Author's response to reviews

Title: Treatment of hyperfunctioning thyroid nodules by percutaneous ethanol injection: 2-year follow up

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We are hereby submitting the revised version of the manuscript “Treatment of hyperfunctioning thyroid nodules by percutaneous ethanol injection”. The changes we have made to the manuscript in response to the referees’ comments are as follows:

Professor Enio Martini:
We have added the paper by Lippi et al (JCEM 1996) to our references. We have deleted Table 1 and the reference to cystic and cold nodules, as requested.

Professor Fabio Monzani:
We have discussed our results in the light of larger studies, especially the one carried out by Lippi et al. We have amended the segment “PEI could not be performed because of nodule fibrosis”. We have clarified that the figure of 0.1ml per ml of nodule volume is a mean value. We have corrected the number of cases complicated by transient dysphonia; the actual figure was two. We have added details of the kits used to test thyroid function, along with the normal ranges in the Methods section. We have provided a definition of complete response in the Patients & Methods section. In the opinion of our consultant biostatistician, given the design of the study, linear regression would not have added anything meaningful to our findings, and so we have not performed regression analysis on our data.

Professor Lazlo Hegedus:
Item 1: We have added long-term anti-thyroid therapy as a therapeutic option.
Item 2: We have clarified in the introduction the reasons for our undertaking this study.
Item 3: We have divided patient population into patients and methods.
Item 4: We have specified our entry criteria and clarified that our sample was a consecutive series of patients who were treated.
Item 5: We have clarified that ethics committee approval was obtained.
Item 6: FNAB was performed to rule out malignancy before starting PEI therapy. As pointed out in the text, all our FNAB specimens were reported as colloidal goitre, which is not easily mistaken for follicular neoplasia. We re-consulted the reporting pathologist and have accordingly stated the criteria sued to define a benign FNAB.
Item 7: The methods for the hormone assays as well as the normal ranges have been included the
appropriate section.
Item 8: The formula used by the ultrasound machine to calculate nodule volume automatically is provided in the Methods section, along with the reference from which the formula has been taken. The reported accuracy of the method is 80-85%.
Item 9: No maximum nodule size was set.
Item 10: The study was not initially designed to differentiate between the three phenotypes reported. That is why we have not distinguished between the outcomes in the three groups. Moreover, the presence of only patient with co-dominant nodules does not lend itself to any significant interpretation.
Item 11: The study was designed to test the clinical efficacy of PEIT. We have succeeded in demonstrating this. We did not seek to quantify the effect of PEIT in this study, but will do so in a larger trial, which we will be starting soon.
Item 12: Only patients suspected of having sustained laryngeal nerve injury were examined by indirect laryngoscopy.
Item 13: Asymptomatic means disappearance of the clinical symptoms of thyrotoxicosis.
Item 14: The number of cases of transient dysphonia was two. The error has been corrected.
Item 15: This has been rephrased.
Item 16: All the procedures were performed by two experienced interventional radiologists. The success rate achieved and the low incidence of complications bear witness to their level of skill. The study, as pointed out in Item 11, was designed to detect clinical and biochemical recovery after PEIT, and not to determine the actual quantity of ethanol required to achieve this.
Item 17: The authors took note of the referee’s recommended references before revising the manuscript. We have not cited the referee in our references, however.
Item 18: Table 1 has been deleted.
Item 19: We have added pre- and post-PEIT nodule volumes in Table 2.

In compiling this covering letter, we revised the manuscript once more and have made a few more changes. Please consider the version forwarded with this covering letter as the final revised manuscript. Thank you for your guidance and patience.

Best regards,
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