

## Peer Review File

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### **Reviewer A**

Thanks for your kindness and suggestions.

Comment 1:

ABSTRACT - Is a very good comprehensive summary of the study which includes all the key points.

KEYWORDS - Good

Reply 1: Thanks for your comments.

Changes in the text: none.

Comment 2:

INTRODUCTION - The introduction is practical, clear and well organized, but few grammatical and spelling mistakes need to be corrected.

Reply 2: Thanks for your suggestions. Introduction was re-read with some mistakes be corrected (See Page5, line 63-66,81-82).

Changes in the text:

Since then, up to 60 names have been reported such as pseudosarcomatoid adenoma and carcinosarcoma. In 1982, the World Health Organization (WHO) officially named it as PT, and divided it into three grades including benign, borderline and malignant. Surgical management is still controversial as the main treatment of PT.

Comment 3:

METHODOLOGY

Good

-Methodology was accurately described so clinician can reproduce the experiments and get the same outcomes

-Authors have included proper references to previously published methodology

Reply 3: Thanks for your comments.

Changes in the text: none.

Comment 4:

RESULTS

Very well presented results with the aid of tables and appropriate statistical analysis.

Reply 4: Thanks for your comments.

Changes in the text: none.

Comment 5:

DISCUSSION

Very good review of literature, including reflection of the authors results as well as the limitations of the study

-appropriate citations used

Reply 5: Thanks for your comments.

Changes in the text: none.

Comment 6:

#### CONCLUSION

A very well-written conclusion that reflects the findings studied and advises for larger studies to develop more robust data.

Reply 6: Thanks for your comments.

Changes in the text:

#### **Reviewer B**

We would like to thank you for your careful reading, helpful comments, and constructive suggestions, which have significantly improved the presentation of our manuscript. And we have carefully considered all comments and revised our manuscript accordingly.

Comment 1:

#### Abstract

Background and conclusion are longer than methods and results that is quite unusual and less informative.

I think that inclusion and exclusion criteria are poorly described although they have a huge importance.

Reply 1:

Thanks for your suggestions. The abstract was revised (See Page3-4, line28-33, 36-42 and 51-57).

Changes in the text:

Background: Information is still controversial ... have significant implications on the surgical management of PT.

The studies were identified following strict inclusion and exclusion criteria ... Visual inspection of funnel plots was used to judge publication bias.

Different surgical management strategies should be considered for different PT grades. ... More studies are still needed to clarify and update the existing conclusions and improve the prognosis of PT patients.

Comment 2:

#### Introduction

Good description of the subject and actual problems.

I understand the plan of the authors is:

- Epidemiology and LR rates
- The role of wider local excision
- Role of margins status
- Conclusion

I think the reading of this part could be optimized by changing plan to

- Epidemiology and LR rates
- Role of margins
- There is a role of margins status, but is there a role for wider local excision?
- Conclusion

I think the conclusion of introduction is too long (more than 10 lines).

Line 104: “the treatment option of benign PT from WLE to observation after biopsy”  
[?] please precise after excisional biopsy

Line 111: this is in methods part 2 lines below (and the abbreviation is described 2 lines below also). I suggest to delete the sentence in the Introduction part.

Reply 2:

1. Thanks for your helpful suggestions. I have re-read the introduction part carefully and change the text as suggested (See Page5-6, line71-86).
2. Line 104 was changed as suggested (See Page6, line91).
3. Thanks for your carefulness but I am sorry that Line 111 was required by the journal.

Changes in the text:

Margin width and status are two important factors affecting the prognosis. Previously, ...Lu et al. proposed that margin status was only found to be associated with LR risk for malignant PT (15).

Surgical management is still controversial as the main treatment of PT... In 2021, the fourth edition of NCCN guidelines modified the treatment option of benign PT from WLE to observation after excisional biopsy (20).

Comment 3:

Methods

Search strategy: well explained and described in table S1

Eligibility criteria:

- I don't understand in Table 1 (The subtypes of PT (benign, borderline and malignant) are investigated.) if studies had to include all the grade or had to describe the PT grade they studied.
- I am surprised by finding: “Studies with margin status below 50 patients were excluded” and observed 2 studies with  $n < 50$  included in Table 2. Could you explain?
- By a quick research on Medline on the most recent years, I don't understand why the publications PMID: 31989361 DOI: 10.1245/s10434-020-08217-y and doi.org/10.1136/esmoopen-2020-000843 were not included.
- Is this study registered/recorded in PROSPERO?

Reply 3:

1. I am so sorry for the confusion and what I mean was the studies had to clearly describe the PT grade they studied. The text was changed (See Table1).
2. The studies of margin contained two parts: either margin status or margin width. Considering the large number of studies containing margin status, studies containing at least 50 patients were included. However, the studies which only contained margin width were all included regardless of the number of cases. This explained the reason for your finding and I am sorry for the confusion.
3. Thanks for your suggestions. The studies you mentioned were conducted by Liso et al. and Neron et al. The studies were completely suitable for our study by reading the title and abstract. However, Liso et al. did not clearly stated the number of LR patients with margin status but only the total number. And the subgroup division of Neron et al. was different from us. They divided the margins into 1–2 mm, 3– 7 mm, and  $\geq 8$  mm margins and what we discussed was the margin  $< 1\text{cm}$  and  $\geq 1\text{cm}$ . So these studies were not included in our research and thanks again for your carefulness.

4. The study has already registered in PROSPERO with the ID: CRD42021292859 (See Page6, line 98-101).

Changes in the text:

The subtypes of PT (benign, borderline and malignant) are clearly described.

This study was reported following Preferred Reporting for Items for Systematic Reviews and Meta-Analyses-Protocols (PRISMA-P) (21). And the systematic review has been registered in the International Prospective Register of Systematic Reviews 'PROSPERO' database (ID: CRD42021292859).

Comment 4:

Results

I find the plan correct here: characteristics / margins status then margin width.

Results are easy to read and understand.

Reply 4: Thanks for your comments.

Changes in the text: none.

Comment 5:

Discussion

- "Surgical management has been a controversial subject in PT, mainly including 226 margin width and margin status. The latest NCCN guidelines recommended that the

227 strategy of "wait and watch" was feasible for benign PT after excisional biopsy, while

228 for borderline and malignant PTs, a second extended resection was still required.

229 However, the correlation between margin and prognosis as well as the necessity of

230 mastectomy for borderline and malignant PTs are still required to be explored. »

è All this paragraph has been ever written above and should be deleted.

For the overall discussion, it is difficult to read due to mixing of informations.

Authors should think a better plan for the discussion to draw conclusions at each step:

- By using the same plan above (margins status/ margin width/ type of surgery)

- Or by drawing conclusion by grade (one paragraph by grade as author did for the borderline, explaining by grade the role of margins and type of surgery) that is easier to read and understand for clinical practice

Reply 5: Thanks for your helpful suggestions. Discussion has been revised according to your second statement of this part (See Page11-14, line 211-259).

Changes in the text:

In this systematic review and meta-analysis grounded on a total of 6431 patients from 34 studies, we assessed the correlation of margin, surgical treatment and LR risk for different grade of PT.

For benign PT, no significant difference in the LR rate..., "wait and watch" strategy may be an optimal option for benign PT with positive margin.

For borderline PT, we found no ... Whether the 1cm margin is sufficient for borderline PT is still controversial with more cases to supplement.

As for malignant PT, ... Mastectomy should be recommended in the situations where the tumor was too large or if the inability to obtain negative margin to reduce LR risk

Comment 6:

Figures

I do not have commentaries for figures that seem correct and easy to read.

Reply 6: Thanks for your comments.

Changes in the text: none.

### **Reviewer C**

Comment 1:

This is a good systematic review and meta-analysis article to discuss the surgical management in phyllodes tumors of the breast. But it needs to be partially modified and clarified some points.

Reply 1: Thanks for your comments.

Changes in the text: none.

Comment 2:

In row 72 and 73, “Studies have shown that LR might occur in 73 every grade with the rate of 10% ~ 17%, 14% ~ 25% and 23% ~ 30% respectively.”, please revised to “10-17%, 14-25% and 23-30%”.

Reply 2: Thanks for your suggestion and the text was changed (See Page5, line 67-68).

Changes in the text:

Studies have shown that LR might occur in every grade with the rate of 10-17%, 14-25% and 23-30% respectively.

Comment 3:

In row 77, “Surgery management is still controversial as the main treatment of PT.”, please revised to “Surgical management of breast-conserving surgery and mastectomy is still controversial as the main treatment of PT.”

Reply 3: Thanks for your suggestion and the text was changed (See Page5, line 81-82).

Changes in the text:

Surgical management of breast-conserving surgery and mastectomy is still controversial as the main treatment of PT.

Comment 4:

In row 80, “wide local excision (WLE)” and “breast-conserving surgery (BCS)” are the same operations in your manuscript?

Reply 4: Thanks for your question. BCS mainly contains two parts including WLE and lumpectomy. The difference between these two surgical therapies is the margin width (WLE: margin  $\geq$  1cm). The WLE mentioned in row 80 was trying to point out the importance to maintain margin  $\geq$  1cm.

Changes in the text: none.

Comment 5:

In row 81, “the LR rate from 21% and 46% to 8% and 29% respectively”, please revised to “21-46% to 8-29%”.

Reply 5: Thanks for your suggestion and the text was changed (See Page6, line83-84).  
Changes in the text:

Studies have shown that for benign and borderline PT, wide local excision (WLE) can reduce the LR rate from 21-46% to 8-29%.

Comment 6:

In row 88, “And re-excision was only suitable for borderline and malignant PTs.”, please add “if safe margin < 1cm”.

Reply 6: Thanks for your suggestion and the text was changed (See Page6, line86).

Changes in the text:

However, some studies indicated that regular follow-up was adequate since the LR rate of benign PT with positive margin was very low. And re-excision was only suitable for borderline and malignant PTs if safe margin < 1cm.

Comment 7:

In row 104, “However, the correlations between margin width, margin status and LR risk are still controversial in the current literature. The systematic review and meta-analysis on the surgical management of PT also need to be updated.”, can be deleted.

Reply 7: Thanks for your suggestion and the text was changed.

Changes in the text:

However, the correlations between margin width, margin status and LR risk are still controversial in the current literature. The systematic review and meta-analysis on the surgical management of PT also need to be updated.

Comment 8:

In row 113 (methods), Please clarify the calculation method of the lumpectomy, wide local excision and breast-conserving surgery in your study.

Reply 8: Thanks for your helpful suggestion. Although these three methods were mentioned in the article, we did not classify the surgical management into such subgroup. Considering we only calculated the cases underwent BCS and mastectomy, we did not think it is necessary to clarify the method of these three methods.

Changes in the text: none.

Comment 9:

In row 269, “Therefore, since the benefits of re-excision on the prognosis of the patient are uncertain and a second operation may bring psychological pressure or cosmetic damage to the patients, "wait and watch" strategy may be an optimal option for benign PT with positive margin.”, in the other opinion, positive margin of benign PT still cause some patients to worry about the recurrence of the disease. Sharing decision making by patients of a second operation of BCS with safe margin over 1 cm or "wait and watch" strategy with regular following up may be the better choice.

Reply 9: Thanks for your advice. The text was changed as you advised (See Page12, line229-230).

Changes in the text:

... "wait and watch" strategy with regular following-up may be an optimal option for benign PT with positive margin.

Comment 10:

In malignant PT, mastectomy refers to the removal of all breast tissue, but what is the safety margin of the affected area of the skin envelope of breast or the base of the pectoralis major is a question. Please find evidence of safe margins of the skin and base during mastectomy and mention it in the discussion.

Reply 10: Thanks for your suggestion. In this study, no significant difference in the LR rate between margin  $\geq 1$ cm and  $<1$ cm, and mastectomy significantly reduced the LR risk were found. Previously we thought 1cm might not be a meaningful boundary for malignant PT. After a deep reading of articles, we found that  $<1$ cm also had the possibility to be sufficient for malignant PT with some studies supported. Neron et al. even indicated that a 3mm threshold was sufficient and explained the positive impact mastectomy have on LR risk as surgical procedures it followed. Therefore, we changed the description of surgical management for malignant PT in the text and we were so sorry for this (See Page 13-14, line 245-259 and Page 14, line 271-277).

Changes in the text:

As for malignant PT, ...Mastectomy should be recommended in the situations where the tumor was too large or if the inability to obtain negative margin to reduce LR risk (7,41).

Regardless of the tumor grade, there was a significant correlation between positive margin and LR risk. ...Mastectomy was recommended in the situations where the tumor was too large or if the inability to obtain negative margin to reduce LR risk.