Reviewer's report

Title: Long-term results of radical prostatectomy with immediate adjuvant hormonal therapy for pT3 prostate cancer

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Reviewer: Brian Chapin

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Single center retrospective study on patients with pT3 disease followed by adjuvant ADT for minimum 5 years. Endpoints were OS, CSS, clinical recurrence and hormone refractory PCa. It is unclear why this patient population received a therapy that is not recommended by any guidelines and seemingly did not receive adjuvant XRT, which has demonstrated advantages through level I evidence. But since the data is available it might be of interest to those planning clinical trials in this area. Given the data this would provide some interest as to the possibility of an alternative or adjunctive therapy to adj XRT. However, the patient population needs to be better described, the analysis needs additional variables and the discussion needs to be edited to provide a more equitable assessment of the available data. Please see below revisions.

Major revisions:

Subjects and methods:

1. Immediate adjuvant hormone therapy implies undetectable PSAs at the time of initiation of systemic therapy. If this is correct please state. If a percentage of patients had failure to nadir to undetectable this information should be provided.

2. The authors state that a pelvic LND was completed on each patient but do not report on node findings. Clearly patients with pathologic node positive disease have a more significant risk of bcf and this information should be provided for the reader. Node positive patients should be looked at separately in the analysis.

3. I assume this was not a single pathologist review as it is not commented on by the authors.

Results:

1. 14 patients received non-standard ADT regimens. This may have been selection bias based on pathology or patient preference. It makes it unclear if equivalent application of this therapy was provided to all patients. If anything this would potentially bias the results, underestimating the risk of recurrence in this population. For example if all 14 pts were NED throughout the study. I would consider excluding the patients receiving casodex, estramustine and other tx.

2. Lymph node status should be included in the univariate and multivariable analysis. If all were pNO this should be stated in the results along with median number of LNs removed. If some were pN+ this should be a variable in the
3. It is unclear if any patients received adjuvant XRT or if XRT was only applied in the salvage setting. If they did not, why did they receive a non-standard/recommended therapy (ADT) without receipt of adj XRT, which has level I evidence to support its use.

4. The table states 16% of patients with pT3 disease were Gleason 5-6. This seems rather high and inconsistent with the findings of others. Was the path re-reviewed or is this the reported path prior to the 2005 Gleason modifications. If these are indeed Gl 6 from pre 2005 they would likely be upgraded to Gl 7s post 2005. Recommend having a single GU pathologist review the path to confirm Gleason grade and stage.

Discussion:

1. The authors make comparison to other retrospective reported series of T3 a or b disease. While it is important to draw attention to the available data making comparisons across retrospective studies is not helpful. This studies population is made up of mostly Gl 7 or less patients, while other studies have majority of Gleason >/=8. The authors comments “surgery alone might thus be of limited use in most patients with stage pT3N0M0 PCA” is not an appropriate conclusion based on the data provided. Please revise the statement to something along the lines of single modality therapy may not be sufficient in a large portion of patients with T3 PCa and a multimodality approach may be more beneficial, or something along those lines.

2. The studies presenting outcomes of T3 pts s/p RP only have fairly high rates of biochemical failure free survival and overall survival. Given those findings and the significant hazard ratio for pT3b disease my conclusions from this study would have been different. May consider revising to state that given the high success rate with RP alone in T3 patients, the greater risk of hormone-refractory biochemical progression free survival in pts with pT3b disease and the reported CSS and hormone refractory bcpfs in this series, future prospective studies are needed comparing additive effects of multimodal therapies in patients with pT3 disease to better select for a population of patients that may receive the most benefit. This is hypothesis generating as to what therapies may provide improved outcomes in a sub group of pT3 patients, but clearly a significant percentage of patients are being over treated with application of systemic therapy to all comers.

3. The final comment is that these findings are based on a pathologic result. The majority of these patients were consider of lower grade and stage at diagnosis and the T3 finding was only after RP. In my opinion this makes RP a very reasonable option for the initial treatment of PCa to help better select for patients who will require additional therapies.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: none