

## Peer Review File

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### Reviewer A

Brandt et al. retrospectively collected data from NSCLC patients with large tumors ( $\geq 5.0$ cm), and negative lymph nodes registered in the National Cancer Database and performed a propensity-scored matching to compare the overall survival between patients submitted to surgery or chemoradiotherapy. They observed that, in general, patients who were submitted to surgery performed better, although patients who did not obtain R0 resection had overall survival similar to patients treated with chemoradiotherapy.

The study is very well written, building upon real-world data. The results are clinically useful in a scenario where active neoadjuvant chemoimmunotherapy and consolidation immunotherapy following CRT are applicable options; however, the second strategy is currently recommended for irresectable, locally advanced tumors only.

### Major comments

1. What was the type of radiation delivery (IMRT x Conformational 3DRT)?
  - **Response:** We have since changed our manuscript dramatically and now are no longer focusing on surgery versus definitive chemoRT and therefore, this point is less relevant. You can see the changes in the aim in lines 118-123.
2. Was there any influence on the kind of surgery employed (lobectomy x pneumonectomy) in OS?
  - **Response:** Because our aims have changed dramatically due to the suggestions of reviewer 2, this point is no longer relevant.
3. How was lymph node compromise ascertained in each group? By image only?
  - **Response:** This is a great question for both studies. Unfortunately, we do not have HOW the pre-clinical lymph node status was determined. Most patients in this cohort had a PET CT scan as that was standard of care, however, the NCDB does not have granularity in how patients are clinically staged at this time.
4. How many patients were submitted to invasive mediastinal staging in each group?
  - **Response:** As above, we do not have information on how many patients had invasive mediastinal staging. We have added a line in our manuscript about the limitation (lines 133-134).
5. Was median overall survival the same (25.8 months) in both groups (surgery x CRT)? What percentage of patients that had incomplete tumor resection received adjuvant radiotherapy?

- **Response:** Again, because of the dramatic changes to our manuscript and clinical question, this information is no longer relevant.
6. It would be interesting if the authors compared both treatments (Surgery versus CRT) separately in the group with chest wall or major structure invasion.
    - **Response:** We agree this would be interesting. After reading the comments by Reviewer #2, we decided to re-work the manuscript towards evaluating risk factors for incomplete resection in this cohort.
  7. I recommend that authors calculate relapse-free or cancer-specific survival to reduce the impact of post-progression treatments and any bias in patient selection to each strategy due to patient performance status or comorbidities at the time of surgery or CRT.
    - **Response:** Thank you for your comments. Relapse-free survival and cancer-specific survival are, unfortunately, not available in the NCDB. Even in the new evaluation we did, we are still unable to calculate this, unfortunately.

#### Minor comments

8. Some typo corrections are in order in the manuscript.
  - **Response:** Thank you. We re-read the manuscript carefully and tried to fix the typing errors as needed.
9. The statement "Complete resection is associated with improved survival in all NSCLC. However, when patients have large, locally invasive tumors, one must outweigh risks of complications and mortality versus" is missing something.
  - **Response:** Thank you for your comments. Due to the new approach this sentence is now changed.
10. The manuscript establishes some background to discuss approaches like perioperative systemic therapy or concomitant CRT followed immunotherapy consolidation. After the suggested adjustments, I believe the manuscript will be ready for publication.
  - **Response:** Thank you for your comments! We really appreciate you reviewing our manuscript.

## Reviewer B

The NCDB should not be used for retrospective comparative effectiveness analyses. Patients who undergo surgery for these tumors are expected to be the "best players", so it is not surprising their outcomes are superior to those who undergo chemoradiation. No amount of propensity matching can correct for this, because the NCDB does not contain granular enough details.

Such articles are a disservice to the thoracic oncology community and only serve to reinforce the authors' pre-existing biases. If the study had found that chemoradiation was associated with superior outcomes to surgery, would the authors (almost exclusively CT surgeons, save the token radiation oncologist) have published this?

The authors might claim that they wish to merely "report an association", but the study will be interpreted as surgery > chemoradiation. Additionally, causal language is clearly written in the Discussion:

"There is a clear advantage to attempted surgical resection over definitive CRT in our study, particularly for those who received a complete resection"

If the authors would like to resubmit the article and focus on factors associated with incomplete surgical resection for these large tumors, and leave out a comparison to chemoradiation, that would be welcome and I would support its publication in the JTD.

**Response:** We understand the reviewer's concerns. We agree, the NCDB is missing granular data that would be useful to truly analyze this and we do not want an unfair analysis with an overly ambitious conclusion. Our intention was to focus on the benefit of surgery if an R0 resections should be obtained. We took the reviewer's comments very seriously and have entirely re-configured our aims to evaluate patients with invasive large, node-negative NSCLC. We then aimed to evaluate risk factors for positive margins. We essentially re-formatted the entire manuscript and therefore, do not respond here with every change but have included the new manuscript with all the tracked changes.