Peer review file

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Reviewer A

Comment 1. Assignment of the subjects into two group seems to be not random. Exclusion criteria is understandable and address the influence of this exclusion criteria on the outcome.

Reply 1: Patients with stage IIIA SCLC were informed of possible treatments without preferential advice, allowing patients to choose their next treatment plan. Assignment of the subjects into two group was not random.

Changes in the text: Page 8, line 107.

Comment 2. SCLC sometimes mean heterogeneous, ranging conventional small cell carcinoma (oat cell carcinoma; historically) to LCNEC histologically. Clarify pathological details of the cancers of the participants; immunohistochemical markers and others.

Reply 2: We added an excel chart which contains pathological details and immunohistochemical markers of the cancers of the participants.

Reviewer B

Comment 1. In this case control study, how the patients divided in two groups?

Reply 1: Patients were divided into two groups after they received 2 cycles induction-chemotherapy according to patients' personal willingness. Patients were informed of possible treatments without preferential advice, allowing patients to choose their next treatment plan.

Changes in the text: Page 8, line 107 and Page 9, line 134.

Comment 2. Was the regimen separated from the start in each group?

Reply 2: The regimen separated after two cycles of induction-chemotherapy. Patients were informed of possible treatments without preferential advice, allowing patients to choose their next treatment plan.

Changes in the text: Page 9, line 133.

Comment 3. Stage IIIA is an aggregate of heterogenous attributes, so, population of each TNM classification is requested.
Reply 3: We added an excel chart which contains the TNM stage of the cancers of the participants.

Comment 4. Contents of line 160 to 162 does not match the data in Table 2.
Reply 4: We have corrected our text as advised.
Changes in the text: Page 12, line 175.

Reviewer C

Lung cancer is the leading cause of cancer related mortality worldwide and these types of studies are helpful in determining the optimal treatment/interventional strategies to treat lung cancer. Small cell lung cancer being the more aggressive type of lung cancer with very high mortality rate and extensive investigations are required to optimize the interventions to improve patient survival. I have some concerns with the study.

Comment 1. The work is purely clinical, involving human participants. Have the authors obtained approval from institutional review board to conduct studies involving human subjects? If so, it has to be mentioned with an approval number.
Reply 1: We have obtained approval from institutional review board to conduct studies involving human subjects. The approval number (K20-196Y) was added in the footnote.
Changes in the text: The footnote, line 6.

Comment 2. There is no information about the written consents to recruit human subjects for this study. Were the patients informed about the study?
Reply 2: This is a retrospective study, and the informed consent was not taken from the patients.
Changes in the text: Page 8, line 109.

Comment 3. Methods section: Mann-Whitney test can ne merged with statistical analysis section.
Reply 3: We moved the Mann-Whitney test to the statistical analysis section
Changes in the text: Page 10, line 153.

Comment 4. Stage IIIA, along with stages I and II are considered early stage. Authors should justify why specifically Stage IIIA SCLC was chosen for the study and not stages I and II?
Reply 4: For patients with stage I or stage II SCLC, the treatment plan at SPH was direct surgery after induction therapy, so few non-surgical patients were enrolled in the control group. Only patients with stage IIIA SCLC were informed of possible treatments without preferential advice, allowing patients to choose their next treatment plan.
Changes in the text: Page 8, line 105.

Comment 5. Were needle biopsies performed to confirm the histological nature of SCLC?
Reply 5: Needle biopsies or endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) was performed in patients with peripheral or central lesions. All patients were confirmed the histological nature of SCLC before induction-chemotherapy.
Changes in the text: Page 9, line 126.

Comment 6. Do you have any data on patients who did not receive any treatment or patients who had surgical resection only?
Reply 6: All confirmed SCLC patients received induction chemotherapy before surgery. Patients who were accidentally diagnosed with SCLC after surgery were not included in this study.
Changes in the text: Page 9, line 136.

Comment 7. English language: Authors should carefully revise the manuscript for English language (consistencies with the use of upper case and lower case, alignment

of paragraphs, typo errors) and get it corrected by a native English speaker.
Reply 7: We have revised the manuscript as advised.

If these issues are addressed, I would suggest the manuscript to be considered for the review process. However, the decision is left to the Editor's discretion.

Reviewer D

Comment 1. Improve written English.
Reply 1: We have revised the manuscript as advised.

2. The discussion correct it and complete comments on previous and randomized studies.
Reply 2: We have modified the comments on previous studies of the discussion as advised.
Changes in the text: Page 14, line 218

3. Reduce and select the comments made in the final part of the discussion.
Reply 3: We have reduced the final part of the discussion as advised.
Changes in the text: Page 16, line 252
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Comment 4. Figure caption missing in 2.
Reply 4: We have added the caption in Figure 2 as advised

Comment 5. There are errors in Table 2 in relation to the text. In this it is indicated that there are 12 complete responses and 17 partial; and in the table he lists 12 stabilizations and 12 partial responses.
Reply 5: We have corrected our text as advised.
Changes in the text: Page 12, line 175.

Reviewer E

In this retrospective study, authors report better outcomes in clinical stage IIIA SCLC patients who underwent chemotherapy with peri-operative chemotherapy, compared to the ones treated with chemo-radiotherapy. As their proposed treatment is not the standard of care and their message can have a relevant impact on SCLC management, I have been quite demanding in my comments.

Comment 1. Since the abstract, please explicit that "surgical" treatment means peri-operative chemo including neoadjuvant. In methods Authors mention neoadjuvant chemo, but I suggest to insist on that, as "surgery with systemic chemotherapy" can be misleading (suggesting surgery is followed by adjuvant chemo).
Reply 1: We have replaced "surgery with systemic chemotherapy" with "surgery with neoadjuvant and adjuvant chemotherapy" in the abstract.
Changes in the text: Page 4, line 46.

Comment 2. In introduction, when dealing with CT-RT as the standard of care, please specify you are referring to limited-stage SCLC.
Reply 2: We have modified our text as advised.
Changes in the text: Page 6, line 71.

Comment 3. In Methods, Authors should not report patients' number, but indeed that the population of interest was clinical stage IIIA SCLC in SPH from 2005 to 2015, the exclusion criteria and the diagnostic/staging procedures. Patients' numbers should be reported in Results.
Reply 3: We have moved the patients' numbers to the Results as advised.
Changes in the text: Page 8, line 104 and Page 11, line 159.

Comment 4. I do not agree with the exclusion criteria for S+C: all patients who were candidate to surgical treatment after neoadjuvant chemo should be included in the analysis. Surgical mortality impact on treatment choice, and "positive surgical margins" detected AFTER surgery are not an element to exclude patients from the analysis. "Palliative operations" should be excluded only in the case of true palliation (to control pain, to "debulk tumor", to remove a source of infection…) where a R0

resection was not envisageable.
Similarly, I do not agree to CT-RT exclusion criteria: all patients candidate to the treatment should be included, regardless of its completion.
Reply 4: This comment is very valuable. For S+C group, we wanted to study the difference between patients who are expected to undergo radical surgery and patients who can tolerate treatment. In SPH, surgical palliative care is rare. We selected these palliative patients during the retrospective study, but the surgeons had known that these patients could not undergo radical surgery. Therefore, these patients are not included in our study. We only gave patients who are expected to be completely resected in the preoperative assessment two choices: to undergo surgery or non-surgical treatment.
There are indeed some problems in the exclusion criteria CT-RT patients. We admitted it as a limitation of the clinical study in the discussion part.
Changes in the text: Page 16, line 258.

Comment 5. The major limitation to this study is the lack of mandatory PET scan. The crucial issue in c IIIA SCLC is nodal mediastinal involvement, and the lack of PET information to concur to a more precise staging is a relevant issue.
Reply 5: Although it is true that not all patients have received PET-CT detection, all of our patients have been assessed for their general condition. Including but not limited to: chest CT, cranial enhanced MRI, abdominal CT, bone ECT, bronchoscopy and a small number of patients received PET-CT. In china, PET-CT was not covered in the social medical insurance, but cranial MR, abdominal ultrasound, and bone ECT are covered, and the price difference is about 10 times. So, some patients are unwilling to accept PET-CT for economic reasons. If the patient decided not to do PET-CT, they were examined separately.

Comment 6. I see a discrepancy between figure 1 and methods, where 157 are mentioned, and text results (412). Please correct accordingly.
Reply 6: We have corrected this careless mistake as advised.
Changes in the text: Page 11, line 159.

Comment 7. PET-CT was available for how many patients in both groups?

Reply 7: 6 patients in CRT group and 14 patients in S+C group underwent PET-CT examination. There were no reports because of the long period, and some patients did it in other hospitals.

Comment 8. “all of these patients received systematic lymph node dissection.”: please provide pathological staging for all patients who underwent surgery. This can help to understand the “real” clinical stage.
Reply 8: We added an excel chart which contains the pathological staging for all patients who underwent surgery.

Comment 9. Please provide details of chemotherapy administered after surgery.
Reply 9: We added an excel chart which contains the details of chemotherapy administered after surgery.

Comment 10. A selection bias is present (and acceptable) in this work, given its retrospective nature: if possible, patients were candidate to S+C, whereas CT-RT was proposed to other cases. Indeed, Authors state that “patients who underwent S+C was associated with younger age, higher partial response to chemotherapy.” This suggest that the possibility to undergo surgery is itself a prognostic factor. In the discussion (and in the abstract) Authors should insist on that: surgery can be an option in c IIIA SCLC after induction CT, in selected patients.
Reply 10: We agree that surgery can be an option in cIIIA SCLC after induction CT, in selected patients. And we added this in the Abstract and Conclusion.
Changes in the text: Page 4, line 62 and Page 13, line 198.

Comment 11. Authors selected patients from 2005 to 2015, with the last follow-up in 2017. Can Authors update the patients’ enrollment and follow-up?
Reply 11: It is a pity that after 2017, the loss ratio of follow-up was relatively high, and it was difficult to meet the study. And we added it as a limitation of this study.
Changes in the text: Page 17, line 264.