Author’s response to reviews

Title: Does External Beam Radiation Boost to Pelvic Lymph Nodes Improve Outcomes in Patients with Locally Advanced Cervical Cancer?

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Author’s response to reviews:

Please kindly refer to the attached supplementary material for our responses.

We would like to thank the editors and reviewers for taking the time to review our manuscript. We have included your valuable feedback in our revised manuscript and would greatly appreciate your comments. Thank you very much.

Reviewer 1:

1. Confusing paragraph - page 5, line 45-51

Initially stated that there are 139 patients. Then it states 53 patients (79.1%) have SCC. However, 53/139 does not equal 79.1%. Same with the following sentence. 60 pts (89.6%) were given concurrent cisplatin-based chemotherapy. 60/139 does not equal 89.6%.
Answer:

We sincerely apologize for the confusion and thank you for clarifying this. We have now included the proportion of SCC and patients receiving concurrent chemotherapy out of 139 patients rather than only calculating the proportion within the 67 patients with positive pelvic nodes. We have now amended the paragraph as follows:

'Squamous cell carcinoma (SCC) histology was most common in 76.2% (n=106) of all patients. In 67 patients with positive pelvic nodes, 79.1% (n=53) had SCC and in 62 patients with negative pelvic nodes, 85.5% (n=53) had SCC.' - Page 6, line 1-7.

'Concurrent cisplatin-based chemotherapy was given in 84.1% (n=117) of all patients. In 67 patients with positive pelvic nodes, 89.6% (n=60) received concurrent chemotherapy and in 62 patients with negative pelvic nodes, 75.8% (n=47) received concurrent chemotherapy.' - Page 7, line 1-11.


Answer:

Thank you for noticing this error. We have now corrected this as follows:

'In 36 patients with positive pelvic lymph nodes who received a nodal boost, 44.4% (n=16) developed recurrence, of which 5.6% (n=2) had local recurrence only, 22.2% (n=8) had distant metastases, and 16.7% (n=6) had both local and distant recurrence.' - Page 7, line 42-49.


Answer:

Thank you for clarifying this. We have added the following to our manuscript:

'Lymph nodes that were < 10 mm on radiological imaging with round, irregular shape, or ill-defined edge, occurring as clusters, enhances with intravenous contrast were deemed to be suspicious and managed as positive pelvic node.' - Page 3, line 49-54.

4. “Patients who did not receive a nodal boost had fewer recurrences and better OS.” Results show there was no significant difference amongst the two groups in recurrences or in median OS – page 8, line 54.
Answer:

Thank you for highlighting this. We have now amended this to:

'Patients with positive pelvic lymph nodes who did not receive nodal boost appeared to have fewer recurrence and better OS, however these were not statistically significant.'  - Page 9, line 13-18.

Reviewer 2:

1. It remains completely unclear how the operative strategy was, esp in cases with FIGO I and II, please clarify if FIGO I and II was without operative strategy why this decision was made.

Answer:

Thank you for clarifying this.

All of the patients included in this study received radical intent pelvic external beam radiotherapy (EBRT) with brachytherapy and did not undergo surgery. We have now included this information on page 3, line 44-47.

As per the National Comprehensive Cancer Network guideline, treatment options with radical hysterectomy or pelvic radiotherapy with concurrent chemoradiotherapy. Patients with FIGO I and II included in this study did not undergo surgery due to multifactorial issues including co-morbidities rendering high anaesthetic and surgical risk and/or personal preference.

2. CT is known to be less significant to lymph node involvement, therefore the question arises if all patients underwent PET-CT.

Answer:

We have included that in our study, only 18.7% (n=26) patients received a PET scan as part of their staging mainly due to cost limitation.  - Page 9, line 49-54.

3. What is about the paraortic lymph node involvement esp in group with positive pelvic nodes?
Answer:

Thank you for discussing this. Please kindly refer to our explanation below:

Out of 67 patients who had positive pelvic lymph nodes, 9 also had positive para-aortic lymph nodes at diagnosis and all received extended field RT covering the involved para-aortic nodes as per our department protocol. Page 6, 51-58.

We have now also added the following detail in our manuscript on page 8, line 9-20.

Two patients had positive PA nodes and positive pelvic LN but did not receive any pelvic nodal boost:

- One patient developed local recurrence as well as distant metastases
- The other patient developed distant metastases only

Seven patients had positive PA nodes and positive pelvic LN with pelvic nodal boost given:

- Three patients developed local recurrence as well as distant metastases
- One patient developed distant metastases only
- The remaining three patients had no recurrence