ORIGINAL ARTICLE

How useful are perioperative biochemical parameters in predicting the duration of calcium and / or vitamin D supplementation after total thyroidectomy?

Running title: PTH & calcium predict supplementation duration

Brian Hung-Hin LANG, MS, FRACS

Kai Pun WONG, MBBS, FRCS

Division of Endocrine Surgery, Department of Surgery, University of Hong Kong, Pokfulam, Hong Kong SAR

Address for Correspondence:

Dr Brian HH Lang

Division of Endocrine Surgery, Department of Surgery,

Queen Mary Hospital,

102 Pokfulam Road,

Hong Kong SAR, China

Tel.: (852) 22554773, Fax No.: (852) 28172291

Email: blang@hkucc.hku.hk

ABSTRACT

Background

Oral calcium and calcitriol are often prescribed after total thyroidectomy to avoid biochemical and/or symptomatic hypocalcemia. We aimed to identify independent perioperative factors which correlated with the duration of calcium and / or calcitriol supplementation after total thyroidectomy.

Methods

Of 271 eligible patients, 48 (17.7%) required calcium and / or calcitriol supplements on discharge. Supplementation was gradually weaned off by one surgeon according to a biweekly algorithm based on serum calcium (Ca). Duration of supplementation was calculated from the date of operation to the date of ceasing all supplementation without biochemical hypocalcemia (i.e. serum adjusted-Ca $\geq$ 8.44mg/dL). The Cox regression analysis was performed to identify independent perioperative factors for duration of supplementation. The best cut-off value for these independent factors was determined by the receiver characteristic (ROC) curve.

Results

In the multivariate analysis, PTH at skin closure (PTH-SC) (RR = 1.742, 95%CI=1.080–2.810) and postoperative day 1 adjusted Ca (Ca-D1) (RR=77.526, 95%CI=3.600–1669.57) were the only two independent determinants for shorter duration of ceasing all supplementation. The best cut-off values in predicting supplementation $\geq$ 6 months for PTH-SC and Ca-D1 were 7.08pg/mL (sensitivity=100%, specificity=60.5%, PPV=40.0% and NPV=100%) and 7.88mg/dL (sensitivity=90.0%, specificity=55.3%, PPV=34.6% and NPV=95.5%), respectively.

Conclusions

Both PTH-SC and Ca-D1 were independently associated with the duration of supplementation after total thyroidectomy. Almost all patients with PTH-SC $\geq$ 7.08pg/mL or Ca-D1 $\geq$ 7.88mg/dL did not require supplementation $\geq$ 6 months whereas about 1/3 of patients with PTH-SC < 7.08pg/mL or Ca-D1 < 7.88mg/dL required supplementation $\geq$ 6 months.

INTRODUCTION

Postoperative hypoparathyroidism leading to hypocalcemia is one of the most frequent morbidities following total thyroidectomy with an incidence ranging between 3 – 40%.[1] However, because potentially life-threatening hypocalcemia does not usually develop until 24 to 48 hours after surgery, hypoparathyroidism may delay early hospital discharge.[2-4] In order to safely manage postoperative hypoparathyroidism / hypocalcemia without unnecessarily prolonging hospital stay, two different approaches have often been adopted, namely routine calcium and / or calcitriol supplementation or selective supplementation, based on postoperative intact parathyroid hormone (PTH) values.[2-4] Some have advocated the latter approach because PTH testing taken within a few hours of surgery could accurately predict clinically-relevant hypocalcemia in the immediate postoperative period.[5-10] However, few studies have focused on its predictive value on persistent / long-term hypocalcemia.[11-14] Wang et al. evaluated the predictive value of postoperative day 1 PTH (PTH-D1) on the need for calcitriol supplementation > 1 month and found that none of the 78 patients with PTH-D1 $\geq$ 5 pg/mL required calcium and calcitriol supplementation lasting > 1 month.[14] The implication is that those with normal to near-normal postoperative PTH level would have a shorter duration or greater chance of ceasing all supplementation than those with low to undetectable initial PTH. This information is relevant to clinicians because the process of weaning off supplementation in patients with hypoparathyroidism often entails multiple clinic visits and blood tests.[11-14] Therefore, knowing which perioperative factors could predict the duration of supplementation could potentially reduce the number / frequency of clinic visits and overall costs. However, to our knowledge, few studies have specifically examined the association between perioperative biochemical factors and duration or chance of ceasing calcium and / or calcitriol supplementation after total thyroidectomy.[9-14] We hypothesized the perioperative PTH and adjusted calcium (Ca) (i.e. the severity of immediate postoperative hypoparathyroidism) might be associated with the duration and the chance of weaning off calcium and / or calcitriol supplementation after a total thyroidectomy.

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METHODS AND PATIENTS

The present study protocol was approved by the local institutional review board. From October 2010 to December 2011, 316 consecutive patients underwent a total or completion-total thyroidectomy. All had PTH at skin closure (PTH-SC) and PTH-D1 taken. To minimize other confounders, those with concomitant central selective neck dissection (n=15), active bone disease (evident by preoperative bone alkaline phosphatase > 150IU/L) (n=3), incomplete / missing postoperative PTH values (n=7) or completion total thyroidectomy (n=20) were excluded. Therefore, 271 patients were eligible for analysis.

Postoperative calcium monitoring, supplementation and follow-up protocol

All postoperative patients were monitored for hypocalcemia. Ca was checked within 4 hours after operation, on the following morning (i.e. on postoperative day 1) (Ca-D1) and every 8-10 hours until stabilized. Clinically-significant hypocalcemia was defined by the presence of hypocalcemic symptoms and/or postoperative serum Ca dropped < 7.60mg/dL (normal range: 8.44 – 10.20mg/dL). Those with clinically-significant hypocalcemia were initially given 2500mg oscal tablets (as calcium supplements) and were further given calcitriol 0.50mcg twice daily if >2500mg oscal tablets alone failed to maintain normcalcemia. The person prescribing the oral calcium and / or calcitriol supplementation was unaware of the PTH results. Patients were discharged from hospital and followed up 7-10 days after surgery with serum Ca checked beforehand. Figure 1 shows the algorithm for weaning off calcium and / or calcitriol supplementation after discharge. To avoid individual variability, one surgeon (BHL) was responsible for weaning off supplementation. As a general rule, the calcitriol supplementation was weaned off stepwise before the calcium supplementation. To avoid the problem of weaning off supplementation prematurely, serum Ca was repeated a week later. Patients on calcium and / or calcitriol supplementation were followed-up every 2-3 weeks until all supplementation had been completely weaned off. The same follow-up protocol was applied to all patients irrespective of their postoperative PTH levels. Patients no longer

on supplementation were followed up every 6-12 monthly. All postoperative patients were followed up for 2 years before discharged to their primary care physicians.

The duration of supplementation (in days) was calculated from the date of primary operation to the date when all supplementation had been completely weaned off with biochemical normocalcemia (i.e. Ca $\geq$ 8.44mg/dL) (to convert mg/dL to mmol/L, multiply by 0.25) To ensure that those not requiring calcium and / or calcitriol supplementation had really not taken any supplementation (such as those who might have taken calcium supplementation from other specialties for other indications), a careful manual search of all patients' medication status in the territory-wide Clinical Management System (CMS) was performed. The CMS is a computerized database which captures all medication entries of all patients in our locality.[15]

Surgical technique

Surgical techniques had been previously described.[16] Any devascularized parathyroid glands were immediately minced and auto-implanted to the ipsilateral sternocleidomastoid muscle. All data were prospectively recorded.

Laboratory methods

Ca and phosphate levels were measured in the hospital laboratory by standard methods using the Roche Diagnostics Modular Analytic system (Roche Diagnostics, Indianapolis, IN). PTH level was measured by Access® 2 immunoassay system (Beckman Coulter, Brea, CA), and the inter- and intra-assay CVs were 5.8 and 4.5%, respectively. The normal range for PTH was 11.3 to 53.8pg/mL (to convert pg/mL to pmol/L, multiply by 0.106). Serum 25-hydroxyvitamin D was measured by using the electrochemiluminescence immunoassay (Elecsys Vitamin D Total assay), and the inter- and intra-assay CVs were 6.2 and 4.8%, respectively. The measuring range was 3.00 – 70.0 ng/mL (to convert ng/mL to nmol/L, multiply by 2.496).

Statistics

Cox proportional hazards regression was used to evaluate the association between potential perioperative parameters and duration of supplementation (or chance of weaning off

supplementation) in both univariate and multivariate analyses. Only significant variables in the univariate analysis were entered into the multivariate analysis. To improve clinical utility of independent continuous variables, the receiver operating characteristic (ROC) curve were performed to calculate the best cut-off value for predicting duration of supplementation ≥ 6 months. The reason for choosing 6 months was because it is often considered a cut-off for temporary and permanent hypoparathyroidism. Test sensitivity = true positive / (true positive + false negative); test specificity = true negative / (false positive + true negative); positive predictive value (PPV) = true positive / (true positive + false positive); negative predictive value (NPV) = True negative / (false negative + true negative). All statistical analyses were conducted using SPSS version 18.0 (SPSS, Inc., Chicago, IL, USA). P<0.05 was considered statistically significant.

RESULTS

Table 1 shows the patient baseline characteristics and follow-up data. Two-hundred and seventy-one patients underwent a total thyroidectomy. On discharge, of the 271 patients who underwent total thyroidectomy, 48 (17.7%) required supplementation. Eleven of the 48 patients were started on supplementation because of symptoms and of these, 8 had Ca < 7.60mg/dL. Under our weaning algorithm, no patient had unexpected symptomatic hypocalcemia over the study period. Those on calcium alone had significantly higher PTH-D1 (10.4 vs. 2.8pg/mL, p=0.029), Ca-D0 (8.56 vs. 8.16mg/dL, p=0.003) and Ca-D1 (8.08 vs. 7.68mg/dL, p=0.004) than those on calcium and calcitriol.

Table 2 shows the univariate analysis for duration of stopping calcium and / or calcitriol supplementation. PTH-SC ≥ 7.08pg/mL (p=0.001), PTH-D1 ≥ 9.43pg/mL (p=0.003) and Ca-D1 ≥ 7.88mg/dL (p=0.001) were significant factors for shorter duration of supplementation. When entered as continuous variables, the PTH-SC (RR=1.44, 95%CI: 1.15 – 1.81, p=0.002), PTH-D1 (RR=1.34, 95%CI: 1.10 – 1.62, p=0.003) and Ca-D1 (RR=69.1, 95%CI: 4.54 – 1054.87, p=0.002) were significant factors associated with the duration of supplementation. Table 3 shows the multivariate analysis for duration of stopping calcium and / or calcitriol supplementation. When entered as continuous variables, PTH-SC (RR = 1.742, 95%CI=1.080 – 2.810, p=0.023) and Ca-D1 (RR=77.526, 95%CI=3.600 – 1669.57, p=0.005) were the two independent factors for duration of supplementation. When the 10 patients on supplementation ≥ 6 months were excluded, PTH-SC and Ca-D1 remained significant (RR = 1.245, 95% CI=1.001 – 1.548, p=0.049 and RR=30.886, 95%CI=1.792 – 532.446, p=0.018, respectively).

Using the ROC, the best cut-off values in predicting supplementation ≥ 6 months for PTH-SC and Ca-D1 were 7.08pg/mL (sensitivity=100%, specificity=60.5%, PPV=40.0% and NPV=100%) and 7.88mg/dL (sensitivity=90.0%, specificity=55.3%, PPV=34.6% and NPV=95.5%), respectively.

Table 4a is a summary table between PTH-SC < 7.08pg/mL and ≥ 7.08pg/mL and those requiring supplements < 6 months, ≥ 6 months and no supplements. Those with PTH-SC ≥ 7.08pg/mL, the

median (range) duration of supplementation was 60 (7 – 126) days whereas those with PTH-SC < 7.08pg/mL, the duration was 140 (7 – 598) days. Of the 10 patients on supplementation ≥6 months, 3 patients still required supplementation at last follow-up (511, 556 and 598 days, respectively) while the other 7 patients stopped supplementation after 231, 283, 297, 204, 339, 350 and 423 days, respectively. No patients with PTH-SC ≥ 7.08pg/mL required supplementation ≥ 6 months.

Table 4b is a summary table between Ca-D1 < 7.88mg/dL and ≥ 7.88mg/dL and those requiring supplements < 6 months, ≥ 6 months and no supplements. Those with Ca-D1 ≥ 7.88mg/dL, the median (range) duration of supplementation was 61 (7 – 556) days whereas those with Ca-D1 < 7.88mg/dL, the duration was 122 (8 – 598) days. Only one patient with Ca-D1 ≥ 7.88 mg/dL required supplementation ≥ 6 months.

Table 5 shows using a combination of PTH-SC and Ca-D1 in predicting the need for supplementation for < 6 months and ≥ 6 months. Nine of 17 patients with PTH-SC < 7.08pg/mL and Ca-D1 < 7.88mg/dL required supplementation ≥ 6 months. By combining both PTH-SC and Ca-D1, the PPV increased to 9/17 (52.9%) while the sensitivity was 14/14 (100%). No patient with a combined PTH-SC ≥ 7.08pg/mL and Ca-D1 ≥ 7.88mg/dL required supplementation ≥ 6 months. The median duration for this subgroup was 36 (7 – 126) days. By using the formula [0.554* (1.740 * PTH-SC)] + [4.350 * (77.523 * Ca-D1)] derived from the Cox Regression model in the multivariate analysis, the AUC for combined PTH-SC and Ca-D1 was slightly higher than the AUC for PTH-SC and Ca-D1 alone (0.955 vs. 0.943 and 0.950, respectively).

DISCUSSION

The proportion of patients requiring calcium and / or calcitriol supplementation to prevent biochemical and / or symptomatic hypocalcemia after total thyroidectomy tends to vary and is dependent on a multitude of factors including preoperative thyroid function, vitamin D level, surgical indications, extent of surgery, underlying metabolic bone disease and individual surgeon's threshold for supplementation.[1,5,17] However, even when selective supplementation (as opposed to routine) is adopted, up to 40% of patients might require some form of supplementation on hospital discharge.[1] Our study aimed to examine what perioperative factors or indicators were associated with the duration of ceasing all supplementation. By knowing these factors, perhaps, the process of weaning off supplementation could become more precise.[8,11-14,17-18] Although previous studies have examined on this issue,[11-14] they did not specifically evaluate the extent of perioperative biochemical factors in predicting the duration of supplementation. Furthermore, it was unclear if their patients were being weaned off the supplementation with a standardized and intensive follow-up protocol.

In our study, 15 patients with concomitant central neck dissection and 3 patients with active bone disease were excluded from analysis because they often require prolonged period of supplementation irrespective of their residual parathyroid function.[11] In the univariate analysis, PTH-SC, PTH-D1 and Ca-D1 were significant factors for shorter duration of supplementation. Based our results, relative to PTH-SC< 7.08pg/mL, those with PTH ≥ 7.08pg/mL had 3.59 times shorter duration of needing supplementation. Similarly, those with PTH-D1 ≥ 9.43pg/mL and Ca-D1 ≥ 7.88mg/dL had 2.84 and 3.20 times shorter duration of supplementation, respectively. However, since PTH and Ca were closely inter-related, a multivariate analysis was performed. In the multivariate analysis, both PTH-SC and Ca-D1 turned out as independent predictors for duration of supplementation and remained significant even when the 10 patients on supplementation ≥ 6 months (i.e. those with possible permanent hypoparathyroidism) were excluded. Relative to PTH-SC < 7.08pg/mL, PTH-SC ≥ 7.08pg/mL had 2.87 times shorter duration

of supplementation while relative to Ca-D1 < 7.88mg/dL, Ca-D1 ≥ 7.88mg/dL had 2.69 times

shorter duration of supplementation. These findings concurred to our latter findings that the median

duration of supplementation for PTH < 7.08pg/mL and ≥ 7.08pg/mL were 140 days and 62 days,

respectively. Similarly, the median duration for Ca-D1 < 7.88mg/dL and ≥ 7.88mg/dL were 122

days and 61 days, respectively. In fact, no patients with PTH ≥ 7.08pg/mL and only 1 patient with

Ca-D1 ≥ 7.88mg/dL required supplementation ≥ 6 months. These findings reconfirmed our initial

hypothesis that both the severity of immediate hypoparathyroidism (as reflected by PTH-SC) and

hypocalcemia (by Ca-D1) could predict the duration of needing supplementation. However, these

findings were not surprising because those with low or near-normal PTH or Ca would be expected

to have their earlier recovery of parathyroid function and shorter duration of supplementation than

those with very low or undetectable initial PTH or Ca. After all, most temporary

hypoparathyroidism is probably a result of transient interruption of parathyroid blood supply and so

those with less compromised blood supply would be expected to recover sooner. This finding

concurred to those by other authors.[12,13] In the second part of the analysis, we evaluated how

sensitive and specific these two factors were in predicting supplementation < 6 months (temporary

hypoparathyroidism) and ≥ 6 months (permanent hypoparathyroidism). We found that both PTH-

SC and Ca-D1 were very sensitive, even though not very specific in predicting supplementation < 6

and ≥ 6 months. None of the 24 patients with PTH-SC ≥ 7.08pg/mL required supplementation ≥ 6

months regardless of the level of Ca-D1 and only 1 of the 23 patients with Ca-D1 ≥ 7.88mg/dL

required supplementation ≥ 6 months. However, it should be noted that the PPV was actually

relatively low (30-40%) (i.e. those with PTH-SC < 7.08pg/mL or Ca-D1 < 7.88mg/dL did not

always require calcium and / or calcitriol supplementation ≥ 6 months). In fact, only 10 of 25

patients with PTH-SC < 7.08pg/mL required supplementation ≥ 6 months and 9 of 26 patients with

Ca-D1 < 7.88mg/dL required supplementation ≥ 6 months. The implication of these findings was

that the majority (or at least two thirds) of patients would have normalization of parathyroid

function to the extent of not needing supplementation in the short- to medium term. These findings

concurred to a study which found no patients with PTH-D1 $\geq$ 5 pg/mL required calcium and calcitriol supplementation lasting > 1 month. [14] Interestingly, relative to using PTH-SC or Ca-D1 alone, combining both PTH-SC and Ca-D1 increased the PPV from 34.6% - 40.0% to 52.9% and the AUC from 0.943 – 0.950 to 0.955. Although this finding might be seen as an improvement, the incremental clinical significance of this remains uncertain. Perhaps, other factors such as parathyroid autotransplantation or presence of ectopic parathyroid glands or rests could potentially reduce the chance of long-term supplementation, although the former factor did not turn out significant in the univariate analysis and so it was not evaluated.[19]

Clinical implications

Instead of having an intensive biweekly follow-up protocol for all patients taking supplementation on discharge (i.e. the blanket approach), our results could be extrapolated for stratifying those requiring supplementation on discharge according to PTH-SC and Ca-D1. Since those with PTH > 7.08pg/mL and / or Ca-D1 > 7.88mg/dL would have a significantly greater chance (>90%) of being weaned off all supplementation < 6 months, a more intensive protocol would appear appropriate in order to minimize the duration of supplementation. In contrast, since those with PTH < 7.08pg/mL and / or Ca-D1 < 7.88mg/dL would have a significantly lesser chance (50-66%) of being successfully weaned off supplementation < 6 months, a less intensive follow-up (perhaps, a 1-2 monthly protocol) would be more appropriate and less troublesome for the patient.

Despite our findings, we would acknowledge the shortcoming that when the duration of supplementation was calculated, for simplicity, we did not make a clear distinction between those who were weaned off from calcium only and those who were weaned off from calcium and calcitriol. It is known that those taking both calcium and calcitriol have more severe hypoparathyroidism than those taking calcium alone and would have taken longer to wean off supplementation.[12,13] The other shortcoming was the fact that some might think that our algorithm of weaning off supplementation was too slow and that might have caused some patients actually taking supplements more than and / or for longer than it was necessary. For example, some might

view that patients with adjusted Ca between 8.44 to 8.80mg/dL probably could be weaned off supplementation rather than waiting until the adjusted Ca > 8.80mg/dL. Nevertheless, it was our policy that we would rather slightly "overtreat" biochemical hypocalcemia with supplementation than to cause transient symptomatic or biochemical hypocalcemia. We are worried that under-replacement my lead to deterioration in bone mineral density in the long term, although it remains unclear what the long-term consequences are. Also it would have been helpful if our data could be further supported by the follow-up or latest postoperative PTH levels and used these to further correlate with duration of supplementation.

CONCLUSION

Our data showed that both PTH-SC and Ca-D1 were independent factors for the duration of supplementation or chance of weaning off supplementation. Relative to patients with PTH-SC < 7.08pg/mL or Ca-D1 < 7.88mg/dL, those with PTH-SC ≥ 7.08pg/mL or Ca-D1 ≥ 7.88mg/dL had at least 2 times shorter duration of supplementation. Almost all patients with PTH-SC ≥ 7.08pg/mL or Ca-D1 ≥ 7.88mg/dL did not require supplementation ≥ 6 months whereas about 1/3 of patients with PTH-SC < 7.08pg/mL or Ca-D1 < 7.88mg/dL required supplementation ≥ 6 months.

Table 1. Patient baseline characteristics, calcium and calcitriol supplements on discharge and at last follow-up

Characteristics	Median / no. of patients	Range or %
Age at operation (years)	51	16 - 87
Female sex	238	87.8
Surgical indication / final pathology		
- Graves' disease / toxic MNG	28	10.3
- Benign pathology	205	75.6
- Malignancy	38	14.0
No. of parathyroid glands identified		
- None or 1	24	8.9
- 2	51	18.8
- 3	35	12.9
- 4	161	59.4
Parathyroid glands auto-transplantation	65	24.0
Preoperative adjusted calcium (mg/dL)	9.16	8.48 – 10.20
Preoperative 25-OHD level (ng/mL)	12.6	3.0 – 31.4
PTH at skin closure (PTH-SC) (pg/mL)	30.19	1.9 – 158.49
PTH on postoperative day 1 (PTH-D1) (pg/mL)	24.53	0.9 – 169.81
Calcium on postoperative day 1 (Ca-D1) (mg/dL)	2.18	1.78 – 2.49
Supplementation on discharge	48	17.7
- Calcium only	20	7.4
- Calcium and calcitriol	28	10.3
Duration of supplementation (days)		
- Calcium on discharge only (n=20)	31	7 – 350
- Calcium and calcitriol on discharge (n=28)	119	10 – 598
Duration of temporary supplementation* (days)		
- Calcium on discharge only (n=20)	23.5	7 – 177
- Calcium and calcitriol on discharge (n=18)	94.5	10 – 180
Duration of follow-up since operation (months)	12.7	6.2 – 20.1
On supplementation for ≥ 6 months	10	3.4
- Calcium only	5	1.7
- Calcium and calcitriol	5	1.7

Abbreviations: MNG = Multinodular goiter; 25-OHD = 25-hydroxyvitamin D; PTH = intact parathyroid hormone.

* after excluding the ten patients who took supplementation for ≥ 6 months

Table 2. An univariate analysis on shorter duration of stopping calcium and / or calcitriol supplementation

	Relative risk (95% confident interval)	p-value
Age at operation (years)	1.00 (0.98 – 1.03)	0.947
Sex		0.498
- Male	1	
- Female	1.51 (0.46 – 4.90)	
No. of parathyroid glands identified		0.356
- ≤ 2	1	
- > 3	1.18 (0.83 – 1.67)	
Parathyroid autotransplantation		0.543
- No	1	
- One gland	0.80 (0.40 – 1.60)	
- Two glands	1.60 (0.46 – 5.51)	
Preoperative adjusted Ca (mg/dL)	53.73 (0.53 – 5466.37)	0.091
Preoperative 25-hydroxyvitamin D (ng/mL)	0.96 (0.86 – 1.09)	0.547
PTH-SC (pg/mL)#		**0.001**
- < 7.08	1	
- ≥ 7.08	3.59 (1.71 – 7.53)	
PTH-D1 (pg/mL)#		**0.003**
- < 9.43	1	
- ≥ 9.43	2.84 (1.44 – 5.59)	
Ca-D0 (mg/dL)#		0.288
- < 8.00	1	
- ≥ 8.00	1.67 (0.65 – 4.30)	
Ca-D1 (mg/dL)#		**0.001**
- <7.88	1	
- ≥7.88	3.20 (1.61 – 6.36)	

the best-cut off value was determined by using the receiver operating characteristic (ROC) curve

Table 3. A multivariate analysis on shorter duration of stopping calcium and / or calcitriol supplementation after surgery

Covariates	ß-coefficient	Relative risk (95% confidence interval)	*p*-value
PTH-SC (pg/mL)#			**0.012**
- < 7.08		1	
- ≥ 7.08	1.053	2.87 (1.27 – 6.49)	
PTH-D1 (pg/mL)#			0.123
- < 9.43		1	
- ≥ 9.43	0.178	1.20 (0.95 – 1.50)	
Ca-D1 (mg/dL)#			**0.012**
- <7.88		1	
- ≥7.88	0.990	2.69 (1.24 – 5.83)	

When the 10 patients on supplementation for > 6 months were excluded, both PTH-SC and Ca-D1 remained significant (RR = 1.245, 95% CI=1.001 – 1.548, *p*=0.049 and RR=30.886, 95%CI=1.792 – 532.446, *p*=0.018, respectively)

the best-cut off value was determined by the receiver operating characteristic (ROC) curve
Abbreviations: PTH-SC = parathyroid hormone at skin closure; PTH-D1 = parathyroid hormone on day 1; Ca-D0 = calcium on day 0; Ca-D1 = calcium on day 1

Table 4a. A summary table between PTH at time of skin closure (PTH-SC) < 7.08pg/mL and ≥ 7.08pg/mL and between those on supplements < 6 months, ≥ 6 months and no supplements

	Supplementation for > 6 months (n=10)	Supplementation for ≤ 6 months (n=38)	No supplementation (n=223)
PTH-SC < 7.08pg/mL (n=25)	10 (TP)	15 (FP)	4
PTH-SC ≥ 7.08pg/mL (n=23)	0 (FN)	23 (TN)	219

Table 4b. A summary table between postoperative day 1 adjusted calcium (Ca-D1) < 7.88mg/dL and ≥ 7.88mg/dL and between those on supplements < 6 months, ≥ 6 months and no supplements

	Supplementation for > 6 months (n=10)	Supplementation for ≤ 6 months (n=38)	No supplementation (n=241)
Ca-D1 < 7.88 mg/dL (n=26)	9 (TP)	17 (FP)	2
Ca-D1 ≥ 7.88 mg/mL (n=22)	1 (FN)	21 (TN)	221

Abbreviations: TP = true positive; FN = false negative; FP = false positive; TN = true negative

Table 5. A summary table between combining PTH at skin closure (PTH-SC) and postoperative day-1 adjusted calcium (Ca-D1) and those on supplements < 6 months and ≥ 6 months

	Supplementation for > 6 months (n=10)	Supplementation for ≤ 6 months (n=38)
PTH-SC < 7.08pg/mL and Ca-D1 < 7.88 mg/dL (n=17)	9	8
PTH-SC ≥ 7.08pg/mL and Ca-D1 < 7.88 mg/dL (n=9)	0	9
PTH-SC < 7.08pg/mL and Ca-D1 ≥ 7.88 mg/dL (n=8)	1	7
PTH-SC ≥ 7.08pg/mL and Ca-D1 ≥ 7.88 mg/dL (n=14)	0	14

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AUTHORS CONTRIBUTIONS

BHH Lang was involved in the review of literature, acquisition of data and drafting and completing the manuscript. KP Wong was also involved in the review of literature and drafting the manuscript. BHH Lang conceived the study, participated in the co-ordination and the acquisition of data and helped to draft the manuscript. All authors read and approved the final manuscript.

DISCLOSURE STATEMENT

Both authors had nothing to disclose. No competing financial interests exist.

LEGENDS

Figure 1 shows the algorithm for weaning off calcium and / or calcitriol supplementation after hospital discharge
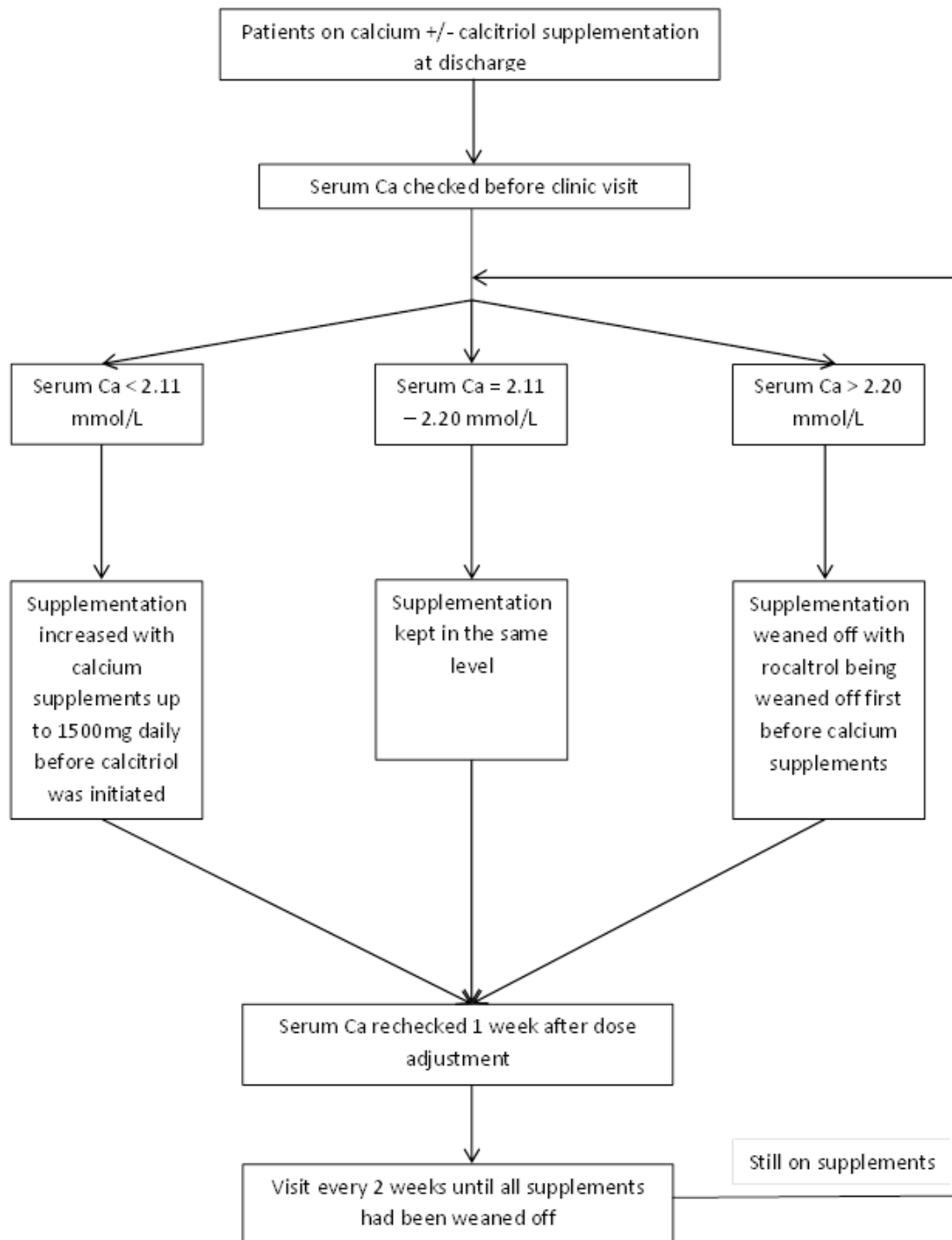
*Normal serum calcium (Ca) = 2.11 − 2.55 mmol/L