Author's response to reviews

Title: Pancreatogastrostomy versus pancreatojejunostomy for REConstruction after partial PANCreatoduodenectomy - A randomized controlled trial (RECOPANC)

Authors:

Ulrich F Wellner (dr.ulrich.wellner@gmail.com)
Sabine Brett (sabine.brett@uniklinik-freiburg.de)
Thomas Bruckner (bruckner@imbi.uni-heidelberg.de)
Ronald Limprecht (limprecht@imbi.uni-heidelberg.de)
Inga Rossion (ingga.rossion@med.uni-heidelberg.de)
Christoph Seiler (christoph.seiler@med.uni-heidelberg.de)
Olivia Sick (olivia.sick@uniklinik-freiburg.de)
Inga Wegener (ingga.wegener@med.uni-heidelberg.de)
Ulrich T Hopt (ulrich.hopt@uniklinik-freiburg.de)
Tobias Keck (tobias.keck@uniklinik-freiburg.de)

Version: 2 Date: 15 December 2011

Author's response to reviews: see over
Dear Mr. Goldsmith,
Dear Members of the Editorial Board,

Hereby we submit the revised version of our manuscript. As requested we include the ethics committees’ votes for all centers.

We thank you for the careful review and include a point-by-point answers to the reviewer’s comments below.

We hope that our manuscript will be eligible for publication in Trials.

Ulrich F. Wellner, first author
Tobias Keck, senior author
Answers to reviewer’s comments:

Ad 1-9: We have adopted the suggested modifications.

Ad 10: The inclusion of all subtypes of PG or PJ leads to a high external validity and makes the study results more generalizable. We feel this is appropriate. A detailed analysis of subtechniques is out of the scope of this trial.

Ad 11: suggested changes were adopted

Ad 12: An additional explanation was necessary and has been added to the manuscript.

Ad 13-15: suggested changes were adopted

Ad 16: This difference was calculated by pooled analysis of the only two available RCTs which employed the POPF consensus definition (ISGPS). This definition is also used for the REcopANC trial. The application of a "minimum clinically important difference" concept to the surgical patients with dichotomous occurrence of complications like POPF is not straightforward. However considering the average hospital caseload of 30-100 pancreateoduodenectomies per year for high-volume centers, a “MCID” of 10% seems reasonable from the surgeon’s point of view.

Ad 17: The suggested minor corrections have been made. A clearer explanation of sample size calculation and interim analysis is given now. The sample size is to be recalculated from the adaptive interim analysis. Assuming a rate of fistula of r=16% in the PJ group and r=6% in the PG group, recalculation of the sample size for stage two results in a mean total sample size of n=158 (ADDPLAN 5.0). We agree that this calculation does not provide added value to the manuscript, so this part is now omitted. We do not feel that it is necessary to inflate the sample size for the centers. Center bias is alleviated by inclusion of only high-volume academic centers with the highest standard of care. The center effect is part of the multivariable analysis.

Ad 18-20: suggested changes were adopted

Ad 21: This is a planned exploratory subgroup analysis and will have to be interpreted with adequate caution. The underlying question is of relevant clinical interest and should not be omitted. However we decided to include all patients (not only high-risk patients) to maintain the highest generalizability of results.

Ad 22: Missing data and loss to follow-up is expected to be marginal, missing data will be handled by an appropriate statistical method. A detailed explanation has been added to the manuscript (paragraph on sample size calculation).

Ad 23-42: suggested changes were adopted