Author’s response to reviews

Title: The modified Glasgow Prognostic Score in prostate cancer: results from a retrospective clinical series of 744 patients.

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Author’s response to reviews: see over
Thank you for your email regarding the above mentioned manuscript. We appreciate the supportive comments of the reviewers. We have considered carefully the reviewers’ comments and made some changes. Below are our point by point responses to their comments.

REVIEWER #1 (Kenneth R Muir):

Thank you very much for your supportive comments.

REVIEWER #2 (Azad Razack):

1. There is no information on the stage and the treatment received by the patients. It will be difficult to compare the prognosis and survival without this information.

Response: We completely agree that stage and treatment have significant prognostic value. A previous paper by McArdle PA et al, showed the effects of CRP has significant prognostic value both on localized as well as advanced prostate cancer patients. We also stratified our analysis based on PSA and Gleason Score, which gives some clue that mGPS is equally important both in low risk and high risk patients. Furthermore, the prognostic value of mGPS was also assessed by excluding patients who died during first year following diagnosis. This was based on the assumption that high risk patients with metastatic disease may die earlier due to their disease and these patients may have higher systemic inflammation due to metastatic disease. By excluding these patients from the cohort, what we may left with is a group of patients with low risk disease. Even in that sub-group the mGPS shows significant prognostic value. We completely agree that treatment and stage specific analyses are also required to better understand the prognostic value of this test in subgroups of prostate cancer patients. However, current Scottish Cancer Registry does not have the complete information of these factors and that remains a limitation of this study which is mentioned in the discussion section on page 14 of manuscript. We also clearly concluded that “Prospective studies are required to validate our results and to test the clinical utility of mGPS in the clinical management of prostate cancer.”
2. The information of the Gleason score i.e. if it is from biopsy or radical prostatectomy specimen is not clear.

(Response: Point taken, the information of Gleason score is obtained from biopsy and it is mentioned on page 8 as “The information on Gleason score was obtained through prostatic biopsy.

3. No information on the number of patients without Gleason score.

(Response: Point taken, following sentence added in result section on page 10, “Thirty five percent of patients (n=262) had high Gleason score (Gleason 8-10), 21.9% had unknown Gleason score (n=163) and nearly half of the cohort (n=362, 49%) had PSA greater than 20ug/l.”)

The baseline table 2 already have the information of those with missing Gleason grade. Relative excess risk of death has been separately reported for those who had missing Gleason score.

4. The cause of death is important but is not available.

(Response: The information on cause of death is available and we also calculated cause-specific survival estimates which were consistent with what we reported in this manuscript. However, we used “relative survival” which is considered as most viable technique for calculating cancer-specific survival in population-based cancer registries. This technique does not rely on cause of death information rather it includes all deaths in cohort of patients comparing it with age, gender and SES specific population mortality rates and provide excess mortality due to cancer. In recent years, it has been considered as most useful way of estimating survival and excess risk of death from population-based datasets.

4. In patients with Gleason score under 7, since the stage and the treatment information is not available it is difficult to conclude on the effect as it is possible that these patients might have other co-morbidity which resulted in more of them having watchful waiting rather than active treatment.

(Response: Previous in-patient bed days have been used as a proxy measure of co-morbidity in population-based studies of cancer (DH Brewster et al, Characteristics of patients dying within 30 days of diagnosis of breast or colorectal cancer in Scotland, 2003–2007). Co-morbidity index (CCI) was not available in the Scottish Cancer Registry Data, so to overcome that limitation we done a further linkage with hospitalisation records to obtain “previous in-patient bed days” from 10 years to 1 year prior to diagnosis. This was particularly important because patients who had higher CRP before diagnosis may have a concurrent co-morbid condition which raised their inflammatory markers. So inclusion of previous in-patient bed days may still be a useful measure as men with concurrent co-morbidity may have higher in-patient bed
days compared to those with no co-morbidity. So analysis presented for Gleason less than 7 are adjusted for co-morbidity (using previous in-patient bed days from 10 years to 1 year prior to diagnosis). These details are mentioned on page 7.

Once again, thank you for the consideration of our manuscript for publication; we will look forward to your reply in due course.

Yours sincerely,

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