

Clinical Image

Is the Female Sex a Predictor of the Severity of Post-Thyroidectomy Hypocalcemia?

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Received: June 11, 2020; **Accepted:** October 09, 2020;
Published: October 16, 2020

Abstract

Background: There are more than 200 million goiter patients throughout the world especially in the areas away from the sea; this makes total thyroidectomy one of the most common endocrine operations performed by surgeons. The particular position of the parathyroid glands, their size and delicate blood supply make injury to them and post-thyroidectomy hypocalcemia one of the most common complications of thyroid surgery; functioning parathyroid preservation is considered a key event during this surgery. Studies have identified the possible risk factors and the helpful ways to predict post-thyroidectomy hypocalcemia with the ultimate goal of limiting its incidence.

Methods: From February 2015 to March 2019, a prospective study has included 250 patients presented with non-recurrent simple nodular goiter underwent total thyroidectomies. Classic operative steps were done for all participants with selective ligation of the branches of the inferior thyroid arteries on both sides, meticulous sharp dissection around parathyroid glands, and preservation of at least two glands. Preoperative serum ionic calcium (SiCa), 24 and 48h levels were measured in all patients. Calculations of the mean SiCa levels before and 24h after surgery for female and male groups were compared. Other comparisons were done for the postoperative incidence of hypocalcemia, the mean hospital stay, and the rate of symptomatic hypocalcemia in each sex group.

Results: The total incidence of hypocalcemia was 21.6% (54 cases) with hypocalcemic incidence of about 21.8% among females (45 patients) and 20.5% among males (9 patients). Female patients have more decrease in the mean SiCa value 24 hours after surgery (from 4.7 ± 0.17 mg/dl to 4.3 ± 0.4 mg/dl). The incidence of symptomatic hypocalcemia was higher in the female group (40% versus 22.2%) with more prolonged mean hospital stay (4.45 ± 1.2 days for females and 3.15 ± 0.9 days for males).

Conclusion: Female sex has no effect on the incidence of post-thyroidectomy hypocalcemia however; its effect was clear on the severity of this developed complication and on the postoperative hospital stay.

Keywords: Simple Nodular Goiter; Total Thyroidectomy; Post-Thyroidectomy Hypocalcemia; Female Sex

Introduction

There are more than 200 million goiter patients throughout the world especially in the areas away from the sea [1]; As many of the patients who suffer from benign thyroid diseases besides cases of thyroid cancer which accounts for more than 90% of cancers of the endocrine glands undergo total thyroidectomy [2], this makes such surgery one of the most common endocrine operations performed by surgeons for different indications [3]. The particular position of the parathyroid glands, their size and delicate blood supply make injury to them and post-thyroidectomy hypocalcemia the most common complications of thyroid surgery and their preservation is considered a key event during this surgery [4-5]. Many predictors of post-thyroidectomy hypocalcemia were suggested by the studies including; greater extent of surgery [6], female gender [7], patients below 45 [8] and above 85 years old [9], limited surgeon's skills and experience [10], huge goiters with retrosternal extension, Graves'

disease [11], repeated neck surgery [12], large thyroid gland volume [11], and the intended systematic search for the parathyroid glands intraoperative may theoretically increase the risk of injuring them [13]. The objective of this study was to assess the effect of gender on the incidence and severity of post-thyroidectomy hypocalcemia and the subsequent consequences on the postoperative hospital stay.

Methods

February 2015 to March 2019, 250 patients presented with simple nodular goiters with classic surgical indications for total thyroidectomy were evaluated, consented, operated and enrolled in this prospective study. Huge and recurrent cases together with end stage renal disease patients were excluded. Preoperative SiCa levels were measured for all patients. Classic operative steps were done for all participants with selective ligation of the branches of the inferior thyroid arteries on both sides, meticulous sharp dissection around parathyroid glands, and preservation of at least two glands. All these

operative steps were done by experienced surgeon in the field of head and neck surgery. SiCa levels were measured 24 and 48h after surgery for all patients and daily thereafter for hypocalcemic patients till hospital discharge. Calculations of the mean SiCa levels before and 24h after surgery for female and male groups were compared. Other comparisons were done for the postoperative incidence of hypocalcemia, the mean hospital stay, and the rate of symptomatic hypocalcemia in each sex group.

Post-thyroidectomy hypocalcemia was defined as SiCa level less than the lower limit of our institutional reference range (from 4.5mg/dl to 5.6 mg/dl). All our participants were kept in the hospital for at least two days after surgery; this postoperative hospital stay has been extended for another 1 to 4 days for symptomatic hypocalcemic patients which were in a need for intravenous calcium gluconate replacement therapy and an extended hospital stay; they were discharged after symptoms control on oral calcium and vitamin D supplements. Asymptomatic hypocalcemic patients were discharged after 48 hours on oral calcium and vitamin D supplements.

Data was collected, coded and analyzed using SPSS software version 18 under windows 7. For quantitative parametric data, we have used the In-dependend student t-Test used to compare measures of two independent groups. Paired t-test in comparing two dependent groups. For quantitative non parametric data, we have used Mann-Whitney test in comparing two independent groups (Non-paired variables) and Wilcoxon tests used in comparing two dependent groups (Paired variables). The level $P \leq 0.05$ was considered the cut-off value for significance.

Results

In this study, Patients presented with age range from 22 to 49 years old (Mean 34 ± 8.1 years). Females constituted 82.4 % of the participants (n=206) and males 17.6% (n=44) with a female to male ratio of 4.68: 1. The total incidence of hypocalcemia was 21.6% (54 cases) with hypocalcemic incidence of about 21.8% among females (45 patients) and 20.5% among males (9 patients). Hypocalcemic incidences in both groups showed no statistical difference. Preoperative mean SiCa levels were calculated for both female and male groups (4.7 ± 0.17 mg/dl and 4.7 ± 0.15 mg/dl respectively). We found no statistical difference between both groups regarding the preoperative mean values. The postoperative values showed that female group has more decrease in the mean SiCa value 24 hours after surgery (from 4.7 ± 0.17 mg/dl to 4.3 ± 0.4 mg/dl) that was statistically significant, and male group has less decrease (from 4.7 ± 0.15 mg/dl to 4.5 ± 0.13 mg/dl) that wasn't significant. The incidence of symptomatic hypocalcemia showed a statistically significant higher value in the female group (40% versus 22.2%) with more prolonged mean hospital stay (4.45 ± 1.2 days for females and 3.15 ± 0.9 days for males) (Table 1) (Figure 1,2).

Discussion

Post-thyroidectomy hypocalcemia remains the most common complication after thyroid surgery; however, there is still no consensus in literature about a definition used for determination of this complication and which parameters we can depend on to properly measure it [9]. We have decided to accurately mention our cut-off point for hypocalcemia and the other used parameters to get

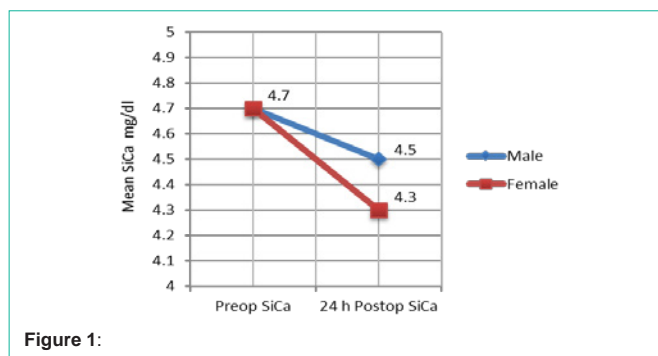


Figure 1:

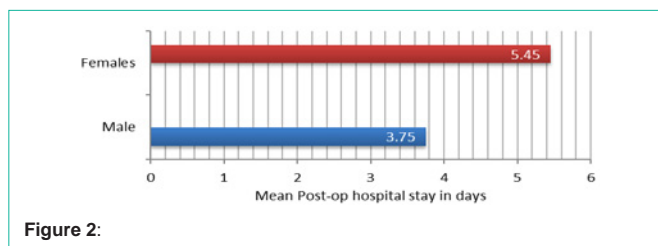


Figure 2:

Table 1: Study statistical results and significance for male and female groups.

	Female	Male	Significance
Number of patients	206	44	
Hypocalcemic cases	45	9	
Incidence of hypocalcemia	21.80%	20.50%	NS difference
Symptomatic hypocalcemia	18 (40%)	2 (22.2%)	Sig. difference
Mean pre-op SiCa	4.7 ± 0.17 mg/dl	4.7 ± 0.15 mg/dl	NS difference
24 hours mean Post-op SiCa	4.3 ± 0.4 mg/dl	4.5 ± 0.13 mg/dl	Sig. difference
Mean Hospital Stay'	5.45 ± 0.7 days	3.75 ± 0.5 days	Sig. difference

Pre-op = preoperative, Post-op= postoperative, NS= Not significant, Sig= Significant, ' for symptomatic hypocalcemic patients.

a precise data and comparable results. Hypocalcemia was considered with serum ionized calcium level less than the lower limit of our institution reference range (4.5-5.6 mg/dl) for total thyroidectomies whether associated with symptoms or not. We have intended to depend only on the biochemical definition for hypocalcemia to exclude the subjective clinical manifestations.

Before the study, we have noticed that female patients undergoing total thyroidectomy have a longer hospital stay than males when symptomatic hypocalcemia complicates the operation. It's well known that hypocalcemia is the most prominent obstacle to the early and safe hospital discharge after thyroid surgery; however the main questions which were in a need for answers are; is this noticed difference really exist? And what is the reason which stands for this?

Our results refer to a total hypocalcemia incidence of about 21.6% (54 cases) for our patients presented with non-recurrent simple nodular goiters performing total thyroidectomies; We surely expect that this incidence will be higher, if our inclusion criteria were expanded to include more difficult cases such as the graves, recurrent, malignant and huge cases with retrosternal extension; on the other hand, our results can be considered a low incidence when compared with the other studies including in their work surgical operations with lower probability of postoperative hypocalcemia development

such as hemi- and subtotal thyroidectomies; this case mix shares in the great variability and the wide range in the incidence of post-thyroidectomy hypocalcemia mentioned in the literature (ranged from 0.3% to 66.2%) [9]. The calculated mean preoperative SiCa values for both female and male patients showed no statistically significant difference; however 24h after surgery, only female patients showed a highly significant decrease in the mean SiCa value that was clearly reflected on the severity of the developed clinical manifestations of hypocalcemia and the mean hospital stay. In the current study, there was no significant difference between the number of female and male patients who have developed post-thyroidectomy hypocalcemia. The mean hospital stay for female patients, who have developed hypocalcemia, has showed longer hospital stay (5.45 ± 0.7 days) than their male peers (3.75 ± 0.5 days) and a higher rate of symptomatic hypocalcemia (40% *versus* 22.2%), so our results agree with the voices that assumed "Hypocalcemia is the most common postoperative complication that prolongs the hospital stay after thyroid surgery" [14-16].

Our results and their statistical analysis demonstrate that female gender cannot be considered a risk factor for the incidence of post-thyroidectomy hypocalcemia but it can be considered a risk factor for the development of more severe hypocalcemia, "females have the same hypocalcemic incidence as for males; it will be more severe and more symptomatic in females". Consistent with our results, some studies showed that gender has no significant effects on the incidence of hypocalcemia [5, 12, 17-19]; however, the association between postoperative hypocalcemia and female sex was assumed by other results [6, 20-23].

The term of post-thyroidectomy hypocalcemia should be studied and considered not only in the form of incidence rate but the issue of severity (level of SiCa drop) should be minded with the subsequent effects on the ways of their management, follow up and hospital stay; therefore, great attention should be directed towards female patients who have developed postoperative hypocalcemia.

Conclusion

Post-thyroidectomy hypocalcemia believed to have a multifactorial background including the experience of the operator, the surgical technique and some risk factors the patients have; all these factors have contributed to incidence of 21.6% in the current study; the good knowledge of the surgical anatomy of the thyroid, parathyroid glands and their embryological origins together with the meticulous surgical technique remain the most valuable points in the prevention of post-thyroidectomy hypocalcemia.

There is almost consensus about the role of the operator experience, skills and the adopted surgical technique in changing the incidence of hypocalcemia but this isn't the same for the risk factors presented with every patient; gender remains one of the controversial issues.

In our study, we can assume that patient's sex has no effect on the incidence of post-thyroidectomy hypocalcemia; however its effect was clear on the hospital stay and the severity of this developed complication. Our results agree with the voices that assumed "Hypocalcemia is the most common postoperative complication that prolongs the hospital stay after thyroid surgery". We suggest that the

term of post-thyroidectomy hypocalcemia should be studied and considered not only in the form of prevalence and incidence rates but the issue of severity should be minded with the subsequent effects on the ways of dealing with the patients and their follow up.

References

Nil