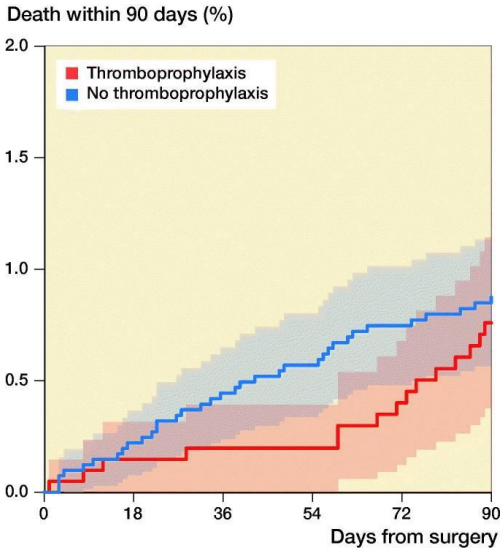


Figure 15. Kaplan-Meier curve showing the death rate up to 90days after surgery in patients with and without thromboprophylaxis. 95% CI is given.

4.2 Paper II

The Delta III and Delta Xtend reverse shoulder arthroplasty. Risk of revision and failure mechanisms: a report on 3,650 cases from the Norwegian Arthroplasty Register 1994-2021

Hole RM, Fenstad AM, Gjertsen JE, Hallan G, Furnes ON. J Shoulder Elbow Surg. 2023 Aug 11:S1058-2746(23)

This study assesed 10- and 20-year survival rates, risks of revision, and reasons for revisions for Delta III (1994-2010) and Delta Xtend (2007-2021) shoulder prostheses, drawing from 3,650 primary RSAs in the Norwegian Arthroplasty Register. Of these, 315 were Delta III (42% cemented stems) and 3,335 were Delta Xtend (88% cemented stems).

Delta III patients were more commonly diagnosed with inflammatory disease or fracture sequela, whereas Delta Xtend were primarily used with acute fracture, osteoarthritis, and cuff arthropathy.

Delta III had a 10-year survival of 93.0% (cemented stem) and 81.6% (uncemented stem), while Delta Xtend showed 94.7% (cemented stem) and 95.7% (uncemented stem) (Figure 16). Notably, Delta III (uncemented stem) demonstrated a 20-year survival of 68.2%.

Glenoid loosening was the primary cause of revision for Delta III (uncemented stem), while instability was the primary cause of revision for Delta Xtend (both cemented and uncemented stems). Men and patients with fracture sequela faced increased revision risks.

The study found a higher revision risk for Delta III (uncemented stem) compared to Delta Xtend (cemented stem) with 10-year follow up (HR 2.9, CI 1.7-5.0). However, this registry study cannot determine whether implant design changes or other factors

that changed during the study period are the cause of the differences. The indication for the primary operation likely influenced the risk of revision.

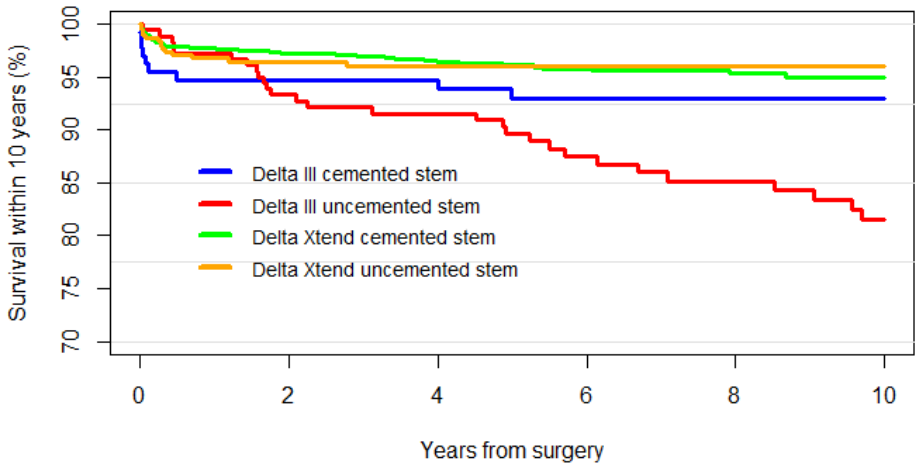


Figure 16. Kaplan-Meier survival with 10-years of follow-up for Delta III cemented stem (blue), Delta III uncemented stem (red), Delta Xtend cemented stem (green) and Delta Xtend uncemented stem (yellow).

4.3 Paper III

Survival of and risk factors for revision of reverse shoulder arthroplasties: results of 5,494 arthroplasties with up to 15 years follow-up reported to the Norwegian Arthroplasty Register 2007-2022.

Hole RM, Fenstad AM, Gjertsen JE, Hallan G, Furnes ON

This study aimed to analyze the survival rates of RSA designs and brands, identifying associated factors contributing to revision. Additionally, reasons for revision were evaluated.

In total 4,696 inlay and 798 onlay RSAs reported to the Norwegian Arthroplasty Register (NAR) in 2007- 2022 were included. Kaplan-Meier estimates of survivorship and Cox models adjusted for age, sex, diagnosis, implant design, humeral fixation, and previous surgery were investigated to assess revision risks. The reasons for revision were compared using competing risk analysis.

The overall 10-year survival rate was 94% (CI 93-95) with all brands surpassing 90% at 5 years. When compared to the Delta Xtend (n=3,865), several brands including Aequalis Ascend Flex (HR 2.8, CI 1.7-4.6), Aequalis Reversed II (HR 2.2, CI 1.2-4.2), SMR (HR 2.5, CI 1.3-4.7), and Promos (HR 2.2, CI 1.0-4.9) demonstrated a higher risk of revision. Onlay and inlay RSAs had similar revision risks (HR 1.2, CI 0.8-1.8) (Figure 17).

Instability and deep infection were the most frequent revision causes. Male sex (HR 2.3, CI 1.7-3-1), fracture sequela (HR 3.1, CI 2.1-5.0) and fractures operated with uncemented humeral (HR 3.5, CI 1.6-7.3) stems had increased risk of revision.

In conclusion the risk of revision after RSA was low. No difference in risk of revision between inlay and onlay designs was found. Some prosthesis brands had a higher rate of revision than the most common implant, but numbers were low. Based on these findings cemented humeral fixation is recommended for proximal humerus fractures.

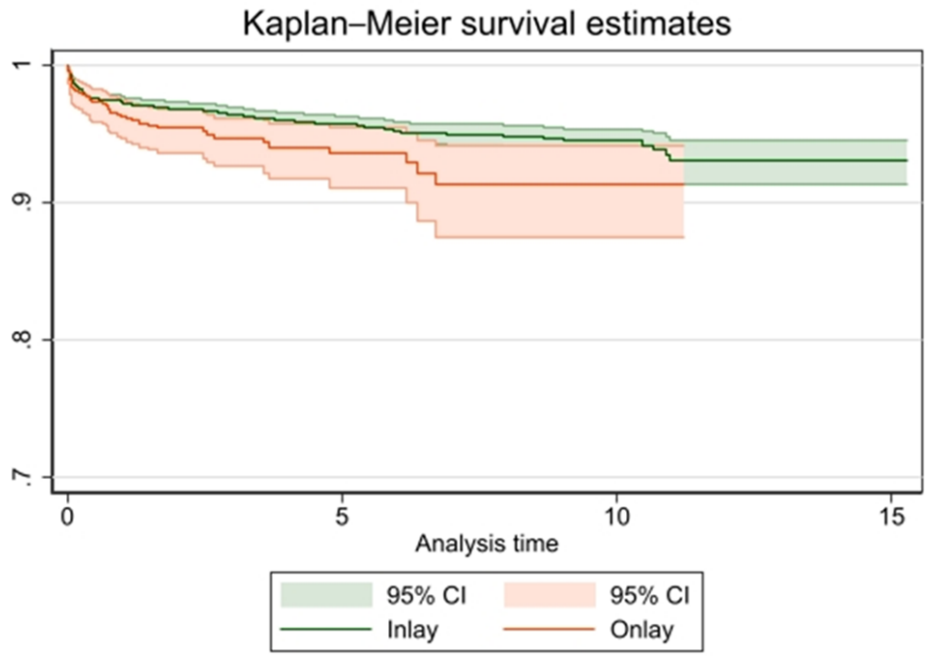


Figure 17. Kaplan-Meier survival for primary reverse shoulder arthroplasty by design (all diagnoses) in NAR 2007-2022.

5. Discussion

5.1 Methodological considerations

In clinical research the objective is to gather evidence that enhances our understanding and guides clinical decision making. This research can be categorized into two main types – observational or interventional/experimental studies. While interventional involve the investigator assigning the exposure or not, observational studies are designed to collect information about individuals, their conditions, and changes over time.

Interventional studies, further classified into randomized and non-randomized studies, commonly favor randomized controlled trials (RCTs) as the gold standard in clinical research. Nevertheless, the prevailing belief that only RCTs produce dependable results, while observational studies are misleading, has been questioned by several authors (21, 23). RCTs are time demanding and often expensive to perform, and to achieve strong statistical power multiple centers needs to be involved which further challenges the logistics. Especially when studying rare outcomes, large observational studies have clear advantages to the RCTs. Observational studies may generate new hypotheses, which can then be explored further in randomized controlled studies. Different designs for observational studies are used (Figure 18).

Registry studies are cohort studies that are prospective in their design. An arthroplasty registry is defined in the bylaws of the International Society of Arthroplasty Registries (ISAR) as “a systematic collection of predetermined data on arthroplasty surgery with established methods for longitudinal follow-up, coverage, and completeness analysis”. The cohort has been exposed to a risk and are observed for outcomes of interest. The cohort studies are more likely to provide an indication of what is achieved in daily medical practice (149). The cohort study is the strongest form of non-experimental evidence (Figure 18) (150). National shoulder arthroplasty registries are currently used to assess incidence, indication, type of prosthesis and revision. Registries are the best

tools for long-term implant surveillance and bridge the gap between implant performance in clinical trials and their use in routine practice over time (151).

Figure 18. Levels of evidence pyramid for study design in health research. Study design in ascending levels of the pyramid generally exhibit increased quality of evidence and reduced risk of bias. The quantity of studies usually declines in ascending levels. Quality varies within each level depending on study design and implementation. (Adapted from Yetley et al, 2017(152))

Variations of this hierarchy have been proposed by different authors, and the use of the evidence pyramid can be criticized as incomplete and not taking into consideration the different quality of studies within each design. At all levels there are strong and weak

studies, depending on methodology and the pyramid may fail to distinguish high quality studies from the lower quality studies (153). In addition the different study designs have different purposes and ranking them in the same hierarchy by the same criteria may be difficult (154).

Recognizing the strengths and limitations of various study designs are important for selecting the appropriate design to answer the research questions at hand.

5.1.1 Strengths of registry studies

New arthroplasties can be released into the market without any evidence of clinical efficacy and safety. The main advantage of arthroplasty registries is post marketing surveillance as demonstrated by national hip and knee arthroplasty registries (24). Data in orthopaedic registries have the potential to answer several clinical research questions. Large study populations make it possible to study rare outcomes at low cost and at shorter time than would be possible with an RCT. In RCTs only patients that are willing to take part in the randomization and comply to strict inclusion criteria are considered. Registry studies also include patients that would possibly be excluded from RCTs and those that are not willing to comply to specific protocols, consequently the findings are more likely to reflect a "real life" situation. All hospitals, surgeons, patients, surgical techniques, and prostheses are included and the goal is as few exclusions as possible.

The primary strengths of registry studies encompass several key points (155):

- **Large sample size**: The large-scale sample ensures robust statistical power, facilitating earlier detection of significant results (133). It also enables the exploration of rare outcomes that would require extensive sample size beyond the feasibility of RCT studies. Merging of several international registers would further increase the strength, but requires harmonization of the variables (133, 156).

- **Efficient data collection**: With data already compiled in a large register, individual research projects benefit from expedited and cost-effective data acquisition. Accessibility to this pre-existing data streamlines the process, lessens patient burden, and mitigates data fatigue.
- **Enhanced generalizability**: The completeness of these databases ensures external validity, allowing for broader generalization across various countries and diverse practice settings. Unlike RCTs conducted in controlled environments, registries encompass all patients regardless of stringent inclusion criteria, providing a more realistic reflection of average surgical practices across multiple hospitals. Shoulder arthroplasty surgery is currently performed at 44 hospitals in Norway and the results from a national registry are likely to reflect an average surgeon at an average hospital.
- **Minimal bias**: Prospective data collection independent of any specific study reduces recall bias and reduces the potential study-induced influences on diagnostic or therapeutic processes.
- **Long-term observations:** Extended follow-up periods offer a reliable platform for observing outcomes manifesting after prolonged latency periods (22). This extended view proves invaluable in studying complications, such as implant loosening, which may present many years after the surgery.
- **Rich demographic insights:** Registries supply crucial demographic data, and merging data sets from multiple registries on an individual level diminishes residual confounding factors, enhancing the accuracy of the analysis.

The validity of the registry consists of four major aspects (22):

- **Coverage** of the registry is defined as the total number of hospitals reporting to the registry out of the total number of hospitals in the country. All hospitals operating shoulder arthroplasties in Norway report to the NAR.
- **Registration completeness of procedures/patients**. The completeness of reporting to the registry is calculated by comparing the number of patients

reported to the registry with the number of patients reported to the NPR on an individual level. NPR is considered the gold standard, and we assume that all operations are recorded in the NPR.This comparison is done regularly to ensure the highest possible completeness. Completeness is published in NAR's annual report to motivate hospitals with low reporting to enhance their reporting routines.

- **Registration completeness of variables** included in the registry. In our studies few patients were excluded due to missing variables. When variables were missing in the database a manual check was done to ensure all information on the paper form was registered correctly. In some cases, hospitals with missing values were contacted to complete the form.
- **Accuracy of registered variables** is evaluated by validation studies. Validation is done by comparing the reported data to the data in the patient charts at each hospital. Validation studies are time consuming, but important to ensure high quality of the register (157-159).

5.1.2 Limitations of registry studies

Limitations of the registry studies are important to be aware of (155):

- **Precollected data constraints**: Researcher face restrictions as they cannot specify criteria for variable selection. Valuable information may remain inaccessible unless multiple registries or supplementary sources like patient charts or x-rays are collected and incorporated. In our studies, the registration for shoulder arthroplasties utilized a generic common form designed for various joint arthroplasties. This lack of customization might lead to different interpretations among researchers and obscure specifics of common complications. For instance, some of the more common complications is not specified in the form, and only reported as "other" with a textual specification from the surgeon and in the recoding process these are "translated" into

predefined groups of complications, potentially losing specificity through recoding.

- **Limited number of variables**: The predetermined variables constrain researchers, possibly omitting confounding factors crucial to the research question. For instance, the NAR lacks data on medications, smoking, BMI and socioeconomic status. Inability to adjust for these variables could impact the outcome.
- **Data completeness and quality**: Despite high coverage, even minimal missing data might influence analyses. Systematic missing data may reflect that the form is unclear and that the surgeons are uncertain of the interpretation of the question. Variables with many missing cases should be used with caution. Variations in data quality across registries necessitate validation through comparison with other registries or individual patient chart reviews, although such validation studies demand substantial time and effort (157, 158). Completeness of the data in the NAR is regularly validated against the Norwegian Patient Registry (NPR) (141, 160).
- **Risk of inflated significance:** Large sample size can inflate statistical significance, magnifying minor differences that may lack clinical relevance, leading to debates about the true clinical significance.
- **Guarding against data biases:** Watchfulness against data fishing or data dredging is crucial in large datasets. Defining research questions and hypotheses before exploring data prevents biased interpretations.

Registries are excellent tools for implant surveillance, and to evaluate the incidence, the indication, the type of procedure and the survival rate of arthroplasties. Registry studies, while offering extensive datasets, face limitations stemming from precollected data constraints, limited variable scope, data completeness, quality variations, potential inflated significance, and the need to guard against data biases, necessitating careful considerations in their utilization and interpretation.

5.1.3 Data quality

Several orthopaedic registries are established worldwide and many now include shoulder arthroplasties (22). The NAR has long follow-up compared to other joint registries. The high registration completeness increases the applicability and external validity of the data. A study with high external validity indicates that the results can be generalized to other patients. Applicability means that the effects observed in a study are likely to be found if the intervention or treatment was used in a large population under "real-world" conditions (161).

Patients in the NAR are identified using the 11-digit Norwegian personal identification number, ensuring accurate age and sex recording as well as establishing a correct link between primary surgery and subsequent revisions. This same identifier connects the NAR to the National Population Registry, enabling comprehensive tracking of deaths and migrations. Moreover, the NAR is linked to the NPR to validate recorded surgical procedures, crucial for assessing the completeness of primary surgeries and revisions. Yet, the codes used for NPR and NAR entries differ, complicating the assessment of completeness, particularly for revision surgery where several procedures and codes can be used. The completeness for revision surgeries is lower than that of primary shoulder surgeries (159, 160). A prior validation study revealed a tendency to underreport infections in the NAR (159), potentially due to these cases often occurring out of scheduled operating hours, and the surgeries may be done by surgeons not so familiar with the reporting system. Validation of registration completeness has been updated regularly and the results are published in the annual report (141). Most validation studies from NAR include data from hip arthroplasties, but the registration forms for all joint arthroplasties are similar. Surgeries are done in the same units and to some extent by the same surgeons. Thus, we can assume that the results from the validation studies are transferrable to shoulder arthroplasties.

The most important measures of quality of an arthroplasty are the risk of revision, reoperation and the patient`s function, pain, and quality of life after surgery. Revision is a common outcome in registry studies, and revision due to any cause was the main outcome in **paper II** and **paper III. The r**isk of revision can be useful information for

patients and surgeons when considering arthroplasty surgery, but revision is not the only outcome that describes the success of an arthroplasty. A patient with an unrevised shoulder arthroplasty does not necessarily have a good shoulder function or satisfactory radiographs. Patients with a poor clinical result may remain unrevised due to concomitant diseases, a high risk of complications, or reluctance by the surgeon or patient to undergo further surgery. Knowledge about patient satisfaction together with the revision risk will hopefully increase our ability to advise patients on shoulder arthroplasty surgery. Collection of patient related outcomes (PROMs) are now widely used in registries in combination with the implant survival (134). Wide variations in registered variables in different national registries makes it difficult to merge data across registries and to compare results. To harmonize registration in the Nordic countries, the Nordic Arthroplasty Register Association (NARA) has been established (133). Western Ontario Osteoarthritis index (WOOS) is used in the Swedish and Danish shoulder arthroplasty registries, and this PROM score was also chosen when PROM was introduced to the NAR in 2021 in addition to the EuroQol questionnaire (EQ-5D-5L). The WOOS is a disease- specific questionnaire for the measurement of shoulder function in patients with osteoarthritis of the shoulder (162) while the EQ-5D-5L is a short generic questionnaire charting the health-related quality of life (163).The completeness of PROMs so far is low (25), but increasing, and future studies will focus on PROMs in addition to survival outcomes.

The registration completeness for primary operations and even for revisions are high (141), but the registration completeness and accuracy of each variable is unknown. Causes of primary arthroplasties and revisions are registered by the surgeon performing the procedure. Each surgeon may classify the causes differently based on experience, local traditions, and subjective assessment. The common paper form has limited alternatives for both primary and revision surgeries, and a perfect match may not be able to be found for the specific patient. For example, an irreparable cuff tear is not an option as a reason for primary operation and may be classified by one surgeon as “rotator cuff arthropathy” even if arthropathy is still not evident, and by another surgeon classified as arthritis while yet another may classify this as “other” and specify

"rotator cuff rupture" as a free text. The same is true for the revision causes as the reason for revision may be unclear, and what may appear as a loosening of the implant or pain and stiffness may turn out to be an infection when tissue samples are cultured. Reasons are given directly after surgery and tissue samples that are collected during surgery may be positive after the form has been submitted. Misclassification is more likely to occur for revision causes that have an unclear definition, like malalignment or instability. Both these causes may lead to loosening of the implant or polyethylene wear and the definition of which cause is the main cause may be difficult. A more accurate definition of the causes may reduce the error of misclassification, and with the electronic registration the variables are more specific to shoulder arthroplasty and are also harmonized with the other Nordic registries to facilitate merging. Several causes of revision can be given. The hierarchy developed by the NARA group for the revision causes (133) was applied when more than one cause was given.

Awareness of different revision causes varies with time. As surgeons' experience has increased with the increasing incidence of shoulder arthroplasties, the reluctancy to revise may also become less. Revisions may be done for causes that were not previously considered as options for revision and surgical techniques are better. In this way the risk of revision may not be feasible to compare between time-periods.

In the registry studies possible confounders are adjusted for in the statistical analyses. Only the registered parameters can be adjusted for, and parameters not included in the registry such as BMI, diabetes, smoking habits, glenoid shape, radiologic parameters, and preoperative shoulder function may be confounders. Some of these are added to the new electronic registration form and may be possible to adjust for in the future. Despite adjusting for registered confounders there may be some residual confounding.

5.1.4 The reporting of cohort studies

The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative provides guidance on how to report research and recommend what should be included in an accurate, transparent, and complete report of an observational study

(164). This checklist consists of 22 items that relate to all parts of a scientific paper. Four of the items are specific to cohort studies, and 18 items are common to cohort, case-control, and cross-sectional studies. The STROBE statement is designed to apply to all observational studies and specific issues related to reporting of registry data are not addressed, and there are some gaps specific to research using data from routinely collected health data. The Reporting of studies Conducted using Observational Routinely collected health Data (RECORD) is an expansion of STROBE to explore and address specific reporting issues relevant to research using routinely collected health data. Consistent with the STROBE approach the RECORD guidelines are not designed to be used in the designing or conducting of studies, but merely to ensure internal and external validity of the research (165). The RECORD checklist was used in **all papers** in this thesis.

5.2 Discussion of results

5.2.1 Thromboprophylaxis in primary shoulder arthroplasty

In **Paper I** we found no association of reduced mortality after primary shoulder arthroplasty with use of thromboprophylaxis.

Thromboprophylaxis in surgery is intended to prevent symptomatic venous thromboembolic events (VTEs), and there is a strong recommendation that thromboprophylaxis should be given to patients undergoing hip and knee arthroplasties (166). The incidence of VTE in upper extremity surgery has, however, in several studies been found to be lower (125, 167) and no strict recommendations for thromboprophylaxis in shoulder arthroplasty surgery exist.
Deaths in the first 90 days after surgery were defined as primary outcome in **paper I**, as deaths after this period were considered less likely to be related to the index procedure. Heit et al found an increased risk of death up to 3months after VTE (130).

Postoperative bleeding may lead to haematoma formation, and subsequently an infection either when there is prolonged wound drainage or persistent swelling. Cheung

et al (123) found that hematoma after shoulder arthroplasty often was accompanied by positive cultures and clinical infection. We could not find any difference in the revision and reoperation rate at one year with or without the use of thromboprophylaxis, and the specific revision rate due to infection was also comparable in the two groups.

Even if we found no correlation to death we do not know if the patients had more thromboembolic events. The NAR does not have any information on complications other than those leading to a revision, and readmissions due to VTE are not considered. As we included only death as outcome variable, we missed other complications such as deep venous thrombosis and pulmonary embolism not leading to death. In addition, we do not have information on the causes of death and accordingly we do not know whether the observed deaths were related to VTE. To examine this, data from the NAR, the NPR and the Norwegian Cause of Death Registry could be compared, and readmission and death causes could be further investigated.

In the analyses we adjusted for possible confounders that we had access to in the NAR, but even if we considered the patient`s ASA classification this did not take into consideration all risk factors for VTE. Risk factors such as earlier thromboembolism and inherited disorders that may affect blood clotting, such as Leiden mutation or deficiencies in antithrombin, protein C, or protein S do not necessarily give a higher ASA classification even if the VTE risk increases substantially.

We found that the use of thromboprophylaxis varied across the hospitals. While some hospitals gave prophylaxis for most surgeries and some did not, some hospitals were not consistent in their use of thromboprophylaxis. This may be explained by surgeon`s preference, by a diversified treatment, or by lack of routines. We found no correlation between the use of thromboprophylaxis and the patients ASA classification.

In accordance with earlier studies (168-170) we found an increased risk of death in the acute fracture setting, and the use of thromboprophylaxis did not alter this risk. High age and high ASA class also increased the risk of death within 90 days. In the cohort

study from Young et al (170) proximal humerus fracture, anemia, congestive heart failure, and chronic lung disease increased the risk of PE.

We concluded that no association of reduced mortality with use of thromboprophylaxis was found and that the routine use of thromboprophylaxis in SA surgery can be discussed.

In 2020 the Norwegian guidelines for thromboprophylaxis in surgery was updated (171). In accordance with our results the new guidelines recommends that no thromboprophylaxis routinely should be given to patients with no earlier VTE. This recommendation is based on the fact that deep venous thrombosis is a rare complication after shoulder arthroplasty with estimates of 2/1000, and even with comorbidity the estimates are not more than 4/1000. The minimal reduction that can be achieved by treating all patients with heparin does not outweigh the risk of complications. The recommendations are, however, based on few studies (172-176) and unpublished meta-analyses and some of the studies included have risk of bias. The recommendations are in line with the results in our study and strengthens the conclusion of not giving thromboprophylaxis as a routine in shoulder arthroplasty surgery.

Patients with a history of VTE has, however, an increased risk of a new VTE after shoulder arthroplasty surgery estimated at 14/1000 by the authors of the updated guidelines, and in these patients the new guidelines recommend giving thromboprophylaxis.

For patients in need of thromboprophylaxis an oral alternative to LMWH may increase compliance and obliviate the need for nursing after the hospital stay. Oral anticoagulants include Vitamin K antagonists and direct oral anticoagulants (DOACs) which directly inhibit factor Xa or thrombin. With the introduction of oral anticoagulants, the administration of thromboprophylaxis is much more feasible to patients after the hospital stay. Guidelines from the UK and the US support the use of

DOACs as thromboprophylaxis (177, 178), however clinical experience with DOAC in shoulder surgery is limited.

5.2.2 Comparison of the Delta III and the Delta Xtend RSAs

In **paper II** we compared the implant survival, risk of revision, and reasons for revision in the Delta III and Delta Xtend reverse shoulder arthroplasties. Delta III with uncemented stem had higher risk of revision compared to Delta Xtend with cemented stem.

Delta III was the second generation of the Grammont reverse arthroplasty and introduced in 1991. The NAR started collecting data on shoulder arthroplasties in 1994, and at that time hemiarthroplasties were the most used shoulder arthroplasty in Norway (26). RSA was used only in a few selected cases. During the study period, the promising results with the early RSA led to a substantial increase in use. This is particularly evident after the introduction of the Delta Xtend in 2007. Indications have changed and RSA is now the most used implant in shoulder arthroplasty surgery in Norway (76% in 2022) (179). The early reverse shoulder arthroplasties faced challenges with high complication rates and inferior results, glenoid loosening and instability were major concerns (41, 43). Delta Xtend was developed to improve on these complications with changes in design and material. In accordance with earlier studies (48, 180), we found glenoid loosening to be the main reason for revision in the Delta III with an almost 17 times increased risk compared to the contemporary Delta Xtend with cemented stem.

Comparing the two different time periods we were faced with some challenges. Firstly, the number of Delta III arthroplasties were much smaller than that of Delta Xtend. Secondly, the indications for reverse arthroplasties changed during the study period. In the early years the RSA was used mainly for inflammatory arthritis and fracture sequela while the indications later were expanded to include acute fractures and osteoarthritis among others (141). This could influence the implant survival. The fracture patients are older and frailer and may be less likely to undergo revision. Thirdly, the experience

of the surgeons increased during the study period. Shoulder arthroplasty is an advanced surgery, and a learning curve must be expected (181). Fourthly, the follow up time was different for the two arthroplasty designs. To ensure as equal conditions for comparisons as possible between the arthroplasties, we censored the follow up at 10 years when comparing Delta III and Delta Xtend, and revisions occurring after more than 10 years were thus excluded from the analyses.

Notching and glenoid loosening was one of the common complications with the early RSAs (48, 109, 182, 183). Changes in the glenoid component with less medialization of the COR, but also increased awareness of the importance of a low placement of the glenosphere on the glenoid (45, 46) has probably led to less scapular notching, and thereby less problems with glenoid component loosening. This is also described by other authors (48).

Instability is however continuing to be the predominant cause of revision in RSA. Even if the overall risk of revision has decreased, the risk of revision due to instability was comparable in all the 4 included designs. Determining the height of the humeral stem may be more difficult when the anatomy is changed, and especially in the acute fracture setting it may be difficult to restore the anatomy and correct tension in the soft tissue. Patients with fracture sequelae may also have an altered anatomy making it difficult to place the implant at the proper height. This can lead to instability of the implant, and as the Delta Xtend was used more often for acute fractures, this may explain why the revisions due to instability have not decreased as one could expect when surgeons are more experienced with the implant. The increased experience and the promising results may also tempt the surgeons to use the implant for other diagnoses and more difficult cases that would earlier not be considered suitable for arthroplasty.

The high overall long-term implant survival for the contemporary Delta Xtend (95% at 10-years follow-up) is important to be aware of when advising patients on shoulder arthroplasty surgery.

5.2.3 Risk factors for revision of reverse shoulder arthroplasties

In **paper III** we compared the survival of different designs and different brands of RSAs after 2007 when several new brands were introduced to the Norwegian market. The two main designs, inlay and onlay humeral stems, were compared. We also investigated factors affecting the risk of revision and the reasons for revision. The main finding from the study was the high survival of all the included brands with more than 90% survival at 5 years follow up. Many different brands have been introduced in the later years, and at 10 years follow up the number at risk was small for many of them. Inlay and onlay designs had comparable risk of revision. While exploring the reasons for revision, differences emerged among the brands and various designs. However, owing to the limited data size, these differences warrant validation in other registries to ascertain whether they are due to the design or to variations in surgical technique.

A registry with detailed information on the implants will to some degree be able to classify the different brands, but when implant factors such as lateralization can be achieved in several different ways both on the implant and with bone grafts, it is almost impossible to classify this exactly for each patient individually. The goal of a registry study must be to compare groups that are as homogenous as possible. Comparing implants that are either inlay or onlay in design, as we have done in **paper III,** is one way of dealing with this problem, even if it does not take into consideration all the other options of lateralization.

In a study from the New Zealand registry, the inlay design RSA had higher survival than the onlay design, but functional outcome at 6 months were better for the onlay RSA (184). On the other hand, the Australian registry reports increased risk of revision for inlay design compared to onlay (185). As the implants evolve there are a lot of parameters that can contribute to changes in biomechanics. Several of the inlay implants now have possibilities of lateralization on the glenoid (bio-RSA or lateralized components), and the possibility of different neck shaft angles resulting in less medialization. As described by Werthel (58) there is a broad spectrum of lateralization, and implants can be customized in many ways. A simple comparison between inlay

and onlay designs cannot take all these modifications into consideration. In our study we chose to classify the implants as either inlay or onlay depending on the position of the humeral tray, but further studies should investigate the actual amount of lateralization achieved.

In our study the Delta Xtend was the most frequently used brand, and a comparison between inlay and onlay can be criticized for being a comparison between Delta Xtend and the onlay brands. We performed a subanalysis where Delta Xtend was excluded. This did not affect the outcome of comparable risk of revision with the two designs. Some brands are used at very few hospitals, and the study can be criticized for comparing surgeons and not brands. The Delta Xtend was the most used brand and the widespread use in many hospitals all over the country gives the results on survival of this brand an excellent external validity.

Even if we found increased risk of revision for some of the brands included in **paper III**, the differences could be influenced by low number of cases and surgeons. The results should be verified by others. The Orthopaedic Data Evaluation Panel (ODEP) benchmark each implant to predefined standards (number of centers using the implant, total cohort, patients at risk at time of benchmarking, and revision rate) and rating is given at www.odep.org.uk. All implants currently in use in Norway have obtain a 7A or 10A in the ODEP. ODEP 10A corresponds to at least 88% survival at 10 years, and 7A corresponds to at least 91% survival at 7 years.

RSA has become the implant of choice for proximal humerus fractures (25). This trend is supported by several studies reporting good outcomes for RSAs in this patient group (73, 74, 88, 186). There are numerous studies assessing RSA for proximal humerus fracture, but few studies explore the differences in outcomes based on fixation of the stem (187, 188). Most of these previous studies included small sample sizes, insufficient follow-up, lack of a control group, fracture sequelae, and different types of implants in the same series (189, 190). There seems to be an international trend going towards uncemented humerus stems in shoulder arthroplasty in general, but also in

RSA for proximal humerus fractures due to several advantages including shorter operation time, no cement-related complications, supposed improved biologic fixation, and ease of revision if necessary (191). A review of clinical outcomes with cemented vs uncemented RSA for proximal humerus fracture (190) found that both cemented and uncemented RSA are viable options with comparable complication rates between the two techniques. They found, however, increased risk of intraoperative humerus fracture for uncemented stems. In **paper III** we found that the use of uncemented humeral stem had higher risk of revision due to instability/dislocation than the use of cemented stem in patients with proximal humerus fracture. Most proximal humerus fractures are osteoporotic fragility fractures. These fractures are most prevalent in elderly women and in these patients the use of uncemented stems carries the risk of periprosthetic fracture both intraoperatively and postoperatively. The height of the stem can also be difficult to determine in a fracture setting where the anatomy of the proximal humerus is altered, and obtaining good stability with the press-fit stem can be challenging.

Glenoid loosening as a reason for revision was prevalent in the Delta III uncemented arthroplasties in **paper** II (6.6%). In **paper III** glenoid loosening was the reason for revision in only 0.3% of the cases, and advancements in both surgical techniques and implants could have contributed to the decreased risk of loosening.

All indications for surgery have been included in our study and in accordance with earlier studies we found the highest risk of revision for patients with fracture sequela (78, 192). The fracture sequela group consisted of both conservatively treated proximal humerus fractures, and fractures that were initially treated with internal fixation, but in the sequelae group we did not find any difference in risk of revision between patients who had previous surgery and those who did not. Previous surgery in the same shoulder has earlier been described as one of the risk factors for infection and revision of RSA in general (193). In our study we did not find increased risk of revision with previous surgery for patients with fracture sequelae, osteoarthritis or rotator cuff arthropathy.

Patients with poor functioning arthroplasty that is not revised for various reasons, for instance severe comorbidity or lack of options for revision surgery, will not be considered an implant failure in the register. These clinical failures are not presented in the implant survival analyses, and other outcomes such as patient-reported outcome measures (PROM) give a more complete view on the total failures after shoulder arthroplasty. PROM scores were added to the shoulder registration when the electronic form was introduced in 2021, and PROM scores are not analyzed in the papers included in this thesis.

In conclusion the risk of revision after reverse shoulder arthroplasty was low and all included reverse shoulder arthroplasty brands had good survival at 5-year follow-up. We found no difference when comparing inlay to onlay design RSA. Factors that were associated with an increased risk of revision were male sex, fracture sequela diagnosis, and uncemented humeral stem in acute fracture patients.

6. Conclusion

In this thesis the results of shoulder arthroplasty in Norway were evaluated.

Paper I

- The use of thromboprophylaxis in shoulder arthroplasty surgery was not associated with a reduced mortality.
- The use of thromboprophylaxis did not influence the risk of intraoperative bleeding complications, all-cause revision or revision due to infection within 1 year.

Paper II

- The Delta III with cemented stem and the Delta Xtend prostheses had a high 10-year implant survival. The Delta III with uncemented stem had a 10-year survival of 81.6% and a 20-year survival of 68.2%.
- Delta III with uncemented stem had a higher risk of revision compared to Delta Xtend with cemented stem.
- Risk of revision due to glenoid component loosening was lower for Delta Xtend, but revisons due to instability/dislocation are still a concern.

Paper III

- Survival of reverse shoulder arthroplasties were high.
- No difference in risk of revision between onlay and inlay design implants was found.
- Men and fracture sequela diagnosis had a higher risk of revision.
- Uncemented humeral stem fixation was associated with a higher risk of revision than a cemented humeral stem fixation for proximal humerus fractures.
- Instability/dislocation was the most common reason for revision in the inlay design arthroplasty, and for both acute fracture and fracture sequela diagnosis.

7. Clinical implication

Observational studies describe the results of established treatments, but cannot prove causality. Caution must be exercised when clinical conclusions are drawn. The results from registry studies can generate new hypotheses that should be tested in experimental studies and, if others observe the same results, it strengthens the conclusion. Some clinical implications can be suggested from our studies and guide clinical decision making.

- As a consequence of the results in **paper I**, one should reconsider the practice of giving all shoulder arthroplasty patients thromboprophylaxis as a routine. Instead, the use of thromboprophylaxis in each patient should probably be considered individually based on known risk factors of VTE.
- The results in **paper II** confirm that the use of Delta Xtend reverse shoulder arthroplasty yields good and predictable long-term results, and the risk of revision is low. Hospitals and surgeons utilizing this prosthesis can confidently continue their use.
- The results in **paper III** support continuous use of the currently employed implants in Norway. However, surgeons should be aware of variations in the risk of revision. Cemented humeral stems with proximal humerus fractures are already the preferred technique, and the trend towards uncemented stems is not supported by our study. As instability continues to be a dominant reason for revision, the surgeons must be attentive to this especially when treating patients with fracture sequela.

8. Future perspectives

The research on shoulder arthroplasties in the NAR is so far limited and several future studies would yield further insight and help the clinicians choose the best option for their shoulder patients.

8.1 Patients in need of thromboprophylaxis

The findings in **paper I** have already raised awareness of thromboprophylaxis in shoulder arthroplasty and there is a trend towards fewer patients receiving thromboprophylaxis with primary shoulder arthroplasties (25). The true risk of venous thromboembolisme (VTE) after shoulder arthroplasty is not known. Some studies suggest that the risk equals that of lower limb arthroplasty (175), but most studies find a lower risk in the upper extremities (125, 167). In **paper I** we found that the mortality after shoulder arthroplasty was not affected by thromboprophylaxis. The causes of death were not investigated in our study, and we do not know whether the cause of death was related to a thromboembolic event or to causes not related to the surgery. A merging of the data from NAR with the Norwegian Cause of Death Registry and with the National Patient Registry (NPR) for causes of readmission to hospital within the first year after surgery will give further insight to the true risk of VTE and causes of death.

8.2 Results of shoulder arthroplasty in the Nordic countries

Data on revision rates have been published by the Nordic arthroplasty registries. However, due to the relatively small number of cases, statistically significant differences between arthroplasty types and brands are difficult to detect. By merging data from several national registries, the amount of shoulder arthroplasties increases, and enables us to study rare complications with higher statistical power. The NARA collaboration is planning for an updated dataset with more detailed information and more variables than earlier datasets have provided. Comparing the causes of revision

in both **paper II and paper III** we found differences between the revision causes for the arthroplasties. Due to small numbers the confidence intervals were wide and concluding on clinically important differences was difficult. We adjusted for diagnosis in our study, but it could provide useful information if numbers were larger and further subdivision into more homogenous groups could be done. This will enable a study with causes of revision on a more detailed level and hence study different diagnoses and brands separately. Even if the implant is the same, the surgery and the patients are very different in shoulder arthroplasties due to fracture, osteoarthritis, or rotator cuff arthropathy. With a larger number of included arthroplasties each indication for surgery may be studied separately to clarify the challenges and risks specific to each group of patients.

8.3 Anatomic or reversed shoulder arthroplasty

In Norway most shoulder arthroplasties in the recent years are reversed shoulder arthroplasties, and in 2022 80% of all shoulder arthroplasties were reversed (25). Total anatomic shoulder arthroplasty shows good clinical results with osteoarthritis and intact rotator cuff tendons (194, 195), but in Norway reverse shoulder artrhroplasties seems to have become the preferred treatment even for primary osteoartrhritis. **Paper III** showed high survival of the reverse shoulder arthroplasties. Arguments for use of reverse shoulder arthroplasty in osteoarthritis with intact rotator cuff may be that the prevalence of rotator cuff tears in the aging population is high even if symptoms are minimal (194, 196) and that even if the cuff is intact at the time of operation, the cuff may deteriorate at a later point. An unrevised arthroplasty does not necessarily mean a well-functioning arthroplasty, and as WOOS score are currently collected from shoulder arthroplasty patients after implementation of the new electronic registration, further research should focus on which implant gives the best clinical outcome with minimal risk of revision. A registry randomised controlled study (R-RCT) with long-term follow-up and focus on both risk of revision and patient related outcome

comparing TSA and RSA in patients with intact rotator cuff would be feasible (197, 198).

8.4 Periprosthetic fractures

In **paper III** we found increased risk of revision for uncemented humeral stems with proximal humerus fractures. We suspect an underreporting of periprosthetic fractures to the registry, especially fractures that are not treated with exchange of the humeral stem (conservative or plate fixation) and a validation of the reporting could be done by comparing the hospital charts. We found 160 patients with uncemented stems for proximal humerus fractures and evaluation of these patients could be done to identify underreporting and compare them to a matched group with cemented stems.

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10. Appendices

10.1 Surgeons form

Nasjonalt Register for Leddproteser
Ortopedisk klinikk, Helse Bergen HFHaukeland
universitetssjukehus, Postboks 1400
Møllendalsbakken 7, 5021 BERGEN
Tlf 55973742/55973743

F.nr. (11 sifre).....

Navn:.....

(Skriv tydelig ev. pasientklistrelapp – **spesifiser sykehus**.)

Sykehus:.....

KNEPROTESER og andre leddproteser

Innsetting, skifting eller fjerning av protese eller protesedeler, samt bløtdelsrevisjoner for infisert protese og protesenære frakturer.

LOKALISASJON, AKTUELL OPERASJON
☐1 Kne ☐6 Håndledd
☐2 Ankel ☐7 Fingre (angi ledd) .....
☐3 Tær (angi ledd) ..... ☐8 Annet .....
☐4 Skulder ☐9 Rygg (angi nivå).....
☐5 Albue

AKTUELLE SIDE (ett kryss) (Bilateral opr. = 2 skjema)
☐1 Høyre ☐2 Venstre

TIDLIGERE OPERASJON I AKTUELLE LEDD (ev. flere kryss)
☐0 Nei
☐1 Osteosyntese for intraartikulær/leddnær fraktur
☐2 Osteotomi
☐3 Artrodese
☐4 Protese
☐5 Synovectomi
☐6 Annet (f.eks menisk og leddbåndsop.).....

AKTUELLE OPERASJON (ett kryss)
☐1 Primæroperasjon ☐2 Reoperasjon (protese tidligere)

OPERASJONSDATO (dd.mm.åå) |__|__| |__|__| |__|__|

ÅRSAK TIL AKTUELLE OPERASJON (KRYSS AV ENTEN I A ELLER B)

A. Primæroper. pga (ev. flere kryss)
☐1 Idiopatisk artrose
☐2 Rheumatoid artritt
☐3 Fraktursequele.....
☐4 Mb. Bechterew
☐5 Sequele ligamentskade
☐6 Sequele meniskskade
☐7 Akutt fraktur
☐8 Infeksjonssequele
☐9 Spondylose
☐10 Sequele prolaps kirurgi
☐11 Degenerativ skivesykdom
☐12 Rotarcuff artropati
☐13 Annet .....

B. Reoper. pga (ev. flere kryss)
☐1 Løs prox.protesedel
☐2 Løs distal protesedel
☐3 Løs patellaprotese
☐4 Luksasjon av patella
☐5 Luksasjon (ikke patella)
☐6 Instabilitet
☐7 Aksefeil
☐8 Dyp infeksjon
☐9 Fraktur av bein (nær protesen)
☐10 Smerter
☐11 Slitt eller defekt plastforing
Hvilken.....
☐12 Progresjon av artrose
☐13 Annet (f.eks tidl fjernet protese)
.....

REOPERASJONSTYPE (ev. flere kryss)
☐1 Bytte el. innsetting av distal komponent
☐2 Bytte el. innsetting av proximal protesedel
☐3 Bytte el. innsetting av hele protesen
☐4 Innsetting av patellakomp.
☐5 Bytte av patellaprotese
☐6 Bytte av plastforing
☐7 Artrodese
☐8 Amputasjon
☐9 Fjernet protesedeler (inkl. sementspacer)
Angi hvilke deler .....
.....
☐10 Bløtdelsdebridement for infisert protese
☐11 Osteosyntese av protesenær fraktur. Angi hvilket ben .....
☐12 Annet.....

BENTRANSPLANTASJON / BENERSTATNING (ev. flere kryss)

Proximalt	☐0 Nei	☐1 Ja	☐2 Benpakking	☐3 Kjegler (cones)
Distalt	☐0 Nei	☐1 Ja	☐2 Benpakking	☐3 Kjegler (cones)

ANTIBIOTIKAPROFYLAKSE ☐0 Nei ☐1 Ja

	Navn	*Dosering*	*Varighet i timer*
Medikament 1	.....	.....	.....timer
Medikament 2	.....	.....	.....timer

TROMBOSEPROFYLAKSE
☐0 Nei ☐1 Ja: Første dose ☐1 Preoperativt ☐2 Postoperativt
Medikament 1.....Dosering opr.dag.....
Dosering videre.....Varighet.....døgn
Medikament 2..... Dosering.....Varighet.....døgn

FAST TROMBOSEPROFYLAKSE
☐0 Nei ☐1 Ja, type: .....

FIBRINOLYSEHEMMER
☐0 Nei ☐1 Ja, medikament: ..... Dosering.....

DREN ☐0 Nei ☐1 Ja. Antatt varighet .....døgn

OPERASJONSTID (hud til hud) .....minutter

BLODTOMHET ☐0 Nei ☐1 Ja **BLODTOMHETSTID**..... minutter
BLODTOMHET UNDER SEMENTERING ☐0 Nei ☐1 Ja

PEROPERATIV KOMPLIKASJON
☐0 Nei ☐1 Ja,hvilke(n): .....

MINI INVASIV KIRURGI (MIS) ☐0 Nei ☐1 Ja
COMPUTERNAVIGERING (CAOS) ☐0 Nei ☐1 Ja Type:.....
PASIENTTILPASSEDE INSTRUMENTER ☐0 Nei ☐1 Ja Type:.....

ASA KLASSE (se baksiden for definisjon)
☐1 Frisk
☐2 Asymptomatisk tilstand som gir økt risiko
☐3 Symptomatisk sykdom
☐4 Livstruende sykdom
☐5 Moribund

PROTESE KNE (Bruk klistrelapper på baksiden, eller spesifiser nøyaktig)

PROTESETYPE
☐1 Totalprot. m/patella . ☐4 Patellofemoralledd prot.
☐2 Totalprot. u/patella ☐5 Bi-compartmental ☐6 Hengslet protese
☐3 Unicondylær prot ☐ Medial ☐ Lateral ☐7 Annet .....

FEMURKOMPONENT
Navn/Type/Str / evt. Katalognr.....
ev. katalognummer .....
Sentral stamme ☐0 Nei ☐1 Ja, ev. lengde .....mm
Sementert stamme ☐0 Nei ☐1 Ja
Metallforing (Wedge) ☐0 Nei ☐1 Ja
Stabilisering ☐0 Nei ☐1 Ja, bakre ☐2 Ja, annen
☐1 Sement med antibiotika – Navn .....
☐2 Sement uten antibiotika – Navn .....
☐3 Usementert

TIBIAKOMPONENT (metallplatå)
Navn/Type/Str / ev. katalognummer .....
Forlenget sentral stamme ☐0 Nei ☐1 Ja, ev. lengde .....mm
Sementert stamme ☐0 Nei ☐1 Ja
Metallforing (Wedge) ☐0 Nei ☐1 Ja
☐1 Sement med antibiotika – Navn .....
☐2 Sement uten antibiotika – Navn .....
☐3 Usementert

TIBIAKOMPONENT (plastkomponent)
Navn/Type/Str / ev. katalognummer.....
Tykkelse ..... mm
Stabilisering ☐0 Nei ☐1 Ja, bakre ☐2 Ja, annen

PATELLAKOMPONENT
Navn/Type/Str / ev. katalognummer.....
Metallrygg ☐0 Nei ☐1 Ja
☐1 Sement med antibiotika – Navn .....
☐2 Sement uten antibiotika – Navn .....
☐3 Usementert

KORSBÅND

Intakt fremre korsbånd før operasjon	☐0 Nei	☐1 Ja
Intakt fremre korsbånd etter operasjon	☐0 Nei	☐1 Ja
Intakt bakre korsbånd før operasjon	☐0 Nei	☐1 Ja
Intakt bakre korsbånd etter operasjon	☐0 Nei	☐1 Ja

PROTESE ANDRE LEDD (Bruk klistrelapper på baksiden, eller spesifiser nøyaktig)

PROTESETYPE
☐1 Totalprotese ☐2 Hemiprotese ☐3 Enkomponentprotese ☐4 Annet .....

PROKSIMAL KOMPONENT
Navn/Type/Str / ev. katalognummer.....
☐1 Sement med antibiotika – Navn .....
☐2 Sement uten antibiotika – Navn .....
☐3 Usementert

DISTAL KOMPONENT
Navn/Type/Str / ev. katalognummer.....
☐1 Sement med antibiotika – Navn .....
☐2 Sement uten antibiotika – Navn .....
☐3 Usementert

INTERMEDIÆR KOMPONENT (f.eks. caput humeri)
Navn/Type/Str/Diameter / ev. katalognummer.....

Lege .....
Legen som har fylt ut skjemaet (navnet registreres ikke i databasen).

RETTLEDNING KNEPROTESER og andre leddproteser

Registreringen gjelder innsetting, skifting eller fjerning av protese i kne, skuldre og andre ledd med unntak av hofter som har eget skjema. Ett skjema fylles ut for hver operasjon. Pasientens fødselsnummer (11 sifre) og sykehus må være påført. Aktuelle ruter markeres med kryss.
På eget Samtykkeskjema skal pasienten gi samtykke til rapportering til Leddregisteret.

Kommentarer til de enkelte punktene

AKTUELLE OPERASJON
Primæroperasjon: Dette er første totalproteseoperasjon.
Kryss av enten i A eller i B. Kryss av for alle årsakene til operasjonen. Bløtdelsrevisjon for infeksjon skal registreres selv om protesedeler ikke skiftes.

REOPERASJONSTYPE
Fjerning av protesedeler må spesifiseres og føres opp, også fjerning ved infeksjon.

BENTRANSPLANTASJON
Påsmøring av benvev rundt protesen regnes ikke som bentransplantat.

ANTIBIOTIKAPROFYLAKSE
Medikament, dose og varighet av profylaksen skal angis f.eks. slik: Medikament: Keflin, Dosering: 2g x 4, med varighet 4,5 timer.

TROMBOSEPROFYLAKSE
Medikament, dose og antatt varighet av profylaksen skal angis separat for operasjonsdagen og senere. Det skal også oppgis om pasienten står fast på tromboseprofylakse (AlbyIE, Marevan, Plavix ol).

FIBRINOLYSEHEMMER
Her føres det på om en benytter blødningsreduserende legemidler i forbindelse med operasjonen (f.eks. Cyklokapron).

PEROPERATIV KOMPLIKASJON
Dersom det foreligger komplikasjon i form av stor blødning, må mengden angis.
Dersom pasienten dør under eller like etter operasjonen, ønsker vi likevel melding om operasjonen.

ASA-KLASSE (ASA=American Society of Anesthesiologists)
ASA-klasse 1: Friske pasienter som røyker mindre enn 5 sigaretter daglig.
ASA-klasse 2: Pasienter med en asymptomatisk tilstand som behandles medikamentelt (f.eks. hypertensjon) eller med kost (f.eks. diabetes mellitus type 2) og ellers friske pasienter som røyker 5 sigaretter eller mer daglig.
ASA-klasse 3: Pasienter med en tilstand som kan gi symptomer, men som holdes under kontroll medikamentelt (f.eks. moderat angina pectoris og mild astma).
ASA-klasse 4: Pasienter med en tilstand som ikke er under kontroll (f.eks. hjertesvikt og astma).
ASA-klasse 5: Moribund/døende pasient

PROTESETYPE
Dersom det er gjort revisjon av totalprotese uten patellakomponent og REOPERASJONSTYPE er **innsetting av patellakomponent,** skal det krysses av for pkt. 1: Totalprotese med patellakomponent (dvs. protesen har nå blitt en totalprotese med patellakomponent). Ved revisjon av unicondylær protese til totalprotese brukes enten pkt. 1 eller 2.

PROTESEKOMPONENTER
Her anføres kommersielle navn, materiale, størrelse og design. Alternativt kan en føre opp protesenavn og katalognummer eller benytte klistrelapp som følger med de fleste protesene. **Denne kan limes på baksiden av skjemaet (vennligst ikke plasser klistrelapper på markeringskryss, som brukes ved scanning av skjema).**
Navnet på sementen som evt. brukes må anføres, f.eks. Palacos R+G. (Bruk helst klistrelapp)
Under femurkomponent skal evt. påsatt **femurstamme** anføres med lengde.
Med **metallforing** under femur- og tibiakomponent menes bruk av en eller flere separate metallkiler (wedges) som erstatning for manglende benstøtte.
Stabilisering er bruk av proteser med stabilisering som kompensasjon for sviktende båndapparat.
Forlenget sentral stamme under tibiakomponent (metallplatå) skal bare anføres ved bruk av en lengre påsatt stamme enn standardkomponenten.

ANDRE LEDD. PROTESETYPE
Ved bruk av hemiprotese med bare en komponent, f.eks. resurfacing i skulder, skrives dette på DISTAL KOMPONENT. Enkomponent-protese i finger/tå, skrives på PROKSIMAL KOMPONENT.

COMPUTERNAVIGERING (CAOS = Computer Aided Orthopaedic Surgery**)**
Angi firmanavn på computersystem.

MINIINVASIV KIRURGI (MIS = Minimally Invasive Surgery**)**
Her menes at kirurgen har brukt kort snitt og at det er brukt spesialinstrument laget for MIS.

PASIENTTILPASSEDE INSTRUMENTER
Her menes kutteblokker eller instrumenter som lages etter MR eller CT bilder tatt av pasienten før operasjonen. Oppgi navn på systemet.

Kopi beholdes til pasientjournalen, originalen sendes Haukeland universitetssjukehus.

Kontaktpersoner vedrørende registreringsskjema er
Seksjonsoverlege Ove Furnes, tlf. 55 97 56 90.
Overlege Randi Hole, kontaktperson (skulder), tlf. 55 97 56 79.
Overlege Yngvar Krukhaug, kontaktperson (albue/hånd), tlf. 55 97 56 88.
Ortopedisk klinikk, Haukeland universitetssjukehus. Besøksadresse: Møllendalsbakken 7.
Sekretærer i Nasjonalt Register for Leddproteser, Ortopedisk klinikk, Helse Bergen:Randi Furnes, tlf. 55 97 37 42.
Epost: nrl@helse-bergen.no Internett: http://nrlweb.ihelse.net/
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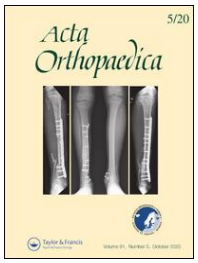
Papers I-III



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Thromboprophylaxis in primary shoulder arthroplasty does not seem to prevent death: a report from the Norwegian Arthroplasty Register 2005–2018

Randi M Hole, Anne Marie Fenstad, Jan-Erik Gjertsen, Stein A Lie & Ove Furnes

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Thromboprophylaxis in primary shoulder arthroplasty does not seem to prevent death: a report from the Norwegian Arthroplasty Register 2005–2018

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Background and purpose — There is still no consensus on whether to use thromboprophylaxis as a standard treatment in shoulder replacement surgery. We investigated the use of thromboprophylaxis reported to the Norwegian Arthroplasty Register (NAR). The primary endpoint was early mortality after primary shoulder arthroplasty with and without thromboprophylaxis. Secondary endpoints included revisions within 1 year and intraoperative complications.

Patients and methods — This observational study included 6,123 primary shoulder arthroplasties in 5,624 patients reported to the NAR from 2005 to 2018. Cox regression analyses including robust variance analysis were performed with adjustments for age, sex, ASA score, diagnosis, type of implant, fixation, duration of surgery, and year of primary surgery. An instrumental variable Cox regression was performed to estimate the causal effect of thromboprophylaxis.

Results — Thromboprophylaxis was used in 4,089 out of 6,123 shoulder arthroplasties. 90-day mortality was similar between the thromboprophylaxis and no thromboprophylaxis groups (hazard ratio (HR) = 1.1, 95% CI 0.6–2.4). High age (> 75), high ASA class (≥ 3), and fracture diagnosis increased postoperative mortality. No statistically significant difference in the risk of revision within 1 year could be found (HR = 0.6, CI 0.3–1.2). The proportion of intraoperative bleeding was similar in the 2 groups (0.2%, 0.3%).

Interpretation — We had no information on cause of death and relation to thromboembolic events. However, no association of reduced mortality with use of thromboprophylaxis was found. Based on our findings routine use of thromboprophylaxis in shoulder arthroplasty can be questioned.

Shoulder arthroplasty (SA) has gained wide acceptance as treatment for a variety of shoulder conditions, and the annual incidence rates are increasing (Lubbeke et al. 2017). Venous thromboembolism (VTE) is a recognized complication after hip and knee arthroplasties (Lie et al. 2002) but has been considered rare after SA. The number of reports of VTE after SA has increased with increasing number of SAs performed (Lyman et al. 2006, Jameson et al. 2011) and fatal outcome has also been reported (Saleem and Markel 2001, Madhusudhan et al. 2009). The true risk of VTE after SA has not been determined, and even though some studies suggest that the risk equals that of lower limb arthroplasty (Willis et al. 2009), most studies find a lower risk in the upper extremities (Isma et al. 2010, Saleh et al. 2013). Chemical thromboprophylaxis reduces the rates of symptomatic VTE following lower limb arthroplasty and is supposed to reduce mortality from thromboembolic complications (Dahl 1998, Senay et al. 2018). Thromboprophylaxis remains controversial among surgeons because it may carry a higher risk of bleeding, wound complication, and reoperation after orthopedic surgery (Kwong et al. 2012).

Guidelines on thromboprophylaxis exist in Norway and in other countries (SIGN 2010, Falck-Ytter et al. 2012, Kristiansen et al. 2014, National Institute for Health and Clinical Excellence 2018, Samama et al. 2018). While thromboprophylaxis is recommended for all patients undergoing hip or knee arthroplasties, there are still no evidence-based guidelines specific for SA. Due to the low number of SAs performed and the low rate of deaths due to thromboembolic events, a randomized trial would not be feasible. Hence, the best option to study the effect of thromboprophylaxis is large cohort studies (Fender et al. 1997). Using an observational population-based design with data from the Norwegian

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Arthroplasty Register (NAR) we studied the use of thromboprophylaxis in patients undergoing SA. Our primary endpoint was the influence of thromboprophylaxis on 90-day mortality. Secondary endpoints were intraoperative bleeding complications and revision due to all causes and due to infection within 1 year.

Patients and methods

This study was performed according to the Reporting of studies Conducted using the Observational Routinely collected health Data (RECORD) checklist.

The NAR started collecting data on shoulder arthroplasties in 1994. All hospitals in Norway performing SAs report to the register (Fevang et al. 2009). After each operation the surgeon fills in a 1-page paper form, which includes details on the surgical procedure and implants with catalogue numbers. In addition, the form includes information on age, sex, indication for operation, duration of surgery, and intraoperative complications including major bleeding. From 2005 information also includes details on chemical thromboprophylaxis and comorbidity according to the ASA classification. The completeness of reporting of primary SAs in the NAR was 95% for primary operations compared with the Norwegian Patient Registry in 2017–2018 (Furnes et al. 2020).

All patients operated on with SA in the period studied were included regardless of the cause for operation. Rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, seronegative arthritis, and systemic lupus erythematosus were grouped together and categorized as inflammatory arthritis. Several diagnoses could be given for each operation, and in cases with more than 1 diagnosis we used the hierarchy developed by the Nordic Arthroplasty Register Association (NARA) (Rasmussen et al. 2016).

The NAR uses the unique personal ID given to each inhabitant of Norway to link the primary shoulder arthroplasty to subsequent revisions and reoperations. Revisions and reoperations are reported equivalent to the primary operation. A revision is defined as the insertion, exchange, or extraction of any of the prosthesis components while a procedure without insertion, exchange, or extraction of components is registered as a reoperation. Multiple reasons for revision can be marked on the form. In cases with more than 1 reason for revision the hierarchy developed by the NARA group was used to determine 1 main reason for revision. Reoperations without the exchange or extraction of components were reported to the register from 2011. In our dataset there were no reported reoperations.

The NAR was linked to the National Population Register and information on death and emigration was available for all patients. Deaths in the first 90 days after surgery were defined as primary outcome, as deaths after this period were considered less likely to be related to the index procedure. Reported intraoperative bleeding complications and revisions during the first year after surgery were also included in the analyses.

All 6,972 primary shoulder arthroplasties reported to NAR in the period 2005–2018 were eligible for inclusion in the study. No patients emigrated during the study period. We excluded 849 operations with missing information in one or more of the variables of interest. Finally 6,123 cases were included in the study.

Statistics

Pearson's chi-square test was used for comparison of categorical variables.

Survival time for the 2 subgroups of patients was calculated using Kaplan–Meier estimates. Endpoint was death of any cause within 90 days. Cox regression analyses were used to calculate hazard ratios (HRs) for postoperative deaths and risk of revision between patients receiving thromboprophylaxis and those not receiving prophylaxis, with adjustments for possible confounding of age, sex, ASA score, diagnosis, type of implant (anatomic total, reversed, or hemiarthroplasty), fixation (cemented or uncemented humerus stem), duration of surgery, and year of surgery.

Bilateral cases were treated in the descriptive part as if they were independent, while the adjusted HRs were calculated using robust variance estimates to account for bilateral SAs. Calculation of the robust variance estimates follows the counting process formula of Andersen and Gill (Andersen and Gill 1982, Therneau and Grambsch 2000).

As an alternative to the adjusted Cox regression, we estimated the causal effect of thromboprophylaxis using an instrumental variable (IV) approach. This analysis follows the methods described by MacKenzie et al. (2014) for IVs in a Cox regression model using the statistical package R (R Foundation for Statistical Computing, Vienna, Austria). As instrument, we applied the hospital's annual propensity for using thrombosis prophylaxis. Hence, the IV approach assumes that the hospital is related to the mortality only through the use of thrombosis prophylaxis, and that the hospital is independent of unobserved covariates. Under these conditions the estimated HR can be interpreted as a causal HR of thrombosis prophylaxis on mortality.

All tests were 2-sided and p-values below 0.05 were considered statistically significant.

Follow-up started on the day of the primary arthroplasty and ended on the date of death or at 90 days for the mortality analyses and at 1 year after surgery for the revision analyses. All analyses were repeated stratifying on age, sex, ASA classification, diagnosis, and arthroplasty type in order to study the potential differences in effect of thromboprophylaxis on outcomes in subgroups of patients.

Analyses were performed using the package IBM SPSS statistics version 24.0 (IBM Corp, Armonk, NY, USA) and the statistical package R Version 4.0.0 (R Foundation, Vienna, Austria).

Table 1. Patient and procedure characteristics at primary shoulder arthroplasties relative to thromboprophylaxis or no thromboprophylaxis reported to the Norwegian Arthroplasty Register 2005–2018

Factor	Thromboprophylaxis No	Yes	p-value
Number of procedures	2,034 (33)	4,089 (67)	
Women	1,429 (70)	2,846 (70)	0.6 [a]
Mean age at surgery (SD)	70.7 (10.8)	70.9 (10.7)	0.6 [b]
Age group			0.07 [a]
≤ 64 years	568 (28)	1,035 (25)	
65–74 years	697 (34)	1,484 (36)	
≥ 75 years	769 (38)	1,570(38)	
ASA class			0.02 [a]
1–2	1,329 (65)	2,546 (62)	
3–4	705 (35)	1,543 (38)	
Arthroplasty type			< 0.001 [a]
TSA	355 (18)	887 (22)	
RSA	816 (40)	1,957 (48)	
SHA	623 (31)	965 (24)	
Other	240 (12)	280 (7)	
Diagnosis			0.01 [a]
Primary arthritis	740 (36)	1,584 (39)	
Acute fracture	583 (29)	1,068 (26)	
Fracture sequelae	294 (15)	578 (14)	
Rotator cuff arthropathy	193 (9.5)	323 (7.9)	
Inflammatory arthritis	156 (7.7)	357 (8.7)	
Other	68 (3.3)	179 (4.4)	
Duration of surgery			
in minutes, mean (SD)	109 (42)	114 (37)	< 0.001 [b]
Fixation of stem			< 0.001 [a]
Cemented	895 (44)	2,396 (59)	
Uncemented	1,139 (56)	1,693 (41)	

TSA = total shoulder arthroplasty, RSA = reverse shoulder arthroplasty, SHA = stemmed hemiarthroplasty.
[a] Pearson's chi-square test;
[b] Student's t-test.

Ethics, funding, and potential conflicts of interests

The NAR has permission from the Norwegian Data Inspectorate to collect patient data based on written consent from the patients (ref 24.1.2017: 16/01622-3/CDG). The Norwegian Arthroplasty Register is financed by the Western Norway health authorities. The authors declare no conflict of interest.

Results

4,089 cases received thromboprophylaxis and 2,034 did not receive thromboprophylaxis. Low molecular weight heparin (LMWH) was the dominant medication used. 2,778 patients were treated with dalteparin and 1,201 patients with enoxaparin (68% and 29% of the patients receiving thromboprophylaxis respectively).

Patient and procedure characteristics for the 2 groups are shown in Table 1. The patients receiving thromboprophylaxis had statistically significantly higher mean ASA class and longer mean duration of surgery. Patients operated on with a reverse shoulder arthroplasty (RSA) more frequently received thromboprophylaxis compared with patients operated on with

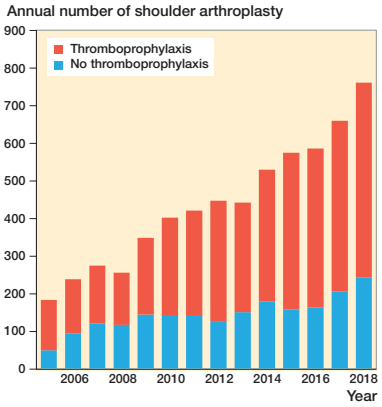

Figure 1. Change in the use of thromboprophylaxis over time, Norwegian Arthroplasty Register 2005–2018.

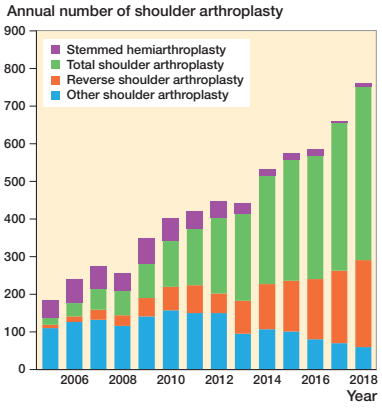

Figure 2. Change in the use of different arthroplasty design over time, Norwegian Arthroplasty Register 2005–2018.

stemmed hemiarthroplasty (SHA) and total shoulder arthroplasty (TSA) ($p < 0.001$).

There was an increase in the use of thromboprophylaxis over time in the period studied (Figure 1). The use of hemiarthroplasty dominated in the earlier years of this period, and the use of RSAs and TSAs increased in the later years (Figure 2).

Risk of death

We identified 50 deaths within 90 days in the period studied, 35 in the thromboprophylaxis group and 15 in the group with no thromboprophylaxis (Figure 3). Adjusted HR showed no significant difference between the two groups (HR 1.2; CI 0.6–2.2) with the no thromboprophylaxis group as reference. Using the IV approach, we found a non-significant causal effect of thromboprophylaxis on 90-day mortality (HR 1.1; CI 0.6–2.4) (Table 2).

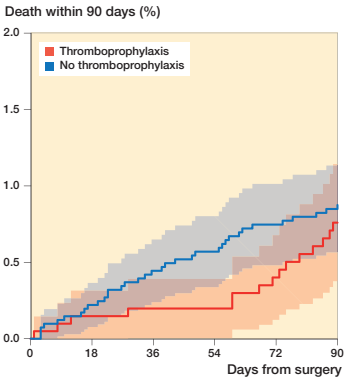

Figure 3. Kaplan–Meier curve showing the death rate up to 90 days after surgery in patients with and without thromboprophylaxis with 95% CI.

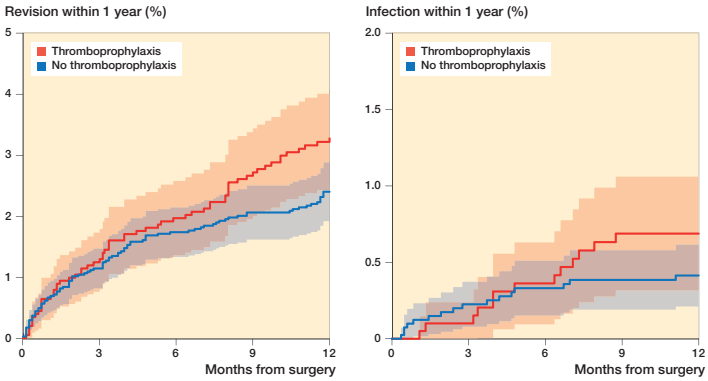

Figure 4. Kaplan–Meier curve showing the revision rate due to all causes (A) and due to infection (B) up to 1 year with 95% CI.

Table 2. Kaplan–Meier (K–M) estimated risk of death at 90 days: shoulder arthroplasties reported to the Norwegian Arthroplasty Register 2005–2018

	Deaths at 90 days	At risk at 90 days	K–M % deaths (95% CI)	Adjusted HR (95% CI)	IV adjusted HR (95% CI)
No thromboprophylaxis	15	1,928	0.8 (0.4–1.2)	1	1
Thromboprophylaxis	35	3,859	0.9 (0.7–1.1)	1.2 (0.6–2.1)	1.1 (0.6–2.4)

Cox adjusted hazard ratio (HR) with robust variance estimates adjusted for age, sex, ASA class, diagnosis, arthroplasty type, use of cement in humerus, duration of surgery and time period.
IV = Instrument variable approach.

Compared with patients with primary osteoarthritis, patients with acute fractures had a higher 90-day mortality (HR 3.4; CI 1.2–9.5). A similar tendency was found for patients with sequelae after fracture, but the difference was not statistically significant. Patients with rotator cuff arthropathy or inflammatory arthritis did not have increased 90-day mortality compared with patients with primary osteoarthritis (Table 3, see Supplementary data). We found higher 90-day mortality after fracture-related surgery (acute fracture and fracture sequelae) than after non-fracture-related surgery 1.6% (CI 1.0–2.2) vs. 0.3% (CI 0.1–0.5).

Old age (> 75 years), high ASA class (≥ 3), and acute fracture diagnosis statistically significantly increased 90-day mortality. The risk of death was not significantly changed in the different time periods studied (Table 3, see Supplementary data).

ASA classification and age

Since both increasing ASA class and high age increased mortality, we also performed Cox regression analysis with patients stratified into 3 different risk groups, dependent on both age (≥ 80 based on the Norwegian guidelines for thromboprophylaxis) and ASA classification. This analysis suggested an even stronger correlation between age, ASA class, and the risk of death. We found no statistically significant difference in the distribution of thromboprophylaxis in the different risk groups and use of thromboprophylaxis did not alter the risk of death at 90 days (Table 4, see Supplementary data).

Revision risk

There were 155 revisions within the first year. Of these, 29 revisions were performed due to deep infections (16 in the thromboprophylaxis group and 13 in the no thromboprophylaxis group). 62 revisions were due to loosening of 1 or more of the components without deep infection recorded. Risks of revision of any cause (HR 0.8; CI 0.6–1.1) and for infection (HR 0.6; CI 0.3–1.2) were similar between the study groups (Table 5, see Supplementary data, Figure 4). No reoperations were recorded.

Intraoperative complications

182 intraoperative complications were registered. Extensive intraoperative bleeding was reported in 17 cases, 12 in the thromboprophylaxis group (0.3%) and 5 in the no throm-

boprophylaxis group (0.2%). Only 3 of the 12 patients with extensive bleeding in the thromboprophylaxis group had preoperative initiation of the thromboprophylaxis.

Discussion

Our main finding was that there was no association between the use of thromboprophylaxis and the risk of death in the postoperative period. As expected, we found that high age, high ASA class, and fracture diagnosis (acute fracture and fracture sequelae) increased the 90-day mortality. Earlier studies on thromboprophylaxis in shoulder arthroplasty surgery include fewer patients, and even though the number of deaths in our study is low the incidence is comparable to earlier studies.

Thromboprophylaxis after shoulder surgery is still a controversial issue: the national guidelines in Norway and other countries are vague. The guidelines in the United Kingdom (National Institute for Health and Clinical Excellence 2018) recommends that the surgeon "Consider VTE prophylaxis for people undergoing upper limb surgery if the person's total time under general anaesthetic is over 90 minutes or where their operation is likely to make it difficult for them to mobilise." Based on these recommendations the vast majority of shoulder arthroplasty patients will require thromboprophylaxis. However, VTE events are rare after planned shoulder surgery (0.01–0.5%) (Lyman et al. 2006, Jameson et al. 2011, Navarro et al. 2013).

In the study from Jameson et al. (2011) the 90-day mortality rates after planned shoulder surgery were low (0.03–0.5%), and no change in the mortality rate after the introduction of the 2007 NICE guidelines could be found. Our results with 0.3% 90-day mortality in non-fracture SA surgery support Jameson's findings.

VTE events are more common in the proximal humerus fracture setting (0.4–1.7%) (Navarro et al. 2013) but compared with other orthopedic procedures the risk is still low (Dahl et al. 2003).

In a large cohort study from Young et al. (2015) proximal humerus fracture, anemia, congestive heart failure, and chronic lung disease were 4 independent predictors for PE after shoulder arthroplasty. As expected, increasing age, fracture diagnosis, and high ASA class correlated with increased mortality in our cohort.

We found increased use of thromboprophylaxis in shoulder arthroplasty surgeries during the studied period. The Norwegian guidelines (Kristiansen et al. 2014) indicating that thromboprophylaxis should be used have probably led to some hospitals changing their use of prophylaxis, but some hospitals were not consistent in their use of prophylaxis. This may be explained by surgeon's preference or by lack of routines. It could also reflect diversified treatment where patients considered at risk are given thromboprophylaxis. The use does not seem to correlate with the patient's ASA class, but the ASA class does not fully account for risk factors like previous DVT or other predisposing factors and may therefore not necessarily be a good measure of the actual risk of VTE and mortality. In our study the use of different arthroplasty types changed during the period studied and some of the differences in the use of thromboprophylaxis in different arthroplasties can be explained by the change of indications for the arthroplasty type.

The lack of consensus on the use of prophylaxis in shoulder replacement surgery is reflected by our data, where some hospitals seem to give thromboprophylaxis as a routine and others do not. Some hospitals perform more elective surgery and have more rheumatoid patients while other perform more fracture surgery, and this may also influence the hospital's routines for thromboprophylaxis. The cost-effectiveness of daily injections of LMWH has to be considered. It is inconvenient for the patient and resource demanding for the healthcare system if patients cannot administer the injections themselves, and there are potential complications. However, we found no difference in intraoperative bleeding complications between the 2 groups and the use of thromboprophylaxis did not seem to affect the risk of revision due to infection. Kwong et al. (2012) found insufficient data in the literature to confirm or refute the hypothesis that postoperative bleeding due to VTE prophylaxis in hip and knee arthroplasty contributes to increased risk for wound infection.

Navarro et al. (2013) observed no difference in 90-day mortality by procedure type (reverse shoulder arthroplasties, total shoulder arthroplasties, or hemiarthroplasties), but a higher mortality in trauma patients compared with elective in his retrospective database review from the Kaiser Permanente registry. In our cohort we found increased risk of mortality in the acute fracture setting, and use of thromboprophylaxis did not alter this risk. Navarro found that only 1 of the 13 deaths observed in his study could be attributed to complications of PE, and this indicates that this is a fragile group of patients with several comorbidities and increased risk of death. In accordance with this we found increased risk of death in the acute fracture group and also higher age in this group.

By dividing patients into risk groups and combining the ASA classification with age, Dale et al. (2020) showed that high-risk patients had nearly 9 times the risk of adjusted perioperative death after primary total hip arthroplasty compared with low-risk patients. In our study the use of thromboprophylaxis did not alter the risk of death within 90 days in any of the risk groups. This does not support the routine use of thromboprophylaxis to prevent death.

The bilateral observations in register studies can be dealt with in different ways (Ranstam et al. 2011). Also, Lie et al. (2004) studied the influence of bilateral hip arthroplasties on survival analyses and concluded that in analyses of arthroplasty survival dependencies should be considered, but ignoring the possible dependencies does not necessarily have an impact on the result. We performed Cox regression analyses

with robust variance analyses to account for the bilateral cases and found only small differences (statistically non-significant) between unadjusted and adjusted risk of death. Using an instrument variable analysis approach to estimate the causal effect of thrombosis prophylaxis confirmed the results from the standard analysis.

Strengths and limitations

This is a nationwide observational cohort study from the Norwegian Arthroplasty Register. The strengths of a register study are the large number of patients and the possibility to study rare events. All hospitals performing shoulder arthroplasties in Norway are reporting to the register and the completeness of reporting primary cases is 95% (Furnes et al. 2020). Information on death and migration was available from Statistics Norway, allowing for nationwide cohort studies with complete follow-up. We do not, however, have access to the cause of death or readmissions to hospital due to VTE or bleeding in these patients. Lie et al. (2002) studied 67,000 hip arthroplasties and early postoperative mortality by linkage to the cause of death registry. They found that vascular causes of death were commonest, with the subcategory thromboembolic complications as the most frequent cause. Even though we do not have access to cause of death in our material we might assume that thromboembolic complications are also a common cause of death in shoulder arthroplasty surgery. This is confirmed in a study from the Danish Shoulder Arthroplasty Registry (Amundsen et al. 2016). They reported the 90-day mortality and the reasons for death between 2006 and 2012. In their study, approximately 30% of deaths were reported with a cardiac or pulmonary cause. In light of the results from Amundsen's study we can assume that the number of deaths related to thromboembolic events in our study, with only 35 and 15 deaths in the 2 groups, were low and probably insufficient to make any clear recommendations.

The use of thromboprophylaxis as a standard method of treatment varies among hospitals. This might influence the result, as different surgeons may have different results. The instrumental variable analysis accounted for these differences by applying the hospitals' propensity for using thromboprophylaxis in the model and the results from the standard analysis were confirmed.

An intraoperative bleeding complication was recorded only if the surgeon considered it to be extensive, and the amount of bleeding was not recorded. The completeness of the registration of complications has not been investigated. The findings regarding intraoperative complications must hence be interpreted with caution, and the incidence of such complications is most likely higher than reported. Until 2011, reoperation due to bleeding or hematoma was not reported to the register unless a revision of the prosthesis was also performed. From 2011 all reoperations should be reported to the register, but the completeness of this registration is not known and may be underreported.

Conclusion

The use of thromboprophylaxis does not seem to reduce the overall low mortality and the use of thromboprophylaxis as a routine in shoulder arthroplasty surgery to prevent thromboembolic complications leading to death can be discussed. We cannot exclude that subgroups of patients with a high risk of VTE, such as earlier VTE events, may benefit from thromboprophylaxis.

Supplementary data

Tables 3–5 are available as supplementary data in the online version of this article, http://dx.doi.org/10.1080/17453674.2021.1906595

RMH performed the analyses of the data and wrote the manuscript. AMF and SAL contributed with statistical advice. All authors contributed to the conception and design of the study, critical analyses of the data, interpretation of the findings, and critical revision of the manuscript through all stages of the study.

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The Delta III and Delta Xtend reverse shoulder arthroplasty—risk of revision and failure mechanisms: a report on 3650 cases from the Norwegian Arthroplasty Register 1994-2021

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Background: The Delta reverse shoulder arthroplasty (RSA) is commonly used worldwide and is the most frequently used RSA in Norway. The aim of this registry-based study was to report 10- and 20-year implant survival, risk of revision, and reasons for revision in 2 consecutive time periods for Delta III (1994-2010) and Delta Xtend (2007-2021) prostheses.
Methods: We included 3650 primary RSAs reported to the Norwegian Arthroplasty Register: 315 Delta III (42% cemented stems) and 3335 Delta Xtend (88% cemented stems). We used Kaplan-Meier analyses to investigate implant survival. The reasons for revision were compared for the 2 designs and fixation technique. Factors that could influence the risk of revision, such as implant design, fixation technique, and patient factors, were investigated using Cox regression analyses with adjustments for age, sex, and diagnosis.
Results: Patients operated with Delta III were more likely to be diagnosed with inflammatory disease or fracture sequela, whereas acute fracture, osteoarthritis, and cuff arthropathy were the most frequent indications for Delta Xtend. Ten-year survival was 93.0% (95% confidence interval [CI]: 87.0-99.0) (cemented stem) and 81.6% (95% CI: 75.3-87.9) (uncemented stem) for Delta III and 94.7% (95% CI: 93.3-96.1) (cemented stem) and 95.7% (95% CI: 88.3-100) (uncemented stem) for Delta Xtend. Twenty-year survival for Delta III (uncemented stem) was 68.2% (95% CI: 58.8-77.6). Compared with DeltaXtend (cemented stem) at 10-year follow-up, we found a higher risk of revision for Delta III (uncemented stem) (hazard ratio [HR]: 2.9, 95% CI: 1.7-5.0), whereas no significant difference was found for Delta III (cemented stem) and Delta Xtend (uncemented stem). The most common reason for revision of Delta III (uncemented stem) was glenoid loosening followed by deep infection and instability. Instability was the most frequent revision cause for Delta Xtend (both cemented and uncemented stem). Men had an overall higher revision risk than women (HR: 2.8 [95% CI: 2.0-3.9]), and patients with fracture sequela had increased risk for revision (HR: 2.8, 95% CI: 1.7-4.7) compared with patients with osteoarthritis.
Discussion: We found that Delta III (uncemented stem) had a higher risk of revision compared with Delta Xtend (cemented stem). The risk of revision for glenoid component loosening was lower for Delta Xtend, but revisions due to instability/dislocation are still a concern. This register study cannot determine whether the differences found were caused by differences in implant design or other factors that changed during the study period. Risk of revision may have been affected by the indication for primary operation.

The Norwegian Arthroplasty Register has permission from the Norwegian Data Inspectorate to collect patient data based on written consent from the patients (ref: 24.1.2017: 16/01622-3/CDG) and comply by the Norwegian and EU data-protection laws.

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In 1985, Grammont introduced his concept for reverse shoulder arthroplasty (RSA) with a medialized and distalized center of rotation, as well as a nonanatomic neck-shaft angle of 155°.[5,17,18] In the second generation of the Grammont (Delta III; DePuy Synthes Warsaw, IN, USA), introduced in 1991, the center of rotation was further medialized to the native glenoid face, and the back of the glenoid baseplate was coated with hydroxyapatite (HA) to improve fixation.

By lengthening the arm and increasing deltoid tension, Delta III was successful in restoring the range of motion in cuff-deficient patients, but still rotation often remained limited, and failure to restore sufficient tension in the deltoid could result in instability.[6] Scapular notching was also a concern because it leads to progressive bone loss of the scapular neck and subsequent loosening of the glenoid component.[22]

Delta Xtend (DePuy Synthes) was introduced in 2006 as a successor to Delta III. The implant had less congruent humeral inserts to prevent polyethylene wear and improve range of motion (Fig. 1). The glenoid component was modified to a smaller baseplate with a curved back surface and the possibility of an eccentric glenosphere to allow inferior overhang.[42,30] The HA coating on the stem intended for uncemented fixation is the same on Delta III and Delta Xtend, but Delta Xtend has higher roughness underneath the coating. Delta III had a modular stainless steel polished stem with (intended for uncemented fixation) or without HA coating (intended for cemented fixation). Delta Xtend has 2 different stem options; the modular Delta Xtend stem is TiA6V grit blasted with HA coating, and the monobloc Delta Xtend stem is polished CoCr intended for cemented fixation. Glenoid components were also changed from stainless steel in Delta III to TiA6V + HA for the metaglene (baseplate) and CoCr for the glenosphere in Delta Xtend. Glenoid components are intended for uncemented fixation in both Delta III and Delta Xtend.

Delta Xtend is widely used globally.[3,26,25] Precise knowledge of the probability and implications of the various complications is imperative for the best choice of implant for RSA patients.

Two papers have reported improved short-term clinical outcomes and survival for Delta Xtend compared with Delta III.[1,21] In addition, some retrospective case series with long-term outcomes have been reported,[4,11] but to our knowledge, this is the first registry-based study to report on 20-year follow-up for RSAs.

Based on data in the Norwegian Arthroplasty Register (NAR), the aim of this study was to report 10- and 20-year implant survival, risk of revision, and reasons for revision in 2 consecutive time periods for Delta III (1994-2010) and Delta Xtend (2007-2021) prostheses.

Patients and methods

The NAR has collected data on shoulder arthroplasties on a national level since 1994.[19]

The completeness of primary shoulder arthroplasty data in the NAR was 90.8% in 2019-2020 and 84.6% for revisions.[15] The NAR collects surgical data reported on a 1-page paper form filled in by the surgeon immediately after the surgery. Data collected include the name of the operating hospital, date of operation, indication for surgery, type of surgery, implant details on product number level, type of fixation, laterality, and intraoperative complications, as well as patient-related factors such as age, sex, ASA score, and information on any former surgery in the shoulder.[12,19] Several diagnoses could be given for each operation, and in cases with more than 1 diagnosis, we used the hierarchy developed by the Nordic Arthroplasty Register Association (NARA).[32] The NAR uses the unique personal ID given to each inhabitant in Norway to link the primary shoulder arthroplasty to any subsequent implant revisions or other reoperations. A revision is defined as the insertion, exchange, or removal of any of the prosthesis components, whereas a procedure without insertion, exchange, or removal of components is registered as a reoperation. Reoperations have been reported since 2011, and these procedures (n = 5) were excluded in the survival analyses in the present study. Reasons for revision are reported. More than 1 reason for revision can be given in each case, and the hierarchy developed by the NARA was used in the analyses for revision causes where more than 1 reason was given.[32]

Information regarding deaths and emigrations was obtained from the Norwegian National Population Register.

Between 1994 and 2021, 11,287 primary shoulder arthroplasties were reported to the NAR, including 5079 RSAs. Delta III and Delta Xtend were used in 3650 of these procedures (Fig. 2). Delta III (n = 315) was used from 1994 until 2010 and was gradually replaced by Delta Xtend (n = 3335) from 2007 (Fig. 3). All primary Delta RSAs were included in the study. We compared the following 4 implant groups, all with uncemented glenoid components:

(1) Delta III, cemented stem (n = 133)
(2) Delta III, uncemented stem (n = 182)
(3) Delta Xtend, cemented stem (n = 2947)
(4) Delta Xtend, uncemented stem (n = 388)

Statistical analysis

Descriptive statistics were used to give an overview of the patient demographics. The median time of follow-up in the groups was

Figure 1 From left to right: Delta III (cemented stem), Delta III (uncemented stem), Delta III glenoid components, Delta Xtend (cemented stem), Delta Xtend (uncemented stem), and Delta Xtend glenoid components. Reprinted with permission from Ortomedic/DePuy Synthes.

estimated by the reverse Kaplan-Meier method. Results are presented with 95% confidence intervals (CIs).

Implant survival with an endpoint of all revisions were estimated by a Kaplan-Meier analysis with 10 years of follow-up in each group and, in addition, 20 years of follow-up for Delta III with censoring at the time of revision, death, emigration, or end of study (December 31, 2021). If a patient had sequential revisions, only the time to the first implant revision was included in the analyses.

To investigate the risk of revision, we compared Delta III and Delta Xtend, with cemented and uncemented stem using Cox multiple regression analyses for each revision cause according to the NARA hierarchy adjusted for age, sex, and diagnosis. We also compared cemented and uncemented stems within each implant. The proportional hazards assumption was evaluated graphically and fulfilled for follow-up of 0-2 years and 2-10 years, respectively.[31] The results are presented for the entire period. In addition, competing risk analyses were performed by calculating the subhazard ratios (SHRs)[14,23] for each cause of revision. The Fine and Gray method is a regression model expressed as SHRs with the possibility to adjust for relevant covariates. The reason to present the SHRs was to calculate correct estimates for revision for each cause separately. The SHRs describe the relative effect of potential covariates on the subdistribution hazard function. The endpoint was revision due to a specific cause, with revision due to all other causes as the competing factor. If the patient died or emigrated, the follow-up time was censored.[2]

All tests were 2-sided, and *P* values below .05 were considered statistically significant.

All statistical analyses were performed using SPSS Statistics (version 26.0.1.0; IBM Corp., Armonk, NY, USA), R version 4.0.2 (R Centre for Statistical Computing), and Stata/SE 17.0.

Results

The mean age of the study population was 73 years, and 75% were women. Female patients were more frequent in all study groups, but there were more men in the Delta Xtend (uncemented stem) group (42%) compared with the other implant groups (13%-24%). Baseline data for each of the 4 implant groups are shown in Table I. Inflammatory arthritis was the most common indication for the Delta III prostheses especially in the uncemented stem group, whereas acute fracture, primary osteoarthritis, and rotator cuff arthropathy were the most frequent indications for the Delta Xtend prostheses.

Risk of revision

In total, 159 arthroplasties were revised. To ensure as equal basis for comparison as possible between the arthroplasties, we censored the follow-up at 10 years when comparing Delta III and Delta Xtend. Revisions occurring after more than 10 years of follow-up (n = 12) were excluded from the SHR analyses. These revisions were all Delta III prostheses and were performed for either deep infection (n = 4), glenoid component loosening (n = 7), or polyethylene wear (n = 1).

Kaplan-Meier survival rates for the 4 implant groups are shown in Table II and Fig. 4.

Delta III (uncemented stem) had poorer survival than the other implant groups at 10 years (82% vs. 93%-96%) and 68% survival at 20 years.

Adjusted for age, sex, and diagnosis, Delta III (uncemented stem) had an almost 3 times higher risk of revision at 10 years compared with Delta Xtend (cemented stem) (HR: 2.9, 95% CI: 1.7-5.0, $P < .001$). No statistically significant difference was found for Delta III (cemented stem) or Delta Xtend (uncemented stem) compared with Delta Xtend (cemented stem) (Table III). When comparing uncemented and cemented stems for each implant separately, there was a tendency toward increased risk for revision for Delta III (uncemented stem) compared with Delta III (cemented stem), but the difference was not

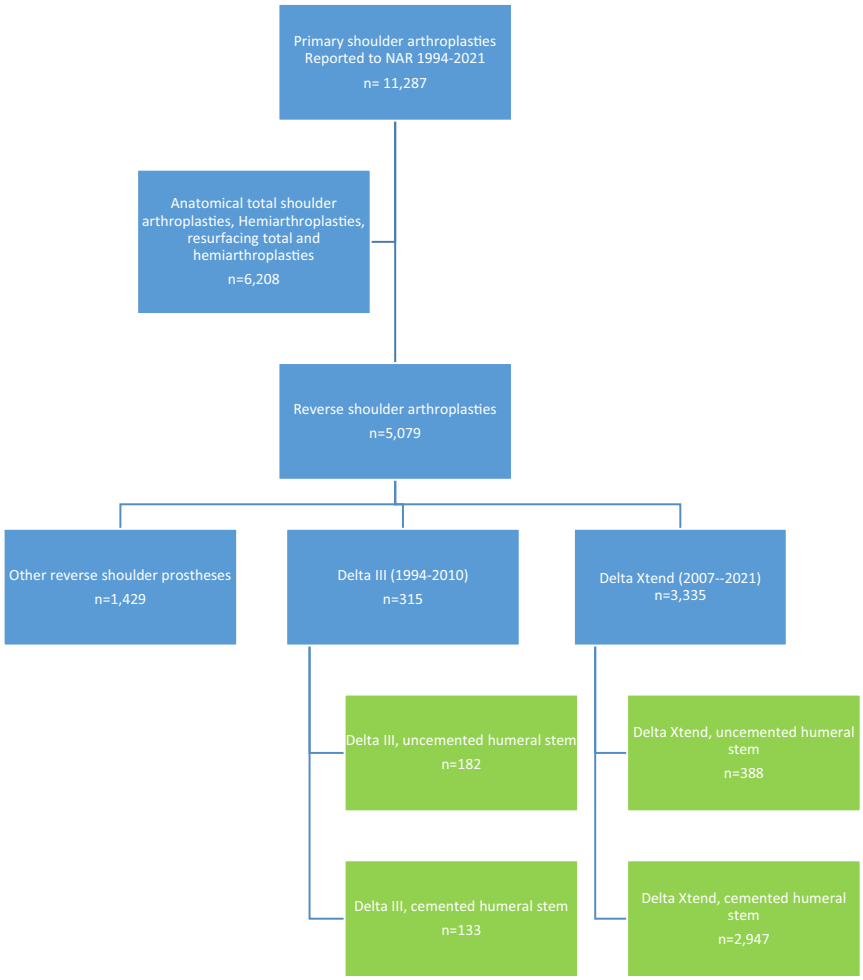

Figure 2 Inclusion and exclusion of shoulder arthroplasty patients from the Norwegian Arthroplasty Register (NAR) from 1994 to 2021. The 4 patient groups are highlighted by green boxes.

statistically significant (HR: 2.3, 95% CI: 0.95-5.30, $P = .064$) (Table IV). There was no statistically significant difference in risk for revision between Delta Xtend (uncemented stem) and Delta Xtend (cemented stem) (HR: 1.0, 95% CI: 0.59-1.95, $P = .808$) (Table V).

Men had almost 3 times increased risk of revision compared with women. This increased risk was mostly due to infection and dislocation. Arthroplasties for fracture sequelae had almost 3 times increased risk of revision compared with arthroplasties for osteoarthritis (Table III).

When used for patients with osteoarthritis, Delta III prostheses with both uncemented and cemented stems had a higher risk of revision compared with Delta Xtend with cemented stem (HR: 6.5, 95% CI: 2.2-19, $P = .001$, and HR: 6.0, 95% CI: 1.2-29, $P = .03$, respectively) (data not shown in the tables). When used for fracture sequelae, inflammatory arthritis, and rotator cuff arthropathy, no statistically significant differences in survival were found. There were too few patients with acute fracture operated with the Delta III prostheses to compare revision risk for this group of patients.

Reasons for revision are given in Table VI. The most frequent reasons for revision with 10-year follow-up were dislocation/instability (n = 51), deep infection (n = 40),

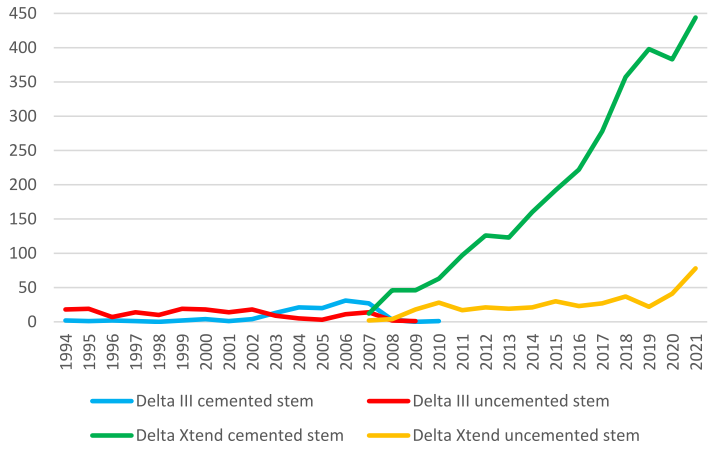

Figure 3 Primary operations with Delta reverse shoulder arthroplasties in the Norwegian Arthroplasty Register, 1994-2021.

Table I Demographics of the study population of 3650 Delta reverse shoulder arthroplasties from the Norwegian Arthroplasty register, 1994-2021; all glenoid components uncemented

	Delta III		Delta Xtend	
	Cemented stem (n = 133)	Uncemented stem (n = 182)	Cemented stem (n = 2947)	Uncemented stem (n = 388)
Women, n (%)	115 (87)	153 (84)	2247 (76)	225 (58)
Age at surgery (yr), mean ± SD	72 ± 10	69 ± 11	74 ± 8.9	72 ± 8.8
Age group (yr), n (%)				
<55	10 (8)	20 (11)	92 (3)	19 (5)
55-64	22 (17)	39 (21)	341 (12)	47 (12)
65-74	42 (32)	60 (33)	1078 (37)	169 (44)
75+	59 (44)	63 (35)	1436 (49)	153 (39)
Diagnosis, n (%)				
Inflammatory arthritis	42 (32)	104 (58)	112 (4)	43 (11)
Fracture sequelae	38 (29)	26 (14)	560 (19)	24 (6)
Primary osteoarthritis	26 (20)	33 (18)	550 (19)	155 (40)
Rotator cuff arthropathy	11 (8)	11 (6)	542 (18)	139 (36)
Acute fracture	2 (2)	5 (3)	1034 (35)	9 (2)
Instability sequelae	1 (1)	1 (1)	73 (3)	12 (3)
Other	13 (11)	1 (1)	67 (2)	7 (2)
Duration of surgery (min), mean ± SD	112 ± 41	94 ± 37	125 ± 39	120 ± 34
Follow-up years, median (IQR)	11.7 (7.9)	11.9 (5.6)	3.2 (4.0)	3.8 (5.5)

SD, standard deviation; *IQR*, interquartile range.

loosening of the glenoid component (n = 20), and loosening of the humeral stem (n = 12). SHRs were calculated at 10-year follow-up with all other revision causes merged as one competing risk in the analyses. Delta III with uncemented stem had significantly increased risk of revision due to glenoid loosening, humeral loosening, and deep infection compared with Delta Xtend with cemented stem. The change in reasons for revisions is also illustrated in Fig. 5, with loosening and infection more frequently observed early in the study period.

Time from surgery to revision

The median time from primary surgery to revision was 5 months (0-292 months). Dislocations and instability were

Table II Kaplan-Meier survival table for reverse shoulder arthroplasties in the Norwegian Arthroplasty Register, 1994-2021 revision due to all causes

	1 yr	2 yr	5 yr	10 yr	20 yr
Delta III					
Cemented stem	94.7 (91.0-98.4)	94.7 (91.0-98.4)	93.0 (88.5-97.5)*	93.0 (87.0-99.0)*	n = 4
Uncemented stem	97.2 (94.8-99.6)	93.3 (89.6-97.0)	89.6 (85.1-94.1)	81.6 (75.3-87.9)†	68.2 (58.8-77.6)†
Delta Xtend					
Cemented stem	97.7 (97.1-98.3)	97.2 (96.6-97.8)	96.1 (95.3-96.9)	94.7 (93.3-96.1)‡	n = 0
Uncemented stem	96.5 (94.7-98.3)	96.2 (94.2-98.2)	95.7 (93.5.2-97.9)§	95.7 (88.3-100)§	n = 0

Data are presented as Kaplan-Meier% (95% confidence interval).
* Last revision at 5.0 years, n = 75 at 10 years.
† n = 88 at 10 years, n = 27 at 20 years.
‡ Last revision at 8.7 years, maximum follow-up = 14.1 years, n = 145 at 10 years.
§ Last revision at 2.8 years, maximum follow-up = 13.1 years, n = 33 at 10 years.

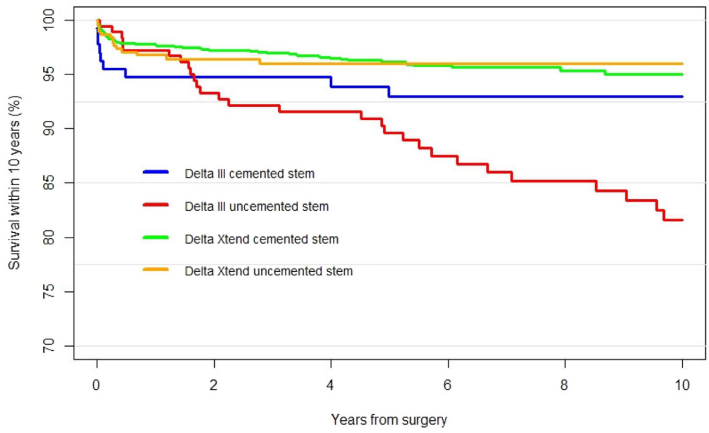

Figure 4 Kaplan-Meier survival with 10 years of follow-up for Delta III cemented stem (*blue*), Delta III uncemented stem (*red*), Delta Xtend cemented stem (*green*), and Delta Xtend uncemented stem (*yellow*).

early reasons for revision with a median time to revision of 2 months (0-102 months), whereas deep infection (19 months, 0-161 months), loosening of components (25 months, 0-292 months), and periprosthetic fracture (22 months, 0-115 months) occurred later (Fig. 6).

Intraoperative complications

Intraoperative complications were registered in 101 procedures (2.8%). Of these, 4 (3.0%) occurred in Delta III (cemented stem), 9 (4.9%) in Delta III (uncemented stem), 79 (2.7%) in Delta Xtend (cemented) stem, and 9 (2.3%) in Delta Xtend (uncemented stem) (Table VII). Bleeding, fracture of proximal or distal bone, and problems because of the patient's anatomy were the most common intraoperative complications.

Discussion

We found that Delta III with uncemented stem was associated with a higher risk of revision compared with Delta Xtend with cemented stem and a tendency toward a higher risk of revision compared with Delta III with cemented stem. Glenoid loosening was the most frequent cause of revision for the earlier design (Delta III uncemented stem). Instability was the most frequent revision cause with the modern design (Delta Xtend), but the rate of revision due to instability was not changed from Delta III to Delta Xtend. Male sex and sequelae after fracture as an indication for surgery were associated with a higher risk of revision.

The improvement in results may be partly due to the early learning curve in both patient selection and the technical procedure for RSA, as described by Walch et al,[41]

Table III Cox model with endpoint all-cause revision at 10-year follow-up, adjusted for sex, age, and diagnosis

	HR (95% CI)	*P* value
Prosthesis type		
Delta III, cemented stem	1.1 (0.54-2.4)	.738
Delta III, uncemented stem	**2.9** (1.7-5.0)	**<.001**
Delta Xtend, cemented stem	1	
Delta Xtend, uncemented stem	1.0 (0.57-1.8)	.945
Sex		
Female	1	
Male	**2.8** (2.0-3.9)	**<.001**
Age group (yr)		
<55	1.5 (0.86-2.7)	.153
55-64	1.0 (0.61-1.6)	.916
65-74	1	
75+	0.8 (0.53-1.6)	.242
Diagnosis		
Acute fracture	0.9 (0.46-1.7)	.665
Fracture sequelae	**2.8** (1.7-4.7)	**<.001**
Inflammatory arthritis	1.5 (0.78-2.9)	.226
Rotar cuff arthropathy	0.9 (0.51-1.7)	.833
Osteoarthritis	1	
Others	1.6 (0.77-3.5)	.203

HR, hazard ratio; *CI*, confidence interval.
Significant values are highlighted in bold figures.

Table IV Cox model with endpoint all-cause revision at 10-year follow-up for Delta III, adjusted for sex, age, and diagnosis

	HR (95% CI)	*P* value
Prosthesis type		
Delta III, cemented stem	1	
Delta III, uncemented stem	2.3 (0.95-5.3)	.064
Sex		
Female	1	
Male	**3.9** (1.9-8.0)	**<.001**
Age group (yr)		
<55	1.2 (0.41-3.4)	.765
55-64	1.3 (0.52-3.1)	.602
65-74	1	
75+	1.0 (0.36-2.5)	.914
Diagnosis		
Acute fracture	1.0 (0.11-8.1)	.969
Fracture sequelae	1.2 (0.37-3.8)	.775
Inflammatory arthritis	1.0 (0.36-2.8)	.993
Rotar cuff arthropathy	0.4 (0.04-3.0)	.347
Osteoarthritis	1	
Others	0.7 (0.08-6.4)	.750

HR, hazard ratio; *CI*, confidence interval.
Significant values are highlighted in bold figures.

Table V Cox model with endpoint all-cause revision at 10-year follow-up for Delta Xtend, adjusted for sex, age, and diagnosis

	HR* (95% CI)	*P* value
Prosthesis type		
Delta Xtend, cemented stem	1	
Delta Xtend, uncemented stem	1.0 (0.59-2.0)	.808
Sex		
Female	1	
Male	**2.6** (1.7-3.4)	**<.001**
Age group (yr)		
<55	1.7 (0.84-3.4)	.142
55-64	0.9 (0.50-1.6)	.686
65-74	1	
75+	0.8 (0.48-1.2)	.190
Diagnosis		
Acute fracture	1.0 (0.47-1.9)	.905
Fracture sequelae	**3.5** (1.9-6.3)	**<.001**
Inflammatory arthritis	1.6 (0.63-4.2)	.319
Rotar cuff arthropathy	1.1 (0.57-2.2)	.758
Osteoarthritis	1	
Others	2.0 (0.87-4.5)	.104

HR, hazard ratio; *CI*, confidence interval.
Significant values are highlighted in bold figures.

but also due to the development in the prosthesis design and surgical techniques.

The use of RSA has increased steadily in the study period, and the indications for RSA have changed from mostly inflammatory arthritis and fracture sequelae toward acute fracture, osteoarthritis, and rotator cuff deficiency and arthropathy. The decreased risk of revision with increased surgeons' experience and due to a change in indication for surgery has also been reported earlier.[41] We found a decreasing risk of revision due to infection during the study period, as opposed to the results from hip arthroplasty, where the risk seems to increase.[9,10] Changes in patient demographics, surgeons' skills, indications for revision, and better reporting probably influence the risk for infection more than the implant design. Although Cho et al's[7] meta-analysis from 2017 showed no increased risk of infection with RSA in inflammatory arthritis, patients with inflammatory arthritis have earlier been shown to have increased risk of revision due to infection.[27,35] The Delta III prosthesis, in particular with uncemented stem, was frequently used in patients with inflammatory arthritis, and this may explain some of the increased risk of revision due to infections and loosening.[7] Even if the risk of revision due to infection is lower for Delta Xtend, our reported rate of infection is still higher than earlier reported for anatomic total shoulder arthroplasties.[13,21,33]

We found increased risk of revision after fracture sequelae. This increased risk has also been described in earlier studies,[39,40] and these patients have also been reported to have poorer clinical results.[8]

Instability and dislocation were the most frequent reasons for revision in our study. The incidence of revision due to instability did not change from Delta III to Delta Xtend. In our study, the incidence was 1.4%, which was lower than

Table VI Reasons for revision by incidence and subhazard ratios (SHRs) for 3650 Delta reverse shoulder arthroplasties reported to the Norwegian Arthroplasty Register between 1994 and 2021

Prosthesis type and fixation of stem*	Deep infection (n = 40)	Instability/dislocation (n = 51)	Glenoid* loosening (n = 20)	Humeral* loosening (n = 12)	Periprosthetic fracture (n = 8)	Other (n = 20)	Total† (n = 151)
Delta III cemented stem, n = 133 (% revised)	1 (0.8)	6 (4.5)	1 (0.8)	0	0	1 (0.8)	9 (6.8)
SHR (95% CI)	0.5 (0.1-4.4)	2.0 (0.7-7.8)	1.9 (0.2-17.0)	–	–	1.0 (0.1-8.8)	1.2 (0.5-2.5)
Delta III uncemented stem, n = 182 (% revised)	9 (4.9)	2 (1.1)	12 (6.6)	5 (2.7)	2 (1.1)	3 (1.6)	40 (22.0)
SHR (95% CI)	**3.0 (1.1-8.5)**	0.6 (0.2-2.5)	**16.6 (5.3-52.0)**	**11.2 (3.4-36.3)**	3.2 (0.2-54.0)	0.8 (0.2-4.0)	**2.9 (1.8-4.8)**
Delta Xtend cemented stem n = 2947 (% revised)	27 (0.9)	36 (1.2)	5 (0.2)	7 (0.2)	6 (0.2)	16 (0.5)	96 (3.3)
SHR (95% CI)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Delta Xtend uncemented stem, n = 388 (% revised)	3 (0.8)	7 (1.8)	2 (0.5)	0	0	2 (0.5)	14 (3.6)
SHR (95% CI)	0.8 (0.2-2.6)	1.4 (0.6-3.4)	1.8 (0.3-10.2)	–	–	0.8 (0.2-3.6)	1.0 (0.6-1.9)

SHR, subhazard ratio; *CI*, confidence interval.

All other revision causes were merged and hence treated as one competing risk in the analyses. Results presented with 10 years of follow-up adjusted for age, sex, and primary diagnosis. Arthroplasties revised after 10 years (n = 12) were not included in the analyses. Delta Xtend (cemented stem) was used as reference comparing the 3 other Delta types. Statistically significant results are in bold (*P* value <.05, 2-sided test).

* All glenoid components are uncemented.

† The surgeons reported 147 revisions. Revisions where both glenoid and humeral loosening were registered are counted for in both groups (n = 4). A total of 151 revisions were included in the analyses.

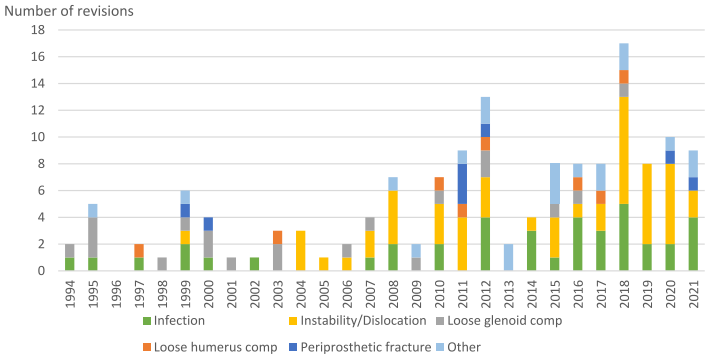

Figure 5 Reasons for revision by year of primary operation of Delta reverse shoulder arthroplasties with primary surgery from 1994 to 2021. Patients with loosening of both humerus and glenoid components are registered in both groups (n = 6): Delta III 1994-2010 and Delta Xtend 2007-2021.

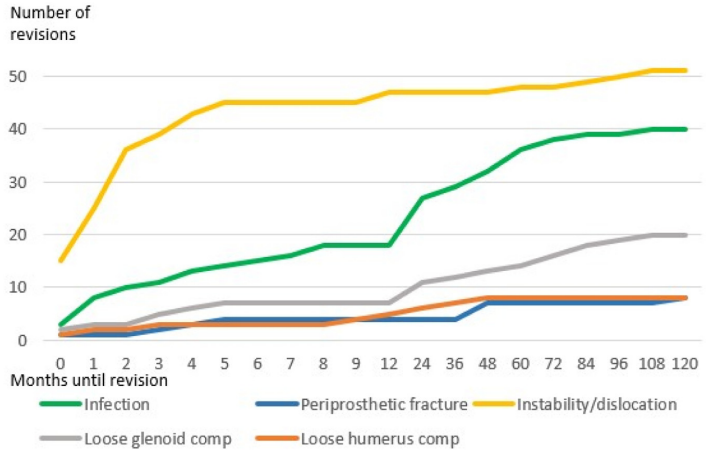

Figure 6 Time from primary surgery to revision (months) according to the cumulative frequency of the different reasons for revision. Note that the first year is given in 1-month intervals; thereafter 12-month intervals are given.

in earlier publications where high incidence (4.7%) of instability with the Grammont designs and the 155° neck-shaft angle have been reported.[43] Most revisions due to instability in our study occurred within the first 6 months after surgery. Delta Xtend was used more frequently with fractures in our population, and a higher rate of instability is expected.[29] The low rate of revision due to instability despite increased use in fracture patients may reflect increased awareness of the challenges with fracture patients.

Notching and glenoid loosening was one of the common complications with the early RSAs.[1,28,34,37,38] The focus on inferior positioning of the glenoid component and the possibility of choosing an eccentric glenosphere are measures taken to prevent loosening. The change to a curved back and HA coating on titanium on the glenoid baseplate may also contribute to less glenoid component loosening with Delta Xtend. Concurrently, we found that glenoid loosening was less common with Delta Xtend than with Delta III (uncemented stem).

We found an almost 3 times higher risk of revision for Delta III with uncemented stem compared with Delta Xtend with cemented stem. Further, even if not statistically significant due to the reduced number of patients, Delta III with uncemented stem had a tendency toward a doubled risk of revision compared with the Delta III cemented stem. On the other hand, no difference was found between Delta Xtend with uncemented and cemented stems. Uncemented

Table VII Intraoperative complications according to humerus fixation in Delta reverse shoulder arthroplasties reported to the Norwegian Arthroplasty register, 1994-2021

	Delta III		Delta Xtend		Total (n = 3650)
	Cemented stem (n = 133)	Uncemented stem (n = 182)	Cemented stem (n = 2947)	Uncemented stem (n = 388)	
Glenoid fracture, n (%)	–	5 (2.7)	12 (0.4)	1 (0.3)	18 (0.5)
Humerus fracture, n (%)	–	–	13 (0.4)	1 (0.3)	14 (0.4)
Extensive bleeding, n (%)	1 (0.8)	–	13 (0.4)	1 (0.3)	15 (0.4)
Anatomic problem*, n (%)	–	2 (1.1)	19 (0.6)	1 (0.3)	22 (0.6)
Technical problem†, n (%)	–	1 (0.5)	6 (0.2)	1 (0.3)	8 (0.2)
Administrative‡, n (%)	3 (2.3)	1 (0.5)	5 (0.2)	1 (0.3)	10 (0.3)
Soft tissue injury§, n (%)	–	–	4 (0.1)	2 (0.5)	6 (0.2)
Other, n (%)	–	–	7 (0.2)	1 (0.3)	8 (0.2)
Total complications, n (%)	4 (3.0)	9 (4.9)	79 (2.7)	9 (2.3)	101 (2.8)

* Includes change of components due to notching/impingement, failed attempt on ostheosynthesis, cementing an uncemented component because of poor bone quality, etc.
† Includes technical problems with components, cement, and instruments.
‡ Includes missing components, breaks in sterile technique, etc.
§ Includes injury of nerve, vessel, or tendon.

stems can lead to proximal bone resorption and signs of stress shielding with stem diameter being related to the degree of bone resorption.[24] In our study, the uncemented stem was used more frequently in Delta III as opposed to the study by Alberio et al[1] where mostly cemented stems were used in Delta III and uncemented stems in Delta Xtend. The Delta III uncemented stem had a smooth surface underneath the HA coating, and this can contribute to the observed increased risk of humeral loosening. The combination of a smooth surface with HA coating has been shown to have inferior results in hip arthroplasties.[20] The glenoid component was the same for Delta III with uncemented and cemented stems, and we cannot explain why the glenoid seemed to come loose more often when combined with an uncemented stem. When compared with Delta Xtend (cemented stem), we cannot conclude on the reasons for increased risk for glenoid loosening for Delta III (uncemented stem), and several factors probably contribute to this. Implant design changes, patient selection, and surgeons' experience may all influence the risk of revision.

Intraoperative fractures can occur both in the humerus and glenoid. These fractures are uncommon complications that can be difficult to manage. Humeral fractures have been more common than glenoid fractures in earlier reports and have been reported in 1.8% of patients.[36] Only 0.8% intraoperative fractures were reported in our study, and there were more fractures on the glenoid side. Only 1 humeral fracture was reported with the use of uncemented stems despite the described increased risk with reaming and press-fit stems.[16] With more experience and more implant options, the surgeon may lower the threshold for revising an implant that earlier would be left in place with a poor functional result. Despite this, we found a lower risk of revision in the later years of the study period.

Strengths and limitations

The primary strengths of this study are the high number of arthroplasties included on a national level, long follow-up time, and the high completeness of reporting to the NAR (90.8% for primaries and 84.6% for revisions).[15] This allowed us to evaluate rare complications that would otherwise be impossible to assess at a single institution.

Only surgical revisions were reported, and we had no information on postoperative complications that were managed nonoperatively or reoperations without involvement of the components. Most acromial and scapular spine fractures were probably managed nonoperatively and not reported. We had no access to X-rays, and, accordingly, radiological findings could not be evaluated. The reasons for revision were reported by the surgeon immediately after surgery. Unexpected positive perioperative bacterial samples from revision surgeries would be identified later and not reported to the register. We suspect that some of the unknown reasons for revision, and some revisions due to aseptic loosening or pain alone, may in fact be low-grade infections that were not suspected at the time of surgery due to the lack of clinical manifestations of infection. As a consequence of this, the register will collect results from bacterial samples from all revision surgeries in the future. The NAR has only recently added patient-reported outcome measures to the registration, and no patient-reported outcome measure results were available for this study. The 2 prostheses compared have been used in 2 different

time periods. This resulted in a longer mean follow-up for the Delta III arthroplasties than for Delta Xtend. Shorter follow-up may underestimate the risk of some of the complications known to occur late such as loosening. To partly compensate for this, we analyzed the risk of revision with endpoint at 10 years for all implants, censoring events occurring after. Also, the fact that the 2 designs were used in different time periods means that other time-dependent differences (ie, surgical technique, surgeon's threshold for revision surgery, instrumentation, and infection prevention strategies) could have influenced our results. Cementing was not a randomized variable; cemented and uncemented stems were used in different patient populations. Delta III with uncemented stem was used in many patients with inflammatory arthritis, whereas the uncemented stem in Delta Xtend was used mainly for patients with primary osteoarthritis and rotator cuff arthropathy who have better bone quality and expected lower risk of loosening. The large increase in the use of shoulder arthroplasties has led to a much larger number of arthroplasties in the Delta Xtend groups than in the Delta III groups, which could also influence the outcome.

Conclusion

We found that Delta III (uncemented stem) had a higher risk of revision compared with Delta Xtend (cemented stem). The reasons for revision have changed, and both loosening and infection have become less of a problem in the more recent years. This register study cannot determine whether the differences found were caused by differences in implant design or by other factors that changed during the study period. Instability is still a main concern, and alternative solutions to the original Grammont design are still being explored to address this.

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