Author's response to reviews

Title: Single- Versus Two- Layer Intestinal Anastomosis: A Meta-Analysis of Randomized Controlled Trials

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Version: 2 Date: 11 September 2005

Author’s response to reviews: see over
Dear editors of BMC Surgery,

We have revised our manuscript “Single- Versus Two- Layer Intestinal Anastomosis: A Meta-Analysis of Randomized controlled Trials” (manuscript No. 3108561095761579) in light of the reviewers’ comments and uploaded the revised version.

Thank you for your kind consideration,

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A list of all changes in the revised manuscript:

(1) “The conclusion that there is no difference between the two methods” is too strong, so this sentence was deleted and we put the following sentence in the “discussion” section:

- there is no evidence of a difference in terms of risk of leak but that there is insufficient evidence to rule out a modest but potentially important difference.

(2) As reviewer’s calculation, the summary estimate and CI for the risk ratio was calculated from the fixed effects model (M-H), not the random effects model (DerSimonian-Laird methods). Therefore, we changed to the following sentences in the “Abstract - results” and “Results- leaks” section.

- Combined risk ratio using DerSimonian-Laird methods was 0.91 (95%CI=0.49 to 1.69)  
  - Inter-study heterogeneity was considered statistically significant ($\chi^2$=10.5, d.f.=5, p=0.06).

(3) Goligher’s study has the largest weight in this meta-analysis. As reviewer’s comment, we performed a sensitivity analysis excluding this study. We changed the sentences as described in (4).

(4) We made the graphical exploration using a L’Abbe plot (= Fig 3). From this plot, Goligher’s study can be considered as an outlier and the source of heterogeneity among the studies. Sensitivity analysis excluding this study showed homogeneity in the residual studies and supported this consideration. Therefore, we replaced the following sentences.
Into “Figure legend” section:
- Figure 3 – L’Abbe plot of risk of leak in single-layer vs. two-layer.

Into “methods – Statistical analysis” section:
- Meta-regression analyses were performed to explore sources of heterogeneity. Variables comprising year of publication, mean age of study participants, and percentage of male patients were examined for significant effects on risk of leak. In addition to that, informal graphical exploration using a L’Abbe plot was made and sensitivity analysis was performed [19,20].

Into “results - Exploring sources of heterogeneity and sensitivity analysis” section:
- Meta-regression revealed that none of the variables for year of publication, mean age of study participants, and percentage of male patients were related to risk of leak. From the graphical exploration using a L’Abbe plot [Fig. 3], we considered the study by Goligher et al. as the source of heterogeneity and we performed sensitivity analysis excluding this study. With the fixed-effect model, the combined risk ratio for leak was 0.63 (95% CI = 0.37 to 1.06 ) and inter-study heterogeneity was not significant ($\chi^2 = 2.96, \text{d.f.}=4, p=0.57$).

Into “discussion” section:
- Sensitivity analysis excluding the study by Goligher et al. suggested it as the source of heterogeneity. In their trial, techniques of vertical mattress sutures in the posterior two-thirds of the circumferences and Lembert sutures of horizontal mattress type in the anterior third of the bowel circumference were performed in single-layer group and reported the highest risk of leaks (45%). Although one possible explanation of this high rate of leaks may be caused by their inclusion criteria, high and low colorectal anastomosis, it is inexplicable for all. On this subject, they described “We are quite unable to explain the difference between Everett’s results and ours” in their report [11]. To say the least, this suture technique is not common in intestinal anastomosis in the present day.

Into “discussion-limitations” section:
- First, the study by Goligher et al. had an effect on the main result strongly. Although the main result was not sensitive to the sensitivity analysis excluding this study, it showed more favorable trend in single-layer.

Into the “reference” section:
- [20] Sharp SJ, Thompson SG, Altman DG: The relation between treatment benefit and

(5) We made the supplementary file (Additional file 1: Appendix - Search strategy.doc) and linked from the Method section. In this, all details concerning the search strategy have been described. And we put the following sentences into “Methods- Search strategy and selection criteria”

- A search of any language literature was performed through August 2004 to identify reports of randomized controlled trials comparing single- with two-layer intestinal anastomosis. Data bases searched were Medline (1966-April 2004), the Cochrane Register of Controlled Trials (Issue2, 2004 ), and EMBASE(1986-August 2004). A detailed description of the search strategy is provided in the Appendix [see Additional file 1]. Electronic searches were supplemented by hand searching reference lists and reviews.

(6) According to reviewer’s comment, in Table 1, the reporting of numbers as single / two-layer is confusing as the usual convention in meta-analysis is (No. in group experiencing event) / (total in group), and also easier to interpret if also as a percentage, e.g. in the form 31/69 (45%). Therefore, we changed Table 1 to this form.

(7) In Figure 2, we replaced “single-layer favor” by “Favors single-layer” and similarly for two-layers.

(8) In the legend of Figure 2, “the pooled risk ratio for leaks in single-layer group is 1.00 (95% CI = 0.71 to 1.42)” was both incorrect and unnecessary (it is obvious from figure) according to reviewer’s comment, we deleted this sentence in the legend of Figure 2.

(9) The risk ratio and CI for the Burch’s study in Figure 2 is incorrect as a thoughtful reviewer’s comment. We appreciated this point-out and changed Figure 2 (risk ratio is 2.24, and CI is 0.21 to 24.04).

(10) We should state the particular routines used and reference their sources and authors. Therefore, we added the following sentences in the “methods - statistical analysis” and “reference” section.

Into the “methods - statistical analysis” section:
- We used a user-written add-on Stata routine "metan", which was written by Bradburn et al.[24].

Into the “reference” section: