Author's response to reviews

Title: Video-assisted Radiofrequency Ablation for Pleural Disseminated Non-small Cell Lung Cancer

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Author's response to reviews: see over
Dear Reviewer,

Thank you for your comments which have proven extremely valuable to us in improving the manuscript. We have made the following revisions as per your points:

The reply to the comments by Dr Stefania Camagni:

1. The hypothesis the authors want to verify is well defined: they compare R-TP and TP to determine whether R-TP is technically safer and oncologically more adequate than TP in the treatment of advanced NSCLC with pleural dissemination. However, I think it is not correct to compare them in terms of safety since RFA is an invasive procedure; moreover, I think it is not correct to compare them in terms of oncological efficacy since RFA is the therapy of the tumor while TP is the prophylaxis or therapy of pleural effusion, which is an epiphenomenon of the tumor. I wonder why the authors did not compare two different therapies of the tumor, like R-TP and lung resection with or without parietal pleurectomy combined with TP.

Re: In terms of the advice on study design, I agreed with the point that the comparison between TP and R-TP was unfair (both on the safety and oncological efficacy). Actually, we conducted this primary study to see whether RFA would prolong patients’ survival without compromising with perioperative results. The test was between RFA+ and RFA−, while the talc pleurodesis was the basic treatment. We do think it would be a very nice idea to have a study between RFA and surgical resection. To be honest, the study is on the way, and we would be pleased to share our further results with you. The manuscript was revised according to your comments (see LOA1). Thank you for your nice suggestion.

2. It is not clear whether the authors propose R-TP as the treatment of advanced NSCLC with pleural dissemination only to patients with poor lung function or to the operable ones too.

Re: The study included operable patients for typical thoracoscopic lobectomy, and patients with poor lung function were not candidates for lobectomy in our department. To make things clear, The inclusion criteria were added in the manuscript (see LOA2).

3. The authors do not specify which kind of study they performed (controlled cohort study?)
Re: This was a retrospective study with historical controls, and we have added details in terms of the study design (see LOA3).

4. The plan of the study is not well defined: paragraphs Patients and Methods and Clinical Features suggest that the patients with intraoperative diagnosis of pleural dissemination underwent TP from December 2005 to June 2006 and R-TP from July 2006 to June 2008, but this is not explicit; if this is true, I wonder why the patients with intraoperative find of pleural dissemination were 24 throughout 6 months and 21 throughout 2 years.

Re: Many thanks for your kindly reminding on this issue. We have checked our database: From December 2005 to June 2006, the number of included patients was 339 (7.08%), and from July 2006 to June 2008, the number of included patients was 413 (5.08%). The incidence was low and close between two time periods. Since some new operation types were tried in late 2006 (mainly the minimally invasive esophagectomy), the lung surgery decreased from that time. This explained why less pleural dissemination were found in the later periods. The details were added in the manuscript (see LOA4).

5. The number and volume of the lesions treated by RFA are not reported.

Re: In this study, all patients included were single lesion and were candidates for thoracoscopic lobectomy. We have added tumor volume in Tab 1, the lesions diameter was comparable between R-TP and TP (see LOA5).

6. The author tell nothing about post-operative treatment (chemotherapy, targeted therapy, supportive therapy), which is mentioned only in Tab 1.

Re: As you may concern, the post-operative treatment weights a lot on patients’ survival. However, the post-op therapy was less detailed in this study. We have recognized this point and added more details on this issue. Thank you for your suggestion (see LOA6).

7. In the paragraph Comment the authors compare the complications of R-TP in their study and the complications of percutaneous RFA. I think it is not correct to compare the data of the current study (2 complications among 21 patients) and the data of the literature, which are about a greater number of patients surely.
Re: Since our research was based on small case volumes with different inclusion criteria from the previous study, it would not be suitable to have the complication ratio compared with other publications in the Discussion part. We have revised manuscript as you have suggested. (see LOA7). Thank you again for your nice suggestions on this manuscript.

The reply to the comments by Dr Tommaso C Mineo:

Re: Thank you very much for your kindly review on this paper, which encouraged our further research on this topic. The study was restricted in the small case volume and retrospective design, and we would conduct RCTs to confirm the primary findings. Many thanks!

List of Action
LOA1: “Radiofrequency ablation combined with TP for the treatment of pleural disseminated NSCLC is safe, feasible, and effective” was revised as “The introduction of RFA to TP offered survival benefits to pleural disseminated NSCLC patients” in page 3.

“technically safer and oncologically more adequate than the traditional treatment” was changed to “technically safe and oncologically beneficial in the treatment of advance NSCLCs” in page 4.

“ is safe and effective” was changed to “does not increase the risks of higher morbidity” in page 10.

LOA2: The inclusion criteria were added in the page 5.

LOA3: The study design was added, it was a retrospective study with historical controls.

LOA4: “The incidence of unexpected pleural dissemination was close between R-TP and TP (21/339 versus 24/413, p=0.832)” was added in page 7.

LOA5: “volume” was inserted in this sentence, and the tumor diameter was added in Tab1.

LOA6: Postoperative therapy was stated in page7-page8.

LOA7: In page 11, “..., which is fewer than that of percutaneous RFA. For tumors not suitable for or at high risk of complications with percutaneous RFA, thoracoscopic guidance was considered a safer and easier alternative” was revised as “… Although the study was based on small population, the relatively low incidence of complication suggested that thoracoscopic guidance could be considered as a safe and easy alternative to conventional therapy.”