Original Article

Evaluation of Parathyroid Gland Angiography with Indocyanine Green Fluorescence in Predicting Postoperative Parathyroid Gland Function in Patients Undergoing Total Thyroidectomy

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ABSTRACT

Background: The most frequent side effect after thyroidectomy is still postoperative hypoparathyroidism. The goal of this pilot research was to evaluate the intraoperative parathyroid gland angiography's ability to predict normal parathyroid gland function following thyroid surgery.

Patients and Methods: Patients undergoing total thyroidectomy at Ain Shams University Hospitals – Endocrine Surgery Unit underwent intraoperative angiography using the fluorescent dye indocyanine green (ICG) to see the vascularization of the parathyroid glands that were detected.

Results: ICG angiography was performed on 40 patients selected as follows: needs total thyroidectomy either due to benign or malignant causes. The study participants did not get prophylactic calcium supplementation. According to the ICG results, all individuals with at least one well-vascularized parathyroid gland had normal parathyroid hormone levels on postoperative day 1. Twenty-seven (67.5%) out of 40 patients in our research had an ICG score of less than or equal to 5, whereas 13(32.5%) out of 40 patients had an ICG score of higher than 5. In this study, 21(52.5%) out of 40 patients had hypocalcemia, whereas 19(47.5%) out of 40 patients did not experience any hypocalcemia following surgery. Ten out of 13 patients with an ICG score higher than 5 did not have postoperative hypocalcemia, while five out of 27 patients with an ICG score less than 5 did not develop any hypocalcemia postoperative.

Conclusion: ICG-enhanced fluorescence imaging should be carefully evaluated before being used in endocrine surgery. This method is noninvasive, nonradiological, and safe. This technique, with a cutoff of fluorescence score 5, had a sensitivity of 77.8% while specificity was 73.9% with an accuracy of 0.760 in predicting postoperative hypocalcemia.

Key Words: Indocyanine green, Parathyroid hormone, Postoperative hypocalcemia, Total thyroidectomy.

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INTRODUCTION

After a total thyroidectomy, postoperative hypocalcaemia is frequent and can significantly affect quality of life. Based on the operator's skill and the technical difficulties of the treatment, postoperative hypocalcaemia is common and has been reported in 15–35% of patients. One to three percent of individuals have been found to have permanent hypocalcemia, which is defined as hypocalcemia that persists for more than 6 months following thyroidectomy. The risk of hypoparathyroidism increases with the extent of thyroidectomy, completion thyroidectomy, reoperative procedures, and central neck dissection[1,2].

Following a total thyroidectomy, hypoparathyroidism resulting from intraoperative trauma, unintentional parathyroid gland removal, or devascularization is the primary cause of hypocalcemia[3].

It is challenging to predict the degree of parathyroid gland injury intraoperatively. It has long been believed that half of a normal parathyroid gland can produce enough parathyroid hormone (PTH)[4,5].

One of the most recent methods for assessing parathyroid gland perfusion and function following thyroidectomy is intraoperative parathyroid gland angiography using indocyanine green (ICG) dye. This technique is used to reduce the chances of hypoparathyroidism after thyroid surgery and can help to preserve postoperative parathyroid remnant function[6,7].

Recently, during various surgical operations, particularly laparoscopic surgery, the concept of angiography using dyes like ICG is utilized to increase visualization and

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offer comprehensive anatomical information. Fluorescent optical guiding improves operational efficiency while reducing unintentional tissue damage. ICG is an anionic amphiphilic tricarbocyanine dye that dissolves in water. When excited by a laser beam or light with a wavelength around 820nm, ICG turns fluorescent and may be injected intravenously with almost no negative consequences[8,9].

The only clinically certified NIR fluorescent dye is ICG, which was initially authorized for usage in (1956). To identify the anatomical structures that contain the dye, such as biliary ducts, arteries and lymph nodes. Angiography can be done using specialized scopes and then transferred to a standard monitor. During surgery, an intravenous injection of ICG allows for the real-time measurement of intestinal perfusion and visceral blood supply. ICG that has been injected binds firmly to lipoproteins and is quickly eliminated into the bile[10].

Aims and objectives

Evaluation of intraoperative ICG angiography in predicting postoperative hypocalcemia in patients after total thyroidectomy.

PATIENTS AND METHODS:

Sample size

The program "Power Analysis and sample size, version-16 (PASS-16)" was used to estimate the population size, confidence interval, and SD (0.5 was a safe choice), then convert the confidence level into z score. Ultimately, 40 patients were collected for the study until the required sample size was attained.

Study type

Interventional.

Inclusion criteria: regardless of sex, patients between the ages of 20 and 60 admitted for total thyroidectomy for benign causes, either simple nodular goiter, toxic nodular goiter, or Graves disease or malignancy.

Exclusion criteria: any history of adverse reactions or known allergies to ICG, iodine, or iodine dyes, pregnancy, cases diagnosed as recurrent goiter, and age restriction (<20 and >60).

Sample method: 40 consecutive patients who presented to Ain Shams University Hospitals – Endocrine Surgery Unit in the period between March 2023 and March 2024.

Study tools: patients included in this study were subjected to preoperative assessment, including taking a whole history, emphasizing hyperthyroidism symptoms and compression symptoms (dysphagia, hoarseness of voice, and dyspnea). A history of thyroid cancer in the family, thyroid disease duration.

Clinical examination (general and local): neck examination for lymph nodes, thyroid gland, tracheal position, or scars of previous operations. Imaging: neck ultrasound and thyroid biopsy when indicated (such as fine-needle aspiration according to TIRADS score).

Operative procedure: following exposure of the thyroid gland, the dye (ICG) is injected intravenously peripherally in either the left or right arm. The operator uses the fluorescence system camera to measure parathyroid gland perfusion intraoperatively after turning off all lights in the operating room once the first parathyroid gland has been located. The interval between the dye administration and the onset of fluorescence is noted as an indirect indicator of vascular failure. ICG with fluorescent properties is exposed to excitation lights (near infrared) with wavelength between 750 and 800nm. It emits at around 830nm and has very low toxicity. This technique is integrated into a specific laparoscopy set. The degree of fluorescence of all the parathyroid glands was recorded in all cases. It was cast on a sterilizable laparoscopic camera. Parathyroid gland imaging was done through direct visualization of the field 1 min post-ICG injection after resection of the thyroid gland.

The degree of ICG fluorescence on parathyroids was measured and classified by the operating surgeon, who is not a member of the research group, into either:

0. black (nonvascularized).
1. gray/heterogeneous (partially vascularized).
2. white (well-vascularized).

Postoperative: within 6–8 hours following the conclusion of the procedure, routine measurements of blood calcium (total and ionized), postoperative PTH levels were made at the same time. Patients with at least one postoperative blood calcium level between 8.0 and 8.4mg/dl (reference range: 8.4–10.2mg/dl) were classified as having postoperative moderate hypocalcemia. Patients who experienced hypocalcemia-related symptoms (diffuse perioral or fingertip paresthesias or numbness, tetany, or a positive Chvostek sign) or who had a postoperative serum calcium level of less than 8.0mg/dl on at least one postoperative test were deemed to have postoperative significant hypocalcemia. Then another measure of blood calcium and PTH is taken 2 weeks later.

The trial participants did not get prophylactic calcium supplementation. Only individuals who are experiencing clinical or biochemical hypocalcemia were given calcium supplements.

Ethical consideration: The ethical committee of the scientific research approval at the Faculty of Medicine – Ain Shams University was obtained.

Statistical analysis

All data (serum calcium level, ICG score) were collected, tabulated, and statistically analyzed by a software package program (SPSS Program).

RESULTS:

Total number of patients – 40.

Demographic profile: out of 40 patients included in our study, 24 of the 40 patients who were selected for the research were females and 16 were males.

Surgical indications

Twenty-eight patients had a benign indication, while 12 had a malignant one.

Table 1: hypocalcemia.

Of the 40 patients, 25(62.5%) had postoperative hypocalcemia, of whom 18(45%) had biochemical hypocalcemia and seven (17.5%) had clinical hypocalcemia. After surgery, 15(37.5%) individuals experienced no hypocalcemia.

According to the ICG results, all individuals with at least one well-vascularized parathyroid gland had normal PTH levels on postoperative day 1.

Table 2: total ICG score.

During ICG angiography, each parathyroid gland was visually given a score of 0 (no vascularity), 1 (moderate vascularity), or 2 (excellent vascularity). Parathyroid fluorescence intensity (FI) was measured numerically; this reflects the amount of ICG taken up by the gland and is, in turn, affected by the richness of the associated blood supply. A higher FI reflects better vascularization. After that scores of 4 glands are summed to give one score for every patient.

Thirteen patients had a score greater than 5, while 27 had a total ICG score less than or equal to 5 (Table 2).

In patients with an ICG score more than 5, 10 out of 13 patients did not have hypocalcemia, while three patients had hypocalcemia (two showed biochemical and only one patient had symptomatic hypocalcemia).

While in patients with an ICG score less than or equal to 5, five out of 27 patients with a score less than or equal to 5 did not have hypocalcemia, and significant hypocalcemia (symptomatic) is present in six patients only, and 16 patients had biochemical hypocalcemia.

In Table (3), true positive means the number of patients who had hypocalcemia (laboratory or clinical) in the ICG score less than or equal to 5 (nonwell-visualized parathyroid glands)[15].

True negative means the number of patients who had a normal level of calcium in the ICG score, more (well visualized parathyroid glands), but false positive means the number of patients who had a normal level of calcium in the ICG score less than or equal to 5 (nonwell-visualized parathyroid glands) and false negative means the number of patients who had hypocalcemia (laboratory or clinical) in the ICG score more than 5 (well-visualized parathyroid glands).

We measured the sensitivity and specificity of an ICG score of 5 or less to predict the occurrence of hypocalcemia.

Table (4) reveals that the median sensitivity rate for ICG fluorescence in the detection of parathyroid gland is 77.8% while the specificity rate for ICG (specific for PTH gland, not LNs or any other neck structures) is 73.9% (Figures 1–6, Tables 3 and 4).

Table 1: Postoperative calcium level (total and ionized):

Postoperative calcium level	Total no.= 40 [*n*(%)]
Normocalcemia	15(37.5)
Hypocalcemia	
Biochemical	18(45)
Clinical	7(17.5)

Table 2 Total indocyanine green score

ICG Score	No. Of Patients
Less than or equal 5	27(67.5%)
More than 5	13(32.5%)

Table 3: Correlation between indocyanine green score and postoperative calcium level:

	True positive	True negative	False positive	False negative
ICG score intraoperative	22	10	5	3

ICG: Indocyanine Green.

Table 4: Results of indocyanine green score according to sensitivity, specificity, positive predictive value, and negative predictive value:

Sensitivity	77.8%
Specificity	73.9%
Positive predictive value	77.8%
Negative predictive value	73.9%
Accuracy	0.760

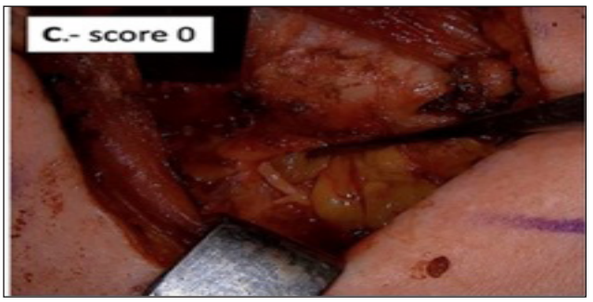

Figure 1: Degree of ICG fluorescence on parathyroids intraoperative (the arrow points to the parathyroid gland) (ICG score 0). ICG, indocyanine green.

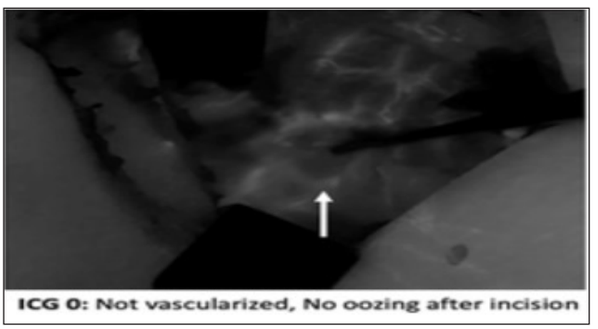

Figure 2: Degree of ICG fluorescence on parathyroids intraoperative (the arrow points to the parathyroid gland) (ICG score 0). ICG, indocyanine green.

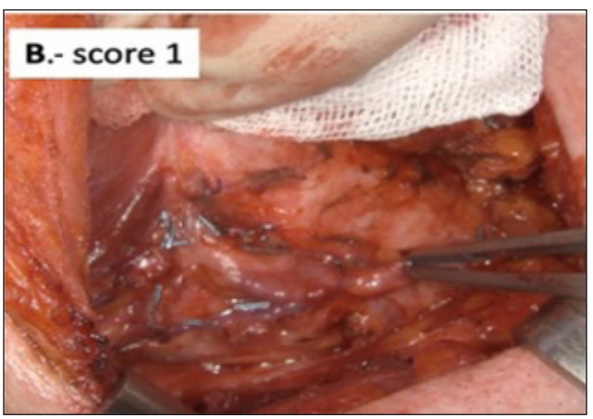

Figure 3: Degree of ICG fluorescence on parathyroids intraoperative (the arrow points to the parathyroid gland) (ICG score 1); ICG: Indocyanine Green.

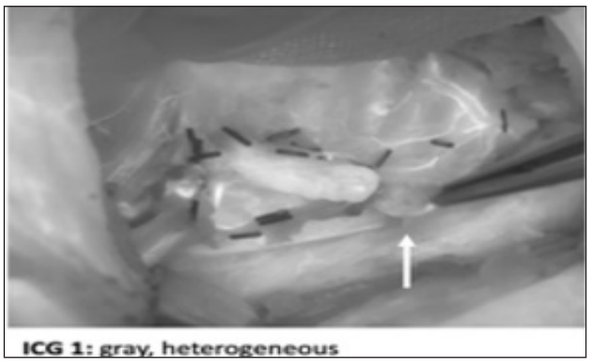

Figure 4: Degree of ICG fluorescence on parathyroids intraoperative (the arrow points to the parathyroid gland) (ICG score 1); ICG: Indocyanine Green.

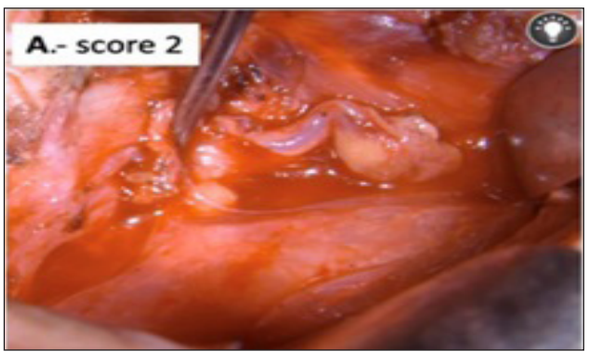

Figure 5: Degree of ICG fluorescence on parathyroids intraoperative (the arrow points to the parathyroid gland) (ICG score 2). ICG, indocyanine green.

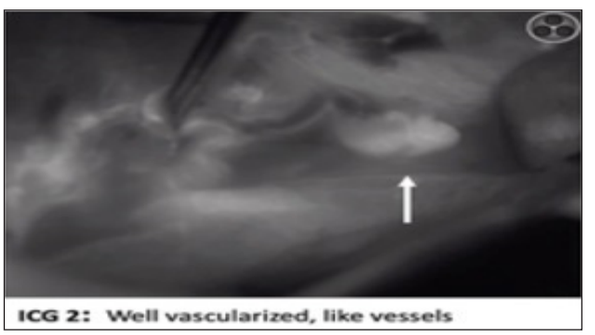

Figure 6: Degree of ICG fluorescence on parathyroids intraoperative (the arrow points to the parathyroid gland) (ICG score 2). ICG, indocyanine green.

DISCUSSION

ICG angiography is safe for patients having a total thyroidectomy. According to this study, the findings indicate a strong relationship between parathyroid function and perfusion. According to the ICG results, all individuals with at least one well-vascularized parathyroid gland had normal PTH levels on postoperative day 1. Twenty-seven (67.5%) out of 40 patients in our research had an ICG score of less than or equal to 5, whereas 13(32.5%) out of 40 patients had an ICG score of higher than 5.

In contrast, another study conducted in (2023) at the Department of Endocrine Surgery, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, found that, of 60 patients, 34 had a total ICG score of less than 5 by percentage (56.66%), and 26 had a score greater than 5 by percentage (43.33%).

In this study, 25(62.5%) out of 40 patients had hypocalcemia, while 15(37.5%) out of 40 patients did not experience any hypocalcemia following surgery.

Compared to the other study, 41(68.33%) patients had hypocalcemia out of 60, of whom 14 developed biochemical hypocalcemia and 27 developed clinical hypocalcemia. After surgery, 19(31.66%) patients did not experience any hypocalcemia. This high percentage of hypocalcemia in our study is biochemical without any symptoms or signs, which did not require any calcium supplementation, either oral or intravenous.

In contrast to the recent Indian study that indicates that the ICG test has a sensitivity of 78.29% and a specificity of 68.42%, this study demonstrates that the ICG test has a sensitivity of 77.8% and a specificity of 73.9%.

A pilot trial for transient postoperative hypocalcemia, including 196 patients who were injected with ICG dye for parathyroid gland angiography posttotal thyroidectomy, was done in (2018) by Vidal Fortuny. Fifty patients had no ICG uptake, while 146 patients had at least one parathyroid gland. Three hundred eighty-seven of the 499 parathyroid glands that were extracted were well visualized and perfused[11].

While none of the 146 individuals had hypocalcemia complaints postoperatively, 11 of the 50 patients did so on the first and tenth postoperative days. The authors advocated ICG angiography as a predictor of the absence of postoperative hypocalcemia and stated that in patients with at least one well-visualized parathyroid gland, calcium and PTH levels may no longer require postoperative testing[12].

As a result, calcium replacement and postoperative hypoparathyroidism may become obsolete if a well-visualized parathyroid gland with high ICG FI can be obtained. To further validate parathyroid gland angiography using ICG as an intraoperative technique for evaluating real-time parathyroid preservation, more randomized clinical studies are required, as there is currently no general agreement on the ideal dosage and timing of ICG delivery[13,14].

CONCLUSION

ICG-enhanced fluorescence imaging should be carefully tested before being used in endocrine surgery. This method is noninvasive, nonradiological, and safe.

This technique can lower postoperative problems and healthcare costs by helping surgeons make crucial decisions, such as the need for intraoperative parathyroid gland autotransplantation in the operating room. This technique, with a cutoff of fluorescence score 5, has a high sensitivity and specificity index as described, which puts this method into consideration.

AUTHORS ' CONTRIBUTIONS

The authors would express their gratitude to all of their colleagues with whom they enjoyed working on this and similar initiatives. The authors learnt about scientific research and life in general from each member, who has also given wealth of professional and personal advice.

CONFLICT OF INTEREST

There are no conflicts of interest.

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