Peer Review File

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Reviewer A

Comment 1: Consider discussing 0.7% of RYGB being a rare pre-condition in thyroidectomy patients, but being relevant due to significant postoperative hypocalcaemia.

Reply 1: Thank you for your interest in our study. We added this comment as advised.

Changes in the text: See page 8, line 179-183

Comment 2: discuss limitations of the clinical suggestions and possible struggles to develop evidence-based guidelines

Reply 2: We implement discussion on this point, as advised.

Changes in the text: See page 8, line 175 -178

Comment 3: consider the discussion o ICG use to optimize surgeons skills during surgery and avoid accidental resection of parathyroid glands

Reply 3: thank you for your suggestion. We added this point as advised.

Changes in the text: please see page 7, line 156-158

Reviewer B: Many thanks for this interesting manuscript on a clinically relevant topic. As the authors state, and to my own knowledge, this is the largest series of total thyroidectomy in patients with a history of bariatric surgery. Previous papers on this subject (Chereau et al., 2017) and a recent meta-analysis (Spartalis et al., 2019) are mentioned in the references list. It is indeed important to gather data on hypocalcemia in TT patients after bariatric surgery, as it is mainly the supplementation after thyroidectomy that poses a challenge. To date, the extent of hypocalcemia, especially in patients with a history of RYGB, is not well documented. Even though this is the largest study to date, the numbers are quite small, and the analysis and interpretation are hampered by the uncertainty of too many other risk factors (% of Graves, # of parathyroids re-implanted…)

Comment 1:

Major issues

- The authors state in their introduction the known risk factors for postoperative hypocalcemia (Graves, length of surgery, bilateral central neck dissection…). However, in their own analysis, they fail to correct for a number of important and well-known risk factors: % of thyroiditis/Graves, % of central neck dissection, % of re-intervention for bleeding, number of reimplanted parathyroid glands, number of parathyroid glands on the resected specimen…

Reply 1: Thank you for your interesting point. As we discussed in the limitations of our study, we did not dispose of the number of parathyroid glands on the resected specimen nor the number of reimplanted parathyroid glands. For all

malignancies we did perform at least a central neck dissection, in accordance to French guidelines. None of the bariatric patients required re-intervention for cervical hematoma.
Further studies will be needed to point out these differences, and we will be privileged to share with you our findings.
Changes in the text: page 8, 187-189

Comment 2: No other risk factors for postoperative hypocalcemia are reported or assessed (besides malignancy), which may be responsible for the apparent increased risk. Therefore, I would recommend presenting the results per indication group, and you could easily calculate the number of expected hypocalcemia cases based on the % in the N=13,152 without bariatric surgery per indication group. Ideally, you would also include other risk factors (e.g. sex, BMI) in this prediction of % expected cases, but assistance from a biostatistician may be required. The authors have a really nice and large series of cases, probably with a lot of clinical detail (hopefully already extracted from the medical records) – therefore it would really increase the strength of this paper. The other alternative would be a matched cohort, in which you match those 90 with bariatric surgery (35, 29, and 26 patients) to 3-5 individuals from the total cohort, by indication, age, sex, BMI, etc. – and analyze if the risk of hypocalcemia is still different
Reply 2: Thank you for your comment. Unfortunately, we did not have enough patients for a matched cohort, since they need to be adjusted for year of surgery, sex, BMI and surgery indication. Although, it is indeed an interesting point that we would like to develop with further studies.
Changes in the text: none

Comment 3:
Introduction
- Line 39: Graves' disease instead of Grave's disease
- Line 42-45: Please rephrase to 'Considering the increasing prevalence of obesity in the western world and the rising number of different bariatric procedures, documenting risk factors for hypocalcemia after TT in this cohort is important to prevent and/or treat this complication.'
- Line 49 belongs to the methods section. Please rephrase to 'The manuscript is presented in accordance with…'
Reply 3: We modified the text as advised, for each suggestion.
Changes in the text: page 2, line 39, line 42-44.
We added to the methods section the statement "the manuscript in present in accordance with.." line 92.

Comment 4:
Methods
1: Please identify details on the center (university, number of annual procedures, tertiary referral, high-volume…)

2: Line 53-55: Please rephrase to 'Patients with a history of thyroid, parathyroid, or other cervical surgeries were excluded'.
3: Line 69: Is there a local protocol that was used to deal with postoperative hypoparathyroidism? Or is this part of the 'perioperative supplementation protocol', mentioned in Line 78? Did the authors measure PTH 4hrs postoperative to predict calcium issues after surgery, or just 20 minutes after surgery?
4: Line 72: Please remove 'which was'
5: Line 76: Change 'and' to 'and/or'. Not all patients required both Vit D and Calcium to maintain normocalcemic.
6: Line 88: Please remove 'the' before 'surgery'
7: Line 90: Please remove 'a' before 'a previous bariatric procedure'
8: Line 92: Please add 'of', as in 'a history of RYGB'
Reply 4: We modified the text as advised, for each suggestion.
Changes in the text:

1. It is a high-volume surgical department specialized in endocrine surgery of a university hospital – See Page 3, line 50-52
2. See line page 3, line 53
3. We do have a preoperative supplementation protocol which includes the administration of alfa calcidiol 1 μg daily during 5 days preoperatively and calcium carbonate 1 day before surgery, mentioned in line 78. This protocol is the same for all patients undergoing TT in our Department (as reported in page 4 line 78)

   We routinely obtain calcium and vitamin D levels preoperatively in all thyroidectomy patients (values in table 1), and supplement it before surgery, considering the elevated rate of vitamin D deficiency in northern Europe population. The supplementation consists in the oral administration of a single dose of cholecalciferol. As it concerns PTH levels, we measure it only 20 min post TT for predicting postoperative hypocalcemia and its supplementation. Postoperative supplementation (after discharge) is based both on post TT PTH and POD1 calcium levels.

4-8. Please see page 3-4, line 70-90.

Comment 5:
Results
1. Try to be consistent in the reporting:
° For example the authors state a percentage followed by n= in between brackets, and sometimes the other way round (line 102 vs 108).
° For example: sometimes percentages are mentioned with one decimal and sometimes without (line 108 vs 114).
2. Line 105-106: Please add percentages
3.Line 108: Please remove the comma after 'women'
Reply 5B (1-3): we made the correction as advised.
Changes in the text: See page 5, line 101-108
4. Line 111-112: Please rephrase: 'no differences in the percentage of thyroid

surgery for malignancy'
5. Line 113: Please add/correct (range: 1-7 years)
6. Line 114: Add 'immediate' to 'postoperative hypocalcemia'
7. Line 114: Try to avoid using the first-person singular and plural in scientific writing. Rephrase the sentence to 'Patients with a history of…'
8. Line 118: Please rephrase to 'one patient with a history of LAGB and 5 with a history of RYGB'
9. Line 120: Please remove 'any patient from'
10. Line 121: Replace 'definitive' with 'permanent'. Try to stay consistent in your use of terminology. The authors defined 'permanent hypocalcemia' in the methods section, so you should continue using the term permanent.
11. Line 128: Please rephrase to 'bariatric surgery is on the rise worldwide'
Reply 5 (4-11): We modified the text as advised.
Changes in the text: See page 5-6, line 110-127.

Comment 6:
Discussion
- Please restructure to
° 1/ Main findings
° 2/ (Possible) explanation of the main findings
- It is remarkable that half of the patients with temporary hypocalcemia become permanent in the RYGB group. Indeed, it is often difficult to supplement Calcium and Vitamin D via oral administration (due to malabsorption). Several case reports have commented on this. Maybe the authors could add a small paragraph commenting on this as well, or even suggest a more aggressive preoperative substitution protocol.
° 3/ Strengths of this study
° 4/ Study limitations
- Please mention all factors that influence postoperative hypocalcemia that were not adjusted for f.e. thyroid cancer stage, % of Graves'….
° 5/ Usefulness in current practice
° 6/ Future studies – Work to be done
- Please mention the importance of gathering big data to further document or identify prognostic factors in this specific cohort (via BAETS, EUROCRINE…)
Reply 6: Thank you for your comment. We corrected our discussion paragraph with your suggestion.
Changes in the text: please see Page 6-8, line 138-146, 188-200,

Comment 7:
- Line 148: Please change 'longer' to 'prolonged'
- Line 149: Please change 'in order to' to 'to'
- Line 150: Please rephrase to '…suggested that candidates for obesity surgery should be screened for…'
- Line 152-156: Please rephrase to 'Controversy remains whether obesity

increases intra- and postoperative morbidity. A recent prospective analysis did not reveal higher complication rates, despite a longer duration of the procedure (30). This finding conflicts with previous studies advocating that bariatric surgery should be performed first (31,32).'
- Line 159: Please change 'On the basis of' to 'Based on'
- Line 173: Please remove the comma after 'suggestion'
- Line 174: Please change to 'by current scientific literature'
- Line 176: Please remove the first 'and' and put a comma after 'anatomy'
Reply 7: we made the corrections as advised.
Changes in the text: page 7, line 149 – 175

Comment 8: Line 175-178: Even though I agree with this statement, this has nothing to do with your research question and is not supported by your results.
Reply 8: we removed this paragraph, as advised.
Changes: Page 7

Comment 9:
Figures & Tables
Table 2:
- It would be nice to have transient and permanent numbers for the non-bariatric cohort for completeness (as it is an impressive cohort).
Reply 9: thank you for your suggestion. We will consider this point in our further studies.