Professor Dr. Fang-Fang Ji
Science Editor
Editorial Office of the World Journal of Clinical Oncology

Dear Professor Fang-Fang,

please find enclosed the edited manuscript in Word format (file name: 10706-revised[1].doc).

Title: World Journal of Clinical Oncology

Author: Feras Al-Shahrabani, Daniel Vallböhmer, Sebastian Angenendt, Wolfram T. Knoefel

Name of Journal: World Journal of Clinical Oncology

ESPS Manuscript NO: 10706

The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer
(1) Reviewer 1:

1. If N2 is unexpected, what is the place of radiation therapy post-op?

Even though some studies suggest that postoperative radiation in case of N2 disease can improve local control, it remains controversial whether it has a prognostic effect.

PORT Meta-analysis Trialists Group. Postoperative radiotherapy for non-small cell lung cancer. *Cochrane Database Syst Rev*. 2005; 2: CD002142. [PMID:15846628]

Based on the National Cancer Institute of Canada and Intergroup Study, the postoperative radiation may be considered in selected patients to reduce the risk of local recurrence, if any of the following are present:
Involvement of multiple nodal stations.
Extracapsular tumor spread.

Pepe C, Hasan B, Winton TL, Seymour L, Graham B, Livingston RB, Johnson DH, Rigas JR, Ding K, Shepherd FA; National Cancer Institute of Canada and Intergroup Study JBR.10. Adjuvant vinorelbine and cisplatin in elderly patients: National Cancer Institute of Canada and Intergroup Study JBR.10. *J Clin Oncol* 2007; 25: 1553-61. [PMID:17442999]

These data/references were added to the discussion.

2. If there is pre-op N2 disease reference 42 does NOT suggest surgery

The paper by Sanli et al. revealed that patients undergoing a complete resection without lymph node invasion show a long lasting survival with radiotherapy or chemoradiotherapy preoperatively and/or postoperatively. Therefore we included this reference in the paragraph.

3. Reference 49, which I could not access, is not a study but a review and, therefore, an opinion.

We agree that the statement from the reference 49 should be considered as an opinion and highlighted that in the paper.

4. It is hard to imagine a role for surgery at any point with N3 disease.

We agree that apart from randomised studies there is no role for surgery in patients with N3 disease

5. Solitary mets: It is probably better to suggest that an isolated adrenal met be resected only if ips-lateral, although no good data exist.

All studies referring to the benefit of the resection of a solitary adrenal metastasis, do not contain a differentiation between ipsi- and contralateral metastasis. Therefore, there is in our opinion no indication that the side of the adrenal metastasis has any prognostic impact.

6. In this group, why should the solitary met be removed prior to the primary?

In case of a cerebral metastasis, the main reason for primary surgery of the metastasis consists in the leading cerebral symptoms.

In case of an adrenal metastasis, the main reason for primary surgery of the metastasis consists in the faster recovery after an adrenalectomy compared after a lung resection.

7. Please define "extended resection

Any resection beyond the anatomical structure of the lung (chestwall, Pericardium, Myocardium, Diaphragm, esophagus, vertebral bodies or distal trachea) is defined as an extended resection.

8. Where discussing T4 lesions it should read as POST- not preoperative.

We agree with the reviewer and added the term “postoperative” to the paragraph.

9. Discussion: give exact reference for NCCN node resection guidelines; same with ESTS guidelines.

We gave exact references to the discussion section.

NCCN guidelines:

Ettinger DS, Akerley W, Bepler G, Blum MG, Chang A, Cheney RT, Chirieac LR, D'Amico TA, Demmy TL, Ganti AK, Govindan R, Grannis FW Jr, Jahan T, Jahanzeb M, Johnson DH, Kessinger A, Komaki R, Kong FM, Kris MG, Krug LM, Le QT, Lennes IT, Martins R, O'Malley J, Osarogiagbon RU, Otterson GA, Patel JD, Pisters KM, Reckamp K, Riely GJ, Rohren E, Simon GR, Swanson SJ, Wood DE, Yang SC; NCCN Non-Small Cell Lung Cancer Panel Members. Non-small cell lung cancer. *J Natl Compr Canc Netw.* 2010;8:740-801. [PMID:20679538]

ESTS guidelines:

Lardinois D, De Leyn P, Van Schil P, Porta RR, Waller D, Passlick B, Zielinski M, Lerut T, Weder W. ESTS guidelines for intraoperative lymph node staging in non-small cell lung cancer. *Eur J Cardiothorac Surg*. 2006; 30:787-92. [PMID:16971134]

(2) Reviewer 2:

The manuscript gives a thorough and careful literature review on surgical strategies of non-small cell lung cancer. The authors introduced the surgical strategies according to disease stages. After that, they also introduced some specific strategies on special occasions, such as in patients with solitary brain or adrenal metastasis; specific strategies such as bronchoplastic lung resection, lymphadenectomy and extended resections, angioplasty and marginal resections using extracorporeal membrane oxygenation (ECMO). In general the writing and language is sound. The contents are detailed with many papers cited from last five years. The tables and figure provided are very explicit. The organization of the last half of the review (section 5~8) seems to be loose and can be better organized. Section 5 can actually be included into section 2. Section 6~8 can be under one section, i.e. 'introduction of surgical strategies advancements'. There are numbering errors in several places. There is missing of section 2.3 and section 4. Or the sections should be re-numbered.

We agree with the reviewer and re-numbered the sections. However, we would like to leave section 5, 6. 7 and 8 separately as specific topics in lung cancer surgery are discussed that deserve in our opinion an individual consideration.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the World Journal of Clinical Oncology.

Sincerely.

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