October 23rd, 2012

Dear Editor,

Thank you for reading our previous manuscript. We have addressed the comments of the reviewers, changed the manuscript accordingly and kindly ask you to consider our resubmission for publication.

Please find enclosed the edited manuscript in Word format (file name: Does availability of an in-house multidisciplinary team incease survival in upper GI cancer\_revised.docx).

**Title:** Does in-house availability of multidisciplinary teams increase survival in upper GI-cancer?

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**Name of Journal:** *World Journal of Gastrointestinal Oncology*

**ESPS Manuscript NO: 658**

We would like to thank the reviewer for the careful reading of our manuscript and are grateful for the suggestion on how to improve the understanding of our findings. The manuscript has been improved according to the suggestions of reviewers:

**Reviewer 1:**

1. *There was “an increase in the number of patients receiving chemotherapy and radiotherapy, but not in surgery. This seems somewhat counter intuative in that studies of high volume v low volume centres in other countries have found that surgical therapies were less likely to be offered by low volume centres, a situation analagous to MDT clinics. A* comment in the discussion may be useful.”

In our work, we analyzed potential life-prolonging interventions and found **NO** increase in the number of irradiation series for the diagnoses in question (p= 1.0, OR= 1.0). In addition, the use of gastro esophageal or bile duct stents was stable during the study period (p= 0.33 OR= 1.04). There was no statistically significant increase in curative UGI cancer surgery (p= 0.3 OR= 1.05). However, as mentioned, the number of lines of chemotherapy regimens used for the total population (p> 0.001, OR= 1.54) in WA/MDT-C.

In light of the reviewers comment, we added the following sentences to the discussion section of the manuscript:

The number of irradiation series or the use of gastro oesophageal or bile duct stents did not increase during the study period and we do not consider that the changes of the palliative services had a major impact on the life expectancy of the study patients, since the in-patient service was established at the very end of the study period.

The role of surgery for survival of the whole study cohort in this setting is more complex, since the group of UGI cancers as a whole has a low rate of curative surgery. Pancreatic and esophageal cancers are operable in less than one of five cases [1](#_ENREF_1), and small changes in this ratio affect median overall survival to a limited extent. Concerning gastric cancer, 43% of cases are operated in Norway [2](#_ENREF_2" \o "Holmebakk, 2010 #20). This proportion was allready higher before (data not shown), but stable throughout the study period, in our clinic. Thus, in light of a relatively high rate of surgery before iMDTa, the rate of surgery was not affected through the establishment of iMDTa in the WA/MDT-Change county.When looking at the results for gastric and esophageal cancers (Table 1), two findings are interesting: Both MDT-No and WA/MDT-Change centralized surgical treatment of esophageal, but not gastric cancer during the second interval of the study period to the MDT-Mix county of Oslo. In the WA/MDT-Change County, a survival benefit was seen for both entities, whereas the survival for these two diagnoses decreased in the MDT-No County (Table 1). These findings may support the theory that, in these particular geographic regions, the presence of oncologists in a hospital may have a greater impact than the place of curative surgery, at least on short term survival.

1. *“Similarly it would be useful to look more at the use of palliative therapies in the centres with MDT, can it e assessed whether these were offered earlier or more frequently.”*

This is a very important aspect, considering the short life-expectancy of the patients in the study. However, we do not consider that the changes of the palliative services had a major impact on the life expectancy of the study patients, since the in-patient service was established at the very end of the study period.

In the county of WA/MDT-Change, as stated in the material and methods section, palliative care services were established in the form of an ambulatory palliative team in 2002, a palliative day center in 2004 and an inpatient palliative care hospital unit in 2007. This implies that there was no palliative in-patient service available during most of the study period. In this regard, we have unfortunately little information about palliative measures used at the hospital.

One important goal of the ambulatory palliative team established in 2002 was to facilitate home. Accordingly, home - and nursing home death rose from 14-18% and 24-30%, respectively. In line with this, number of hospital death declined from 60-51% (p< 0,0001)[3](#_ENREF_3).

The following sentence was added in the discussion section:

...we do not consider that the changes of the palliative services had a major impact on the life expectancy of the study patients, since the in-patient service was established at the very end of the study period.

**Reviewer 2:** The reviewer did not request any changes.

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

**Reviewer 3:**

*“This study assessed the impact of availability of multidisciplinary teams (MDT) on improving survival in some upper GI-cancer patients. By comparing data between two 5-year periods – i.e. before and after MDT introduction – the Authors observed a significant decrease in mortality rate (calculated as HR) for both oesophageal and gastric cancer patients, but not for pancreatic cancer patients. Moreover, the overall median survival for the considered cancers significantly increased from 129 to 300 days.*

*Data of this study could be interesting. However, as pointed out by the Authors, the only substantial difference between the period before and after the MDT introduction was a distinct increase in chemotherapy use, which increased from only 2.4% to 42.9%. Therefore, the significant improvement in the overall patients management mainly depends on increased chemotherapy use. According to our opinion, the rate of chemotherapy performed in the 2000-2004 period (2.4%) in these patients is astonishingly low. Indeed, the 42.9% rate calculated in the second period is still lower than that currently performed in clinical practice in developed countries. Therefore, the Authors have to discuss their data on chemotherapy use as compared to what performed in other countries. In other words, it would appear the overall increase in patients survival for the considered cancers mainly depends on a significant increase in chemotherapy use which still appears to be astonishingly lower than what happens in other countries. Probably, a similar result may be achieved in other Norvegian counties by simply implementing chemotherapy use, with or without a MDT introduction.”*

Dear reviewer, thank you for this important comment! In fact, we discussed it more thoroughly in a previous version of the manuscript, but left it out in order to keep the discussion concise.

The increased use of chemotherapy is correctly stated and we consider the role of the oncologists in the team as important in this setting. However, the gain in survival is too large to be solely attributed to the effect of chemotherapy – other factors play a role as well. The HR for survival over time, adjusted for use of chemotherapy, was 0.95 (95% CI 0.91-1.0) with a p-value of 0.04. In that respect, the increased use of chemotherapy should be interpreted as an effect modifier for survival, since the HR from stratified analysis with (0.89) and without chemotherapy (0.97) flanks the HR for the group as a whole, HR=0.93 (data not shown). As mentioned, we decided not show these data, in order to keep the number of figures and tables as low as possible and to keep the message clear.

In conclusion, we were not able to identify interventional factors other than increased use of chemotherapy to explain the striking improvement in survival in WA/MDT-Change. However, the MDT members in WA/MDT-Change agree upon a during the study period gradually improved team spirit and more effective communication, although it seems easier to measure the results, rather than formally proof the process of such increased human interdependency.

Thus, we added the following two sentences into the discussion:

“A 50% increase in the use of chemotherapy for every year of the study period may be a result of more patients getting therapy. In that respect, MDT seems to result in increased referral of UGI patients to the medical oncologist.”

“In this respect, the increased use of chemotherapy should be interpreted as an effect modifier for survival and the MDT members in WA/MDT-Change agree upon a during the study period gradually improved team spirit and more effective communication, although it seems easier to measure the results, rather than formally proof the process of such increased human interdependency.”

We hope to have addressed the comments of the reviewers sufficiently an thank you again for publishing our manuscript in the *World Journal of Gastrointestinal Oncology.*

Sincerely yours,

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3. Albert E KC. European Journal of Palliative Care 2009.