Author's response to reviews

Title: Risk factors for early recurrence after inguinal hernia repair

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Version: 2 Date: 6 October 2009

Author's response to reviews:

To the editor:
We revised our manuscript exhaustively according to the reviewers comment. A detailed list of the revisions added.

Response to reviewer 1:

Abstract
1. Number was corrected (75 instead of 74)
2. Our statement in the conclusion is misleading, indeed. The new finding of our study is that family history is not only a risk for primary hernias but also and especially for hernia recurrence and this subgroup might be of special interest for genetic studies. With regard to your later comments conclusion of abstract and discussion were adapted.

Background
1. Line 1: common was changed; “The question is if patients with more than one recurrence are not treated sufficiently or if their recurrences are based on disturbances of the extracellular matrix” was added.
2. Line 3: pathobiological deleted
3. Line 4-7: was changed
4. Line 12-14: Alterations of collagen metabolism are reported for inguinal and incisional hernias independent of age. Recently, Type III collagen gene was also reported to play a role in hiatal hernias (Asling et al, Gut 2009). The only exception, to my knowledge, are congenital hernias in young children (Taniguchi al., Ped Surgery Int 2006)
5. Type III collagen gene was added.
6. “We investigated patients having more than one recurrence where the primary and secondary hernia repair failed. Differences in the risk profile of primary and recurrent inguinal hernia patients might help to identify ‘biological subgroups’ of patients at risk. Referring to the European Hernia Society guidelines the identification of biological subgroups can be of importance to develop a tailored
approach for hernia surgery.” was added, including the respective literature.

Materials and Methods
1. Line 1: re-recurrent was changed to recurrent hernia patients
2. Line 1: study range was changed as suggested
3. Line 3: correct number is 75, paragraph was put in the result section, and inclusion criteria were added.

Results
1. Age range of patients with only one recurrence is not available because these patients were excluded. All Patients were operated because of hernia recurrence, infections were not observed.
2. p-values were added
3. older was corrected
4. p-values were added
5. Your comment to paragraph: “Coronary heart disease and hypertension were predictive factors for high recurrence rates (Table 3). These data correlated with anti-hypertensive medication and ACE inhibitors (data not shown)”. –See discussion, page 6 Paragraph 1: Regarding the fact that patients with coronary heart disease are significantly older, the increased recurrence rate can result from a prolonged observation period for these patients rather than from the coronary heart disease. However, coronary heart disease is known to be associated with disturbed collagen metabolism[24].

Discussion
1. Line 3-4: paragraph was changed
2. Line 6: “an significantly” was changed
3. Line 11-15: was changed to “…our cohort more than 5 recurrences could be observed exclusively for patients that were older than 50 years…”
4. The predictive value of coronary or the corresponding medication has to be discussed
5. Several studies suggest a disturbed wound healing due to overexpression of type III collagen in hernia patients. Type III collagen is the immature collagen normally only present in the early phases of wound healing. The expression of collagens can not be influenced by the operative technique.
6. Incisional hernias were excluded
7. How to improve wound healing: “The identification of susceptible genes could permit causative treatment options as realized for the treatment of aortic aneurysm by distinctive blockage of gene transcription in animal models1. Meshes can be used as carrier systems for potential drug treatment.”
8. The conclusion of the discussion was adapted to the abstract conclusion.

Tables and figures
Table 1: an explanation was added
Table 2 and 3: (range) was added
Table 4: we would prefer to keep this table because it gives a schematic overview on the known risk factors for specific hernia phenotypes
Figure 1: recurrence rates was changed to number of recurrences


Response to reviewer 2:
1: “Both authors equally contributed” was deleted
2. The primary operation was not conducted in our clinic. Moreover, time between recurrent and primary operation was 5 years in average (Table 2). Therefore operative data at the primary operation are not available. Because of the 5 year time interval between primary hernia repair and operation of re-recurrent hernia in our clinic postoperative complications such as infection leading to early recurrences can be excluded and were not observed during the operation. To exclude “technical faults” we excluded all patients that had just on recurrence.
3. The reviewer is right, BMI is important, but BMI in relation to recurrence was not investigated in our study. We performed this study based on the well reported finding that especially recurrent hernia patients have a decrease type I/III collagen ratio that may be caused by genetic factors. Therefore BMI was not in our focus though this data are important
4. Was corrected.
5. Was deleted.

Response to reviewer 3:
The new finding of our study is that family history is not only a risk for primary hernias but also for hernia recurrence. This study was based on the assumption that hernias have a genetic background. Several studies hint on collagen genes as candidate genes. Collagens are very important for a sufficient wound healing. Family history as a risk factor for early recurrence independent of gender would support the hypothesis that collagen genes, or genes associated to collagen metabolism play a role for hernia disease.
This comment was also included in the discussion.