

The Netherlands; April 17, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 17183-Edited.doc).

Title: Diagnostic value of drain amylase to detect intrathoracic leakage after esophagectomy.

Author: Gijs HK Berkelmans, MD; Ewout A Kouwenhoven, PhD, Boudewijn JJ Smeets, MD, Teus J Weijs, MD, Luis C Silva Corten, MD, Marc J van Det, PhD, Gerard AP Nieuwenhuijzen, PhD, Misha DP Luyer, PhD.

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 17183

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated and *American Journal Experts* have reviewed the English text.

2. Revision has been made according to the suggestions of the reviewer

(1) Question by 00227449: "In some cases, amylase increased after the clinical symptoms were observed (p. 9 top). Thus, amylase increases may be in addition can serve as an indicator of infection/poor wound healing." *This remark by reviewer 00227449 states the fact that amylase in drain fluid could be an indicator for infection/poor wound healing. Amylase levels were measured for the correlation with anastomotic leakage. Anastomotic leakage is a result of poor wound healing of the esophago-gastric anastomosis. We did not find any effects of elevated amylase levels on poor wound healing in this study. A possible explanation could be the manipulation of the anastomosis at endoscopy or surgical intervention. Page 14, line 357.*

(2) Question by 00227449: Format issue: "The figure legends should be in a different section, not as part of the main text." *This format issue is solved, by moving the figure legend next to the enclosed figures.*

(3) Question by 00225277: "Recommendations for further research In Discussion - studies on the influence of the outcome of early AL detection should also be considered." *We have incorporated this remark in the manuscript discussion, page 15, line 370.*

(4) Question by 00225277: "On page 5 -The signs and symptoms of AL recorded; it is difficult to consider data such as atrial fibrillation and delirium as having a relationship with this complication, even if these data had been observed in the series studied." *Atrial fibrillation is related to the presence of anastomotic leakage. The study conducted by Stawicki et al (PMID: 21674306 PMID: 4069196 DOI: 10.1007/s11748-010-0713-9) describes the relationship of atrial fibrillation with complications after an esophagectomy. Furthermore, delirium is possibly a consequence of complications after surgery and critical illness as stated by Shi et al. (PMID: 20497703). Delirium and atrial fibrillation can occur when complications such as AL arise. Therefore, we choose to record all possible relations with the presence anastomotic leakage and mentioned atrial fibrillation and delirium. Page 10, line 211.*

(5) Question by 00225277: "Why did the percentage of AL treatment refer to the whole series of patients included in the study and not to the patients with complications?" *In our cohort 15 out of 89 patients developed AL. Four patients required surgery as intervention. $4/89 = 4.5\%$, when we present the numbers related to the patients with AL 26.7% ($4/15$) is the percentage. In order to show similarities with today's literature, where percentages are presented in relation to the total cohort, we choose to present the percentages in this particular way.*

(6) Question by 02544637: "It would be better if they combined Figure2A and Figure2B, and represented the "Median amylase levels for patients with or without AL" in the same figure." *I agree with the reviewer that 1 figure could improve visualization of the differences between both groups. We have combined these figures into 1 graph in an earlier stage; however, the Inter Quartile Range bars were overlapping*

when combining the two figures into one. We choose not to combine the figures in order to show true IQR bars and visualize the large spread in the anastomotic leakage group. To illustrate the effect of combining these figures, we have enclosed an additional Figure for this reviewer.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

A handwritten signature in black ink, appearing to be 'G. Berkelmans', written over a circular stamp or mark.

Gijs HK Berkelmans, MD
PhD-candidate
Catharina Hospital Eindhoven
The Netherlands