Peer Review File

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Reviewer A:

Comment 1: The authors description was limited on a limited sample size of libanese people. Which kind of clinical aspect was covered? Which kind of clinical applicability in the scientific community?

Reply 1: We would like to thank the reviewer for the comment and the question. We covered the prognosis and clinical presentation of Lebanese patients with gastric cancer and we determined if age had an effect on the prognosis or on the clinical presentation.

We found that the majority our patients present with advanced disease and that a minority qualify for curative resection. This highlights the importance of having a low threshold for investigating patients with symptoms and for screening patients at high risk. Furthermore, young patients (those below 65 years of age) present with more aggressive disease compared to older ones. They have more poorly differentiated tumors and their cancers are more likely to progress than older ones. This mandate having again a low threshold for investigating young patients with unexplained upper gastrointestinal symptoms, weight loss or anemia. It also suggests that screening patients with risk factors may be needed. Finally, we did not find a significant difference in disease free survival between young and old patients. This may be because older patients have more comorbidities, while younger ones have more aggressive disease. Larger studies are needed to determine the effect of age and comorbidities on survival in gastric cancer.

Reviewer B:

Comment: This is a single institution retrospective study evaluating the impact of age on prognosis of 156 gastric adenocarcinoma patients, treated at the American University of Beirut Medical Centre, a tertiary hospital, between January 2005 and December 2014.

The authors state that it is the first study to evaluate age as a prognostic factor in Lebanon. This information should be important for people and physicians living in the country.

A review of the introduction, results, tables and figures should be done to improve comprehension.

Reply: We have reviewed the introduction, results, tables and figures and the changes are now highlighted.

1)Lines 82-92: References are not in accordance with the text

Reply: We have reviewed and corrected the references (Lines 395-405)

2**)Line 101:** It would be interesting to characterize the institution and type health care system (public or private)

Reply: The American University of Beirut Medical Center (AUBMC) is a private, tertiary care facility that operates 420 beds, serving around 22,000 in-patients per year. AUBMC provides a wide spectrum of medical, nursing, and paramedical training programs at the undergraduate and post-graduate levels in different specialties and subspecialties and is considered a referral medical center in the Middle East region.

Changes in the text: We added the above paragraph that characterizes AUBMC to the Methods section under Study Design and Setting, lines 103-107.

3)Line 103: Provide information about inclusion criteria and exclusion criteria.

Reply: Inclusion: Lebanese adult patients diagnosed with gastric adenocarcinoma between 2005 and 2014.

Exclusion: Patients who had other types of gastric cancer (lymphoma, Gastrointestinal stromal tumor, carcinoid tumors). Non-Lebanese patients with gastric adenocarcinoma.

Changes in the text: the information is mentioned in the Methods section, under Participants, lines 111-117.

4)Line 108: Why patients non-Lebanese were excluded? Lebanese were patients born in Lebanon? Were people born in other countries, but permanent inhabitants of Lebanon, excluded from the analysis?

Reply: We wanted to study a homogenous group of patients that have the same environmental background and have similar genetic factors as those might influence the clinical presentation, clinical behavior and outcome of patients with gastric cancer. We included patients whose medical records indicate they are Lebanese, but we don't have information as to whether they acquired Lebanese citizenship as long-term inhabitants of Lebanon**.**

5)Line 106 - 109: After exclusions, number of patients do add up 99 and not 156, as stated on line 109

Reply: Total number of patients included was 415 patients (correction on line 114)

Changes in the text: the information is mentioned in the Methods section, under Participants, line 114.

6) Provide the number of patients lost to follow up. The last date of inclusion was December 2014. Lines 213-215: median follow up of 3 and 4 years (below 65, equal or above 65y, respectively)

Reply: the total number of patients lost to follow-up was 5 patients- updated on line 172.

Changes in the text: This is indicated in the Results section, page 11, line 172.

Line 126: Provide information for fixing the cut off age at 65.

Reply: We found from some previous studies that overall survival in patients with gastric cancer is worse in older individuals compared to younger ones. Some of those studies have used cutoff points of 60, 65 or 70 years. Kindly refer to the studies by Saito H et al; Lai et al; Yang et al; and Wang et al; cited in our manuscript and expanded on in Table 4. Furthermore, number of comorbidities increases substantially in patients older than 65, and we felt that comorbidities could affect prognosis in gastric cancer.

Line 147: in a separate analysis, patients were further subdivided in 3 categories. Please provide the basis for this subdivision.

Reply: In some studies, on the effect of age on prognosis in gastric cancer, survival worsens progressively with increasing age (kindly see the studies by Lai et al and Yang et al referred to in Table 4). We did not want to miss a possible difference in survival between those who are very young (less than 45 years) and older patients.

Line 195 - Table 1

A review of the numbers and percentages is advised.

The number of patients shown for the variables do not add up 156. Missing information should appear in the table and the total number of patients analyzed for each variable.

Presenting signs and symptoms

Stage at diagnosis (n=111): missing information: 45; stage 2: 21/111 (18.9%) instead of 8.9

Histology (n=134): missing information = 22

Reply: Added missing information to Table 1- Line 205

Line 196: SD: standard deviation: **Removed**

Table 2: A review of the numbers and percentages is advised.

The number of patients shown for the variables do not add up 156. Missing information should appear on the table, as well as the total number of patients that were analyzed for each variable

Reply: We added the numbers for missing patients for each variable to table 2 and the information is now shown in the foot notes of Table 2 lines 351-352.

Table 2 Progression: young: 36 (70.6%) vs elder: 21 (48.8%)

These numbers are not clear. What is the denominator?

Line 204: progression of the disease (the numbers on the table are not clear)

Reply: We corrected the percentages in table 2- denominator is total number of patients within each category. The number of missing patients for each variable is now indicated in the foot notes of Table 2, lines 351-352.

Line205-206: "Patients < 65y…were significantly more likely to have lower BMI"

If we check information on table 2: Underweight and normal - <65y: 45.4% vs >= 65y: 50%;

Obese and severely obese - <65y: 19.5% vs >= 65y:18.6%

This table should be carefully analyzed, and the statement should be rephrased, because the only difference is that there were no severely obese young patients (<65y: 0 vs >=65y: 7.1%):

Reply: We agree with the reviewer and we corrected the mistake. Severe obesity was more prevalent in patients > 65 years of age (p=0.05).

Changes in text: lines 214-216

Figure 1: please inform the X axis: years vs months

Reply: The survival in the Kaplan Meir graph is in years not months. This is now indicated in line 225.

Line 227-230: “Patients were subcategorized into 3 groups according to age…Please see table 2

These results do not appear on table 2.

Reply: We agree with the reviewer and reference to table 2 was removed. This is mentioned in line 233.