Reviewer's report

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

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Reviewer: Prof Laszlo Hegedus

Level of interest: A paper of limited interest

Advice on publication: Reject

The manuscript by Larijani et al. concerns the effect on thyroid function and thyroid nodule size of percutaneous ethanol injection treatment (PEIT). The method with this indication has been used for more than a decade. Numerous publications are available, also dealing with larger groups of patients. In this respects the study offers no novelty.

Specific comments:

1. Introduction page 3. Long-term antithyroid therapy is also an option. Not just 131I and surgery.

2. Since so many studies are already available, the authors should state in the introduction why specifically they undertook this one.

3. Page 4. "Patient population", should be divided into patients and methods.

4. Page 4, first line. What were the entry criteria? Is this a consecutive series of patients or a consecutive series of patients who were treated?

5. Page 4, line 3. Was Ethics Comittee aproval also obtained?

6. Why did the authors perform FNAB in all their subjects? In this kind of nodule you risk obtaining a highly cellular material and little colloid which is often interpreted as follicular neoplasia. Most
endocrinologists would advise against FNAB in this setting. the authors do not state what the criteria for a benign FNAB were.

7. The methods for the hormone assays as well as the normal ranges should be stated, Page 4 line 11-13.

8. Page 4, methodology. There are no data on which method for thyroid nodule volume determination the authors used. observer variation regarding this variable should also be given.

9. Was any maximum nodule size set?

10. Page 6. First 5 lines. The authors describe 3 distinct phenotypes. Does this influence their subsequent data analysis and interpretations?

11. Page 6. The results are almost impossible to evaluate since there are no data on number of treatments, total volume of alcohol given and most important, total volume of alcohol per cc of nodule volume. otherwise the interpretation of the effect on shrinkage is uninterpretable.

12. page 7, complications. Were all patients investigated with indirect laryngoscopy before and after PEIT?

13. Page 8, discussion line 8. What does " became asymptomatic" cover?

14. Page 9, first line. Here one case of vocal cord paralysis is stated. However, on page 7 it is two cases!

15. Page 9, line 2-3. The use of US cannot in itself prevent extranodular alcohol leakage. The authors should rephrase.

16. Page 9, last 3 lines give little meaning. The most important factor in predicting response to treatment is probably amount of alcohol/ cc of nodule volume, but this isnot given by the authors. Since we have no data on number of subjects performing the procedure and their level of skill how can we evaluate whether this influenced the results?


18. Table 1 is superfluous and could be deleted.

19. Table 2 or a separate table or figure, should include thyroid nodule volume and total thyroid volume, if available.

**Competing interests:**

None declared.