ABS ANNALS OF BREAST SURGERY
AN OPEN ACCESS JOURNAL TO BRIDGE BREAST SURGEONS ACROSS THE WORLD

Peer Review File

Article information: https://dx.doi.org/10.21037/abs-22-1

Reviewer A

Comment 1: *Theoretically, DCIS is a limited lesion to the ductal mammary system without capability to produce distant metastases. Nevertheless, we know some predictive factors associated with an increased risk of local recurrence and progression to invasive carcinoma. Would the use of standardized nomograms modified the physicians decisions and the survey results?*
Reply 1: Unfortunately, we did not specifically ask physicians if they use a nomogram to predict progression of DCIS. One could assume that these nomograms could help with the decision to place a patient with DCIS on active surveillance; however, more than half of the physicians answered that there was not enough strong evidence to support the observation of DCIS (page 8, line 21). Therefore, it appears that physicians do not feel there is adequate information out there right now to predict progression to invasive disease.

Comment 2: *It is remarkable that, despite of endocrine therapy being accepted when tumor over-expresses hormone receptors, 46% of physicians felt uncomfortable with observation in these subgroups of patients. How do you explain that?*
Reply 2: Our study results demonstrate that the majority of physicians are still not comfortable observing DCIS, even with low grade or hormone positive tumors. It appears that physician's biggest concern is DCIS progression. As presented in the discussion on page 11 and 12, the data on which tumors will and will not progress and how hormonal therapy affects that is lacking. Hopefully, the COMET trial results will shed further light on if active surveillance with endocrine therapy for estrogen receptor positive DCIS is a sufficient treatment pathway. A phase II study published in Journal of Clinical Oncology did show that preoperative letrozole for women with ER positive DCIS resulted in decreased volumes of disease on MRI but this study was published after our survey was distributed.

Comment 3: *On the other hand, you do not specify whether associating hormonal treatment is a conditioning factor to decide observation, endocrine therapy is offer in all patients regardless of treatment?*
Reply 3: We did not specifically ask in the survey if the ability to give hormone

therapy has an impact on the clinician's decision to observe patient with DCIS. However, as seen in Table 3, nearly 90% of clinicians are uncomfortable observing hormone receptor negative DCIS in contrast to approximately 46% that were uncomfortable observing ER positive DCIS. Therefore, one could deduce that the ability to give endocrine therapy is a significant factor in active surveillance. The LORD and LORIS trial did not include hormone receptor positivity as an inclusion criterion. It will be interesting to see how many hormone receptor negative patients were enrolled in these trials and their outcomes.

Comment 4: *In table 2, you classified physician knowledge in "high" or "low" but you do not differentiate the results based on the level of knowledge which could condition a bias. Have you taken this situation into account in the analysis of the data?*

Reply 4: In supplementary table 3, we show the results of a multivariate model of factors associated with physician opinion on the ease of placing patients in DCIS observation trials. Physicians with high knowledge had a 1.34 odds of responding that they felt it was easy to place a patient in a DCIS observation trial compared to those with low knowledge, but this was not statistically significant (p-value = 0.091).

Comment 5: *Some published studies include other factors like palpable mass, multicentricity, biopsy grade or presence of microinvasion associated with upstaging. In table 4 one of the reasons to exclude patients from observation strategy is a high-risk of disease progression. Are the above factors included in high risk of progression? How do you define high-risk disease?*

Reply 5: We did not define "high risk" in the survey, specifically, instead we let each respondent use their own definition of what is "high risk" of disease progression. Factors associated with upstaging that have been defined in the literature are included in the discussion on page 12. We would agree that these factors can help define "high-risk" disease.

Comment 6: *You conclude that you are unable to identify any factors that would allow clinicians to decide observation in patients with DCIS. How do you think it could be identified the subgroup of low-risk DCIS patients who might benefit from observation alone? You should mention this in the conclusion.*

Reply and changes in the text 6: Thank you for your suggestion. We have included in the conclusion that the ongoing trials and future studies would need to identify a sub-

group of DCIS patients that have a low risk of tumor progression and upstaging, and could therefore be safely observed (page 13, last paragraph).

In summary, explaining the above remarks will improve significantly the objectives of this study.

Reviewer B

Comment 1: *In oncology there are many unanswered questions, one of which is certainly when to treat DCIS of the breast, several ongoing studies on this topic have been mentioned (COMET, LORD and LORIS). The article gives us a clear view of what the doctors involved in the treatment of this tumor think and their concerns.*
We generally know what to do when there are publications with sufficient evidence, but when this is not the case, we are unaware of the practice of other centers. We have seen in this article that young age, negative hormone receptors or high grade are considered by most to be factors that discourage observation.
The methodology is correct and the discussion has seemed excellent to me with abundant updated references. The number of respondents and centers is high and can be quite representative.
Reply 1: Thank you for your comment. We do agree the strengths of our studies include the high responder rate and the methodology.