Reviewer’s report

Title: Heterogeneity in high-risk prostate cancer treated with high-dose radiation therapy and androgen deprivation therapy

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Reviewer: Seungtaek L Choi

Reviewer's report:

This paper looks at a very relevant issue in the treatment of prostate cancer by trying to improve risk classification of patients to better personalize treatment.

However, I had several questions/issues:

1) I would not recommend adding patients with 2-3 intermediate risk features in the "favorable" high risk group. They should be either excluded from this analysis, or be used as a comparison for the patients with 1 high risk feature to see they have similar outcomes.

2) Also, as the patients with very unfavorable high risk patients received a lower dose of radiation (median dose of 70 Gy) and shorter duration of hormone ablation therapy, it's difficult to know if the reason for their worse outcome is the disease or the treatment given.

3) Gleason score of 7 is used as the cutoff point for the analysis. Was Gleason 8 or 9 looked as well?

4) The current standard of care for high-risk prostate cancer is to give long-term hormone ablation therapy (defined as greater than 28 months). Looking at Table 3, less than 30% of patients received that duration (or longer).

5) Was image guidance used for the 3D CRT or IMRT treatment?

I therefore recommend analysing only patients with high-risk prostate cancer who received modern radiation therapy (74 Gy or higher, ideally with image guidance) of radiation therapy.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
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Unable to assess

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No

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I am able to assess the statistics

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