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Intraoperative Parathyroid Hormone Measurement vs Indocyanine Green Angiography of Parathyroid Glands in Prediction of Early Postthyroidectomy Hypocalcemia

The identification of predictors of postoperative hypocalcemia in thyroid surgery is a focus of interest. Perioperative measurement of parathyroid hormone (PTH) levels and angiography of the parathyroids with indocyanine green (ICG) have been explored, with different conclusions.¹⁻⁵ In this study, we compared the diagnostic accuracy of intraoperative measurement of intact PTH (ioPTH) levels and parathyroid gland

angiography with ICG to predict early hypocalcemia in a cohort of patients in whom at least 4 glands were identified.

Methods | The study was approved by the institutional review board of Hospital Universitari de Bellvitge, and all patients gave written informed consent. Patients undergoing total thyroidectomy with or without central neck dissection between May 2016 and October 2018 were included in a prospective cohort. Inclusion criteria were identification of 4 parathyroid glands intraoperatively or if the sum of in situ glands plus autotransplanted glands plus those in the histopathologic report was at least 4. Previous thyroid-parathyroid surgery and treatment with calcium were exclusion criteria. Intraoperative angiography after thyroidectomy was performed as previously described.³ The degree of ICG fluorescence on parathyroids was classified as 0, black (nonvascularized); 1, gray/heterogeneous (partially vascularized); and 2, white (well vascularized). The ioPTH levels were measured preoperatively and 10 minutes after completion of thyroid surgery using a chemiluminescent immunometric assay (reference, 17.1-74.2 pg/mL; to convert to nanograms per liter, multiply by 1).⁵ The percentage of PTH decline was calculated as (preoperative PTH - postresection PTH)/preoperative PTH × 100. Criteria for predicting hypocalcemia were a decrease in ioPTH level of at least 62.5% or less than 17.1 pg/mL. The serum calcium

Table 1. Distribution of Patients According to Predictors of Early Postoperative Hypocalcemia

Variable	No. (%)			P Value
	All Patients (N = 50)	Postoperative Hypocalcemia Absent (n = 39)	Postoperative Hypocalcemia Present (n = 11)	
ioPTH level, pg/mL, mean (SD)				
Baseline (preoperative)	52.4 (2.0)	51.4 (2.1)	56.2 (1.8)	.45 ^a
Final (10 min after thyroidectomy)	25.7 (1.5)	25.5 (1.4)	11.4 (0.6)	<.001 ^a
ioPTH-based hypocalcemia criteria				
No decrease in ioPTH level ≥62.5%	30 (60)	30 (100)	0	<.001 ^b
Decrease in ioPTH level ≥62.5%	20 (40)	9 (45)	11 (55)	NA
No final ioPTH <17.1 pg/mL	33 (66)	31 (93.9)	2 (6.1)	<.001 ^b
Final ioPTH <17.1 pg/mL	17 (34)	8 (47.1)	9 (52.9)	NA
Neither criteria	34 (70)	33 (94.3)	2 (5.7)	<.001 ^b
Both criteria	15 (30)	6 (40)	9 (60)	
ICG score 2, No. of glands				
0	11 (22)	2 (18.2)	9 (81.8)	
1	16 (32)	15 (93.8)	1 (6.2)	
2	15 (30)	14 (93.3)	1 (6.7)	<.001 ^b
3	5 (10)	5 (100)	0	
4	3 (6)	3 (100)	0	
ICG score 2, any gland				
Present	39 (78)	37 (94.9)	2 (5.1)	<.001 ^b
Absent	11 (22)	2 (18.2)	9 (81.8)	
Surgeon's evaluation of functioning glands				
0	26 (52)	17 (65.4)	9 (34.6)	
1	8 (16)	6 (75)	2 (25)	
2	7 (14)	7 (100)	0	.16 ^b
3	7 (14)	7 (100)	0	
4	2 (4)	2 (100)	0	
Surgeon's evaluation				
Functioning glands	24 (48)	22 (91.7)	2 (8.3)	.04 ^b
Nonfunctioning glands	26 (52)	17 (65.4)	9 (34.6)	

Abbreviations: ICG, indocyanine green; ioPTH, intraoperative measurement of intact parathyroid hormone; NA, not applicable.

SI conversion factor: To convert parathyroid hormone levels to nanograms per liter, multiply by 1.

^a t Test.

^b Fisher exact test.

Table 2. Diagnostic Accuracy of ioPTH Measurement, ICG Angiography, and Surgeon's Macroscopic Assessment for Predicting Early Postoperative Hypocalcemia^a

Measures	Rate (95% CI)		
	ioPTH	ICG Score 2	Surgeon's Assessment
Sensitivity	0.818 (0.482-0.977)	0.818 (0.482-0.977)	0.818 (0.482-0.977)
Specificity	0.846 (0.695-0.941)	0.949 (0.827-0.994)	0.564 (0.396-0.722)
Diagnostic accuracy	0.840 (0.709-0.928)	0.920 (0.808-0.978)	0.620 (0.472-0.753)
Predictive value			
Positive	0.600 (0.323-0.837)	0.818 (0.482-0.977)	0.346 (0.172-0.557)
Negative	0.943 (0.808-0.993)	0.949 (0.827-0.994)	0.917 (0.730-0.990)

Abbreviations: ICG, indocyanine green; ioPTH, intraoperative measurement of intact parathyroid hormone.

SI conversion factor: To convert parathyroid hormone levels to nanograms per liter, multiply by 1.

^a Positive tests for postoperative hypocalcemia: ioPTH decline of at least 62.5% and less than 17.1 pg/mL; ICG no gland scored as 2 (well vascularized).

level was measured using a colorimetric assay (reference, 8.60-10.00 mg/dL [to convert to millimoles per liter, multiply by 0.25]). Also, the surgeon scored the macroscopic appearance of the parathyroid glands as 0, nonfunctioning gland; 1, uncertain; and 2, functioning gland, always before ICG. The primary end point was the need for calcium supplementation. Criteria for the administration of calcium were the presence of symptoms of hypocalcemia or calcium levels less than 7.20 mg/dL in asymptomatic patients.

Results | Fifty patients (33 women [66%]) with a mean (SD) age of 52 (12.9) years diagnosed as having thyroid cancer (n = 35 [70%]), multinodular goiter (n = 13 [26%]), and Graves disease (n = 2 [4%]) underwent total thyroidectomy, associated with central neck dissection in 30. Calcium supplements were needed by 11 patients (22%) postoperatively. Differences in baseline data between patients with and without hypocalcemia were not found. Results of ioPTH levels, ICG angiography, and surgeon's evaluation of glands viability are shown in **Table 1**. Of the 39 patients (78%) who did not require calcium supplementation, ioPTH correctly identified 32 of them (64%) and ICG correctly identified 37 (74%). As shown in **Table 2**, the diagnostic accuracy of ICG angiography and ioPTH was similar.

Discussion | Prevention of the parathyroid function during thyroidectomy is clinically relevant owing to serious adverse effects of permanent hypoparathyroidism. Reported studies of PTH levels measured at different times during or after thyroidectomy have shown controversial results.^{1,2} Indocyanine green angiography has been proposed as a useful technique for evaluation of the viability status of the glands, with encouraging results. However, the first reported studies^{3,4} failed to identify all parathyroid gland tissue, and therefore, these missing glands could be responsible for a positive outcome. On the contrary, here we identified all parathyroid glands. In our study, the diagnostic accuracy of ICG angiography and ioPTH were similar to predict hypocalcemia, but this may be a type II error, and a larger sample size would find that ICG angiography could be superior to ioPTH. With all the parathyroid tissue identified, it seems that visualization of at least 1 well-perfused gland on ICG angiography is highly suggestive of normocalcemia in the immediate postoperative period. Also, ICG angiography would allow immediate decision-making without the need of waiting for ioPTH measurement, although a learning curve to score gland vascularization is needed. Limitations of the study include the nonrandomized design and the relatively small study sample.

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Characterization of High Mortality Probability Operations at National Surgical Quality Improvement Program Hospitals

The decision to operate on high-risk patients can be challenging. To our knowledge, there is little evidence available for guidance and wide variability in practice.¹ Surgeons may encounter clinical scenarios in which they believe that the chances of