

# Study on The Effect of Recurrent Laryngeal Nerve Identification Technique in Thyroidectomy on Recurrent Laryngeal Nerve Paralysis and Hypoparathyroidism



## Medical Science

### KEYWORDS :

Thyroidectomy, recurrent laryngeal nerve, hypoparathyroidism

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## ABSTRACT

### AIMS AND OBJECTIVES

1. To study the correlation between the technique of recurrent laryngeal nerve identification i.e superior-inferior OR inferior-superior during thyroidectomy and post operative RLN paralysis.
2. To study the incidence of hypoparathyroidism in relation to the technique of identification of RLN .
3. To study the predictive value of i-PTH in predicting the hypocalcemia in post operative period following total thyroidectomy.

### MATERIAL AND METHODS

This is a prospective study, including all patients who underwent thyroid surgery in the Department of General Surgery & ENT in Gandhi Hospital, Secunderabad and in Government ENT Hospital, Koti from July 2012 to October 2012. The study included 96 patients who underwent surgery for thyroid disorders between July 2012 and October 2012. Patients with multinodular goiter, unimodular goiter, thyroid cancer, thyroiditis, and recurrent goiter were included in the study.

### RESULTS

This is a prospective study, including all the patients who underwent surgery for thyroid disorders from July 2012 to October 2012. The cases were taken from the Department of General Surgery & ENT , Gandhi Hospital and Government ENT Hospital, Koti.

The patients were separated in to 2 groups according to the RLN identification technique.

The first group included thyroidectomies performed in a superior- inferior direction by fixing the nerve where it enters into the larynx, followed by superior pedicle ligation.

The second group included thyroidectomies performed in an inferior- superior direction , following inferior pedicle ligation and determination of the nerve in the tracheoesophageal groove.

Post operative RLN paralysis was observed in 2 patients. None of the patients developed post op hemorrhage or wound infection.

Hypocalcemia was observed in 4 patients out of 12 operated cases. Out of these patients in 3 cases total serum calcium level was lower than 8.0mg/dl

In the group of patients with hypocalcemia the average level if i-PTH 1 hr after surgery was 12.33pg/ml. average level of serum calcium after 24 hr was 7.53 mg/dl

### CONCLUSION

1. Different techniques are followed by different surgeons for identification of recurrent laryngeal nerve during thyroidectomy. The superior-inferior technique has least incidence of RLN injury (nil in our study). Hence superior-inferior technique is recommended for identification of RLN during thyroidectomy.
2. The Superior – Inferior technique for identification of RLN prevents post op hypoparathyroidism.

## INTRODUCTION

Thyroid disorder prevalence is more than 2 billion in the world and with prevalence of more than 40 million in India<sup>[1]</sup> Thyroid disease is being increasingly diagnosed and is one of the commonest non communicable disease.<sup>[2]</sup> Thyroid disorders are among the most commonly seen diseases in the department of General Surgery. Thyroidectomy is one of the frequently performed surgery and Recurrent laryngeal nerve (RLN) paralysis and Hypoparathyroidism are the most serious postoperative complications in thyroid surgery.

Difference of opinion exists in the technique to be adopted to prevent RLN injury. The text book of Bailey and Love states that to prevent injury "RLN should be identified first below the level of inferior thyroid artery, where it runs upwards and forwards in the tracheo esophageal groove ".<sup>[3]</sup> The text book of surgical anatomy by Skandalakis states "visual identification of RLN with avoidance of traction , compression, and stripping of connective tissue should be done to prevent injury"<sup>[4]</sup>

The text book of Mastery of Surgery states "initial step is to divide the superior pole vessels to mobilize the upper lobe. The RLN should always be identified and is visualized after pushing superior parathyroid gland laterally where it enters the larynx on the posterolateral aspect of the cricothyroid muscle."<sup>[5]</sup>

Jatzko et all study shows increased rate of injury (5.2%)

when RLN is not identified compared to when identified(1.2%). Pelizzo et all study states RLN should be identified at the zuckermandles tubercle which is the most posterior extension of the lateral lobe of thyroid gland at the level of ligament of berry.

According to Bayram Veyseller et all study "The RLN should definitely be identified in total thyroidectomies performed using an extracapsular approach. However, excessive dissection of the tracheoesophageal groove during the search for the RLN may devascularize the parathyroid, leading to temporary or permanent hypoparathyroidism".

Thyroidectomies performed for recurrent disease are the reason for the most frequently reported complications: hypoparathyroidism and the RLN paralysis.<sup>[6]</sup> In thyroid surgery, several studies have examined the association between the type of surgery (total, subtotal, or near-total) and prevention of severe complications such as RLN damage and hypoparathyroidism, according to whether the nerve is identified and whether nerve monitoring is used.

Hermann et all, in their review of 16,443 patients who underwent thyroidectomy, showed that the incidence of temporary and permanent RLN paralysis was significantly reduced if the nerve was identified.

Robert et al. in their study quoted an incidence of nerve paralysis three to four times greater in cases in which the recurrent nerve was not localized compared with cases in

which it was identified. However, no prospective study has compared RLN identification techniques.

Two different methods are used for RLN identification during thyroidectomy. The superior-inferior technique which identifies the nerve where it penetrates the larynx, following superior pedicle ligation, and the inferior-superior technique which traces the nerve in the superior direction after identifying it in the tracheoesophageal groove.

In this study, incidence of RLN paralysis and hypocalcemia is compared in thyroidectomies that were performed using 2 different technical paths of RLN identification and also when the RLN was not identified.

Hypocalcemia remains the most common complication after total thyroidectomy. Its reported incidence varies from 0.5% to 50% of operated cases. Following thyroid surgery, hypoparathyroidism may develop owing to the dissection leading to destruction or total removal of the parathyroid glands, decrease of blood flow, or necrosis secondary to hematoma.<sup>[7]</sup> The reported frequency of hypoparathyroidism varies, and the frequency of potential postoperative hypoparathyroidism is affected by the thyroid pathologic characteristics, type of surgery performed, dexterity and experience of the surgeon, and his/her knowledge of parathyroid anatomy.<sup>[6-9]</sup>

The lowest calcium levels are typically recognized 24-48hr after thyroidectomy, though hypocalcemia may be delayed and present on 4<sup>th</sup> POD or later. This leads to longer hospitalisation and increased final cost of treatment. The traditional approach involves in-hospital clinical assessment and monitoring of calcium levels requiring repeated blood sampling.<sup>[10-12]</sup>

The half-life of PTH being 2-5min, it was repeatedly suggested that measurement of intact PTH after thyroidectomy is very useful in prediction of post operative hypocalcemia.<sup>[13-14]</sup>

**This study assesses the correlation between the i-PTH levels after the operation and development of hypocalcemia, i.e the positive predictive value of i-PTH levels will be assessed.**

## MATERIAL AND METHODS

This is a prospective study, including all patients who underwent thyroid surgery in the Department of General Surgery & ENT in Gandhi Hospital, Secunderabad and in Government ENT Hospital, Koti from July 2012 to October 2012. The study included 96 patients who underwent surgery for thyroid disorders between July 2012 and October 2012. Patients with multinodular goiter, uninodular goiter, thyroid cancer, thyroiditis, and recurrent goiter were included in the study.

All patients admitted for surgery of thyroid disease were followed prospectively. Routine surgical profile including CBP, serum creatinine, serum electrolytes, RBS, blood urea, was obtained. Patients with hypertension and diabetes were made fit for the surgery by appropriate anti-hypertensive drugs and daily FBS monitoring. Thyroid profile was obtained for all patients and all patients were in euthyroid state.

All patients underwent FNAC and ultrasonography of the neck and guided FNAC was done for indeterminate or suspicious areas. X-ray neck was done to look for tracheal deviation and compression. Indirect laryngoscopy was done

for all patients and preoperative vocal cord movement was noted.

All surgeries were performed by specialist surgeons by professors or assistant professor. The method of identifying the RLN was based on the preference of the attending surgeon. Also mentioned whether RLN was identified or not during surgery.

The patients were separated into 2 groups according to the RLN identification technique.

The first group included thyroidectomies performed in a superior- inferior direction by fixing the nerve where it enters into the larynx, followed by superior pedicle ligation.

The second group included thyroidectomies performed in an inferior- superior direction, following inferior pedicle ligation and determination of the nerve in the tracheoesophageal groove.

The first, second and third group included 77 and 18 patients respectively.

The first group included 12 total and 65 lobectomy hence 89 RLN dissections were done.

The second group included 1 total and 17 lobectomy hence 19 RLN dissections were done.

Vocal cord function was assessed post operatively by the anesthetist on table and by IDL before the patient was discharged. Data on the incidence of wound infection and hemorrhage was also collected. The patients were followed till the date of discharge. This study compared the complication rates with the two different surgical techniques.

Of the 13 cases of total thyroidectomy, 1 case was excluded from the study regarding assessing the correlation between i-PTH and development of hypocalcemia, as intra operative calcium was given for the patient.

For the remaining 12 cases, total calcium levels before the surgery and 24 hr after the surgery were assessed. The i-PTH level was assessed before and 1 hr after the surgery. Specificity and sensitivity of i-PTH level 1 hr after surgery was calculated aiming to evaluate its potential usage as a predictor of post operative hypocalcemia.

Serum calcium levels were measured in mg/dl with a reference range 8.7-11.0mg/dl. Hypocalcemia was considered when the level was below 8.2mg/dl.

Typical hypocalcemia related symptoms such as paresthesia in the face or upper and lower limbs, nervousness and anxiety were observed.

The reference value for i-PTH were 15-65 pg/ml.

## RESULTS

This is a prospective study, including all the patients who underwent surgery for thyroid disorders from July 2011 to October 2012. The cases were taken from the Department of General Surgery, Gandhi Hospital, Secunderabad.

The study included 96 patients, of which 13 underwent total thyroidectomy and 83 underwent hemi thyroidectomy. 1 patient who underwent isthmectomy was excluded from the study. And out of 13 total thyroidectomies 1 case was excluded as intraoperative Calcium was supplemented.

The patients were separated in to 2 groups according to the RLN identification technique.

The first group included thyroidectomies performed in a superior- inferior direction by identifying the nerve where it enters into the larynx, followed by superior pedicle ligation.

The second group included thyroidectomies performed in an inferior- superior direction , following inferior pedicle ligation and determination of the nerve in the tracheoesophageal groove.

The first, second and third group included 52 and 13 patients respectively.

The first group included 6 total and 46 hemithyroidectomy hence 57 RLN dissections were done .

The second group included 2 total and 11 hence 15 RLN dissections were done.

In about 30 patients RLN was not identified during the surgery.

Post operative RLN paralysis was observed in 2 patients (1.3%) both in group 2 i.e inferior-superior approach. None of the patients developed post op hemorrhage or wound infection.

Thyroidectomy complications :

Complication	S-I group 1	I-S Group 2	RLN – not identified	Total
Wound infection	0	0	0	0
Hemorrhage	0	0	0	0
RLN paralysis	0	2(1.3%)	0	2(1.3%)
Hypocalcemia	1(8.3%)	2(16.6%)	1(8.3%)	4(33.3%)

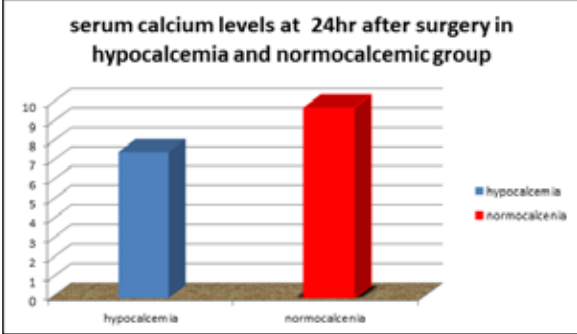
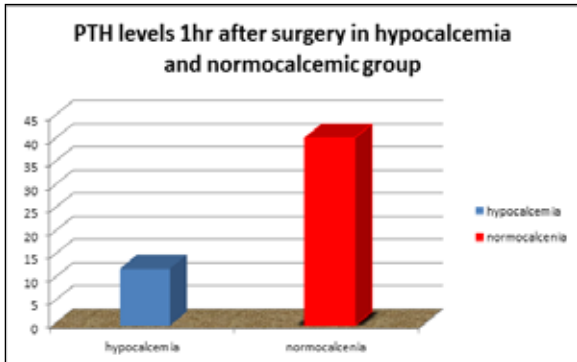
S-I = superior-inferior technique

I-S = inferior-superior technique

Symptomatic hypocalcemia was observed in 4 patients out of 12 operated cases,1 in group 1(8.3%), 2 in group 2(16.6%) and 1 in which RLN was not identified(8.3%). Out of these patients in 3 cases total serum calcium level was lower than 8.2mg/dl

As a result, RLN palsy(1.3%) was only seen in group 2 i.e inferior-superior technique and incidence of hypocalcemia was 4 cases out of 12 (33.3%) of which 2 cases(16.6%) were in group 2.

In the group of patients with symptomatic hypocalcemia the average level if i-PTH 1 hr after surgery was 12.33pg/ml, average level of serum calcium after 24 hr was 7.53 mg/dl



**Sensitivity :**  $(\text{No.of true positives} / \text{No.of true positives} + \text{No.of false negative}) \times 100$

$= (4/4+0) \times 100$

$=100\%$

**Specificity :**  $(\text{No. of true negatives/ No. of true negatives} + \text{no. of false positives}) \times 100$

$= (8/8+0) \times 100$

$= 100\%$

**Positive predictive value** =  $(\text{no.of true positives/ no.of true positives} + \text{no.of false positives})$

$= 4/ 4+0$

$= 1$

Most of the patients in this study are in the age group 21-30yrs (36.4%).

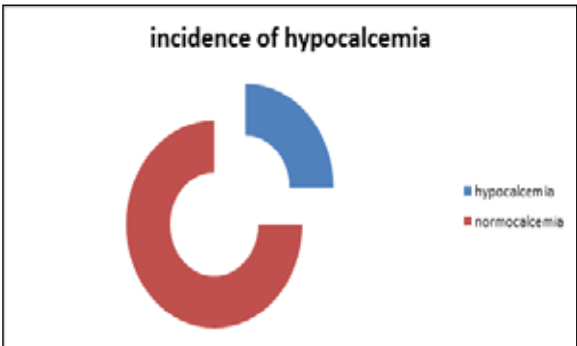
Among the 96 cases of thyroid surgery, majority of them were females with a male to female ratio of 1:6

Solitary nodule is the most common indication for thyroidectomy in this study(64.6%).

**Incidence of Hypocalcemia:**

In this study out of 12 patients who underwent total thyroidectomy, 03 patients developed hypocalcemia in the post-operative period. The incidence of hypocalcemia following total thyroidectomy is 25%.

No. of patients	Hypocalcemia (S.ca ≤ 8.2mg/dl)	No Hypocalcemia (S.ca > 8mg/dl)
12	03(25%)	09(75%)



**Incidence of Symptomatic and Asymptomatic hypocalcemia:**

Symptoms	Hypocalcemia (serum calcium- <8.2mg/dl)	Percent
Symptomatic Patients	03	100%
Asymptomatic Patients	00	0%
Total	03	

In this study, among the 03 patients who developed hypocalcemia (<8mg/dl), symptoms of hypocalcemia were observed all 3 patients (100%)

**Onset of symptoms and signs:**

Day of onset	Cases	Percent
2 <sup>nd</sup> day	2	66.33%
3 <sup>rd</sup> day	1	33.33%
Total	3	

During this study, symptoms and signs of hypocalcemia were observed in 2 out of 3 cases (66.33%) on the 2<sup>nd</sup> post-operative day.

Tingling and numbness was observed to be the initial presenting symptom of hypocalcemia in 66.33% of cases and carpo-pedal spasm (33.3%).

**DISCUSSION****RLN PARALYSIS**

Thyroidectomy is one of the frequently performed surgery and Recurrent laryngeal nerve (RLN) paralysis and Hypoparathyroidism are the most serious postoperative complications in thyroid surgery. Difference of opinion exists in the technique to be adopted to prevent RLN injury.

Two different methods are used for RLN identification during thyroidectomy. The superior-inferior technique which identifies the nerve where it penetrates the larynx, following superior pedicle ligation, and the inferior-superior technique which traces the nerve in the superior direction after identifying it in the tracheoesophageal groove.

In this study, incidence of RLN paralysis and hypocalcemia is compared in thyroidectomies that were performed using 2 different technical paths of RLN identification and also when the RLN was not identified.

In this study the incidence of RLN paralysis is 1.3%. Higher rates of RLN paralysis (1.3%) were observed in thyroidectomies using an inferior-superior technique.

The reported frequency of RLN paralysis is between 0.3% and 1.7% [44]. In 1% to 2% of cases, nerve paralysis due to accidental injury of RLN is reported even by most experienced surgeons.[44]. The result of this study with respect to the incidence of RLN palsy coincides with other studies.

Searching for RLN in the tracheoesophageal groove and following it where it enters the larynx requires more dissection and can lead to nerve injury. The superior-inferior approach to the RLN allows the surgeon reach to the region directly and involves less dissection and less injury to RLN.[45] Lower rates of RLN palsy was observed in thyroidectomies using superior-inferior technique, coinciding with Bayram veyseller et al study where incidence of RLN paralysis was 1.5% seen in inferior-superior technique and nil in superior-inferior technique.

The third group in which RLN was not identified during surgery was very small (10 cases) hence no conclusions could be made.

Of the two RLN paralysis both were seen in cases diagnosed as malignancy, agreeing to previous studies that paralysis of RLN is more common in thyroid cancers.[46-47]

During the surgery, nerve monitoring is a useful tool for identifying the RLN and its major advantage is that it can demonstrate whether the nerve is intact post operatively. Nevertheless, owing to the expense of nerve monitoring, it is not recommended in all cases. Nerve monitoring is recommended in revision surgery, thyroid cancer, patients with retrosternal extension or a giant goiter, and those who previously received radio therapy.[48-49]

**HYPOPARATHYROIDISM**

The incidence of hypoparathyroidism in this study was 25%, as seen in several studies reporting frequency from 1.6% to 50%. [44,46,50-52] Incidence of hypocalcemia was less (8.3%) in superior-inferior technique compared to inferior-superior technique (16.6%), which was also reported in Bayram Veyseller et al study, incidence of 7.4% in superior-inferior technique and 22% in inferior-superior technique.

Rimple et al [53] demonstrated that postoperative hypocalcemia was caused by extensive thyroid resection and parathyroid gland manipulation

Searching for RLN in the tracheoesophageal groove and following it where it enters the larynx requires more dissection and can lead to parathyroid devascularisation, which can cause ischemia and necrosis and lead to hypoparathyroidism. The superior-inferior approach to the RLN allows the surgeon reach to the region directly and involves less dissection and less parathyroid damage.[45]

Meticulous hemostasis and the delicate technique are required to prevent nerve and parathyroid gland injury. Systematic dissection of RLN reduces RLN paralysis but increases hypoparathyroidism, mainly by devascularising the parathyroid glands.[54]

In this study, lower rates hypoparathyroidism were observed in thyroidectomies using superior-inferior approach.

**i-PTH ESTIMATION**

This study showed that the i-PTH level estimated at 1 hr after surgery is a reliable predictor of hypocalcemia after total thyroidectomy. Hence, i-PTH level estimation at 1 hr after surgery can identify the patients who are at risk of hypocalcemia. Similar results were seen a study by Monika proczko et al. [55]

The prospective analysis of perioperative i-PTH kinetics could help to explain the mechanism of postoperative hypoparathyroidism and calculate the cut off iPTH levels prognostic for postoperative hypocalcemia. Robert et al study suggest that early postoperative total or ionized calcium levels predicts hypoparathyroidism after total thyroidectomy.[56-57] Intra operative iPTH levels are thought to be an accurate predictor of symptomatic hypocalcemia[58], but this method can not be used in many surgical centres due to financial conditions.

The alternative method could be the early post operative measurement of i-PTH to identify the patients at risk of developing hypocalcemia.

In our study, i-PTH levels were 1hr after surgical procedure and strong correlation was found between i-PTH level measured 1 hr after surgery i.e 1 hr after skin suturing, on the development of hypocalcemia. We presume that early

postoperative measurement of PTH might be as accurate as results obtained several hours after surgery, because the half life of PTH is 2-5 min.

In other trials different combinations of PTH and calcium measurement were also used. Payene et al. published results of PTH measurements at 6,12,20 hr after thyroidectomy, concluding that PTH and calcium level at 6 hr accurately identified patients at risk of PTH levels after surgical precedure.<sup>[59]</sup>

In other studies compared PTH levels assessed 1-12 hr post operatively with those of 24hr, finding that early results are equally accurate.

As a result, PTH levels measured 1 hr after surgery is a good predictor of post operative hypocalcemia with sensitivity of 100%. There were no cases in this study with hypocalcemia and reference PTH levels.

## CONCLUSION

Different techniques are followed by different surgeons for identification of recurrent laryngeal nerve during thyroidectomy. The superior-inferior technique has least incidence of RLN injury (nil in our study). Hence superior-inferior technique is recommended for identification of RLN during thyroidectomy.

The Superior – Inferior technique for identification of RLN prevents post operative hypoparathyroidism.

The i-PTH level estimated at 1 hr after surgery is a reliable predictor of hypocalcemia after total thyroidectomy. Hence, i-PTH level estimation at 1 hr after surgery can identify the patients who are at risk of hypocalcemia. This will facilitate the management and prevention of hypocalcemia and its complication.

## References:

- Shah Joshi SR. Goitre and Goitrogens- some insights. *JAPI* 2000;48:13-14
- Shah SN, Joshi SR. Thyroid as an endocrine organ. *JAPI* 2000;48:7-8
- Text book of Bailey and Love 25<sup>th</sup> edition
- Text book of surgical anatomy –Skandalakis.
- Text book of Mastery of Surgery by Fischer, 6<sup>th</sup> edition.
- Chao TC, Jeng LB, Lin JD, Chen MF. Reoperative thyroid surgery. *World J Surg.* 1997;21(6):644-647
- Lo CY. Parathyroid autotransplantation during thyroidectomy. *ANZ J Surg.* 2002;72(12):902-907
- Bellantone R, Lombardi CP, Bossola M, et al. Total thyroidectomy for management of benign thyroid disease: review of 526 cases. *World J Surg.* 2002;26(12):1468-1471
- Giles Y, Boztepe H, Terzioğlu T, Tezelman S. The advantage of total thyroidectomy to avoid reoperation for incidental thyroid cancer in multinodular goiter. *Arch Surg.* 2004;139(2):179-182
- Schwartz AE, Clark OH, Ituarte P et al.: Therapeutic controversy: Thyroid surgery - the choice. *J Clin Endocrinol Metab* 1998; 83:1097-1105.
- Lo Gerfo P, Gates R, Gazetas P: Outpatients and short-stay thyroid surgery. *Head Neck* 1991; 13:97-101.
- McHenry CR: "Same-day" thyroid surgery: an analysis of safety, cost savings, and outcome. *Am Surg* 1997; 63: 586-89; discussion 589-90.
- Higgins KM, Mandell DL, Govindaraj S et al.: The role of intraoperative rapid parathyroid hormone monitoring for predicting thyroidectomy - related hypocalcemia. *Arch Otolaryngol Head Neck Surg* 2004; 130: 63-67.
- Barczyński M, Cichoń S, Konturek A et al.: Applicability of intraoperative parathyroid hormone assay during total thyroidectomy as a guide for the surgeon to selective parathyroid tissue autotransplantation. *World J Surg* 2008; 32: 822-28.
- Mishra A, Agarwal A, Agarwal G, Mishra SK. Total thyroidectomy for benign thyroid disorders in an endemic region. *World J Surg.* 2001;25(3):307-310
- Chao TC, Jeng LB, Lin JD, Chen MF. Reoperative thyroid surgery. *World J Surg.* 1997;21(6):644-647

- Bron LP, O'Brien CJ. Total thyroidectomy for clinically benign disease of the thyroid gland. *Br J Surg.* 2004;91(5):569-574
- Cohen-Kerem R, Schachter P, Sheinfeld M, Baron E, Cohen O. Multinodular goiter: the surgical procedure of choice. *Otolaryngol Head Neck Surg.* 2000;122(6):848-850
- Megherbi MT, Graba A, Abid L, Oulmane D, Saidani M, Benabadji R. Complications and sequelae of benign thyroid surgery. *J Chir (Paris).* 1992;129(1):41-46
- Rimpl I, Wahl RA. Surgery of nodular goiter: postoperative hypocalcemia in relation to extent of resection and manipulation of the parathyroid glands. *Langenbecks Arch Chir Suppl Kongressbd.* 1998;1151063-106
- Friedman M, Pacella BL Jr. Total versus subtotal thyroidectomy: arguments, approaches, and recommendations. *Otolaryngol Clin North Am.* 1990;23(3):413-427
- Bhattacharyya N, Fried MP. Assessment of the morbidity and complications of total thyroidectomy. *Arch Otolaryngol Head Neck Surg.* 2002;128(4):389-392
- Thomusch O, Machens A, Sekulla C, et al. Multivariate analysis of risk factors for postoperative complications in benign goiter surgery: prospective multicenter study in Germany. *World J Surg.* 2000;24(11):1335-1341
- Rimpl I, Wahl RA. Surgery of nodular goiter: postoperative hypocalcemia in relation to extent of resection and manipulation of the parathyroid glands. *Langenbecks Arch Chir Suppl Kongressbd.* 1998;1151063-1066
- Megherbi MT, Graba A, Abid L, Oulmane D, Saidani M, Benabadji R. Complications and sequelae of benign thyroid surgery. *J Chir (Paris).* 1992;129(1):41-46
- Monika proczko-Markuszevska, Jaroslaw Kobiela. Postoperative PTH measurement as a predictor of hypocalcemia after thyroidectomy. *przegląd Chirurgiczny.* 2010;82(1):24-28
- Luu Q, Anderson PE, Adams J et al. The predictive value of perioperative calcium levels after thyroid/parathyroid surgery. *Head neck* 2002;24:63-67
- Moore C, Lampe H, Agrawal S. Predictability of hypocalcemia using early post-operative serum calcium levels. *J Otolaryngol* 2001; 30:266-70.
- Richards ML, Bingener-Casey J, Pierce D et al. Intraoperative parathyroid hormone: an accurate predictor of symptomatic hypocalcemia following thyroidectomy. *Arch Surg* 2003;138:632-35.
- Payne RJ, Hier MP, Tamilia M et al. Post operative parathyroid hormone assay predicts hypocalcemia after total thyroidectomy. *ANZ Surg* 2007; 77:362-67.