Peer Review File

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Reviewer A

Comment 1

Although concurrent CHRT may be considered as therapeutic standard in locally advanced inoperable NSCLC several controversies exist over optimal selection of patients for such therapy. Frail/elderly patients are of particular concern when concurrent treatment is considered. Elderly patients (>70) may not benefit from concurrent treatment, as compared to sequential chemo-radiotherapy (see e.g. Miller ED, Fisher JL, Haglund KE, et al. J Thorac Oncol 2018;13:426-35). Also, regarding the future there is ongoing interest in sequential treatment followed by immunotherapy (see e.g. PACIFIC6 trial design ClinicalTrials.gov Identifier: NCT03693300). Clearly, patient selection for concurrent/sequential treatment is of importance in view of the added toxicity of concurrent approach. I would expect in this review a short paragraph focusing on this issue.

Reply

Thank you for your comment on such important issue. Indeed, the population of elderly patients with lung cancer will continue to increase and necessitate special attention. The best treatment strategy for elderly patients with locally advanced non-small-cell lung cancer is not yet defined. We added a separate paragraph addressing this issue.

Comment 2

Lines 295-296 “Whereas the reasons for such a dramatic difference in favor of the 60 Gy dose remain unclear…”

One of discussed explanations of the outcomes observed in RTOG 0617 trial might be radiation treatment planning practice in this trial. To follow radiation dose constraints delineated in the protocol tighter radiation fields to avoid toxicity could be responsible for underdosing of the target.

See e.g. https://www.ascopost.com/issues/april-10-2015/results-of-rtog-0617-reconsidered/

Reply

Results of RTOG 01617 were surprising. Patients receiving higher conventionally fractionated RT dose (74 Gy) combined with concomitant CHT had worse outcomes than those administered standard dose of 60 Gy (median OS of 20.3 and 28.7 months, respectively). Higher dose was also associated with lower quality of life at three months, and higher incidence of severe esophagitis (21% vs. 7% in the low-dose group). We added the abovementioned possible explanations for such difference in favor of 60 Gy.

Reviewer B

Comment 1

My only comment is that a paragraph on the systemic treatments of concomitant chemotherapy in the elderly people who constitutes nevertheless an important part of these patients should be added, with some references.

Reply

Thank you for the positive evaluation of our article. As mentioned above (comment 1, Reviewer A), we added a paragraph focusing on chemoradiation in the elderly.