Author’s response to reviews

Title: Mortality after Primary Shoulder Arthroplasty: An analysis of 4,019 patients from 1976-2008

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Author’s response to reviews: see over
Reviewer’s report Title: Mortality after Primary Shoulder Arthroplasty: An analysis of 4,019 patients from 1976-2008 Version: 1 Date: 21 June 2011 Reviewer: Jos Jam JAM Van Raay

Reviewer's report:
It concerns an article whose findings are important to those with closely related research interests. Especially the finding that a high BMI is protective for 90 day mortality after shoulder replacement. The other findings are well known and does not add important information. Major revision is necessary before a decision on acceptance or rejection can be made.

The question posed by the authors is well defined. Why did they take a 90-day postoperative period into account and for example not one year down the line?

One can imagine that after cardiopulmonal or neurological complications during the period shortly after operation, patients decease in the first postoperative year because of these complications. This could increase the mortality rate or do the authors hypothesize that from 90 days after operation, mortality rate does not increase further. This has to be cleared up. It would be interesting to determine the 1 year mortality.

Response: The reason for choosing 90-day mortality was to have outcome assessed at a time-period relevant to post-operative period after shoulder arthroplasty. While 1-year mortality is an important outcome that could be assessed, it was not the focus of this study. Most surgeons do not consider complications or death after 90-days to be related to the stress of surgery. We have clarified this in the introduction.

“Mortality within 90-days of arthroplasty could be potentially linked to surgery and/or its complications and is of more interest to the surgeon and the patient, as opposed to long-term mortality (1- or 5-year post-surgery), which may indicate baseline mortality risk, rather than related to the surgery.”

Introduction: First sentence: Shoulder arthroplasty is an.... refractory shoulder pain. Does the authors mean “end stage of degenerative arthritis of the shoulder and other causes” that cause refractory shoulder pain? At the end of introduction: 1: determine risk factors and 2 (instead of 3) influence type of procedure
Response: We have added this phrase as suggested.

“Shoulder arthroplasty is an effective surgical procedure for the treatment of refractory shoulder pain due to end stage shoulder disease due to osteoarthritis and other causes.”

Methods: They are not very appropriate and well described. Predictors of interest: The authors anticipated that the numbers of death would be too small to analyze HHS and TSA separately. This contradicts with the second aim of the study i.e assessing whether mortality differed by the type of procedure (HHS vs TSA) Whether TSA or HHS is a predictor of interest is also not mentioned in results and conclusions in the abstract.
Response: We have clarified the methodology, which we believe is the state-of-
The aims were stated before data were obtained. In fact we examined both the aims, albeit with small number of deaths as anticipated, even in this largest series to date. We did not think it was appropriate to delete this aim a posteriori. Each model was adjusted for type of surgery (HHR vs THR) to account for the differences by surgery, which is an appropriate way to adjust in epidemiological studies, where the outcome is rare, such as death. We do not believe that adjusting for surgery in the first analysis for other factors and examining the differences by the type of surgery are contradictory, in fact the way analyses are conducted, they are complimentary.

The results regarding HHR vs. TSA are presented as a paragraph titled “Differences between TSA and HHR”. We have added these to abstract and conclusions, as recommended.

“In this study, our aims were to: (1) determine the risk factors and rate of 90-day mortality following primary shoulder arthroplasty (TSA or HHR); and (2) if data allows, to assess whether mortality differed by the type of procedure (TSA versus HHR).”

Abstract:
“BMI ≥ 30 was associated with lower risk of 90-day mortality (OR, 0.25; 95% CI:0.08,0.78). In univariate analyses, patients undergoing TSA had significantly lower 90-day mortality of 0.4% (8/2,580) compared to 1% in HHR (20/1,411) (odds ratio, 0.22 (95% CI: 0.10, 0.50); p=0.0003).

Conclusions: 90-day mortality following shoulder arthroplasty was low. An underlying diagnosis of tumor, higher comorbidity and higher ASA class were risk factors for higher 90-day mortality, while higher BMI was protective. Pre-operative comorbidity management may impact 90-day mortality following shoulder arthroplasty. A higher unadjusted mortality in patients undergoing TSA versus HHR may indicate the underlying differences in patients undergoing these procedures.”

Under diagnosis, the category tumor is missing. The Deyo-Charlson index has to be cleared up with literature/reference.

Response: The category tumor was provided in the first table as the third row under diagnosis (n=182 (5%)) and also in table 2. We have added additional explanation regarding Deyo-Charlson index as suggested.

“(c) Deyo-Charlson Index, a validated measure of medical comorbidity (11), is a summative weighted scale of 17 comorbidities (including cardiac, pulmonary, renal, hepatic disease, diabetes, cancer, HIV etc.), for example, conditions such as myocardial infarction, dementia, peptic ulcer disease etc. each get a score of “1”; diabetes with end-organ damage, hemiplegia, renal disease, malignancy each get a score of “2”; moderate-severe liver disease a score of “3”; metastatic solid tumor and AIDS/HIV each get score of “6”– this was categorized as 0 or ≥1, since the median for this population was zero”

What is the mortality of an matched (age, gender, comorbidity, Deyo-Charlson, ASA class) population in comparison to the study group? It were all elective cases except trauma? Were fracture cases operated
immediately or in a later phase?

Response: Our objective was to assess the predictors of 90-day mortality and not to assess whether mortality is increased in shoulder arthroplasty patients compared to a control population, which may be a question for a future study. Data on general population matched for those characteristics are not available, to our knowledge (there would be no reason to have ASA in the general population, which is performed in preoperative assessment). All cases were elective except trauma, we have clarified this in table 1 legend.

*“Except for trauma, all other underlying diagnoses are associated with elective arthroplasty”*

**Statistical analysis:** The authors want to assess mortality risk factor in patients undergoing HHS and TSA together. Also this contradicts again the second aim of the study whether mortality differs by the type of the procedure. Does they want to assess mortality risk factors or mortality? This is unclear and conflicting in the introduction and methods text

Response: We have clarified this as suggested. Our main aim, as stated, was to assess the predictors of 90-day mortality. We believe it compliments rather than contradicting the second aim, we have clarified as follows (please also see the response to a similar comment above)

“For the main aim assessing predictors of mortality, we assessed univariate associations of predictors of interest (age, gender, BMI, ASA, Deyo-Charlson, diagnosis and implant fixation) with 90-day mortality using logistic regression. For each predictor, we also performed multivariable-adjusted analyses by adjusting analyses for the type of arthroplasty (TSA versus HHR) based on our clinical prediction that arthroplasty type might be associated with mortality. The objective of adjusting for the type of surgery was to assess if each variable of interest (age, gender, Deyo-Charlson comorbidity index, diagnosis and implant fixation) was independently associated with the outcome, after adjusting for the effect of the type of surgery. Since our main objective was to assess mortality risk factors in patients undergoing shoulder arthroplasty, the HHR and TSA groups were combined for analyses. We decided not to perform additional analyses adjusted for multiple variables to avoid over-adjusted models, since the total number of outcomes was <30. For analysis of the second aim of whether type of surgery had an impact on mortality, univariate associations of type of surgery with mortality were assessed. We also examined each of the multivariable analyses performed for main aim for significance of type of surgery variable, since all models were simultaneously adjusted for this variable.”

**Results 1:** The data are sound but not complete. More information is needed concerning clinical and sociodemographic characteristics. Age upper and lower limit and median? Tumor: primary bone tumour or osseous metastasis? Rotator cuff disease: Massive rotator cuff rupture with and without cuff arthropathy?

Response: We provide additional details regarding tumor type as suggested in the table. Mean age was 65 years [median 67, range 18 to 67]. For rotator cuff
disease, the diagnosis was not classified as massive rupture with or without cuff arthropathy, therefore this detail could not be added.

The manuscript adheres to the relevant standards for reporting and data deposition. 
Response: Thank you.

Results 2: 90 day mortality: mostly during the First 24 h period postoperatively or within several days after operation or later for example after 2 or 3 months? 
Response: We have added this to the results section, as recommended. No patients died in the first 24 hr period.

“Of the 20 HHR patients, 5 died between day 16 and day 30, 6 died between day 31 and day 60, 9 died between day 61 and day 90. Of the 8 TSA patients, 3 died between day 2 and day 30, 4 died between day 31 and day 60 and one died between day 61 and day 90. No patients died within the first 24 hours after HHR or TSA.”

Cause of death? Cardiopulmonal or neurologic event, thrombo embolic? Or directly related to the operative procedure? These data are missing. What comorbidity is associated with an increased mortality risk? 
Response: One of the senior orthopedic surgeon (J.S.) attempted to perform a chart review to assess cause of death, since the total joint registry captures the time, but not cause of death. The cause of death was not documented in medical records for most patients, related to one or more of the following reasons: (1) Most shoulder arthroplasties, and therefore most deaths occurred in patients referred to the medical center for whom the cause of death was not documented in medical records; (2) autopsy data were missing for most patients.

We have provided data that Deyo-Charlson index was not significantly associated with mortality in this study, but this may be due to a small sample size, which is acknowledged in the limitations section.

“We included a large sample size, but found only 28 events during the 33-year study period, which may have led to type II error, i.e., missing a significant association due to small sample size when such an association really existed.”

Discussion: Is balanced and supported by data. Limitations are stated i.e. BMI and ASA data are not available for the whole period. Additional adjustment could be performed without influencing the adjusted model or conclusion. Especially with such a low mortality incidence (28 cases) it is possible to study the cases individually especially when they can be isolated from the prospectively collected information from Total Joint Registry. 
Response: We have added data regarding the time of death to results section, as recommended.
“Of the 20 HHR patients, 5 died between day 16 and day 30, 6 died between day 31 and day 60, 9 died between day 61 and day 90. Of the 8 TSA patients, 3 died between day 2 and day 30, 4 died between day 31 and day 60 and one died between day 61 and day 90. No patients died within the first 24 hours after HHR or TSA.”

The authors acknowledge the published work upon they build. There are no unpublished data reorted.
Response: Thanks, we agree

The title does not comprise what has been found, this could be mentioned in a subtitle as “predictors of mortality”.
Response: We have added this to the title as suggested.

“Title: 90-day Mortality and its Predictors after Primary Shoulder Arthroplasty: An analysis of 4,019 patients from 1976-2008
Running title: Predictors of Mortality after shoulder arthroplasty”

The finding of a low mortality in higher BMI patients is novel and unexpected. A high BMI is protective. What is the explanation of this finding? This does not mean that a low BMI carries a greater mortality risk after shoulder replacement. reference 15 and 16 deal with BMI in relation to groin hernia and cardiac surgery concerning postoperative mortality. There is no reference concerning BMI and postoperative mortality in relation to joint replacement surgery in general and shoulder replacement surgery specifically. How could a large BMI play a protective role in joint replacement surgery?
Response: We have speculated on this in the discussion section.

“Our finding of association of higher BMI with lower mortality following shoulder arthroplasty is novel. To our knowledge, there is only one published study that assessed association of BMI with mortality in arthroplasty cohort (14). In a sample of total hip arthroplasty patients, there was no association of BMI with a composite end-point of mortality, readmission, re-operation or intensive care unit admissions (14). However, the end-point was composite, not mortality. On the other hand, several studies have shown that lower BMI was a risk factor for postoperative complications after hernia surgery (15), postoperative pulmonary complications after cardiac surgery (16), major adverse cardiac events after percutaneous coronary intervention (17) and postoperative adverse cardiac adverse events after hip fracture repair (18). Studies in non-arthroplasty populations have shown that low BMI is a risk for higher in-hospital postoperative mortality (16) and 30-day mortality after coronary artery bypass grafting (19). The “obesity paradox” with worse outcomes noted in patients with lower BMI has also been reported in patients with heart failure (20). A systematic review of cohort studies of patients with coronary artery disease found lower than normal BMI was associated with higher total mortality and cardiovascular mortality compared to patients with normal BMI (21). To our knowledge, our study is the first study to observe this association in patients who underwent shoulder arthroplasty. Underweight patients are likely to have low caloric and functional reserve compared to overweight/obese patents, which might make them more vulnerable to complications and subsequent mortality, especially in a stressful postoperative period after arthroplasty. It is also possible that obese people who survive to old age (patients who commonly undergo shoulder arthroplasty) have a survival advantage as compared to non-obese and lean patients. Adipose tissue is
considered a metabolic organ, and the underlying mechanisms for this association need to be investigated further. This emerging body of evidence suggests a protective role for normal and/or higher BMI with regards to post-surgical survival. We believe this needs further study.”
Reviewer's report Title: Mortality after Primary Shoulder Arthroplasty: An analysis of 4,019 patients from 1976-2008
Version: 1 Date: 27 June 2011
Reviewer: Ashley Blom

Reviewer's report:
Major Compulsory revisions.
This is an interesting body of work and is well presented and clear. The methodology is sound. Mortality after relatively less common surgical procedures such as shoulder replacements is difficult to accurately quantify and the author's large prospective database allows this to be done.

However, I feel the authors can greatly add to their manuscript by providing a little more detail.
Firstly, the diagnoses would be very helpful. Particularly an analysis of trauma versus elective indications, as one would expect mortality to be higher after fracture as has been shown in hip arthroplasty.
Response: We have added these analyses related to diagnoses to table 1, as suggested. There were no significant differences in risk of mortality between trauma versus other diagnoses (elective).

"We also compared elective versus non-elective (trauma) cases. There were no significant differences in risk of mortality between trauma versus other diagnoses (elective)."

Secondly, a day by day analysis of risk of death as done in Blom et al Acta Orthopaedica 2006; 77(3) 347-350 would better present the relative risk as it is unlikely to be linear over the 90 days.
Response: We have added the data regarding the postoperative day of death to the results. Due to small number of events and due to risk of over-interpretation of only 28 events, we decided to not do additional analyses of this small dataset. Future studies with higher number of events can perform additional analyses as suggested

Thirdly, the cause of death would be very valuable to know as this would enable clinicians to address the problem of mortality after shoulder replacement.
If the authors could provide this data, I would recommend publication.
Response: One of the senior orthopedic surgeon (J.S.) attempted to perform a chart review for these 28 cases to assess cause of death, since the total joint registry captures the time, but not cause of death. The cause of death was not documented in medical records for most patients, related to one or more of the following reasons: (1) Most shoulder arthroplasties, and therefore most deaths occurred in patients referred to the medical center for whom the cause of death was not documented in medical records; (2) autopsy data were missing for most patients.
Level of interest: An article whose findings are important to those with closely related research interests.