



BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242 Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com <http://www.wjgnet.com>

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Reviewer 00504183

This is an interesting retrospective study comparing the effects of adjuvant vs. salvage RT on biochemical recurrence free survival of high risk PCa pts with initially undetectable post-op PSA. This is well-written work and both the results and limitations of the study are adequately documented.

Thank you for your comments. We feel our study adequately demonstrates an improved biochemical recurrence-free survival following administration of adjuvant radiation therapy in the setting of adverse pathologic features. We anxiously await the results of the ongoing prospective trials on this subject.

Reviewer 00505643

Dear Editor: The authors compared retrospectively the results of adjuvant and salvage radiotherapy after radical prostatectomy. They found that patients in the adjuvant group had better biochemical recurrence-free survival but no other benefit.

Comments: 1. The authors should define "undetectable PSA".

Thank you for this comment. Our the assay at our institution detects serum PSA to a value 0.05 ng/mL, as such, a value of <0.05 was used as the cutoff for undetectable in this study. The methods section of the manuscript has been updated as follows:

“For this study, an undetectable PSA was defined as a PSA with a value of <0.05ng/mL.”

2. Median follow-up (53 months) is too short. With longer follow-up other benefits of the adjuvant treatment may come-up.

We agree with the reviewer that our follow-up is limited, which is a problem with many studies of the treatment of prostate cancer. With time we will need to re-evaluate this cohort and determine if any differences in overall survival, bone metastases, or time to hormonal therapy become apparent.

3. There is no mention of side effects, not even in the discussion. To be clinically relevant this issue cannot be ignored.

Thank you for this comment and we agree that the potential side effects of radiation therapy require special attention. Unfortunately, we feel a detailed discussion is beyond the scope of this manuscript, however have added the following statement into the discussion addressing the side effects of radiation on patient/provider decision making, and have included references to work from our group and others on the subject.

“Further, the potential side-effects of radiation therapy (including urethral stricture disease, hematuria, proctitis, cystitis, etc) are well documented^[24-30], and play an integral role in the decision making process for both the patient and provider.”

4. Since the study is retrospective, it is subjected to selection bias. Yet this bias would probably favor the salvage group.

We agree with this assessment and the phrase “selection bias” was specifically incorporated into the discussion. As outlined in the discussion patients were not randomized to adjuvant vs salvage radiation, and as such the decision-making process that led to each patients’ treatment choice introduces selection bias. We feel our analysis actually favors the adjuvant radiotherapy group, as this group includes

patients who may have never recurred if they had chosen to undergo observation and salvage at the time of recurrence. The salvage radiotherapy group, however, includes only patients who have undergone a recurrence, and as such have demonstrated they may, in fact, have a more aggressive disease state. While our results must be interpreted within this context, they echo results from prior studies by Ost^[17] and Trabulsi^[18], and provide the basis for the ongoing prospective trials^[20-22] assessing the outcomes in this patient population.