Reviewer’s report

Title: Comparison of laparoscopic and open postchemotherapy retroperitoneal lymph node dissection in patients with advanced testicular cancer a single center analysis

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Reviewer: Wade Sexton

Reviewer’s report:

Dr. Busch and colleagues report the clinical outcomes of patients undergoing open or laparoscopic post-chemotherapy retroperitoneal lymph node dissection (PCRPLND) for metastatic testis cancer. Those of us who manage advanced testis cancer patients would certainly agree that PCRPLNDs can at times be quite challenging requiring experienced surgeons with expert skill and knowledge of dissection techniques. In the post-chemotherapy setting, patient candidates for a laparoscopic approach have to be selected carefully due to the inherent difficulties associated with nodal and vascular dissection. A more important consideration is the premise that the first opportunity to cure (surgically) in the post-chemotherapy setting is absolutely the best opportunity to cure as re-do PCRPLNDs are even more challenging with greater risks for vascular injury and inferior surgical outcomes. To the authors’ credit, they correctly emphasize patient selection. However the purpose of this study is to compare the outcomes between patients undergoing Lap-PCRPLND and Open-PCRPLND. In order to compare these patient groups, they should be similar in their clinical characteristics. Unfortunately the two groups are not comparable which limits any conclusion the authors suggest other than stating that a Lap-PCRPLND is feasible in highly selected patients with very limited post-chemotherapy tumor volume. Furthermore, in many instances, the authors’ reporting of the data appears incomplete and at times is misleading.

Major Compulsory Revisions:

1. The groups undergoing underwent L-PCRPLND and O-PCRPLND are not comparable. This poses the biggest problem with the manuscript and substantially biases the authors’ results. The authors should further address the following points and possibly reassess the aims of the study.

a. A significantly greater percentage of patients with good prognosis disease was managed with lap vs open PCRPLND.

b. The median tumor diameter was significantly less in the lap group (2.2 cm) compared to the open group (6.7 cm). Most certainly, residual tumor size is associated with Clavien grade III complications, need for subsequent procedures, organ or vascular resection.

c. The extent of the retroperitoneal dissection was significantly greater in the open group (61.9% of open patients undergoing full bilateral dissection vs. 26%
of lap patients undergoing full bilateral dissection. Obviously, the surgical times would have been impacted tremendously if patient groups were comparable (longer operative times in the lap group).

d. Two patients in the lap cohort underwent a simple lumpectomy – a procedure clearly recognized to not reflect the standard of care for the management of testis cancer.

e. Comparing and analyzing the differences in Clavien complications (vascular injuries, nephrectomies, etc.) is difficult as again the groups are simply not comparable.

2. The abstract should be revised to reflect both methods and results sections standard to almost all journal formats.

3. Unless specified by the journal, the methods section in the manuscript should be inserted following the background section.

4. Results section first sentence. If 26% and 28.5% of 18 patients with seminomatous elements in the primary orchietomy specimen underwent L-PCRPLND and O-PCRPLND respectively, what transpired with the remaining 45.5% of patients? Maybe the authors have worded this sentence incorrectly?

5. The authors never defined the modified templates they chose to utilize. For instance, in the modified right template, did they respect reports reflecting potential for right to left crossover of nodal involvement and resect the left paraaortics? For left sided templates, did they resect the interaortocaval nodes? In the post-chemotherapy setting, did they completely mobilize the aorta and vena cava by dividing lumbar arteries and veins?

6. Did the authors perform nerve preservation – especially given that the median tumor volume reported for the lap cohort was only 2.2 cm. Thus, approximately ½ of the patients had tumor volumes less than 2.2 cm.

7. How many patients in each of the groups had a complete response following chemotherapy (defined as normal tumor markers with a residual mass less than 1 cm or no residual mass)? In the setting of a complete response, retrospective data from two recent reports support observation following chemotherapy rather than PCRPLND.

8. Did any of the patients have elevated markers at the time of PCRPLND?

9. What criteria did the authors utilize to determine which patients would undergo open vs. lap PCRPLND?

10. Table 1, the percentages of good, intermediate, and poor risk IGCCCG do not account for 100% of the patients in either of the lap or open groups. Either data are missing or the reporting of the results is inaccurate.

11. Table 2, data is missing for residual tumor histology in at least one or more of the patients undergoing open surgery. Furthermore, please specify whether you are reporting lap patients with more than one histology (totals 50 patients).

12. Table 3. Grouping patients by clinical stage IIa through IIc and IIIa through IIlc and then comparing the patients with statistical analysis is terribly misleading – especially when comparing lap vs. open surgical approaches. The authors
should subdivide into separate stages (i.e. IIa, IIb, IIc, IIIa, etc) and simply show the numbers. There is a tremendous difference between a IIa patient with a 1.5 cm residual paraaortic mass and a IIc patient with a 10.0 cm interaortocaval mass (+/- S1 markers).

13. Report the number of chemotherapy cycles in both groups. How many patients in each group were treated with salvage chemotherapy regimens following induction chemotherapy prior to undergoing PCRPLND?

14. Table 5. In regards to further treatment, there must be 10 patients in the Lap group lost to follow-up and at least 2 patients in the open group lost to follow-up. The authors make no comment in this regard and do not explain the results. Although they errantly include a “surveillance group” in the “further treatment” section of this table, it seems that they should indicate the status of these other unaccounted for patients.

15. Table 6. The subgroup analysis is still non-comparable due to significantly different post-chemotherapy median tumor sizes and other unknown clinical factors.

16. Discussion section. The first sentence needs to be revised. In addition, the authors’ data do not support their statement that long-term oncological outcomes were comparable due to many treatment biases as described, although the authors briefly discuss the study biases in the early part of the discussion section.

17. Table 3 and Table 6. In the manuscript, the authors suggest that no drainage tubes were inserted in the lap group, but in these two tables data show that drains were indeed placed in some patients undergoing Lap PCRPLND. (see results section, operative characteristics, duration of drainage tube 0 days). Why were drains placed in some and not in others? Is this a common practice for this group of surgeons? What criteria did the authors use to select patients for drains?

18. Last sentence of the results section: Were the authors surprised by the findings that neither the IGCCCG classification nor the clinical stage correlated with survival? This is contrary to what has been reported for patients with good, intermediate, and poor prognosis disease. The discussion should be expanded in this regard.

Minor Essential Revisions:

19. 18/67 primary tumors were pure embryonal carcinoma (a higher percentage than what would normally be expected). Was a urologic pathologist utilized for this study to re-review the specimens and standardize pathologic analysis?

20. Table 4, how can the estimated overall survival be significantly greater than the median followup?

21. In the Results section, Outcome characteristics subheading, it is difficult to determine in which group patients 1-7 belong (lap vs open). The details regarding relapse would be presented better in a table format.

22. Table 4. Correct several misspelled words.
Discretionary Revisions:

23. In the two patients with pure seminoma in the primary tumor that subsequently underwent L-PCRPLND (table 1), did they undergo surgery for tumors greater than 3 cm in diameter or for a positive post-chemotherapy PET scan?

24. Table 3. Why were there more major vascular injuries in the Lap group and what was the outcome?

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I declare that I have no competing interests.