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Prediction of Permanent Hypoparathyroidism after Total Thyroidectomy

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Abstract

Background Hypoparathyroidism is a common complication with thyroid surgery. The ability to predict a high risk of permanent hypoparathyroidism is important for individual prognosis and follow-up.

Methods Permanent hypoparathyroidism, defined as continuing need for vitamin D medication at 1-year post-operatively, was investigated in patients after total thyroidectomy. Blood levels of calcium and parathyroid hormone (PTH) were measured intra-operatively, the day after surgery and at 1 month post-operatively. Logistic regression analysis was performed to investigate the risk of vitamin D treatment at last follow-up, calculated as odds ratios (ORs) with 95 % confidence intervals (CIs). Patients were followed until cessation of vitamin D and/or calcium medication, until death, loss to follow-up, or end of follow-up, whichever came first.

Results A total of 519 patients were included. The median (range) follow-up in patients unable to cease vitamin D was 2.7 (1.2–10.3) years. The rate of permanent hypoparathyroidism was 10/519, 1.9 %. Parathyroid auto-transplantation was performed in 90/519 (17.3 %) patients. None of these developed permanent hypoparathyroidism, nor did any patient with normal PTH day 1 (>1.6 pmol/l or 15 pg/ml). The adjusted risk (OR, 95 % CI) for permanent hypoparathyroidism for log PTH on day 1 was 0.25 (0.13–0.50). In patients not auto-transplanted and with unmeasurable PTH day 1 (<0.7 pmol/l or 6.6 pg/ml), 8/42 (19.2 %) developed permanent hypoparathyroidism.

Conclusions Auto-transplantation protects against permanent hypoparathyroidism, whereas low PTH day 1 is associated with high risk.

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Introduction

Permanent hypoparathyroidism is an important complication after total thyroidectomy. Associated morbidity includes hypocalcemic symptoms such as tingling and numbness, but also calcification of basal ganglia and renal impairment [1, 2]. Costs to society in terms of sick leave, medical treatment, and surveillance, including frequent and repeated laboratory testing and treatment, are considerable [3]. Permanent hypoparathyroidism is usually caused by injury to the parathyroid glands at operation, either by inadvertent removal, direct damage, or through disturbance of their blood supply. Auto-transplantation of at least one parathyroid gland, with or without histological confirmation, has been found by some [4], but not all [3], to protect against long-term hypoparathyroidism.

Total thyroidectomy is one of the most commonly performed endocrine operations, and most patients recover fully without any adverse events [5]. It would be beneficial to be able to predict the risk of permanent hypoparathyroidism at an early stage after surgery, in order to avoid risks of hypo- and hypercalcemia and counsel the individual patient on prognosis. It has been suggested that aggressive vitamin D and calcium substitution is associated with improved recovery of parathyroid function [3] and that hypoparathyroidism might be treated successfully with

recombinant parathyroid hormone (PTH) [6]. This would further make it important to identify patients at risk.

Previous studies have indicated that lymph node dissection in addition to total thyroidectomy [7], inadvertent removal of parathyroids [8], surgeon's volume [5, 9, 10], post-operative calcium levels [11], and post-operative levels of PTH [12, 13] are helpful predictors of the risk of post-operative hypoparathyroidism. The aim of the present study was to investigate the risk of permanent hypoparathyroidism, defined as the need for continuing medication with oral calcium or vitamin D supplementation at 1 year after total thyroidectomy. It was hypothesized that low calcium or PTH levels immediately after surgery might predict the risk for permanent hypoparathyroidism, and that these variables could be used to construct a risk score.

Methods

Patients

Data on patients treated with total thyroidectomy at Lund University Hospital were entered into a database, held in accordance with legislation contained in the Personal Data Act and approved by the Swedish Data Inspection Board. Indications for surgery, pre- and post-operative levels of calcium and PTH, as well as medication with calcium or vitamin D supplements were routinely recorded during the hospital visit, at discharge, and at 1- and 6-month follow-up or later if necessary. Calcium and vitamin D was supplemented on demand, and ceased as soon as possible. From the database, we extracted data on patients operated between 1991 and 2011.

Biochemical variables

Serum total calcium (reference range 2.15–2.50 mmol/l or 8.6–10.0 mg/dl) was measured with routine methods on a Hitachi 917, with a coefficient of variation (CV) of 2.0 % at 2.40 mmol/l or 9.6 mg/dl. Levels of plasma PTH were analyzed by an assay for intact PTH (Hitachi Modular -E) (reference range 1.6–6.9 pmol/l or 15–65 pg/ml). The analysis has a total CV of 5.9 % at 7 pmol/l or 66 pg/ml and 5.9 % at 100 pmol/l or 938 pg/ml.

Surgical technique

Total thyroidectomy was performed in a standardized manner, by specialized endocrine surgeons or surgeons in training under supervision. The number of parathyroid glands that were visualized was recorded. Accidentally removed or devascularized parathyroid glands were cut into small pieces of approximately 1 mm^3 in volume and auto-transplanted into the sternocleidomastoid muscle, at the discretion of the surgeon; whether auto-transplantation was performed or not was also recorded.

Follow-up

Plasma levels of PTH and total calcium were routinely analysed at the end of surgery and at 6:00 AM on the following morning, respectively. PTH and calcium were measured on the first post-operative day, and 1 month after surgery. Any medication with oral or intravenous calcium or with vitamin D supplements in hospital, at discharge, and at 1- and 6-month follow-up was recorded. Patients unable to cease either calcium or vitamin D at 6 months were followed for at least a further 6 months, with PTH and calcium testing if necessary. Based on our clinical experience, we chose a pragmatic definition of permanent hypoparathyroidism, as the need for vitamin D and/or calcium treatment due to hypocalcemia at 1 year post-operatively, regardless of the PTH values. We meticulously searched the patients' records to exclude individuals who were taking vitamin D and/or calcium for other reasons. The long-term follow-up was part of the ongoing quality control of the department of surgery, and in accordance with national legislation. Hence, ethical approval was not deemed necessary.

Statistical analysis

Data analysis was performed with STATA v 12.0 (StataCorp LP, TX, USA). Values are expressed as numbers (%) and medians (interquartile range [IQR]) unless stated otherwise. Indication for surgery was classified into three groups: thyrotoxicosis, non-toxic benign goiter, and malignancy. A greater proportion of patients had missing levels of PTH immediately after surgery than on day 1. There was good correlation between these levels and thus, if PTH levels at day 1 were missing, they were replaced by PTH levels immediately after surgery. Medians (IQR) of PTH and calcium were calculated in groups defined by medication with calcium and/or vitamin D at different times of follow-up.

Binary logistic regression analysis, yielding odds ratios (ORs) with 95 % confidence intervals (CIs), was performed using oral calcium or vitamin D analog medication at last follow-up as outcome, with PTH and calcium levels the first day after surgery as independent (predictor) variables. PTH levels were log-transformed due to skewness, and calcium levels in mmol/l were multiplied with 100 before being entered into the multiple logistic regression. The regression analysis also included age as a continuous variable; gender; pre-operative PTH and calcium levels, which were transformed in the same way as post-operative values; the number of parathyroid glands identified, divided into three

Table 1 Pre- and peri-operative characteristics

Characteristic	
Age (y)	46 (32–61)
Gender	
Female	405 (78.0)
Male	114 (22.0)
Pre-operative diagnosis	
Cancer	100 (19.3)
Non-toxic benign goiter	179 (34.5)
Thyrotoxicosis	240 (46.2)
Pre-operative laboratory values	
Total calcium (mmol/l)	2.33 (2.26–2.40)
Total calcium (mg/dl)	9.3 (9.0–9.6)
PTH (pmol/l)	4.0 (3.0–5.2)
PTH (pg/ml)	38 (29–50)
Number of identified parathyroid glands	
0	3 (0.6)
1	17 (3.3)
2	128 (24.7)
3	196 (37.8)
4	174 (33.5)
5	1 (0.2)
Parathyroid auto-transplantation	
Yes	90 (17.3)
No	429 (82.8)

Data are presented as *n* (%) or median (IQR)

IQR interquartile range, *PTH* parathyroid hormone

categories (0–1, 2, 3–5); whether or not parathyroid auto-transplantation was performed; and whether the operation was performed due to thyrotoxicosis, benign goiter, or malignancy. Finally, the rate of permanent hypoparathyroidism was compared in categories of PTH and calcium: for PTH < 0.7 pmol/l or 6.6 pg/ml, 0.7–1.6 pmol/l or 6.6–15 pg/ml, and >1.6 pmol/l or 15 pg/ml; for calcium: <2.00 mmol/l or 8.0 mg/dl, 2.00–2.15 mmol/l or 8.0–8.6 mg/dl, and >2.15 mmol/l or 8.6 mg/dl, using two-sided Chi^2 and Fisher's exact test, where appropriate. A p value of <0.05 was considered significant.

Results

Altogether, 519 patients were included: 114 (22 %) men and 405 (78 %) women, with a median (IQR) age of 46 (32–61) years. Some 179 patients (34.5 %) were operated due to non-toxic benign goiter, 100 (19.3 %) due to malignancy, and 240 (46.2 %) due to thyrotoxicosis. Three or more parathyroid glands were identified in 371/519 (71.3 %) of the patients, and parathyroid auto-transplantation was performed in 90/519 (17.3 %), Table 1.

Overall, the rate of permanent hypoparathyroidism, defined as inability to cease vitamin D and/or calcium at 1 year or earlier, was 10/519 (1.9 %) and 12/519 (2.3 %), respectively. The median (range) follow-up in these patients was 2.7 (1.2–10.3) years. There was a gradual decrease in the proportion of patients needing calcium and/or vitamin D medication at increasing times after surgery. Thus, 99/519 patients (19.1 %) had vitamin D at discharge, 42/519 (8.1 %) at 1 month, 8/519 (1.5 %) at 6 months, and 10/519 (1.9 %) at 1 year (Table 2 and Fig. 1).

A total of 66 (12.7 %) patients with missing information on PTH level the day after surgery had their PTH levels on post-operative day 1 replaced by the PTH value immediately after surgery. After this transformation, there was information on PTH post-operative day 1 in 506 patients (97.5 %).

In the multivariable analysis, PTH and calcium at post-operative day 1 after surgery were significantly associated with risk of long-term hypoparathyroidism. The adjusted risk (OR, 95 % CI) for oral vitamin D at 1 year post-operatively for log-PTH day 1 was 0.25 (0.13–0.50). No patients with auto-transplantation developed permanent hypoparathyroidism. Age, gender, indication for surgery, pre-operative PTH and calcium, and number of parathyroid glands identified were not associated with permanent hypoparathyroidism in the present study (Tables 3 and 4).

After dividing PTH and calcium measured on post-operative day 1 into categories, the rate of permanent hypoparathyroidism was 5/30 (16.7 %) in patients not auto-transplanted and with PTH < 0.7 pmol/l or 6.6 pg/ml and calcium < 2.00 mmol or 8 mg/dl. There was no permanent hypoparathyroidism in patients with PTH > 1.6 pmol/l or 15 pg/ml. Patients not auto-transplanted, with a normal calcium level, e.g. >2.15 mmol/l or 8.6 mg/dl, but with a PTH level < 0.7 pmol/l or 6.6 pg/ml had a high frequency of permanent hypoparathyroidism; two of five patients in this group developed permanent hypoparathyroidism. When not considering the calcium level post-operatively, the rate of permanent hypoparathyroidism in patients not auto-transplanted and with PTH < 0.7 pmol/l or 6.6 pg/ml was 8/42, 19.1 % (Table 5). Of ten patients with permanent hypoparathyroidism, eight had PTH levels <0.7 pmol/l or 6.6 pg/ml on day 1, and two had PTH levels between 0.7 and 1.6 pmol/l or 6.6 and 15 pg/ml (Table 5).

Discussion

The overall complication rate after total thyroidectomy is low [14, 15], and, with increasing experience, total

Table 2 Distribution of parathyroid hormone and calcium levels, and management of parathyroid glands during surgery, among patients with calcium and/or vitamin D substitution post-operatively

Factor	All	Gender (male)	Pre-op PTH (pmol/l, pg/ml)	Pre-op calcium (mmol/l, mg/dl)	No. glands id (mean, SD)	Auto-transplantation	PTH day 1 (pmol/l, pg/ml)	Calcium day 1 (mmol/l, mg/dl)	PTH 1 month[a] (pmol/l, pg/ml)
All	519 (100)	114 (22.0)	4.0 (3.0–5.2)	2.33 (2.26–2.40)	3.0 (0.9)	90 (17.3)	2.5 (1.4–4.7)	2.05 (1.95–2.14)	3.7 (2.7–4.9)
			38 (29–50)	9.3 (9.0–9.6)			24 (13–45)	8.2 (7.8–8.6)	35 (26–47)
Intravenous Ca	13 (2.5)	3 (23.1)	3.7 (3.4–6.0)	2.37 (2.26–2.42)	3.0 (0.6)	7 (53.9)	0.7 (0.7–1.7)	1.88 (1.76–1.99)	2.3 (1.5–6.0)
			35 (32–57)	9.5 (9.0–9.7)			6.6 (6.6–16)	7.5 (7.0–8.0)	22 (14–57)
Ca discharge	170 (32.8)	32 (18.8)	3.8 (2.9–5.0)	2.31 (2.25–2.38)	3.1 (0.9)	46 (27.1)	1.0 (0.7–1.9)	1.94 (1.85–2.01)	2.8 (2.2–4.0)
			36 (28–48)	9.2 (9.0–9.5)			9.5 (6.6–18)	7.8 (7.4–8.0)	27 (21–38)
D discharge	99 (19.1)	18 (18.2)	3.9 (2.9–5.2)	2.31 (2.25–2.38)	3.0 (0.8)	29 (29.3)	0.8 (0.7–1.2)	1.91 (1.82–1.98)	2.5 (1.7–3.2)
			37 (28–50)	9.2 (9.0–9.5)			7.6 (6.6–11)	7.6 (7.3–7.9)	24 (16–30)
Ca 1 month	75 (14.5)	15 (20.0)	3.8 (2.9–4.9)	2.31 (2.25–2.41)	3.1 (0.8)	21 (28.0)	0.7 (0.7–1.1)	1.88 (1.78–1.98)	2.6 (1.7–3.7)
			36 (28–47)	9.2 (9.0–9.6)			6.6 (6.6–10)	7.5 (7.1–7.9)	25 (16–35)
D 1 month	42 (8.1)	7 (16.7)	3.6 (2.8–4.8)	2.29 (2.25–2.39)	3.0 (0.9)	13 (31.0)	0.8 (0.7–1.1)	1.90 (1.79–2.04)	2.2 (1.0–3.0)
			34 (27–46)	9.2 (9.0–9.6)			7.6 (6.6–10)	7.6 (7.2–8.2)	21 (9.5–29)
Ca 6 months	15 (2.9)	1 (6.7)	3.4 (2.7–4.3)	2.27 (2.23–2.31)	2.6 (0.9)	2 (13.3)	0.7 (0.1–0.7)	1.81 (1.70–1.97)	1.2 (0.8–2.4)
			32 (26–41)	9.1 (8.9–9.2)			6.6 (1.0–6.6)	7.2 (6.8–7.9)	11 (7.6–23)
D 6 months	8 (1.5)	1 (12.5)	3.4 (2.8–5.2)	2.29 (2.27–2.41)	2.6 (0.7)	1 (12.5)	0.7 (0.2–0.8)	1.80 (1.70–1.94)	0.8 (0.7–2.4)
			32 (27–50)	9.2 (9.1–9.6)			6.6 (1.9–7.6)	7.2 (6.8–7.8)	7.6 (6.6–23)
Ca FUP	12 (2.3)	2 (16.7)	3.6 (2.7–5.4)	2.28 (2.24–2.38)	2.5 (0.9)	0 (0)	0.4 (0.1–0.7)	1.78 (1.69–2.09)	1.3 (0.8–2.3)
			34 (26–51)	9.1 (9.0–9.5)			3.8 (1.9–6.6)	7.1 (6.8–8.4)	12 (7.6–22)
D FUP	10 (1.9)	2 (20.0)	3.6 (2.5–5.5)	2.28 (2.23–2.35)	2.7 (0.8)	0 (0)	0.7 (0.1–0.7)	1.78 (1.67–2.12)	1.3 (0.8–2.5)
			34 (24–52)	9.1 (8.9–9.4)			6.6 (1.0–6.6)	7.1 (6.7–8.5)	12 (7.6–24)

Data are presented as *n* (%) or median (IQR) unless otherwise indicated

Intravenous Ca treatment with intravenous calcium during hospital stay, *Ca* administration of oral calcium, *D* administration of oral vitamin D analog. *FUP* at last follow-up (>1 year), *IQR* interquartile range, *SD* standard deviation

[a] 14.5 % missing

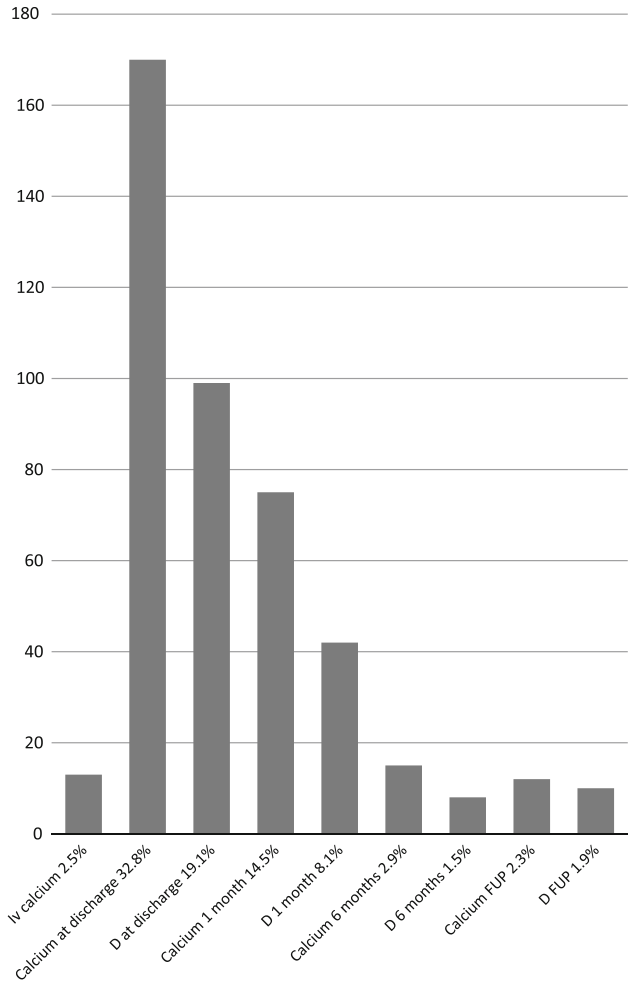

Fig. 1 Number of patients with calcium and/or treatment with vitamin D at different stages of follow-up. *FUP* follow-up, *IV* intravenous

thyroidectomy has become an effective treatment not only for thyroid malignancy, but also for benign thyroid disease.

Permanent hypoparathyroidism is the most common long-term complication after total thyroidectomy, and, though rarely fatal, it can cause significant morbidity for the patient, and is associated with increased costs for the healthcare system.

In this study, the overall rate of permanent hypoparathyroidism was 1.9 %, which is in line with previous reports from high-volume centers [12, 13]. On the other hand, the rate of transient hypocalcemia was rather high, as one-fifth of patients were discharged with a prescription for oral vitamin D analogs.

PTH levels measured early post-operatively were strongly associated with risk of permanent hypoparathyroidism—the rate of permanent hypoparathyroidism was 19.2 % in patients with PTH < 0.7 pmol/l or 6.6 pg/ml the day after surgery. This is in line with other reports, suggesting a strong correlation between PTH levels after total thyroidectomy and long-term hypoparathyroidism [12, 13].

The parathyroid glands are vulnerable at operation, and previous studies suggest that increased surgical volume might be associated with a lower risk of post-operative hypoparathyroidism [5, 9, 10]. In the present study, surgical volume was not specifically recorded, but all surgeons performed at least 50 thyroid operations per year.

Identification of all parathyroid glands was the goal in every operation, and the number of identified parathyroid glands was recorded in all patients. The number of identified parathyroid glands during surgery could not predict permanent hypoparathyroidism in the present study.

Auto-transplantation of parathyroid glands was not routinely performed, but rather at the surgeon's discretion. However, there was no long-term hypoparathyroidism in patients after auto-transplantation. This conflicts somewhat with results of other studies, where some [4], but not all, [3] have found auto-transplantation very useful.

Other researchers have suggested that patients with Graves' disease are at increased risk of hypoparathyroidism after total thyroidectomy [16–18]. This finding was not corroborated in the present study, as indication for surgery, whether for benign non-toxic goiter, thyrotoxicosis, or malignancy, was not associated with risk for permanent hypoparathyroidism. Further, a previous study found no higher risk for post-operative hypocalcaemia in patients with Graves' disease compared with non-toxic nodular goiter [1].

The present study has several limitations. First, information on all risk factors for hypoparathyroidism were not collected in all patients. For instance, there was a lack of data on operation time; the weight of the specimen; and whether lymph node dissection was performed or not. The advantages of the study are the homogenous dataset and that patients were operated by the same surgical team, in the same hospital, with similar surgical technique. Outcome measures were meticulously recorded, and all patients taking oral calcium and/or vitamin D at 6 months were followed for at least 1 year.

Conclusions

A very low PTH early after total thyroidectomy is associated with a high risk of permanent hypoparathyroidism, and normal levels exclude long-term hypoparathyroidism. There is no clear cut-off to indicate high or low risk for permanent hypoparathyroidism by calcium, and post-operative levels of calcium cannot be used to accurately predict long-term risk. Parathyroid auto-transplantation

Table 3 Risk of treatment with calcium at different times of post-operative follow-up

Factor	Intravenous calcium		1 month		6 months		Longterm	
	OR (95 % CI)	OR[a] (95 % CI)	OR (95 % CI)	OR[a] (95 % CI)	OR (95 % CI)	OR[a] (95 % CI)	OR (95 % CI)	OR[a](95 % CI)
Age	0.96 (0.93–0.99)	0.95 (0.91–1.00)	1.00 (0.98–1.01)	0.99 (0.96–1.01)	0.98 (0.95–1.01)	0.97 (0.93–1.02)	1.00 (0.97–1.03)	0.97 (0.93-1.02)
Gender								
Male	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Female	1.07 (0.29–3.95)	1.00 (0.14–7.06)	0.87 (0.47–1.60)	0.83 (0.34–2.04)	0.25 (0.03–1.90)	0.27 (0.03–2.76)	0.71 (0.15–3.27)	0.90 (0.14-5.93)
Pre-operative diagnosis								
Non-toxic goiter	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Toxicosis	1.50 (0.87–6.10)	1.21 (0.16–9.03)	1.15 (0.59–2.24)	0.76 (0.32–1.82)	0.74 (0.23–2.32)	0.53 (0.08–3.37)	0.59 (0.16–2.23)	0.68 (0.08-5.53)
Cancer	2.44 (0.54–11.2)	3.18 (0.47–21.6)	0.84 (0.48–1.46)	0.79 (0.30–2.03)	0.89 (0.22–3.62)	0.76 (0.13–4.35)	1.08 (0.25–4.60)	1.01 (0.15-6.73)
Pre-operative calcium[b]	1.03 (0.98–1.08)	1.00 (0.93–1.07)	1.00 (0.97–1.02)	1.01 (0.98–1.04)	0.93 (0.88–0.98)	0.95 (0.87–1.03)	0.98 (0.92–1.03)	1.01 (0.94-1.09)
Pre-operative PTH	2.19 (0.52–9.23)	4.05 (0.60–27.9)	0.85 (0.45–1.59)	1.04 (0.43–2.53)	0.35 (0.10–1.31)	0.32 (0.05–2.23)	0.64 (0.14–2.86)	0.83 (0.19–2.76)
Identified parathyroid glands								
0–1	0.28 (0.06–1.34)	0.25 (0.03–2.35)	1.12 (0.59–2.12)	1.48 (0.60–3.67)	2.76 (0.82–9.36)	3.74 (0.75–18.5)	3.19 (0.81–12.6)	3.34 (0.56–19.7)
2	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
3–5	0.24 (0.05–1.13)	0.06 (0.01–0.65)	1.54 (0.87–2.75)	1.81 (0.83–3.98)	0.84 (0.18–3.79)	0.67 (0.10–4.65)	0.74 (0.12–4.50)	0.70 (0.08–6.00)
Parathyroid auto-transplantation								
Yes	1.00	1.00	1.00	1.00	1.00	1.00 No events		
No	0.17 (0.06–0.51)	0.14 (0.03–0.61)	0.47 (0.27–0.83)	0.64 (0.30–1.38)	1.38 (0.31–6.22)	0.85 (0.14–5.32)		
Calcium POD 1[b]	0.93 (0.89–0.96)	0.92 (0.87–0.98)	0.90 (0.88–0.93)	0.93 (0.90–0.95)	0.92 (0.89–0.95)	0.94 (0.90–0.98)	0.92 (0.89–0.96)	0.94 (0.90–0.98)
PTH POD 1[c]	0.48 (0.31–0.74)	0.88 (0.37–2.06)	0.17 (0.11–0.26)	0.26 (0.18–0.38)	0.26 (0.17–0.39)	0.26 (0.14–0.49)	0.23 (0.14–0.38)	0.25 (0.13–0.50)

Logistic regression with odds ratios with 95 % confidence intervals in single and multiple adjusted models

CI confidence interval, *OR* odds ratio, *POD* post-operative day, *PTH* parathyroid hormone

[a] Adjusted for all factors in table

[b] Calcium level in mmol/l × 100

[c] log PTH in pmol/l

Table 4 Risk of treatment with oral vitamin D analog at different times of post-operative follow-up

Factor	Discharge		1 month		6 months		Longterm	
	OR (95 % CI)	OR[a] (95 % CI)	OR (95 % CI)	OR[a] (95 % CI)	OR (95 % CI)	OR[a] (95 % CI)	OR (95 % CI)	OR[a](95 % CI)
Age	1.00 (0.99–1.01)	1.00 (0.98–1.02)	1.00 (0.98–1.02)	0.99 (0.96–1.01)	1.00 (0.96–1.04)	0.99 (0.94–1.04)	1.00 (0.96–1.03)	0.98 (0.93–1.02)
Gender								
Male	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Female	0.75 (0.43–1.31)	0.56 (0.22–1.42)	0.69 (0.30–1.60)	0.55 (0.18–1.66)	0.50 (0.06–4.13)	0.48 (0.05–4.89)	0.89 (0.19–4.23)	0.98 (0.15–6.47)
Pre-operative diagnosis								
Non-toxic goiter	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Toxicosis	0.99 (0.54–1.83)	1.28 (0.54–3.04)	0.68 (0.32–1.44)	0.74 (0.25–2.17)	0.49 (0.30–9.16)	0.47 (0.04–5.22)	0.55 (0.12–2.51)	0.30 (0.03–2.88)
Cancer	0.87 (0.53–1.42)	0.81 (0.31–2.11)	1.83 (0.74–3.59)	1.77 (0.63–4.97)	1.81 (0.08–2.89)	1.82 (0.27–12.3)	1.35 (0.30–6.17)	0.99 (0.15–6.57)
Pre-operative calcium[b]	0.99 (0.97–1.01)	0.99 (0.96–1.02)	0.98 (0.95–1.01)	0.99 (0.95–1.03)	0.96 (0.90–1.04)	0.99 (0.90–1.08)	0.96 (0.90–1.03)	1.01 (0.94–1.09)
Pre-operative PTH	1.02 (0.58–1.79)	1.43 (0.60–3.37)	0.54 (0.23–1.25)	0.54 (0.18–1.60)	0.78 (0.14–4.49	0.71 (0.08–6.72)	0.59 (0.12–2.86)	0.47 (0.05–4.36)
Identified parathyroid glands								
0–1	1.07 (0.62–1.86)	1.52 (0.64–3.61)	1.76 (0.77–3.99)	1.95 (0.69–5.53)	1.79 (0.39–8.11)	1.60 (0.26–9.71)	2.25 (0.53–9.57)	1.81 (0.31–10.65)
2	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
3–5	1.19 (0.71– 2.00)	1.08 (0.50–2.74)	1.81 (0.82–3.98)	1.48 (0.55–3.97)	0.37 (0.04–3.59)	0.31 (0.03–3.72)	0.74 (0.12–4.50)	0.74 (0.09–6.43)
Parathyroid auto-transplantation								
Yes	1.00	1.00	1.00	1.00	1.00	1.00 No events.		
No	0.41 (0.25–0.68)	0.49 (0.23–1.06)	0.43 (0.21–0.86)	0.53 (0.22–1.31)	1.48 (0.18–12.15)	1.40 (0.13–15.2)		
Calcium POD 1[b]	0.91 (0.89–0.93)	0.94 (0.92–0.97)	0.94 (0.91–0.96)	0.97 (0.94–0.99)	0.91 (0.87–0.96)	0.94 (0.89–0.99)	0.92 (0.88–0.96)	0.95 (0.90–0.99)
PTH POD 1[c]	0.06 (0.04–0.11)	0.10 (0.06–0.19)	0.27 (0.19–0.38)	0.29 (0.19–0.43)	0.34 (0.20–0.97)	0.45 (0.22–0.89)	0.28 (0.17–0.45)	0.32 (0.17–0.60)

Logistic regression with odds ratios with 95 % confidence intervals in single and multiple adjusted models

CI confidence interval, *OR* odds ratio, *POD* post-operative day, *PTH* parathyroid hormone

[a] Adjusted for all factors in table

[b] Calcium level in mmol/l × 100

[c] log PTH in pmol/l

Table 5 Distribution of oral medication with vitamin D analogs for permanent hypoparathyroidism in 415 patients not auto-transplanted and with information on PTH and calcium day one

		Calcium day 1		
		<2.00 mmol/l or 8.0 mg/dl 7/141 (5.0)	2.00–2.15 mmol/l or 8.0–8.6 mg/dl 1/161 (0.6)	>2.15 mmol/l or 8.6 mg/dl 2/113 (1.8)
PTH day 1	<0.7 pmol/l or 6.6 pg/ml 8/42 (19.1)	5/30 (16.7)	1/7 (14.3)	2/5 (40.0)
	0.7–1.6 pmol/l or 6.6–15 pg/ml 2/69 (2.9)	2/47 (4.3)	0/15	0/7
	>1.6 or 15 pg/ml 0/304	0/64	0/139	0/101

Chi^2, Fisher's < 0.001

Data are presented as n/total (%)

seems to be warranted as a way of minimizing risk of permanent hypoparathyroidism.

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