Title: Changes of Serum 25(OH) D3 and IGF-1 Levels in Patients with Thyroid Nodules

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Reviewer: Rosa Maria Paragliola

Reviewer's report:

The paper "Changes of Serum 25(OH) D3 and IGF-1 Levels in Patients with Thyroid Nodules" is aimed to evaluate the relationship between 25OH vitamin D levels and IGF1 levels and thyroid nodules. The paper is interesting about the topic, but it presents major criticisms in its form and it should be carefully and extensively revised.

Page 2, line 17: "The incidence of deficiency of vitamin D has gradually increased worldwide, becoming a universal health problem that cannot be ignored". In my opinion this sentence is out of the context of the paper and should be omitted.

Page 2, line 21: The sentence is not clear and should be rephrased. Please add a reference.

Page 2, line 23: The sentence is out of the context. The relationship between vitamin D and IGF1 and cancer is well known. However, the aim of this paper is not focused on thyroid cancer.

Page 2, Line 43: The section is very confused and should be completely rewritten. Why did subjects perform thyroid ultrasound? Screening? Known thyroid disease? Signs or symptoms of thyroid diseases? Is this the first US evaluation? I think that exclusion criteria have been applied for both groups (the so called "nodule group" and control group). However, this should be better specified. Furthermore, it is mandatory to specify that patients (I assume that this is so) do not take therapies that can influence the parameters considered (LT4, cholecalciferol etc.).

Page 3, line 7: Perhaps the section about the US features of the thyroid nodules should be included in a different paragraph and not in "Collection of general data". Furthermore, technical data about US should be added (probe, frequency etc.). Unfortunately, no information about US characteristic of thyroid nodules has been reported. I think that it is important to add data about the size and the US features of thyroid nodules detected. In fact, the Authors stated that they excluded thyroid nodules with malignant US features.

IGF1 levels are different based on age. It should be useful to specify in the text that Authors considered only adult patients and to include the mean age.

Page 3, line 58: Please check the brackets.

Page 3, line 61: Please rephrase the sentence.
Page 10, line 17: What does "thyroid and thyroid nodules" mean?

The discussion section is too long and confused and should be rewritten focusing on the most important topics. In my opinion, the crucial question is the "protective" role of IGF1 which, considering the conflicting data reported in literature, should be better argued.

English language should be carefully revised throughout the text.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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Not suitable for publication unless extensively edited

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