Author’s response to reviews

Title: Fast track hip fracture care and mortality – an observational study of 2230 patients.

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Author’s response to reviews:

We would like to thank Cecilia Rogmark and Anne Garland for taking the time to re-evaluate our manuscript. We would also like to thank Henrik Jorgensen for reviewing our manuscript and appreciate his positive response and constructive criticism. The specific comments are addressed point by point.

Henrik L. Jorgensen (Reviewer 3): This is a retrospective register study of the effect of fast track hip fracture care versus conventional hip fracture care on a relatively large number of patients before and after the introduction of the fast track hip fracture care. A prospective, randomized study of the two different pathways would, of course, have been preferable but such a study would be almost impossible to conduct due to a number of practical and ethical problems. Thus, the design of the present study is probably one of the best alternatives, having the advantage of presenting data from a routine, clinical setting into which the fast track program was implemented. Furthermore, the study is one of the largest studies to date on this subject.

The study is well designed and well written. The discussion of the weaknesses / strengths of the study and of the possible reasons for not finding a significant reduction in mortality in the fast track group is clear and thorough.
Specific comments:

1) What kind of pain relief did you give the patients upon arrival in the A&E department? Reading the description of the fast track hip fracture care, it seems as if pain relief (apart from the prehospital treatment) is first initiated upon the return of the patient from the X-ray department to the orthopaedic ward.

Authors’ comments:

This observation is correct. Hip fracture patients do not routinely receive additional pain medication between prehospital treatment and arrival on the orthopaedic ward. It would be preferable to administer the fascia iliaca compartment block before the x-ray examination. However, this would require an available examination room in the A&E department. Since this is a sparse resource in our institution the patients would have to wait for a prolonged time in the A&E department. Therefore, we prioritize ‘fast tracking’ hip fracture patients to the orthopaedic ward. If, however, the nursing staff considers the patient to be in more pain than acceptable, the orthopaedic surgeon on call is contacted and additional intravenous pain medication, usually an opiate, is administered in the A&E department.

Changes made:

Added: “If deemed necessary, additional intravenous opiates are administered in selected cases.” (Methods, Fast track hip fracture care, lines 107 – 108, page 5) (At what point in the admission pathway this is the case becomes clear from the context)

2) Time to surgery has been shown in several studies to have a substantial influence on mortality after hip fracture. The reduction in time to surgery from a median of 25.7 hours in the conventional group to 23.6 hours in the fast track group is not very large which could be part of the explanation of the missing effect on mortality.

Looking at the description of the adjusted analyses, I do not see time to surgery included as a co-variate:

"In the adjusted analyses, age, male gender, cognitive impairment and increasing ASA score were independent predictors of increased mortality while surgeon's experience, type of fracture, type of operation, type of anaesthesia, operating time and municipality were not."
I suggest new analyses including this variable. In addition to its inclusion as a continuous variable, you could also try to include it as a dichotomous variable instead: Operated within 12 hours (0/1) or Operated within 24 hours (0/1).

Authors’ comments:

We agree with the reviewer that time to surgery was only modestly reduced in the fast track group and that this may have had an influence on the association between fast track care and mortality. We have added a comment to this effect in the discussion.

Reducing ‘time to surgery’ is one of the intended effects of fast track care. Therefore, including ‘time to surgery’ in the regression analysis estimates the effect of the other components of fast track care excluding the effect of reducing ‘time to surgery’ and not the whole ‘care package’. We did, however, perform the suggested analyses: In univariate analysis longer ‘time to surgery’ (in hours) was significantly associated with a higher 90-day mortality (OR = 1.01, 95%CI: 1.003–1.017; p = 0.005) while an association with 30-day mortality (OR = 1.008, 95%CI: 0.999–1.017; p = 0.077) and 1-year mortality (OR = 1.006, 95%CI: 1.000–1.012; p = 0.65) bordered on statistical significance. However, in the logistic regression model ‘time to surgery’ was not a significant predictor of 30-day or 1-year mortality while it only bordered on statistical significance in the final model for 90-day mortality (OR = 1.008, 95%CI: 1.000–1.016; p = 0.05). When ‘time to surgery’ was included as a dichotomized variable (with both 12 and 24 hours as cut-off) its association with 90-day mortality no longer bordered on statistical significance. We concluded that there was no clear evidence for an association between ‘time to surgery’ and mortality in our cohort. We have added a comment in the ‘statistical analysis’ section and modified the sentence describing the predictors of mortality in the ‘results’ section.

We realized that the sentence "In the adjusted analyses, age, male gender, cognitive impairment and increasing ASA score were independent predictors of increased mortality while surgeon's experience, type of fracture, type of operation, type of anaesthesia, operating time and municipality were not." also should include ‘fast track care’ as a covariate that did not have a statistically significant effect on mortality. This was added.

Changes made:

Added: “Reducing time to surgery is one of the intended effects of fast track care. Therefore, the logistic regression model analyzing the effect of fast track care on mortality was run with and
without including time to surgery as an independent predictor. This did not relevantly change the result for the effect of fast track care on mortality.” (Methods, Statistical analysis, lines 235 – 239, page 10)

Changed:

“In the adjusted analyses, age, male gender, cognitive impairment and increasing ASA score were independent predictors of increased mortality while surgeon’s experience, type of fracture, type of operation, type of anaesthesia, operating time and municipality were not.”

to

“In the adjusted analyses, age, male gender, cognitive impairment and increasing ASA score were independent predictors of increased mortality while fast track care, time to surgery, surgeon’s experience, type of fracture, type of operation, type of anaesthesia, operating time and municipality were not.” (Results, Mortality, lines 297 - 300, pages 13/14)

Added: “Thus, the rather modest reduction in time to surgery of just over two hours in the fast track group compared to the conventional treatment group might have contributed to not finding a statistically significant effect of fast track care on mortality. However, time to surgery was not an independent predictor of mortality in our cohort.” (Discussion, lines 392 – 395, page 18)

3) A table should be made with the results of the logistic regression analyses showing the odds ratios of the individual, independent predictors of mortality.

Changes made:

Added: A table with the results of the logistic regression analyses showing the odds ratios of the individual, independent predictors of mortality. (Results, Mortality, table 4, line 320, page 15)

Added: “… (table 4) …“ (Results, Mortality, table 4, line 298, page 14)
4) You only analyze the effect of the fast track program on postoperative infections as a whole. Have you tried looking at individual infections (urinary tract infections, pneumonia etc.) separately?

Authors’ comments:

We realize that our terminology was not quite clear. By postoperative infection we meant surgical site infection. We have revised the manuscript accordingly. Information on urinary tract infections, pneumonia etc. was, unfortunately, not available.

Changes made:

Changed: “… postoperative …” to “… surgical site …”

(Abstract, lines 41 and 45, page 2)

(Keywords, line 45, page 3)

(Background, lines 81 and 82, page 4)
5) In your discussion, you state "other recent approaches to improve hip fracture care, such as geriatric co-management, have also largely failed to decrease mortality [33-35]". I do not agree with this statement. Several studies have shown reductions in mortality after hip fracture with orthogeriatric care. You should include references to these studies as well and modify the text accordingly.

Authors’ comments:

We concede that this statement may be too bold. However, we would argue that the effect of geriatric co-management on mortality after hip fracture is not entirely unequivocal. While some studies found significant effects, other studies, amongst others the ones we cited, did not find statistically significant effects. In the results section of the Cochrane review that we refer to in the manuscript (Eamer G et al.: Comprehensive geriatric assessment for older people admitted to a surgical service. Cochrane Database Syst Rev 2018) it is stated that “Comprehensive geriatric assessment probably reduces mortality in older people with hip fracture (RR 0.85, 95% CI 0.68 to 1.05; 5 trials, 1316 participants, P = 0%; moderate-certainty evidence).” The authors’ statement, which includes the word ‘probably’ is cautious since the 95% CI for the odds ratio includes 1 such that, according to ‘classical’ frequentist thinking, the effect of comprehensive geriatric assessment on mortality is not statistically significant. We have added two references to studies which did show a significant effect of geriatric co-management on mortality and have modified our statement citing the conclusion drawn by Eamer et al..

Accordingly we also added a statement on geriatric co-management at the end of the discussion where we propose which areas one might focus on to further improve hip fracture treatment. Since the existing statement already includes the word ‘probably’ (‘Efforts to further improve hip fracture care should probably focus on …’) we simply added geriatric co-management as another possible area of improvement.
Changes made:

Changed:

“This notion seems to be supported by the fact that also other recent approaches to improve hip fracture care, such as geriatric co-management, have largely failed to decrease mortality.”

to

“This notion seems to be supported by the fact that also other recent approaches to improve hip fracture care, such as geriatric co-management, had mixed results with some studies reporting a statistically significant effect on mortality {Middleton, 2017; Baroni, 2019} while other studies did not {Friedman, 2009; Watne, 2014}. A recent Cochrane review was not quite conclusive concerning mortality, but stated that comprehensive geriatric assessment probably reduces mortality in older people with hip fracture (risk ratio 0.85, 95% CI 0.68 to 1.05; 5 trials, 1316 participants, inconsistency (I²) = 0%; moderate-certainty evidence) {Eamer, 2018}.”

(Discussion, lines 409 – 415, page 19)

Changed:

“Efforts to further improve hip fracture care should probably focus on even shorter preoperative waiting times {Pincus, 2017} in combination with a fast track care system and intensified rehabilitation after hospital discharge {Hansson, 2015}.”

to

“Efforts to further improve hip fracture care should probably focus on even shorter preoperative waiting times {Pincus, 2017} in combination with a fast track care system, geriatric co-management {Eamer, 2018} and intensified rehabilitation after hospital discharge {Hansson, 2015}.”

(Discussion, lines 480 – 482, page 22)

Additional changes:

Authors’ comments:

The authors’ e-mail addresses were marked with higher case numbers. However these numbers did not correspond with the numbers used to indicate the authors’ affiliations. Since the authors’ names correspond with the e-mail addresses, an additional specification seemed unnecessary.
Changes made:

The higher case numbers were deleted from the e-mail addresses. (Title page, lines 14-16, page 1)

Authors’ comments:

During the first revision of this manuscript, the editor remarked that “absence of evidence does not equal evidence of absence” and we revised the manuscript accordingly. However, we realized that one statement claiming ‘no effect’ had escaped our scrutiny.

Changes made:

Changed:

“Thus, the relatively high percentage of patients who were not “fast tracked” to the orthopaedic ward may have contributed to not finding an effect of fast track care on mortality.”

to

“Thus, the relatively high percentage of patients who were not “fast tracked” to the orthopaedic ward may have contributed to not finding a statistically significant effect of fast track care on mortality.” (Discussion, line 385, page 18)