

# Use of parathormone as a predictor of hypoparathyroidism after total thyroidectomy

## *Utilización de la parathormona como predictor de hipoparatiroidismo posttiroidectomía total*

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### Abstract

**Background:** Post-operative hypoparathyroidism is the most frequent complication after total thyroidectomy. It represents one of the main causes of prolonged hospital stay and is associated with a significant increase in health costs. The identification of patients with higher risk of suffering this complication allows early treatment, reduces clinical complications and adequate the use of health resources. Throughout history, several predictors have been used to stratify patients at risk. In recent years, the use of parathormone parathyroid hormone (PTH) has taken particular interest. **Objective:** The objective of the study was to review the existing literature on the use of PTH as a predictor of hypocalcemia after thyroidectomy. **Methods:** A Medline search was performed. We reviewed the existing evidence on efficacy of PTH as a predictor of post-operative hypocalcemia, economic impact, optimal time for sampling, and implementation mode. **Conclusions:** The use of PTH predicts with adequate sensitivity, specificity, and negative and positive predictive values the risk for the patients to suffer post-operative hypocalcemia. Cut-off values and sampling number and time vary among authors; as a result, more data are needed to reach a conclusion about the standardization of use after a total thyroidectomy procedure. Its use could be beneficial not only for patients but also for care providers as health cost might be diminished.

**Key words:** Hypocalcemia. Hypoparathyroidism. Parathyroid hormone. Thyroidectomy.

### Resumen

**Antecedentes:** El hipoparatiroidismo posoperatorio constituye la complicación más frecuente de la tiroidectomía total. Se asocia, entre otras cosas, a internación prolongada y múltiples pruebas de laboratorio, y con ello a un incremento en los costos de salud. La identificación de pacientes con mayor riesgo de padecer esta complicación permite realizar un tratamiento precoz, disminuyendo el costo económico y evitando complicaciones asociadas a un retraso en la extirpación. Se han descrito diversos predictores para identificar tempranamente a los pacientes en riesgo; en los últimos años, ha tomado particular relevancia el uso de la parathormona (PTH). **Objetivo:** El objetivo del presente trabajo es revisar la literatura existente sobre la utilidad de la PTH como predictor de hipocalcemia posttiroidectomía. **Método:** Se realizó una búsqueda en PubMed revisando la evidencia existente sobre eficacia de la PTH como predictor de hipocalcemia posoperatoria, su repercusión económica, el tiempo óptimo para la toma de muestra y el modo de implementación. **Conclusión:** El uso de la PTH permite predecir con adecuada sensibilidad, especificidad, valor predictivo negativo y valor predictivo positivo los pacientes en riesgo de padecer hipocalcemia posoperatoria. Sin embargo, los valores de corte, los tiempos de toma de muestra y la cantidad de estas varían entre los autores, por lo que persisten algunos interrogantes acerca de la estandarización de su uso.

**Palabras clave:** Hipocalcemia. Hipoparatiroidismo. Hormona paratiroidea. Tiroidectomía.

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## Introduction

Calcium homeostasis is of critical importance to human physiology. Hypocalcemia can have repercussions that range from mild paresthesias to life-threatening complications, such as severe confusion episodes, tetany, or severe arrhythmias<sup>1-3</sup>. During thyroid surgery, as a consequence of devascularization or parathyroid glands removal, a decrease in serum parathyroid hormone (PTH) concentrations may occur, causing transient or persistent hypoparathyroidism<sup>4</sup>. This phenomenon, together with other factors, causes a decrease in serum calcium concentrations in the post-operative period<sup>5</sup>.

Post-operative hypoparathyroidism represents the most common complication after total thyroidectomy<sup>6,7</sup>. It is classified as transient when its duration is < 6 months and as permanent when it lasts longer. Transient hypoparathyroidism occurs in 1.7-68% of patients, while its permanent form affects 1-12% in different published series<sup>4,8-11</sup>. This complication appears within the first 24-96 h after surgery, which is why in many institutions patients remain hospitalized during this period of time<sup>4,7,8</sup>. Once hypoparathyroidism is installed, it requires treatment with calcium replacement and Vitamin D, and strict monitoring to prevent, detect, or treat severe manifestations of hypocalcemia (arrhythmias, tetany, etc.)<sup>2</sup>.

Patient stratification according to the risk for suffering from hypocalcemia allows effective treatment to be implemented in those categorized as being at high risk and enables rapid discharge for those at low risk, which translates into lower hospital costs<sup>7,10,12</sup>. Serum calcium serial testing has been the most widely used biochemical predictor for post-operative parathyroid function monitoring, mainly due to its relative accessibility<sup>7,8,13</sup>. However, it has multiple limitations, such as the cost that analyzing several blood samples represents discomfort or potential complications resulting from repeated punctures, as well as the fact that blood calcium normal values within the first 24 h appear not to adequately predict serum calcium behavior over the 1<sup>st</sup> post-operative hours<sup>4,7-9</sup>. This would be because post-operative blood calcium plateau is reached at between 48 and 72 h after surgery<sup>4</sup>. This relatively low sensitivity to predict post-operative hypocalcemia (a sample at 24 h of surgery would have a sensitivity of 19-91%)<sup>7,8</sup> justifies that some centers prolong hospital stay or preventively and systematically medicate their patients, even with the harm this entails<sup>3,7,9,10,14</sup>.

There are other predictors that try to identify patients at risk of hypoparathyroidism, including pre-operative serum Vitamin D concentration, post-operative blood phosphate, calcitonin and magnesium levels, the number of glands identified in surgery, the need for a parathyroid autoimplantation<sup>8</sup>. However, post-operative blood PTH levels are the predictor that has been increasingly used in recent years and that generates numerous debates regarding its systematic implementation during hospitalization, hormone metabolization, excretion variables, costs, etc.<sup>7</sup>.

The purpose of this work is to make a non-systematic review of the literature published in PubMed between 1998 and 2017 about PTH as a hypocalcemia predictor in the immediate and mediate post-operative period of total thyroidectomy.

## Methods

A search was carried out in PubMed for papers in English language using the following MeSH terms and key Boolean operators: parathormone AND/OR hypocalcemia AND/OR thyroidectomy AND/OR post-operative. Those studies that described PTH efficacy as a predictor of post-operative hypocalcemia, economic factors associated with its use, optimal time for sample taking, and implementation mode were included in the study. The search was limited to articles published between 1998 and 2019.

### *PTH efficacy as a predictor*

PTH is an 84-amino acid peptide synthesized in the parathyroid glands. Its secretion depends on serum ionized calcium concentration: the lower the blood calcium, the higher the PTH secretion. It elevates serum calcium concentrations through different mechanisms. It has a short half-life of 1-4 min, with rapid liver metabolism and renal elimination<sup>2</sup>.

Numerous studies have used PTH as a predictor of post-thyroidectomy hypocalcemia, demonstrating adequate sensitivity and specificity values, as well as negative and positive predictive values, with a slight superiority versus calcium monitoring<sup>7,8,10,13</sup>. Although the studies are quite heterogeneous in terms of variables and measurement methods, the proposed sensitivity varies from 69% to 100% in a sample taken between the 1<sup>st</sup> and 24<sup>th</sup> h of the post-operative period<sup>7,8,15</sup>.

This evidence would allow claiming that normal intraoperative or post-operative PTH values exclude the

possibility of developing significant hypocalcemia<sup>10,14</sup>. Although infrequently, patients with normal intraoperative PTH values might experience hypocalcemia, but negligible<sup>16,17</sup>. Conversely, low post-operative PTH values are associated with a high rate of hypocalcemia, which is why stricter follow-up and eventual medication would be recommended<sup>16</sup>. One of the most recent works is that by Calvo Espino et al.<sup>18</sup> who demonstrated that PTH measurement on the 1<sup>st</sup> post-operative day with a result < 5 pg/mL has a sensitivity of 95% and specificity of 77% to predict permanent hypoparathyroidism; in addition, serum calcium testing showed a slightly lower sensitivity (92%) and an even lower specificity (65%). Almquist et al.<sup>19</sup> referred similar conclusions, since they establish that very low post-operative PTH values indicate a high risk of permanent hypoparathyroidism; thus, normal post-operative PTH values would allow the possibility of its occurrence to be excluded. In the same line, they state that post-operative blood calcium monitoring, given its variables, does not adequately predict the risk of permanent hypoparathyroidism (> 6-month duration). In turn, Hermann et al.<sup>20</sup> determined that PTH values equal to or lower than 6 pg/mL would have a sensitivity of 100% and a positive predictive value of 15% for permanent hypoparathyroidism<sup>20</sup>. However, other studies, such as that by Sahli et al.<sup>15</sup>, rule out this correspondence. Their work, which included 218 patients, ruled out PTH measured within the 1<sup>st</sup> h after surgery as a reliable predictor of hypocalcemia, arguing its low sensitivity (36.5%); among their conclusions, the need for randomized studies to reach a more accurate conclusion stands out.

### ***Economic impact***

The impact on health costs generated by PTH measurement varies between each center and country, but as a general rule, absolute cost is usually higher than blood calcium analysis<sup>21</sup>. Notwithstanding, PTH monitoring is associated with a decrease in total costs<sup>7,8,10,12,13,21,22</sup>. This is because, since PTH descent curve reaches its plateau within the first few minutes after surgery or, for many, before the conclusion of surgery, a single analysis would suffice<sup>4</sup>. In contrast, blood calcium measurement requires numerous extractions.

Another point to consider in total costs' reduction is that, since a single sample can be obtained (in the immediate post-operative period or very close to the conclusion of surgery), discharge can be granted

early, thus shortening hospital stay and saving on unnecessary medication<sup>7,22</sup>. It is important highlighting that, although PTH accuracy as a predictor is not 100%, hypocalcemia is highly infrequent with perioperative PTH normal values. Following this concept, a single post-operative PTH normal value would allow early discharge, even on the same day of surgery<sup>10,22,23</sup>. In accordance with the above, Payne et al.<sup>12</sup> showed in their series a saving of USD 760 per patient when they compared PTH monitoring with blood calcium serial measurements, which was explained by hospitalization shortening.

### ***Optimal sample collection timing and implementation method***

Despite the clear advantages offered by PTH as a predictor of post-operative hypocalcemia, there are still controversies regarding optimal timing for sample collection and implementation logistics (Table 1).

Perhaps, the biggest question is the timing for carrying out the measurement. Various authors propose collecting the sample during surgery or at skin closure; others, an analysis throughout the first 24 h, at 1, 4, 6, and 8 h postoperatively; and others propose collecting it directly during the 1<sup>st</sup> post-operative day<sup>1,7,9,12,14-16,18,22,24-27</sup>.

As previously mentioned, there are groups that propose collecting the sample intraoperatively or immediately postoperatively with the patient still under anesthesia. Quiros et al.<sup>1</sup> established a relationship between PTH values < 10 pg/mL at the moment of skin closure and post-operative hypoparathyroidism and hypocalcemia, and therefore suggested early Vitamin D replacement in patients with these values. Accordingly, Lang et al.<sup>3</sup> also concluded that a single sample at the completion of surgery, at the time of skin closure, with the patient anesthetized, would allow stratifying risk and avoiding extraction discomfort. Both studies thereby justify that the ideal moment for obtaining the sample is intraoperatively or in the immediate post-operative period. Galy-Bernadoy et al.<sup>22</sup> also collected the sample at the time of skin closure, but the interesting thing about their study is that they used two kits for PTH measurement, thus obtaining two cutoff values with each one. The purpose of the study was to identify patients without risk for hypocalcemia with a negative predictive value of 100%. For this group, cutoff values were  $\geq 9$  and  $\geq 19$  ng/L, each with a negative predictive value and sensitivity

**Table 1. Summary of studies with their designs and main findings and conclusions**

| Authors                           | Year | Design        | n    | PTH    | Timing for PTH                        | Control                                   | PTH cutoff value                | Conclusion                                                                                                                   |
|-----------------------------------|------|---------------|------|--------|---------------------------------------|-------------------------------------------|---------------------------------|------------------------------------------------------------------------------------------------------------------------------|
| Quiros et al. <sup>1</sup>        | 2005 | Prospective   | 72   | iPTH   | Closure; month 1 post                 | Blood calcium at 1 month                  | < 10 pg/mL                      | Single iPTH measurement at skin closure predicts hypoparathyroidism                                                          |
| Lang et al. <sup>3</sup>          | 2012 | Prospective   | 117  | qPTH   | Closure; 24 h post                    | Blood calcium                             | 1 pmol/L                        | PTH value at closure has > S, Sp, and PV than blood calcium and PTH at 24 h                                                  |
| Cahill et al. <sup>4</sup>        | 2005 | Prospective   | 31   | qPTH   | Pre-op; intra*; closure               | Pre, 24, 48, and 72 h post blood calcium  | > 50%                           | The use of PTH as predictive value is relative, requires subsequent controls                                                 |
| Lombardi et al. <sup>5</sup>      | 2006 | Prospective   | 523  | iPTH   | 4 h post                              | 24, 48, day 7 post blood calcium          | > 15 pg/mL                      | PTH value at 4 h post does not adequately predict hypoparathyroidism                                                         |
| Karatzanis et al. <sup>7</sup>    | 2017 | Prospective   | 100  | iPTH   | Pre-op; 18 and 24 h post              | Blood calcium, Mg, P, and alb every 12 h† | 56%                             | PTH values 1 <sup>st</sup> day post can be used as hypocalcemia predictor                                                    |
| Pisanu et al. <sup>9</sup>        | 2012 | Prospective   | 112  | iPTH   | Pre-op; 6, 24, and 48 h post          | Pre, 6, 24, and 48 h blood calcium and P  | ≤ 12.1 pg/mL                    | Single iPTH measurement same day post (6 h) and blood calcium (24 h) predicts hypocalcemia                                   |
| Pattou et al. <sup>11</sup>       | 1998 | Prospective   | 1071 | iPTH   |                                       | Blood calcium, P                          | ≤ 12 pg/mL                      | PTH values ≤ 12 pg/mL predict permanent hypoparathyroidism                                                                   |
| Payne et al. <sup>12</sup>        | 2005 | Prospective   | 95   | iPTH   | 1 and 6 h post                        | 1 and 6 h post blood calcium              | ≤ 8 ng/L                        | PTH and blood glucose values at 1 and 6 h of same day post translated into decrease in hospital costs                        |
| Graff et al. <sup>13</sup>        | 2010 | Prospective   | 69   | iPTH   | Post                                  | 6 and 18 h post blood calcium             | < 14 pg/mL                      | Single iPTH measurement same day post predicts hypocalcemia; increases sensitivity if combined with blood calcium at 6 h     |
| Sahli et al. <sup>15</sup>        | 2018 | Prospective   | 218  | iPTH   | Pre; 1 h post                         | Blood calcium                             | < 10 and < 20 pg/mL; > 50% drop | PTH values are not reliable to predict hypocalcemia                                                                          |
| Carr et al. <sup>16</sup>         | 2014 | Prospective   | 77   | iPTH   | 4 h post; day 1 post                  | Blood calcium, Vitamin D                  | < 10 pg/mL                      | Single iPTH measurement same day post predicts the need for oral calcium replacement or blood calcium control (4 h)          |
| AES Guidelines <sup>17</sup>      | 2007 | Retrospective | 458  | i/qPTH | Between 1 h and 18 h post             | Blood calcium                             |                                 | PTH normal values predict normal blood calcium, preferably at 4 h post                                                       |
| Calvo Espino et al. <sup>18</sup> | 2019 | Retrospective | 481  | iPTH   | 16-20 h post                          | Blood calcium 16-20 h post                | < 5 pg/mL                       | PTH value < 5 pg/mL 1 <sup>st</sup> day post predicts permanent hypoparathyroidism                                           |
| Almquist et al. <sup>10</sup>     | 2014 | Prospective   | 519  | i/qPTH | Intra; day 1 and 14 post              | Blood calcium                             | < 6.6 pg/mL                     | Low PTH values 1 <sup>st</sup> day post predicts permanent hypoparathyroidism                                                |
| Hermann et al. <sup>20</sup>      | 2008 | Prospective   | 208  | iPTH   | Pre-op; intra*; 3 h; day 1, 2, 3 post | Blood calcium                             |                                 | Normal PTH values measured the same day post predict risk of persistent hypocalcemia better than at the end of surgery (3 h) |

(Continue)

**Table 1. Summary of studies with their designs and main findings and conclusions (Continued)**

| Authors                              | Year | Design        | n   | PTH  | Timing for PTH      | Control                             | PTH cutoff value | Conclusions                                                                                                   |
|--------------------------------------|------|---------------|-----|------|---------------------|-------------------------------------|------------------|---------------------------------------------------------------------------------------------------------------|
| Khafif et al. <sup>21</sup>          | 2006 | Prospective   | 40  | iPTH | Pre-op; 30 min post | Blood calcium                       | > 50% drop       | A 50% relative decrease in PTH predicts hypocalcemia                                                          |
| Galy-Bernadot et al. <sup>22</sup>   | 2018 | Prospective   | 257 | iPTH | Closure (2 kits)    | Blood calcium                       | < 7 and < 4 ng/L | Single iPTH measurement at skin closure predicts hypoparathyroidism                                           |
| Grodski and Farrell <sup>23</sup>    | 2007 | Prospective   | 76  | iPTH | 4-12 h post         | 24 h blood calcium                  | 12 pg/mL         | Single iPTH measurement at 4-12 h post predicts hypocalcemia risk                                             |
| Lim et al. <sup>24</sup>             | 2009 | Prospective   | 21  | iPTH | 1 h post            | Blood calcium                       | ≤ 2.5 pmol/L     | Single iPTH measurement same day post predicts symptomatic hypocalcemia (1 h)                                 |
| Kim et al. <sup>25</sup>             | 2011 | Retrospective | 112 | iPTH | 1 h post            | Blood calcium                       | < 10 pg/mL       | Single iPTH measurement same day post predicts symptomatic hypocalcemia (1 h); S increases with serum calcium |
| Le et al. <sup>26</sup>              | 2014 | Retrospective | 125 | iPTH | 1 h post            | Blood calcium                       | < 12 pg/mL       | Single iPTH measurement same day post stratifies patients according to the risk of hypocalcemia (1 h)         |
| Kim et al. <sup>27</sup>             | 2013 | Prospective   | 108 | iPTH | 6 h post            | Blood calcium, Mg, P                | < 10.6 mg/dL     | Single iPTH measurement same day post predicts hypocalcemia (6 h)                                             |
| Sywak et al. <sup>28</sup>           | 2007 | Prospective   | 100 | iPTH | 4 h; 24 h post      | Blood calcium                       | ≤ 3 ng/L at 4 h  | Single iPTH measurement same day post predicts hypocalcemia (4 h)                                             |
| Pradeep and Ramalingam <sup>30</sup> | 2014 | Prospective   | 203 | iPTH | Pre-op; 8 h post    | 24-48 h blood calcium and vitamin D |                  | Decreased PTH in patients with vitamin D deficiency does not predict hypocalcemia                             |

Alb: albumin; intra: intraoperative; Mg: blood magnesium; P: blood phosphate; post: post-operative; PTH: parathyroid hormone; pre: pre-operative; iPTH: intact PTH; qPTH: quick PTH; PV: predictive value; S: sensitivity; Sp: specificity.

\*After thyroid mobilization/when resecting the gland.

<sup>†</sup>Up to three consecutive normal measurements.

<sup>‡</sup>10 min after each lobectomy.

of 100%, and somewhat lower specificity. Between 14% and 28% of patients remained in a “gray” or intermediate zone with regard to the cutoff values and were preventively treated. On the other hand, in contrast, Cahill et al.<sup>4</sup> claimed that, due to the usual intraoperative PTH decrease in bilateral thyroid surgery, a low intraoperative value does not allow predicting the risk of hypocalcemia; therefore, they suggest that measurements should be performed after surgery.

Other groups carry out the measurement in the immediate or mediate post-operative period, with sample collection between at 4 and 6 h postoperatively predominating. Khafif et al.<sup>21</sup> demonstrated the applicability of the method with samples taken 30 min after surgery. In turn, Payne et al.<sup>12</sup> demonstrated adequate PTH sensitivity with samples taken 1 and 6 h after surgery. Lombardi et al.<sup>5</sup> obtained samples at different post-operative intervals, initially finding greater precision in values obtained 4-6 h after surgery. In a later

work, with a larger number of patients, they concluded that a value obtained at 4 h would not be accurate enough and that blood calcium should continue to be measured. In turn, Carr et al.<sup>16</sup>, with 77 patients, obtained good results with a sample taken at 4 h. On the other hand, the Australian Endocrine Surgeons group<sup>17</sup> carried out a retrospective review that included 458 patients from different hospitals; although they do not refer a cutoff value for PTH, they recommend its measurement 4 h after surgery and point out that normal PTH values predict normal blood calcium values, and patients can thus be discharged at the 1<sup>st</sup> post-operative day<sup>16,17</sup>. Accordingly, Sywak et al.<sup>28</sup> have also recommended using a single sample taken at 4 h. Grodski and Farrell<sup>23</sup> concluded that patients with post-operative PTH normal values can be safely discharged at the 1<sup>st</sup> postoperative day. In their work, measurements were carried out 4 and 12 h after surgery. On the other hand, in the work by Kim et al.<sup>27</sup>

with 108 patients, a value lower than 10.6 mg/dL 6 h after surgery had a sensitivity of 89%, specificity of 88%, and a positive predictive value of 85%. Calvo Espino et al.<sup>18</sup> demonstrated that a measurement on the 1<sup>st</sup> post-operative day has a sensitivity of 95% and a negative predictive value of 99.6% to demonstrate permanent hypoparathyroidism if PTH values are below 5 pg/mL. Thus, they conclude that, although there are still no absolute values, those obtained in their work can predict those patients at risk due to the high negative predictive value they obtained.

Another key point that also generates discrepancy between authors is the number of samples. Although many suggest a single sample, others prefer repeating the analysis at variable intervals as, for example, every 1, 6, and 12 h; therefore, an extrapolation cannot be made for systematic use. As previously mentioned, the hormone short half-life explains why PTH plateau is reached during the first few minutes after surgery<sup>24,27</sup>. As a consequence of this, many argue that PTH serial measurements would not be justified, since there would be no significant variations between each value. Furthermore, the current evidence allows asserting that a single PTH sample has adequate sensitivity and specificity, regardless of collection timing<sup>7,8,10,29</sup>.

PTH value interpretation is also controversial. Some authors prefer using an absolute PTH value, for example, 5 pg/mL<sup>18</sup>, 10 pg/mL<sup>9</sup>, 8 mg/dL<sup>1</sup>, and 1 pmol/L<sup>3</sup>, while others consider that the highest accuracy is achieved by comparing pre-operative, intraoperative, and post-operative values, that is, relative values. Khafif et al.<sup>21</sup>, in their prospective study with 40 patients, demonstrated a sensitivity of 92% and specificity of 66% when there is 50% decrease between pre-operative PTH values and those determined at 30 min; 23% and 75%, respectively, when PTH decrease is 75% at the same interval; and 46% and 100%, respectively, when an absolute value is taken as the limit (normality). Logically, the lower the established PTH cutoff value, the higher the specificity and the lower the sensitivity. Karatzanis et al.<sup>7</sup>, prospectively enrolling 100 patients, used relative values, indicating calcium at discharge or prolonging hospitalization when the decrease was larger than 56% and 62%, respectively. Regarding current evidence, it can be concluded that both an absolute value and a relative decrease would allow predicting post-operative hypoparathyroidism and hypocalcemia risk. However, relative analysis requires having a baseline value before surgery.

Some authors have associated PTH analysis with that of blood calcium to increase predictive efficacy. Pisanu et al.<sup>9</sup> associated an absolute PTH cutoff value of 12 pg/dL or a decrease equal to or > 70.5% in pre-operative and post-operative PTH (at 6 h) with a blood calcium cutoff value of 7.97 mg/dL taken at 24 h, and demonstrated a sensitivity and specificity of 100% to predict hypocalcemia. Furthermore, Graff et al.<sup>13</sup>, prospectively, also demonstrated an increase in specificity from 83% to 88% for detecting hypocalcemia by combining PTH values (14 pg/dL) with those of blood calcium (8.0 mg/dL), with samples collected 6 h after surgery. Similarly, Kim et al.<sup>25</sup> demonstrated higher sensitivity and specificity by combining PTH and blood calcium. Certainly, these associations imply higher economic costs and in many cases discharge delay (blood calcium taken at 24 h), but they would evidently be associated with an increase in predictive capacity.

Regarding the applicability of PTH use as a clinical predictor, some studies question its use in patients with Vitamin D deficiency and in those with Graves' disease. In their study, Pradeep and Ramalingam<sup>30</sup> analyzed the usefulness of PTH with samples taken 8 h after surgery and found a lower sensitivity to predict hypocalcemia in patients with pre-operative Vitamin D deficiency. According to the authors, this would be justified because patients with this deficit have a later PTH postoperative decrease and higher pre-operative and post-operative PTH absolute values. For these patients, they suggest pre-operative Vitamin D supplementation and later PTH sample collection, at between 12 and 24 h. As for diffuse toxic goiter, Annerbo et al.<sup>31</sup> analyzed PTH variations in patients undergoing thyroidectomy for Graves' disease. In them, monitoring with PTH would not be recommended, since, despite having normal values of this hormone, a not negligible percentage required calcium or Vitamin D supplementation, or both.

## Conclusions

Post-operative hypoparathyroidism is a common and potentially serious complication of total thyroidectomy. It is associated with a significant increase in health costs.

The need for an adequate predictor has motivated numerous studies on the use of PTH. Although the method lacks 100% sensitivity, PTH is almost certainly a predictor that is currently increasingly and safely being used. The current evidence supports its use to stratify patients, alone or accompanied by other

predictors, but questions remain about the best way to implement its use. Most studies show good results during the first 4, 6, and 24 h after surgery. Furthermore, serial blood calcium measurement would benefit patients and health-care centers by reducing processing costs, hospitalization time, and supplementary medication.

The heterogeneity of published studies with regard to sampling intervals, cutoff value, measured variables, etc., threatens the performance of systematic reviews. However, on the other hand, this shows the versatility of the method, even with discrepancies in implementation logistics.

At present, an increasing number of protocols include PTH. Their prospective study will probably allow in the future answering questions that do not have a clear answer today.

## Conflicts of interest

The authors declare that they have no conflicts of interest.

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## Ethical disclosure

**Protection of people and animals.** The authors declare that no experiments were performed on humans or animals for this research.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

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