

Peer review file

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Reviewer A

In this study, the authors evaluated the factors which affected for surveillance imaging adherence in surgically resected pStage I NSCLC patients, and showed that tumor size, being married and living <100 miles from the medical center were associated. This is interesting for me.

But I have some comments and concerns listed below.

Major comments

Comment 1: Of 1288 patients, two-thirds did not receive MSSIS. I think this is quite more. Why could not they receive? The authors should address.

Reply 1: We appreciate the question and comment from the reviewer. We have discussed this issue within the Comment section of the revised manuscript.

Given the retrospective nature of the data, comparisons of the study groups can suffer from some degree of bias. Theoretically, patients could have been seen outside of our institution by other local physicians accounting for a degree of under capturing. Nonetheless, it is our practice to have thorough involvement in survivorship follow-up and studies performed by other institutions are routinely captured and screened into our system.

We believe that patients are more likely to follow up for the first surveillance imaging because this is the time when they have the most investment/motivation to comply with their care. As the time from the operation becomes more remote, the patient may be experiencing a sense of normalcy and hence may be less motivated or inclined to get further interventions since they may believe to have been “cured”. Of course, this is only a theory, but finding strategies to target these specific groups that are less likely to meet adherence to surveillance guidelines seems very relevant.

Additionally, we accounted for CT scans of the chest or PET-CT performed after the date of operation. If the patient underwent an additional CT chest after their operation for a different reason, this would increase their surveillance imaging number per our methodology. We were not able to elucidate the indication for imaging from these data. We recognize that for some patients, this may introduce some confounding factors but believe that in general, we are capturing surveillance scans for patients with early stage lung cancer.

Comment 2: The authors showed just OS, which is not significant difference. As they mentioned, I also think that the role of postoperative surveillance imaging is to detect not only recurrences but also the other diseases earlier, resulting in to lead the longer survival. However, I think they should at least show the recurrence rates, the diagnostic yields of CT or PET-CT and DFS because the target population of this study is pStage I early lung cancer patients. The necessity of surveillance imaging for the less recurrence rate should be discussed.

Reply 2: We appreciate the reviewer's comments. We agree that recurrence rates are a crucial part of surveillance strategies and certainly play an important role worth discussing. Unfortunately, our methodology did not capture this variable and as such these data are not available at this time. We would be interested in exploring this in the future.

Comment 3: Are there any ideas to accomplish MSSIS for much more patients? The authors mentioned the potential of telemedicine. I agree this. Any other ideas? There is not always necessary to perform surveillance imaging in a single large medical center. I think to build better regional cooperative relationships and follow-up system with community physicians and nearby imaging centers is much important.

Reply 3: We agree with the reviewer's excellent suggestions. Telemedicine is likely to have a positive effect on adherence to surveillance guidelines and survivorship care. Furthermore, additional ways to improving the frequency of surveillance imaging could to be to strengthen relationships with different medical centers around the country, more collaborative electronic medical record platforms, and optimizing patient education.

Ultimately, in order to improve surveillance compliance, we need to understand the barriers, and, thus, a needs assessment would be very helpful to clarify the challenges faced by patients who travel further. We have elaborated on this in our revised manuscript discussion.

Minor comments

Comment 1: Table 1: Total patients number is 1288. But no MSSIS is 537, and MSSIS is 464 (n=1001). Is that okay?

Reply 1: We appreciate the reviewer pointing out this discrepancy. The data have been corrected on Table 1.

Comment 2: References: ref. 4 is quite old. There are many articles which discussed about the same matter. Please change.

Reply 2: Thank you. This reference has been updated in the manuscript.

Reviewer B

The authors compared the degree of surveillance by imaging studies after surgery for pathologic Stage I- non-small cell lung cancer between the MSSIS group and the No MSSIS group, and showed in this paper that the difference in hospital travel distance is the main limiting factor. It shows the grounds for the spread of remote diagnostic imaging in the near future, and shows very interesting and important findings for postoperative follow-up doctors.

Comment 1: Part of the data interpretation on which the main assertion is based, there are some inappropriate expressions and it requires correction. Line 205: The authors defined statistical significance as $p < 0.05$ (line 174), so $p = 0.06$ (Table 2) cannot be said to be significant on multivariate analysis. Therefore, expressions such as "there was a tendency to have a significant difference" will be more appropriate.

Reply 1: This phrase has been revised in the resubmitted manuscript in accordance with this insightful comment. Thank you.

Minor corrections

Comment 2: Line 56, “pI-NSCLC” to “pathologic Stage I-NSCLC”

Reply 2: This has been corrected in the manuscript.

Comment 3: Line 65, it need to insert at first appearance, “MSSIS group vs. No MSSIS group, 2.63 +/- 0.04 cm vs. 2.49 +/- 0.05 cm; p = 0.03).

Reply 3: This issue has been corrected in the revised manuscript.

Reviewer C

Comment: Surveillance for lung cancer is an interesting topic because there is no data that it actually helps improve outcomes. We all do it and know that it helps identify second primary tumors, but the benefits of surveillance and the appropriate intervals are based on expert opinion. This study looks at retrospective data from a large cancer center to determine factors that may influence surveillance adherence. Unfortunately, there is very little novel information in this study. Travel distance is a well known factor for impeding care and even more importantly, one could imagine that many of these patients receive imaging closer to home that may or may not be identified in this study as the methodology is poorly described.

Reply: We appreciate the reviewer’s comments. We believe our study is relevant to the literature because it highlights some important findings, particularly that despite well established surveillance guidelines, two-thirds of patients do not receive appropriate imaging at our institution. With regard to the methodology, we have elaborated in our revised manuscript to provide clarity in that we did capture external imaging within our follow ups. Moreover, we have discussed the possibility of external imaging that was not captured in our limitations of the revised manuscript. Finally, we must reiterate that we do believe, to some extent, that geographic barriers and socioeconomic challenges impede adequate post-treatment surveillance. This study can help fuel further investigations to elucidate predictors of inadequate surveillance, improve survivorship strategies, and potentially lead to efforts to address such barriers as they are identified.

Reviewer D

Minor comments:

Title:

- the title should state that distance is not the only barrier to surveillance imaging adherence in this study

The title has been changed in the manuscript.

Results

- Table 1 specify percentage of MSSIS et NO MSSIS

The percentages have been added to the revised manuscript.

Major comments

Patients and methods

- How patients are called to their follow up exams: phone, mail, E-mail ...and are there any reminders?

Thank you for this question. We have updated our methods to provide clarity in the revised manuscript. Patients are usually followed using phone, email, and “My Chart” (web based application in our electronic medical record, Epic). We send frequent reminders to all patients regarding upcoming testing and appointments. Additionally, we have a robust survivorship department that is in charge of ensuring adequate follow up for patients.

- Have Socio economic and educational level been measured

We appreciate the reviewer’s question. This particular variable was not captured in this study. We are planning on a subsequent study using zip code data to analyze the influence of socioeconomic status on adherence to surveillance guidelines and we have added to our discussion that this is an important future direction.

Results

- Is there a significant difference for adherence to surveillance between married women and married men

Married men were found to have MSSIS in 84% of patients, compared to married women who had MSSIS in 68% of cases ($p= 0.007$). This comparison is included in the revised manuscript.

Comment

- Specify what types of strategies could optimize access to local imagery: give some examples

We appreciate the reviewer's question. Telemedicine is likely to have a positive effect on adherence to surveillance guidelines and survivorship care. Furthermore, additional ways to improving the frequency of surveillance imaging could be to strengthen relationships with different medical centers around the country, more collaborative electronic medical record platforms, and optimizing patient education. We have added this to the discussion.

- Define the way survivor care in this institution

It is our practice to have a thorough involvement in survivorship follow-up and studies performed by other institutions are routinely captured and screened into our system. Patients are usually followed using phone, email, and "My Chart" (web based application in our electronic medical record, Epic). We send frequent reminders to all patients regarding upcoming testing and appointments. Additionally, we have a robust survivorship center and specific clinics that are in charge of ensuring adequate follow up for all patients. These details are included in the revised manuscript.

- Explain the absence of significant difference during the first scan regardless of the distance not found for the following exams

We believe that patients are more likely to follow up for the first surveillance imaging

because this is the time when they have the most investment/motivation to comply with their care. As the time from the operation becomes more remote, the patient may be experiencing a sense of normalcy and hence may be less motivated or inclined to get further interventions since they may believe to have been “cured”. Of course, this is only a theory, but finding strategies to target these specific groups that are less likely to meet adherence to surveillance guidelines seems very relevant. We have discussed these issues in our revised manuscript.

Reviewer E

Study on the surveillance adherence is interesting and of importance. I believe that your conclusion that the distance has an effect on the adherence could be true, but there is also a possibility of a selection bias. In No MSSIS group, tumors were smaller with a higher frequency of stage IA tumors. This could have an effect on the surveillance interest.

My questions and suggestions:

Comment 1: Authors have categorized patients in two groups based on the distance travelled from their homes (Methods/lines 154-155). In multivariate analysis, it seems, however, that you have used distance as a continuous parameter. Is that true? Why is that? I believe multivariate analysis should be calculated with the categorized distance parameter. Furthermore, all parameters used in the model should be clearly stated.

Reply 1: We appreciate the reviewer’s question. For the purposes of the multivariable analysis, distance to the institution was included as a categorical variable (<100 miles vs >100 miles).

For this analysis, we used a forward stepwise multivariate logistic regression model was created using MSSIS as the dependent variable and an entry threshold of $p < 0.05$ for entry of potential predictor variables into the model. We included all of the variables listed in table 1 that were found to have a statistically significant difference between groups.

Comment 2: Conclusion and the title of the study are, at this point, somewhat misleading. As you state yourself in the results, only tumor size and marital status was associated with obtaining MSSIS. If in the new multivariate analysis distance remains as a non-significant parameter, it could reasonable to concentrate more on the marital status as an important factor to the adherence of surveillance.

Reply 2: We appreciate the reviewer's comments. We have changes the title in the manuscript as per recommendations from the reviewer team.

Comment 3: You state that 1288 patients met the inclusion criteria in line 177 and refer to Table 1. In Table 1, the overall number of patients is only 1001?? Furthermore, those numbers in Table (gender/Caucasian/married) differ from those in the Results??

Reply 3: We appreciate the reviewer's question. The data have been corrected in the manuscript.

Comment 4: I feel Figure 2 is misleading. It compares the number of imaging studies between those living within 100 miles to those living further away. Authors seem to automatically assume that more imaging studies is better. There is no data in this study to support this. What is the optimum number of imaging studies within 60 months? In both ESMO 2017 and ACCP 2013 guidelines, the recommendation is the same as the minimum stated is the manuscript. Numbers above these recommendations could be considered as over-surveillance. Therefore, the comparison should be made similar to Figure 1 (MSSIS vs No MSSIS).

Reply 4: We appreciate the reviewer's comments. The objective of Figure 2 was to focus the travel distance variable and show the trend/changes overtime in each of the groups. We accounted for CT scans of the chest or PET-CT performed after the date of operation. If the patient underwent an additional CT chest after their operation for a different reason, this would increase their surveillance imaging number per our methodology. We were not able to elucidate the indication for imaging from these data. We recognize that for some patients, this may introduce some confounding factors but

believe that in general, we are capturing surveillance scans for patients with early stage lung cancer.

Comment 5: Authors report very shortly that no survival difference was detected between No MSSIS vs. MSSIS. In conclusion, in lines 263-264 they state “not specifically powered to meet this objective”. I feel this is somewhat awkward comment. First, this is a retrospective study without power calculations. Second, with 1288 Stage Ia and Ib patients, I am sure, authors could have done multivariate analysis and evaluated the survival difference between different surveillance strategies.

Reply 5: The referenced comment has been removed from the manuscript.

Comment 6: Minor comments:

a. There seems to be a mistake in Table 2. OR of Distance was 1.01 but 95% CI was 0.99-1??

The result is correct. This variable did not reach a statistically significant difference.

b. Smoking history would be important parameter to be included.

Unfortunately, this data point was not available for this particular study. We agree that this is a relevant and important variable to report.

c. The used TNM-edition should be stated in the Methods.

This change has been included in the manuscript.

d. In Table 1 “vital status” is not commonly used.

This change has been included in the manuscript.

e. The sentence in lines 194-195 is somewhat misleading. Should be for example: ... <100 miles from hospital did have more postoperative imaging studies (10.7...

This change has been included in the manuscript.

Reviewer F

The authors retrospectively evaluated characterize surveillance practices after lobectomy for early-stage NSCLC and to identify the impact of various demographic factors on patterns of surveillance. They found that two-thirds of patients at our institution did not undergo recommended surveillance imaging. Tumor size, being married, and living.

I have the following concerns.

Comment 1

Abstract/ Method

P3. L59

Please add the standard nomenclature of CT and PET.

This change has been made in the manuscript.

Comment 2

Abstract/ Result

P3. L65

Please add the standard nomenclature of OR and CI.

This change has been made in the manuscript.

Comment 3

Abstract/ Result

P3. L66

Add 95% CI for having larger tumor size.

This change has been made in the manuscript.

Comment 3

Patients and Method

P6. L154

Why did the authors divide the distances by 100 miles?

We appreciate the comments from the reviewer. We chose the distance variable to be 100 miles because we wanted to capture out of state patients. Since the majority of the patients we take care of (about 70%) live in the state of Texas, we felt like this distance could be reflective of a more rural environment or at least a barrier to return to our facility for their survivorship care. We have added this justification to our methods section.

Comment 4

Patients and Method

Please describe exclusion criteria.

Overall, patients lost to follow up were considered as having no imaging after surgery. It is possible that the patients were obtaining imaging elsewhere and were not captured by our system but we believe that this event would be rare given the way survivorship care is handled at our institution. If there was incomplete data, the patients were not included in the study. This has been added to our methods section of the revised manuscript.

Comment 5

Patients and Method

P6. L168

The authors used Chi-square or Mann-Whitney tests to evaluate categorical variables. However, were Mann-Whitney tests used for continuous variables?

We used Chi-square or Mann-Whitney for variables deemed appropriate for each methods as highlighted by the reviewer.

Comment 6

Patients and Method

P6. L172-173

The author used Kaplan-Meier analysis to estimate all-cause mortality.

Did you use log-rank test to evaluate OS between obtained MSSIS and NO MSSIS groups?

Please add a figure that showed the Kaplan-Meier curve and p-value analyzing the OS between obtained MSSIS and NO MSSIS groups.

There was no difference in overall survival between the patients that obtained MSSIS compared to those who did not (78% vs. 75%; $p = 0.34$) with a mean follow up period of 54.2 36.3 months. This analysis was performed with a simple Z-score test for proportions. A formal survival analysis was not performed given that we did not have long term follow up data for this calculation.

Comment 7

Patients and Method

Do you have data regarding smoking history?

Unfortunately, these data is not available for this study.

Comment 8

Result

Please describe how you deal with the excluded data.

Overall, patients lost to follow up were considered as having no imaging after surgery. It is possible that the patients were obtaining imaging elsewhere and were not captured by our system but we believe that this event would be rare given the way survivorship care is handled at our institution. If there was incomplete data, the patients were not included in the study.

Comment 9

Result

P7. L186-189

Please add the outcome of distance to institution, which showed essentially statistical difference.

This change has been made in the manuscript.

Comment 10

Result

P10.243-244

In this study, the authors considered that married status had potentially affected their long-term oncologic outcomes.

I think this view lacks grounds.

Please supplement your comments on marriage and prognosis using the original data analysis and prior references.

Prior reports in the literature have described the association of marital status on oncologic outcomes for different solid tumors. For example, in a recent study by Zhang et al on patient with gastric adenocarcinoma, married patients had a better 5-year OS (32.09% vs 24.61%, $p < 0.001$) and 5-year cancer-specific survival (CSS) (37.74% vs 32.79%, $p < 0.001$) than their unmarried counterparts. The authors hypothesized that these observations could be explained by undertreatment and lack of social support in unmarried patients (18). Further, in a population based study describing the effect of marital status on lung cancer patients in Belgium, both men and women appeared to benefit from being in a relationship with a highly-educated partner. Men appeared to benefit the most from the educational level of their partner and women benefited more by their housing conditions (19); one could hypothesize that interventions to target specific high risk groups, such as single cancer survivors, would be beneficial. These findings have been added to the manuscript.

Comment 11

Result

P10.L273

...of bias..

Please modify this period.

This change has been made in the manuscript.

Comment 12

Introduction

A statement should be included at the end of the “Introduction” to indicate which reporting checklist was followed (eg, “We present the following article / case in accordance with the STROBE reporting) checklist. ”).

This change has been made in the manuscript.

Comment 13

Footnote

Reporting Checklist, Author Contributions, Ethical Statement, Acknowledgments, and Conflicts Of Interest are incomplete.

The missing documents will be added to our submission.

Comment 14

Please modify the style of References.

This change has been made to the manuscript.