Early discharge after total thyroidectomy: a retrospective feasibility study

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SUMMARY: **Early discharge after total thyroidectomy: a retrospective feasibility study.**

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Aim. *The continued hospitalization after total thyroidectomy is often due to the onset of hypocalcemic complications more than 24 hours after surgery. So it would be important to predict which patients will not develop the hypocalcemic complication to discharge them early. This was the aim of our study.*

Patients and methods. *Our retrospective study was conducted on 327 consecutive thyroidectomized patients, operated on for benign and malignant diseases. We evaluated the values of preoperative serum calcium levels (Cal0) and of the first postoperative day (Cal1) and two new variables were calculated (dCal and dCaln). The same thing was made on a subgroup of 111 patients in whom also parathiroyd hormone (PTH) values were detected. Statistical analysis was performed with the goal of determining if we could establish a safe criterion for discharge at 24 hours after surgery and if there is a correlation between suitability for discharge and diagnosis.*

Results. *As to discharge, the predictive power of the discriminant function applied was significant both on the total of patients and in the subgroup of 111 patients, but it was clinically unacceptable because it would expose us to a 21% to 27% error rate. It is not possible to identify a threshold, below which to consider patients surely dischargeable. The diagnosis does not appear correlated with the suitability for discharge.*

Conclusion. *On the basis of serum calcium and PTH levels in the first postoperative day, it is impossible to predict which patients can be discharged 24 hours after surgery without incurring in hypocalcemic complications.*

KEY WORDS: Total thyroidectomy - Early discharge - Hypocalcemia - Postoperative bleeding - Recurrent laryngeal nerve palsy.

Introduction

In the last years the need to contain health spending has been a must to research the possibility of outpatient surgical services, day hospital and day surgery, for an increasing number of diseases (1, 2). Thyroid surgery was no exception. In Italy thyroid surgery is performed on an inpatient basis, mostly consisting in short admissions in week surgery departments with discharge to 48-72 hours after surgery, but several were the contributions in the literature in favour of an early discharge surgery (3-7), and some recommend at least an overnight stay (8, 9). In the United States for years outpatient surgery with discharge on the same day of surgery has had a broad appeal and the rate of thyroid surgical procedures on an outpatient basis over the past 10 years has risen to 39% (10), thanks to the use of outstanding centers.

The causes that are opposed to early discharge are possible bleeding complications, inferior laryngeal nerves palsy and hypocalcemia (11-14), but unlike the first two which are generally well detectable within the first 24 hours after surgery, the latest one is called into question, as often detectable beyond 24-48 hours after surgery (6, 15-20).

Therefore in recent years the goal of researchers has been to predict which patients will undergo postoperative hypocalcemia or worse symptomatology related to it which could lead to a readmission in Hospital, through the evaluation of certain parameters that could have this predictive role. In particular total serum calcium, ionized calcium, the serum phosphorus, serum intact PTH have been used with different qualitative and

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quantitative methods, that make it difficult to compare across studies (21-30, 31, 32, 33). We too in the past published our studies on the subject (34-40) without getting to definitive results. Still open is also the controversy about postoperative calcium and Vit. D supplementation as prophylaxis of hypocalcemia (40-44) and the influence that the malignancy can determine on the percentage of transient or permanent hypoparathyroidism (45-48).

The aim of this study was to assess whether, having only the serum calcium and PTH values of preoperative and in the first postoperative day, we can identify with sufficient certainty, that is, making few mistakes, which patients can be discharged 24 hours after total thyroidectomy without incurring in hypocalcemic complications that could lead to a readmission in Hospital.

Patients and Methods

Our retrospective study considered 355 consecutive patients treated by total thyroidectomy in our Department, both for benign and neoplastic disease, between January 1, 2013 and June 30, 2016. Exclusion criteria from the study were: completion thyroidectomy, Basedow disease, association of central and/or laterocervical lymphadenectomy procedures, autotransplantation of the parathyroid glands during surgery, occurrence of postoperative bleeding that led to a new surgery, onset of mono or bilateral inferior laryngeal nerves palsy, medications that interfere with the metabolism of calcium. Therefore, the number of patients who met the inclusion criteria of the study were 327 in total, 58 men (17.74%) and 269 women (82.26%). The average age was 53.25 years of total patients (57.2 for men and 52.42 for women).

The values of preoperative serum calcium (Cal0) and in the first day after surgery (Cal1) were evaluated and two new variables (dCal and dCaln) were calculated, corresponding respectively to the difference and the normalized difference in percentage between the preoperative serum calcium values and those of the the first day after surgery (dCal = Cal0 - Cal1; dCaln = dCal/Cal0x100).

In 111 of 327 patients preoperative PTH values (PTH0) and on the first postoperative day (PTH1) were also reported.

Even for PTH two new variables were constructed (dPTH and dPTHn), corresponding respectively to the difference and the normalized difference in percentage between the preoperative PTH values and those of the first postoperative day (dPTH = PTH0 - PTH1; dPTHn = dPTH/PTH0x100).

We classified patients retrospectively into "dischargeable" or "not dischargeable", on the basis of their postoperative courses and the presence or absence of signs and / or symptoms of hypocalcemia.

We then divided the total of patients into two groups: benign (Diag=0) and neoplastic (Diag=1), according to the definitive histological diagnosis, to see if the presence or absence of neoplasia could influence the performance of the considered variables and the suitability for discharge. In the entire group neoplastic patients were 83, while the benign ones were 244. In the subgroup of 111 patients with PTH values there were 26 neoplastic and 85 benign patients.

The statistical analysis of data was performed with linear discriminant analysis and with two-way analysis of variance (ANOVA); the correlation coefficients were calculated with Pearson's coefficient; the Student t test was used to compare the two groups of suitability for discharge. A p <0.05 was considered as significant.

Results

Descriptive statistics on the entire set of 327 patients tell us that the dCal value is on average 1.06 mg/dl (SD 0.77), corresponding to a decline average of 11.34% (SD 28.8) while in the 111 patients who also had the PTH values, the dPTH was an average of 24.92 pg/L (SD 24.47) (Table 1).

Patients safely dischargeable to 24 hours after surgery were 228 (69.72%) and those not dischargeable were 99 (30.28%).

We then applied a discriminant function to find the best linear criterion, function of the 4 parameters of difference (dCAL, dCaln, dPTH, dPTHn), to separate the two groups of suitability for discharge making the fewest errors. Applying the discriminant function to the total of patients we see that the criterion has a significant but rather low predictive power, at around 73.25%. The same procedure applied to the group of 111 patients with PTH values also shows a predictive power that reaches 78.75% (Table 2).

The next step was to see if we could identify a threshold, of one or more variables, that would allow us to discharge safely (below the threshold) a patient in

TABLE 1 - DESCRIPTIVE STATISTICS OF THE ENTIRE GROUP OF PATIENTS (N=327) AND OF THE SUBGROUP OF PATIENTS WITH PTH VALUES (N=111).

Variable	N	Mean	StdDev
dCal	327	1.06	0.77
dCaln	327	11.34	8.21
dPTH	111	24.92	24.47
dPTHn	111	45.97	37.48

Table 2 - DISCRIMINANT ANALYSIS. NUMBER OF OBSERVATIONS (ENTIRE GROUP AND PTH GROUP) AND PERCENT CLASSIFIED INTO DISCHARGE24H. THE CASES YES-YES AND NO-NO (IN BOLD) ARE THE RIGHT PREDICTIONS.

Entire group			
For Discharge24h	No	Yes	Total
No	**69** **69.70%**	30 30.30	99 100.00%
Yes	61 26.75%	**167** **73.25%**	228 100.00%
Total	130 39.76%	197 60.24%	327 100.00%
PTH subgroup			
For Discharge24h	No	Yes	Total
No	**24** **77.42%**	7 22.58%	31 100.00%
Yes	17 21.25%	**63** **78.75%**	80 100.00%
Total	41 36.94%	70 63.06%	111 100.00%

the first postoperative day, agreeing to have false positives (not discharging dischargeable patients) but not false negatives (discharging not dischargeable patients). This can be achieved only if there is a sufficient number of dischargeable patients below the not dischargeable patient with the lowest delta. The two groups are significantly different for all 4 parameters but observing the minimum and the maximum values it is not possible to achieve the desired purpose (Table 3).

Finally, we applied the same statistical tools, dividing patients according to the diagnosis. Descriptive statistics tell us that there are major differences between the two groups, but we wanted to control, with a two-way analysis of variance (GLM procedures), if the differences between dischargeable and not dischargeable patients were different entities for the two diagnostic groups (malignant/benign).

The result is that there are small but significant differences for dCal and dCaln in the malignant / benign comparison, but no significant difference in the interaction between the suitability for discharge and diagnosis (Table 4).

Table 3 - THE CLASSIC t-test (POOLED) IS USED AS THE VARIANCES IN THE TWO GROUPS ARE COMPARABLE, THEREFORE THE SATTERTHWAITE CORRECTION IS NOT NECESSARY.

t-Tests					
Variable	Method	Variances	DF	t Value	Pr> |t|
dCal	Pooled	Equal	325	6.79	<.0001
dCal	Satterthwaite	Unequal	168	6.49	<.0001
dCaln	Pooled	Equal	325	7.13	<.0001
dCaln	Satterthwaite	Unequal	169	6.82	<.0001
dPTH	Pooled	Equal	109	5.50	<.0001
dPTH	Satterthwaite	Unequal	40.5	4.60	<.0001
dPTHn	Pooled	Equal	109	4.92	<.0001
dPTHn	Satterthwaite	Unequal	64.4	5.31	<.0001
The MEANS Procedure					
Discharge24h=yes					
Variable	N	Mean	StdDev	Minimum	Maximum
dCal	228	0.88	0.69	− 0.90	2.60
dCaln	228	9.35	7.36	− 10.58	26.80
dPTH	80	17.85	18.66	− 19.50	72.70
dPTHn	80	36.06	35.50	− 43.03	93.39
Discharge24h=no					
Variable	N	Mean	StdDev	Minimum	Maximum
dCal	99	1.47	0.78	− 2.00	3.20
dCaln	99	15.91	8.24	− 23.25	34.40
dPTH	31	43.15	28.32	− 14.60	102.20
dPTHn	31	71.54	29.91	− 32.15	95.68

TABLE 4 - TWO-WAY ANALYSIS OF VARIANCE (GLM PROCEDURE). IN BOLD SIGNIFICATIVE VALUES.

The GLM Procedure					
Dependent Variable: dCal (327 observations)					
Source	DF	Type I SS	Mean Square	F Value	Pr> F
Diag	1	2.70	2.70	5.14	0.02
Discharge24h	**1**	**22.26**	**22.26**	**42.27**	**< 0.0001**
Diag*Discharge24h	1	0.99	0.99	1.89	0.17
Dependent Variable: dCaln (327 observations)					
Source	DF	Type I SS	Mean Square	F Value	Pr> F
Diag	1	318.42	318.42	5.47	0.02
Discharge24h	**1**	**2719.38**	**2719.38**	**46.70**	**< 0.0001**
Diag*Discharge24h	1	112.89	112.89	1.94	0.16
Dependent Variable: dPTH (111 observations)					
Source	DF	Type I SS	Mean Square	F Value	Pr> F
Diag	1	1415.98	1415.98	2.98	0.08
Discharge24h	**1**	**12997.63**	**12997.63**	**27.36**	**< 0.0001**
Diag*Discharge24h	1	627.31	627.31	1.32	0.25
Dependent Variable: dPTHn (111 observations)					
Source	DF	Type I SS	Mean Square	F Value	Pr> F
Diag	1	2268.29	2268.29	1.92	0.16
Discharge24h	**1**	**25955.56**	**25955.56**	**22.00**	**< 0.0001**
Diag*Discharge24h	1	89.07	89.07	0.08	0.78

As expected, the discriminant analysis predictive power is always the same, at around 70%, as in the global set, for the two separate groups (a bit higher, at around 80%, for patients with benign diagnosis in the PTH subgroup) (Table 5).

Similar arguments are for the correlations between parameters within classes that follow the same pattern of the undivided group.

Discussion

The possibility to perform thyroid surgery in day surgery regimen must be obviously linked to the achievement, in a shorter time, of the same results as in traditional surgery regimen. Major complications of thyroid surgery that may object to an early discharge are well known and consist essentially in postoperative bleeding, inferior laryngeal nerves palsy and especially hypocalcemia. Risk factors for thyroid surgery complications include older age, male sex, thyroid malignancy, greater extent of operation, reoperative procedures, increasing nodule size, and surgeon inexperience (49, 50). Recent improvements in hemostasis (including proliferation of advanced energy devices), widespread implementation of nerve monitoring, and routine postoperative calcium supplementation appear to have decreased these risks (51). The bleeding is usually evident within the first 24 hours after surgery and more frequent in the first 6 postoperative hours, being late hemorrhages rare (8, 50, 52). Inferior laryngeal nerves palsy also generally arises early, in about 87% of cases, with the appearance of dysphonia within the first 24 hours after surgery, but later onsets are also described, up to 14 days after surgery, in the remaining 13% of cases (53-57). Conversely postoperative hypocalcemia may also occur after 48-72 hours after surgery, and is the most common cause of prolonged hospitalization after thyroid surgery (15, 58). Transient hypocalcemia may occur in 25% of patients undergoing bilateral thyroid surgery and is permanent in 0.9-14% of cases (59, 60). So, predicting which patients will be affected by hypocalcemic complication within the first 24 hours, is critical for planning an early discharge. There are many studies in the literature that have used determination of serum calcium and PTH in the immediate postoperative hours, as predictive values for hypocalcemia, In our study we also used these parameters, because they are of easier acquisition, but comparing these to the preoperative values, convinced that the predictive value against suitability for discharge is related more to the variation of these pa-

TABLE 5 - DISCRIMINANT ANALYSIS. THE CASES YES-YES AND NO-NO (IN BOLD) ARE THE RIGHT PREDICTIONS.

Entire group		
Number of Observations (No) and percent classified into Discharge24h		
Diag=Benign		
From discharge24h	No	Yes	Total

From discharge24h	No	Yes	Total
No	**44** **70.97%**	18 29.03%	62 100.00%
Yes	44 24.18%	**138** **75.82%**	182 100.00%
Total	88 36.07%	156 63.93%	244 100.00%
Diag=Cancer			
From discharge24h	No	Yes	Total
No	**25** **67.57%**	12 32.43%	37 100.00%
Yes	15 32.61	**31** **67.39**	46 100.00%
Total	40 48.19	43 51.81	83 100.00%

PTH subgroup			
Number of Observations (No) and percent classified into Discharge24h			
Diag=Benign			
From discharge24h	No	Yes	Total
No	**16** **84.21**	3 15.79	19 100.00%
Yes	10 15.15	**56** **84.95**	66 100.00%
Total	26 30.59	59 69.41	85 100.00%
Diag=Cancer			
From discharge24h	No	Yes	Total
No	**8** **66.67**	4 33.33	12 100.00%
Yes	4 28.57	**10** **71.43**	14 100.00%
Total	12 46.15	14 53.85	26 100.00%

the best straight-line basis, according to the 4-parameter difference (dCal, dCaln, dPTH, dPTHn), to separate the two groups of suitability for discharge making fewer errors. The discriminant function is immediately usable by multiplying its coefficients to the values for each patient. You have thus obtained a score for the "no" and a score for the "yes". If the score for the no is higher than the score for the yes, the patient is not dischargeable and vice versa. The matrix that is generated is called "confusion matrix" where the rows are the true state of suitability for discharge observed, while the columns are the forecasts of the mathematical criterion (discriminant function). The yes-yes and no-no cases are the right predictions, the others are errors. The predictive power of the criterion for the entire group of patients, around 73%, appeared significant, but still too low and clinically unacceptable because it is unthinkable to apply it without incurring in the 27% of errors. Although the predictive power, calculated only on the group of patients with the values of PTH, is significant and with an almost 79% higher value, even in this case the clinical inapplicability is evident, since in any case we would experience a 21% rate of error. Then the determination of PTH adds something in terms of predictability but it is not sufficient.

Even the attempt to identify a threshold value of one or more parameters that allow us to safely discharge a large number of patients agreeing to have false positives (not discharging dischargeable patients) but not false negatives (discharging not dischargeable patients) has not produced the desired results, as observing the minimum and maximum values of the two groups, it appears how the threshold below which we can be sure that the patient is dischargeable would identify only a small number of patients.

Finally the analysis made by dividing patients according to the diagnosis (benign vs malignant) has shown us that, apart from the great differences already known about the suitability for discharge, there are slightly significant differences for dCal and dCaln but no differences in the interaction between suitability for discharge and diagnosis in the two groups. This means that although there is a global difference in serum calcium values between benign patients and those with cancer, this difference is unsignificant as to the differential suitability for discharge of the two groups, because the differences dischargeable/not dischargeable are of the same magnitude.

Several studies have shown that the costs of traditional thyroid surgery are significantly higher than those of thyroid surgery in the short hospitalization regimen (61-63), but we believe that, beyond a fair health economical planning, patient safety must always be a priority.

rameters than to their absolute value. For this purpose we have built dCal, dCaln, dPTH and dPTHn variables. Descriptive statistics have revealed to us how the difference between the preoperative serum calcium values, and those in the first postoperative day was 1.06 mg/dl on average, while the dPTH was an average of 24.92 pg/L. So not particularly big differences.

We then applied a discriminant function to find

Conclusion

Our study has shown that no one can use the values of serum calcium and PTH, 24 hours after total thyroidectomy, to define which and how many patients can be discharged without incurring in hypocalcemic complication. Of course, along with laboratory criteria, also clinical considerations can affect the choice. We believe that early discharge to 24 hours after surgery, in the absence of structures such as American outstanding centers, is not safe and we will continue to monitor our patients for at least 48 hours after surgery, until a safe criterion of early discharge is identified.

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