

## Recent advances in early stage lung cancer

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Handling editor:

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1<sup>st</sup> Editorial decision  
22-Sep-2020

Ref.: Ms. No. JCTRes-D-20-00082  
NEW ADVANCES IN EARLY STAGE LUNG CANCER  
Journal of Clinical and Translational Research

Dear Dr Luna-Tirado,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

Please pay particular attention to addressing the state of the art, focusing on novel techniques as pointed out by reviewer 2. Also, the text exacts thorough proofreading. We can help with that if you fail to find a native speaker to assist or by any other means necessary cannot improve the linguistics, grammar, and spelling.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by Oct 22, 2020.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: This manuscript is an updated review discussing the current therapies for the treatment of early-stage lung cancer. The authors discuss the mainstays of early-stage lung cancer treatment, which includes surgery and radiation. Recent advances in surgical techniques and the utility of molecular markers and adjuvant therapies such as immunotherapies are also highlighted in this review.

A few comments for our authors:

Within surgery, there is some debate regarding mediastinal lymph node sampling versus dissection with lymphadenectomy. A full lymphadenectomy adds complexity and potential morbidity to a case. With the advent of more minimally invasive techniques such as VATS, a lymphadenectomy is very difficult. The ACOSOG Z0030 trial should be discussed. In addition to the Japanese trial regarding sublobar resection versus lobectomy, there is also another multi-center clinical trial that should be included. Some preliminary data of the CALGB 140503 have been presented and published (Altorki NK Lancet Respir Med 2018; 6:915-924).

In regards to the role of immunotherapy for surgically resectable lung cancer, the authors should include Forde PM et al. N Engl J Med. 2018; 378(21):1976-1986. Pathologic down-staging was seen in 40% of patients and the administration of neoadjuvant immunotherapy did not delay or increase the morbidity of the surgery. This study, however, did not present data regarding long-term survival.

Reviewer #2: In this manuscript the authors provide a review of currently used modalities in the treatment of early stage lung cancer. Despite the title there is little in the manuscript that describes truly new advances.

- 1) The authors might want to include some of the technologies being used to treat lung cancer via the bronchoscope.
  - 2) While uni-portal VATS and awake surgery are being performed, they have not been widely incorporated into practice especially for more complex resections. Might want to focus on other aspects of minimally invasive surgery.
  - 3) Discussion of adjuvant therapy should include some reference to the histologic sub-types of the tumors. Also much better survival curves are available based on the size of the tumors
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Authors' response

REPLIES TO THE REVIEWERS

Reviewer #1:

**Comment 1: “Within surgery, there is some debate regarding mediastinal lymph node sampling versus dissection with lymphadenectomy. A full lymphadenectomy adds complexity and potential morbidity to a case. With the advent of more minimally invasive techniques such as VATS, a lymphadenectomy is very difficult. The ACOSOG Z0030 trial should be discussed”.**

In the revision we have discussed in more detail the issue of lymphadenectomy extension and its performance with minimally invasive techniques. We have also commented on the main findings of the ACOSOG Z0030 trial.

**Comment 2: “In addition to the Japanese trial regarding sublobar resection versus lobectomy, there is also another multi-center clinical trial that should be included. Some preliminary data of the CALGB 140503 have been presented and published (Altorki NK Lancet Respir Med 2018; 6:915-924)”.**

The main results of CALGB/Alliance 140503 trial have now also been added in the surgery section of the manuscript.

**Comment 3: “In regards to the role of immunotherapy for surgically resectable lung cancer, the authors should include Forde PM et al. N Engl J Med. 2018; 378(21):1976-1986. Pathologic down-staging was seen in 40% of patients and the administration of neoadjuvant immunotherapy did not delay or increase the morbidity of the surgery. This study, however, did not present data regarding long-term survival”.**

In the section of adjuvant systemic treatment, we have modified the whole Immunotherapy issue, highlighting the main characteristics and results of Foster's trial.

Reviewer #2:

**Comment 1: “The authors might want to include some of the technologies being used to treat lung cancer via the bronchoscope”.**

We have included a new section in the manuscript about other local treatments, among which we have highlighted techniques like Image-guided thermal ablation or bronchoscopic ablative techniques.

**Comment 2: “While uni-portal VATS and awake surgery are being performed, they have not been widely incorporated into practice especially for more complex resections. Might want to focus on other aspects of minimally invasive surgery”.**

In this revision of the manuscript we have introduced other aspects of minimally invasive surgery, such as evidence in the performance of sublobar resections as oncological surgery and the management of lymphadenectomy with VATS.

**Comment 3: “Discussion of adjuvant therapy should include some reference to the histologic sub-types of the tumors. Also much better survival curves are available based on the size of the tumors”.**

In the first version of the manuscript we had already commented on existing evidence in adjuvant treatment according to tumor size and other risk factors (references from 29 to 37). We have referred to the evidence according to major clinical guidelines (references 16, 17), including the NCCN guide (ref 17) which alludes to the indication of adjuvant treatment according to tumor size.

We have also commented on the interesting research development of molecular markers that are likely to define in the future the subgroups of patients within the early stages of NSCLC who do benefit from adjuvant treatment.

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2<sup>nd</sup> Editorial decision  
26-Jan-2021

Ref.: Ms. No. JCTRes-D-20-00082R1  
NEW ADVANCES IN EARLY STAGE LUNG CANCER  
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

The acceptance of the paper depends on an upgrade of the English language to academic standards, in conformity with the journal's author guidelines. Please engage a native speaker or paid service (also possible through JCTR - please contact the editor).

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at <http://www.jctres.com/en/author-guidelines/> under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Feb 25, 2021.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: The authors have done a great job incorporating the reviewers recommendations into their new draft. Please have the manuscript reviewed for grammatical and typographical errors.

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3<sup>rd</sup> Editorial decision  
28-Feb-2021

Ref.: Ms. No. JCTRes-D-20-00082R2  
RECENT ADVANCES IN EARLY-STAGE LUNG CANCER  
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Comments from the editors and reviewers: