

## Peer Review File

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### Reviewer A

The criticism argues (based on another paper) that invasive carcinoma always has a solid component. Generally, this is true but not always. I have had lesions which appeared completely ground glass by CT scan but then did have an invasive component - which admittedly was surprising but it happens. Therefore, I think the crux of this criticism is flawed. Unfortunately, there is some subjectivity to what is called pure GGO and I think the original paper is still valid.

Secondly, I understand where the criticism is coming from, i.e., we have to be careful that all ggo lesions will have such good outcomes out to 10 years. This criticism would make sense if the lesions are very small or very indolent and therefore not high-risk. However, the criticism focuses on lesions that had invasive adenocarcinoma and therefore were higher risk. Even with the higher risk lesions the outcomes were still excellent. So instead of criticizing this point, it makes more sense to highlight it and suggest ways to make GGO or part-solid lesion identification more objective.

### Reply to Reviewer A

First of all, we thank you for your revision. Similar to your experience, we have had some lesions apparently pure GGO in the CT scan that at the final histologic examination were invasive tumors. We agree with you that it can happen, but it is the exception not the rule. Furthermore, here the question is different. As reported in our editorial, the topic is the taxonomy. The CTR is a helpful radiologic tool to preoperatively classify the lesions, but the histological pattern remains crucial to confirm the definition of “pure GGO”. To avoid misunderstanding, we believe that the series should be as homogenous as possible also considering the histological findings and excluding lesions that, for histological definition, are part-solid nodules. Regarding your second objection, we also agree with you about the excellent long-term survival and once again we believe that it is important in the evaluation to clearly distinguish pure GGO lesions to part-solid or solid lesions.

### Reviewer B

Well explained point of view.

### Reply to Reviewer B

Thank you for your comment.

### **Reviewer C**

Your commentary points out the real weak points of the Li et al. (1) study. In their paper there is no clear reference about the follow-up timing (i.e., Every 3 or 6 months, either with a HRCT or a contrast-enhanced CT). Moreover, there is no detailed reference on nodal dissection in wedge and sublobar resections. However, some statements in your commentary should be revised. In particular, from page 1 line 24 there is a comparison between Travis et al. paper and the study by Li et al. The Li et al. case series implies “pure GGO” (CTR=0) as a selection criteria. In their case series there are also invasive adenocarcinomas in pure GGOs (i.e., Results paragraph). Those patients have to be considered in their study because of the radiological appearance (pure GGO).

Page 1 line 4-5: would it be better rephrasing: “to develop computed-tomography screening programs aiming at improving the detection of early-stage LC. A complementary...”

Page 1 line 9: “According to...”

Page 1 line 14: “These findings imply that a correct...”

### **Reply to Reviewer C**

First of all, thank you for your comments and suggestions. Our purpose by mentioning the paper by Travis was not to compare it with the paper by Li, but just to emphasize that the radiological finding of pure GGO should be confirmed also at histology so to have a real and homogenous population of pure GGO lesions and to assess its long-term survival. For this reason, we believe that patients with histological findings of part-solid lesions should be excluded from the analysis.

According to your suggestions, we have corrected the manuscript (yellow parts).

### **Reviewer D**

Good comment/letter to the editor about the management of GGOs. I would suggest an emphasis on more prospective trials on lung cancer surgeries (and not just database analysis). Large database is interesting, but selection bias is a huge problem, especially for smaller centers.

Also, in line 43, it is mentioned "third". It is out of pattern as the other reasons presented with numbers before.

### **Reply to Reviewer D**

First of all, thank you for your comments. We agree with you regarding the need to emphasize prospective trials on management of GGOs, but the aim of this editorial was only to comment the results of the paper by Li. Once again, we agree with you about the selection bias and the taxonomy.

According to your suggestions, we have corrected the “Third” with “Finally” (yellow line).

**Reviewer E**

Dear Authors, I read with interest your editorial commentary on the paper by Li et colleagues entitled " Ten-year follow-up results of pure ground-glass opacity-featuredlung64 adenocarcinomas after surgery".

Authors offered some food for thought on the GGO management.

In the daily practice, GGO is a very common finding, especially in screening programs, and an invasive approach may lead to an over treatment of non-malignant lesions.

In the editorial, authors hit the spot of the GGO management pointing out the strengths and weaknesses of the abovementioned article.

I have no issues or concerns to address.

**Reply to Reviewer E**

[Thank you for your comments.](#)

**Reviewer F**

Thanks for your Editorial commentary,

The authors summarize the current situation in the difficult management of GGO-type lung lesions, which are increasingly common in our daily lives thanks to the improvement of imaging techniques and the implementation of screening programs. It is crucial to have new guidelines that recommend the management of these cases without forgetting the stress component that it can cause both in the patient and in their referring doctors.

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It is important to highlight that we must be able to clearly identify the type of lung injury at a radiological level, a key point to be able to obtain satisfactory therapeutic management afterwards. As the authors list, once the type of lung injury has been identified, conservative or aggressive management must be decided and, if it is a lung resection, decide what type of lung resection we are going to perform.

**Reply to Reviewer F**

[Thank you for your comments.](#)