Peer Review File
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Reviewer A

Major comments

Comment 1: I thought that this article contains recent trends about small-sized pulmonary nodules detected in CT check-up, and the psychological problems of the patients with indeterminate pulmonary nodules. However, I thought that this article was lacking impact because the results of the psychological factor analysis were common and expected. Although the authors also described the importance of doctor/patient communication, I thought that the patients' psychological status mainly depends on the communication with a doctor. If the doctor provides precise information to the patients with indeterminate lung nodules, and relieves the patients' stress, the psychological status of the patients will be favorable. In this article, there were no analyses about the communication factor between the doctor and the patients although the authors slightly commented this on point in the discussion section. Could this study analyze some communication factors? If the factors will be included in the analysis, this article will be more useful for the readers. What do the authors think about this points?

Reply 1: Thank you for your comment. We strongly agree with your opinion. The communication between doctors and patients is the crucial factor influencing patients' psychological status. Therefore, we conducted this research to analyze the potential risk or protective factors for making the communication more directional. In fact, the communication factors had been involved in our questionnaires. We investigated the perceptions of patients on the communication (Will you follow your doctor's advice? Do you think the follow-up recommended by your doctor is appropriate?). The results showed that 1141 (96.3%) patients would follow the doctor's advice, while 1018 (85.9%) thought the timing of follow-up was just right, which reflected how important the view and the advice of doctors are for the patients. We will present these results and discuss more about the communication.

Changes in the text: Page 7, line 127-128： Communication factors including adherence to doctors' recommendation and perception of follow-up periods recommended by doctors were also incorporated into the investigation. **Page 9, line 181-83：** The results also showed that 1141 (96.3%) patients would follow the doctor's recommendation, while 1018 (85.9%) thought the timing of follow-up was just appropriate. **Page 12, line 246-248：** As for communication factors, patients who thought the follow-up periods recommended by doctors too long would more strongly prefer surgery ($\chi 2 = 18.198$, $P < 0.001$). **Page 17, line 347-359; Page 18, line 360：** It

is gratifying to note that adherence of patients in this study was remarkably high, although a part of patients thought the follow-up periods recommended by doctors was not appropriate. It is not surprising that this part of patients with extremely high risks of anxiety and depression were more willing to choose surgery. Apparently, doctors play a significant role in the medical behavior of patients. When doctors communicate with patients, they should not just only tell patients what it is and how to do but pay attention to what patients doubt. Our results provide ideas for understanding what patients really concern about. For example, patients regarded cough as a risk factor leading to a high level of anxiety, likewise, patients with family history of malignancy would be more anxious. Implementing targeted patient education can promote healthy behavior and alleviate negative emotions. As for patients with anxiety or depression, management strategies can be adjusted appropriately, such as a shorter follow-up period. Surgery should also be included in the discussion when the patient is extremely distressed, especially for those nodules that can be wedge resected. Of course, where necessary, psychosocial interventions can be implemented in collaboration with psychologists.

Comment 2: It was unclear how the authors would manage the patients with indeterminate pulmonary nodules from the results of this study.
Reply 2: Thank you for your comment. We have highlighted it and modified the manuscript.

Changes in the text: Page 17, line 347-359; Page 18, line 360： It is gratifying to note that adherence of patients in this study was remarkably high, although a part of patients thought the follow-up periods recommended by doctors was not appropriate. It is not surprising that this part of patients with extremely high risks of anxiety and depression were more willing to choose surgery. Apparently, doctors play a significant role in the medical behavior of patients. When doctors communicate with patients, they should not just only tell patients what it is and how to do but pay attention to what patients doubt. Our results provide ideas for understanding what patients really concern about. For example, patients regarded cough as a risk factor leading to a high level of anxiety, likewise, patients with family history of malignancy would be more anxious. Implementing targeted patient education can promote healthy behavior and alleviate negative emotions. As for patients with anxiety or depression, management strategies can be adjusted appropriately, such as a shorter follow-up period. Surgery should also be included in the discussion when the patient is extremely distressed, especially for those nodules that can be wedge resected. Of course, where necessary, psychosocial interventions can be implemented in collaboration with psychologists.

Comment 3: I could not understand the methods of the questionnaire; whether the questionnaire was performed in the first visit to the hospital or after the follow-up. When was the questionnaire performed?

Reply 3: Thank you for your comment. The questionnaire was performed in the first visit to the hospital. Regardless of whether the patient has been diagnosed with a pulmonary nodule for the first time or has had a pulmonary nodule detected for some time, as long as he visited our clinic for the first time, he would be invited to complete the questionnaire. And we will also carry out the follow up survey to explore the trajectory of psychological status change.

Changes in the text: Page 6, line 113-114： PN patients who first visited the outpatient clinic were invited to complete self-administered questionnaires.

Comment 4: I wonder if there are some guidelines for follow-up methods of indeterminate pulmonary nodules in the authors' country. If there are some guidelines, it is better to show those guidelines.

Reply 4: Thank you for your comment. There are some guidelines for follow-up methods of indeterminate pulmonary nodules in our country. The following is the relevant reference added to the manuscript.

Changes in the text: Page 22, line 453-454 He J, Li N, Chen WQ, et al. [China guideline for the screening and early detection of lung cancer(2021, Beijing)]. Zhonghua Zhong Liu Za Zhi 2021;43:243-68.

Comment 5: One of the variables in Table 2, "Initial impression of doctors"was described. While the benign group (34%) selected surgery, the malignant group (56.3%) selected follow-up. I felt that these results were very strange. I wondered if the doctors provided sufficient information about the lung nodules to the subjected patients. I don't think that the patients would be so anxious if the doctor could provide information about the perspective or the nature of lung nodules. What do the authors think about this point?

Reply 5: Thank you for your reminder. Indeed, we have not elaborated enough on this question. The question set in our questionnaire are actually: For potentially malignant pulmonary nodule, if the doctor tells you that it is safe to follow up in the short term, which of the following medical options are you more inclined to prefer? Therefore, all the participants answered this question at the same situation. The choice of different options reflects their values and preferences.

Changes in the text: Page 12, line 234-235: All the patients answered what treatment options they would prefer if the nodule was clinically characterized as suspicious for malignancy but it was safe to follow up in the short term.

Minor comments

Comment 1: In line 54-55, is the following sentence needed? "Unfortunately, no minimally-invasive methods is available at the current stage to immediately reach a definite diagnosis, unless a transthoracic biopsy or surgical resection is performed." I think this is very well-known.

Reply 1: Thank you for your comment. This sentence has been deleted.
Changes in the text: Page 4, line 67-69.

Comment 2: In the lines 222-223, although the authors described as follows; "Therefore, effort should be put into popularization of knowledge about nodules to patients for avoiding psychological burden", in detail, how do the authors decrease the psychological burden? The effort should be described more.
Reply 2: Thank you for your comment, the manuscript has been modified.
Changes in the text: Page 14, line 291-293: Some strategies can be developed from other studies, such as a brochure that explained the safety and favorable outcomes for most nodules(11) and tailoring patient-centered communication(16).

Comment 3: Please check the parenthesis and semi-colon spaces.
Reply 3: Thank you for your reminder, we have reviewed and corrected the full text.

Reviewer B

Comment 1: Would you please explain the criteria to determine the diagnosis of anxiety or depression? Is it based on HDAS only or there is any expert to support your diagnosis?
Reply 1: Thank you for your comment. We evaluated the anxiety and depression of patients based on HADS only. At the outpatient clinic, due to time constraints, it is hard to allow the psychologist to give a professional assessment of the psychological status. Therefore, we adopted the HADS which is a validated screening tool for anxiety and depression. We can initially judge the psychological status from the results of the HADS.

Comment 2: You provide the univariate analysis on choice of treatment strategy and report that symptomatic patients ($\chi2= 9.696$, $p = 0.021$) and those with 42 progressive nodules ($\chi2= 18.198$, $p = 0.033$) choose more aggressive. Could you observe similar results in the multivariate analysis?
Reply 2: Thank you for your comment. Similar results could not be observed in the multivariate analysis. The reasons for treatment preferences are varied and complex. Further prospective studies are therefore needed to explore the determinants of patient preference. The results we have obtained through one-factor analysis also provide clues for more in-depth research.

Comment 3: Do you have the data of HDAS change before and after receiving follow-ups or surgeries?
Reply 3: Thank you for your comment. The data of HDAS change before and after receiving follow-ups or surgeries are being collected and will be presented in a future study (please refer to our previous study protocol: Zhuang W, Tang Y, Xu W, et al.

Should psychological distress be listed as a surgical indication for indeterminate pulmonary nodules: protocol for a prospective cohort study in real-world settings. J Thorac Dis. 2022 Mar;14(3):769-778. (ClinicalTrials.gov Identifier: NCT04857333)). We are highly interested in psychological changes influenced by the alteration of medical behaviors. The data of this article was from the first visit of the patients and this cross-sectional study also provided some clues. For example, psychological status has a significant impact on treatment preferences. And this is the focus of our follow-up longitudinal research.