**Author’s response to reviews**

**Title:** Parathyroidectomy improves cardiovascular risk factors in normocalcemic and hypercalcemic primary hyperparathyroidism

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**Author’s response to reviews:**

We express our special thanks to the reviewer for his/her careful reading of the paper, and for providing valuable comments and suggestions which have helped improved both the content and the presentation. We believe that the revision has been successful and the paper has been improved. The responses to reviewer’s comments are available in this document.

Cardiovascular risk factors are increased in normocalcemic primary hyperparathyroidism.
Main comments

Reviewer reports:

Giorgio Borretta (Reviewer 1): This study compares cardiovascular risk factors in HPHPT and NPHPT: no differences are found between these groups, which have an increased cardiovascular risk compared to control. It this to be taken into account that subjects with diabetes and subject using antilipidemic and antihypertensive drugs were excluded from the control group. This choice is not justified by the Authors and can affect the results.

- Controls without using antilipidemic and antihypertensive drugs were included study, but % 16.7 and 15.0 of controls were newly diagnosed as dyslipidemia and hypertension at population-based screening programs during this study. HbA1c levels from controls were measured to diagnose diabetes at population-based screening programs. When we looked at our reports, % 8.7 of controls had prediabetes according to Hb1Ac level. These sentences were included in material-method and result part.

Authors should specify if the serum total calcium concentration was albumin correct.

- Albumin-corrected calcium was shown in our report, but I forgot to write in our study. We added this data in Material-method part.

Moreover, considering that most normocalcemic patients were referred from the osteoporosis outpatients clinic, Authors should specify whether they were treated with bisphosphonates. This treatment can affect PTH levels.

- Bisphosphonates can affect serum calcium levels. In our reports, 54 patients had normocalcemia with elevated PTH level, 19 normocalcemic patients treated with bisphosphonates were excluded from study. So, only 35 normocalcemic subjects without using bisphosphonates were included. In our reports, 42 hypercalcemic patients treated with bisphosphonates were excluded. So, only 60 hypercalcemic patients without using bisphosphonates were included. This data were added material-methods part.
Finally, it would be interesting to know the evolution of cardiovascular risk factors after surgery.

- The data including post-parathyroidectomy was added the study. Parathyroidectomy was decreased cardiovascular risk factors in groups with normocalcemic hyperparathyroidism and hypercalcemic hyperparathyroidism. This data was shown in Table 2.

Jessica Pepe (Reviewer 2): The authors of "Cardiovascular risk factors are increased in normocalcemic primary Hyperparathyroidism" found that normocalcemic and hypercalcemic PHPT patients had a similar increase in cardiovascular risk compared to controls, even independently of serum calcium. The paper may be ameliorated with the following suggestions.

* Is there any difference between female and male PHPT patients?

- In our study, cardiovascular risk score was more increased in male. The other variables did not differ between gender. Cardiovascular risk score is increased when gender is male based on The Framingham Cardiovascular risk score. This score would add extra point if gender is male, so we did not show these results in manuscript.

* Medications used in the sample should be added, in particular, as regards dyslipidemia and diabetes.

- Medications including antilipidemic, antihypertensive and oral antidiabetic/insulin drugs were included in Table 1 and results part.

* How many patients had fractures? Did those with fractures have more severe cardiovascular risk?

- In our study, 6 patients with hypercalcemic (% 10) and 2 patients with normocalcemic (% 5.7) had fractures (p=0.624), this data was included in Table 1. After parathyroidectomy, patients with fractures had more severe cardiovascular risk, compared to patients without fractures. This sentence was added to results part. This data was not shown in Table 3 but not included in manuscript.

Table 3. Data according to having fractures