Peer Review File

Article information: https://dx.doi.org/10.21037/gs-23-425

Reviewer A

The study size is a little small compared to the other papers in the literature. It would be instructive to include the relative availability and cost of RFA (and thermal ablation in general), in comparison to radioactive iodine and surgery in Ecuador to provide to more context to patients' decision-making.

Results:
The main outcome when treating autonomously functioning thyroid nodules is whether the hyperthyroidism has resolved (not the volume reduction). So, it is important to mention how many patients became euthyroid after treatment.

Line 49: Hyperthyroidism automatically means the TSH is suppressed so both things don't need to be mentioned.
Thank you for the comment. We corrected it.

Line 52: VRR = volume reduction ratio – this is not a ratio; this is a percentage. Please replace with VRP or simply VR (volume reduction).
We replaced it.

Line 54 – 55: Would comment on the relative success of RFA in this series and whether this is consistent with other studies; and the feasibility of RFA as a treatment option for AFTNs in Ecuador rather than just state more research is needed.
Thanks for the comment. We added it.

Introduction:
Line 58: **Plummer's disease is the correct term and this actually refers to toxic multinodular goiter rather than a single toxic adenoma so would remove this terminology.**
Thank you. We corrected it.
Line 60 – 61: Antithyroid drugs may be employed (it is not necessary)
Done.
Line 68 – 69; Please keep terminology consistent – should be AFTNs rather than toxic goiter nodules.

Done.

Methods:

Line 78 – 80: Was this all of the RFA procedures performed on AFTNs during this time period?

Yes

Line 84 – 86: Did all the thyroid undergo thyroid scintigraphy.

Yes

Line 90: 3 years' experience of doing RFA or 3 years' experience as a head and neck surgeon?

Doing RFA

Line 93: Was the electrode inserted from medial to lateral in all nodules?

Trans-isthmic approach

Line 96: By drug use do you mean the use of antithyroid medications? Should be US neck.

Yes.

Line 97: Not a "ratio"

Results:

Line 113 – 114: The results section in the abstract implies that all patients had symptomatic hyperthyroidism – this provides more detail. This is should be clarified in the abstract e.g., "all patients had suppressed thyroid-stimulating hormone (TSH)"

Done.

Line 115: Would say pre-procedure or pre-RFA rather than pre-operative as this is specifically a non-surgical technique.

Done.

Line 116: Why does the abstract report a mean time and the main text reports a median follow-up time? They should be consistent.

Median

Line 120: Not a "ratio"

Line 129 – 130: Was this median or mean time, power and energy? Was the time the active ablation time or the total time? How is the power calculated? It is 38.57 W rather than 38,57 W? Was the power adjusted during the RFA procedure? Is it 9.28 KJ or 928 KJ? Would give ranges as well as standard deviation.
The RFA machine gives the power. It is 38.57 W.
The machine adjusts the power. It is 9.28 KJ.

Line 132 – 135: How many patients had the TSH normalize after RFA and how long did it take for the TSH to normalize i.e., did it normalize by the 1, 3 or 6-month follow-up?
Before RFA, five patients used anti-thyroid medication (tapazol 5-10 mg). All the patients stopped the anti-thyroid medication after RFA (1 month= 2 patients; 3 months= 2 patients; 4 months= 1 patient).

Discussion:
Line 138 – 139: This sentence is unnecessary – and if it is to point out that this is first case series from Ecuador it needs to rewritten.
Thanks for the comment. It was removed.

Line 140: this is not a volume reduction "rate". The reduction of hyperthyroidism symptoms was not reported in the results – how was this measured? It was also not clarified **how many patients were and weren't on antithyroid drugs before and after the RFA**. **Also, which anti-thyroid drugs were they on and how long before they stopped them?** How many patients remained on them?
Before RFA, five patients used anti-thyroid medication (tapazol 5-10 mg). All the patients stopped the anti-thyroid medication after RFA (1 month= 2 patients; 3 months= 2 patients; 4 months= 1 patient).

Line 142 – 143: The European, AHNS international, NASOIE and ATA guidelines also state RFA is an option for AFTN – with the European guidelines being the most conservative. It may be worth discussing this in more detail rather than simply saying there is no consensus.
Done

Line 145: When the authors say they followed the Korean guidelines to include patients – does this mean that certain patients were excluded? In that case the

exclusion criteria will need to be included in the methods section.
We did not have exclusion criteria. The 8 patients included met the Korean guideline.

Line 146 – 155: volume reduction should not be described as a ratio if expressed as a percentage. Also, important to stress the percentage/number of patients who became euthyroid after RFA in these studies.
All the patients stopped the anti-thyroid medication after RFA (1 month= 2 patients; 3 months= 2 patients; 4 months= 1 patient).

Line 157: Please define technical efficacy and its relevance? A 50% volume reduction that does not result in euthyroidism would not be a successful procedure in case of AFTNs.
Thanks for the comment. Technical is an incorrect term. It was removed.

Line 158 – 159: Was the volume less than 12 ml because of chance or deliberate selection?
Chance

Line 160: Not clear what this sentence means? I believe the authors are trying to say that a patient with a single AFTN may respond better than a patient with a toxic multinodular goiter. One AFTN or a single AFTN would be better terminology than "isolated AFTN".
Thanks for the comment. You right. We clarified it.

Line 167: What extra data were patients needing? Was all the data not available for the 8 patients in the study?
In the followed-up there was some missing data.

Line 169: These statements are fine to make, however these are not strengths of the study, rather are an advertisement for the center. Particularly, the multidisciplinary team's contribution to the study should be in the acknowledgements section as that has nothing the do with the study.
We agree. We improve it.

Line 178: Does total nodule volume refer to the volume before RFA? If so, this needs to be specified.
Yes, it does. We specified it.

Line 180 – 181: Was this measured in any objective way?
Not. It is subjective. In the appointments post-RFA, the patients referred feel better.

Figure 4: This figure indicates missing data and patients that were not followed up at the specified intervals – this should be indicated in the results as the way it is written it appears all 8 patients were followed for 6 months.

It was indicated in the result section.

Figure 5: It would be much better too present TSH changes in a table.
Thanks for the comment. We added this change in table 2.

Table 2: Again – not a ratio. Please clarify in the text how many patients do not have follow-up.
Done.

Please review grammar and syntax throughout the paper.

Reviewer B

I appreciate your endeavours on the introduction of radiofrequency ablation for autonomously functioning thyroid nodules into Ecuador a lot. I consider your work worth to be published in Gland Surgery, however, two things should be corrected prior to eventual acceptance: 1) The results in your abstract do not resemble the results in your manuscript as far as VRR is regarded. 2) Please, shortly introduce into the topic with a report on the incidence of AFTN in Ecuador, the number of centers treating such patients in your country and how many surgical procedures are performed annually in Ecuador for this reason.

Reviewer C

This is a single institution small case series of RFA for AFTN from Ecuador. The main takeaway is that there appeared to be some volume reduction in the already not-very-large nodules, and that the procedure is safe. There appeared to be no significant effect on thyroid function, which is likely the primary indication for intervention in the first place. There is already existing literature on the safety of RFA for AFTN, as well as on its less-than-stellar results in normalizing thyroid function compared with surgical

excision.

Reviewer D

Nice case series. Small number of patients and short follow-up interval.

Page 6 line 136 - does this mean you didn't have any complications, or you're just not reporting them.
We did not have complications.

Reviewer E

Question research of this study is interesting, and I suggest accepting this paper after major revision.

This study evaluates the efficacy and safety of thyroid RFA for treating autonomously functioning thyroid nodules.

Sample size is quite not sufficient to have significant results, but data become interesting since it is a fist experience in a Country (Ecuador).
We added it as a limitation

Citations are missing some important papers, specified below.
Language needs to be improved. Consider a medical writing support.

There are some major issues:
- Abstract: data on the trend of TSH are missing. More the thyroid nodule volume, the TSH is the real indicator of success during follow up in thermally ablated AFTN.

- Introduction: expant deeper the problem. Cite what different guidelines tells about thermal ablation for AFTN (DOI: 10.1159/000508484, DOI: 10.1002/hed.26960; doi: 10.1089/thy.2023.0281)
- Introduction: go deeper why propose thermal ablation for AFTN: scars? Economic? (Consider: DOI: 10.1007/s12020-023-03403-w)

Thank you for the comment. We improved the introduction.

- Figure 1 is not useful in understanding the manuscript. Please remove it.
We have improved this figure.

- Line 92: substitute “catheters” with “needles”
Done.
- Line 92: 7 mm “active tip”
Done.
- Line 95: remove index
Done.
- Line 126: “6.59” specify minutes and seconds
Done.
- Line 133-136: The entire paragraph needs to be revised. Please be clear and easier to be read.