Quality of Life after Total Parathyroidectomy in Patients with Secondary Hyperparathyroidism

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Research

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Abstract

Background. Patients with end-stage renal disease (ESRD) have a decreased quality of life (QoL), which is attributable in part to secondary hyperparathyroidism (SHPT). Surgery is the definitive treatment for SHPT. The aim of this study is to assess the effect of total parathyroidectomy (PTX) with deltoid autotransplantation on QoL.

Methods: A total of 201 ESRD patients with SHPT were enrolled. The operation efficacy was evaluated by analyzing preoperative and postoperative values, including the levels of intact parathyroid hormone (PTH), serum phosphorus, serum calcium, alkaline phosphatase (ALP) and calcium-phosphorus product. The QoL was evaluated by scores on the Medical Outcomes Study 36-item short-form (SF-36) health survey preoperatively and 6 months postoperatively.

Results: Compared with preoperatively, postoperatively, the levels of iPTH (2033 pg/ml vs 62.5 pg/ml), serum phosphorus (2.30 mg/dl vs 1.60 mg/dl), serum calcium (3.62 mg/dl vs 1.84 mg/dl), and calcium-phosphorus product were all decreased. Variations in the number and anatomic location of thyroid glands were found in the patients. QoL improved significantly in all 8 individual and 2 component summary scales, with a more significant decrease in the physical health scales.

Conclusion: PTX significantly improves QoL in patients with SHPT.

Introduction

In the past 10 years, chronic kidney disease has received increasing attention as a leading public health problem. The overall prevalence of chronic kidney disease is 10.8% in China and 13.0% in the USA.[1]

Chronic renal failure is the cause of serious alterations in parameters related to mineral metabolism. Underlying renal disease leads to calcium excretion and loss, inability to activate vitamin D, and hyperphosphatemia. This ultimately results in hypocalcemia and ongoing parathyroid gland stimulation.[2] Furthermore, hyperparathyroidism (HPT) contributes to progressive disturbances in calcium-phosphate homeostasis and, eventually, to hypercalcemia.[3]

Secondary HPT (SHPT) is an adaptative process that ultimately becomes maladaptive in response to an impairment of renal function. Elevated parathyroid hormone (PTH) levels are associated with many complications, such as psychological and neurological disorders, mineral bone disorders, ectopic calcifications in the cardiovascular system, malnutrition, and inflammation.[4] These complications can severely compromise the quality of life (QoL) of already impaired SHPT patients due to both the symptoms of end-stage renal disease (ESRD) itself and the burden of dialysis treatment.[5] SHPT occurs commonly in patients with ESRD (30–50%).[6] In one study, the prevalence was as high as 90% by the time ESRD was achieved.[7]

Parathyroidectomy (PTX) can significantly reduce serum PTH levels and, to a lesser degree, phosphate levels, but PTX can exacerbate hypocalcemia.[7] The Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend PTX in patients with severe HPT (> 800 pg/mL) who are refractory to medical therapy.[8] The beneficial effects of PTX for SHPT have been reported by quite a few studies.[9–12] After PTX, serum Ca and P levels generally reach the recommended target values easily.(9) Bone metabolism(10) and diastolic cardiomyopathy(11) are markedly improved, and they also reduce the incidence of major cardiovascular events. Bone pain, malaise, pruritus and calciphylaxis are likely to improve after PTX.(12)

The aim of this study is to assess the evolution of QoL in patients with SHPT and ESRD who receive surgical treatment and to identify the different clinical, biological and pathological variables that influence this evolution.

Materials And Methods

Subjects

During a 5-year period, from July 2013 to July 2018, a series of 201 consecutive unselected patients with SHPT underwent total PTX by a single surgical team.

All patients had been on peritoneal dialysis or hemodialysis for more than three months, were older than 18 years of age, had no mental disorders, were able to speak clearly, and had no evidence of malignancy. During hospital admission, we explained the research purposes to the potential subjects and their families and obtained informed consent. Demographic, biochemical, radiological, operative, and histological details were recorded in a prospective database. Demographic data included age, sex, education, occupation, primary disease that resulted in ESRD, dialysis modality (hemodialysis or peritoneal dialysis), dialysis frequency, total months of dialysis, and the presence of other chronic diseases. Routine blood biochemistry, blood cell counts, and serum calcium, inorganic phosphate, and PTH levels were measured preoperatively, on the day after the operation, 5-7 days postoperatively and at a scheduled 6-month follow-up visit.

QoL and symptom measurement tools

QoL was measured using the Medical Outcomes Study 36-item short-form (SF-36) health survey(21) adapted for the Chinese population.(22) This instrument was selected because it is practical, well suited for clinical use, and inexpensive, and it has been validated in a variety of disease conditions in adults, including those with ESRD.(23) The SF-36 is a commonly applied questionnaire with 36 simple questions pertaining to eight health domains. Each dimension can be transformed into a 0–100 scale, where a higher score represents better self-perceived well-being and QoL. By means of 36 simple questions that are scored from 1 to 6, the SF-36 allows reproducible measures of patient perceived wellness on eight dimensions: physical functioning (PF), social functioning (SF), role functioning emotional (RE), role

functioning physical (RP), vitality (VT), pain (BP), mental health (MH) and general health (GH). These eight domains are divided into two summery scores: the physical component summary (PCS) score and the mental component summary (MCS) score.

Patients completed the SF-36 questionnaire at 2 distinct times: after admission, prior to surgery and at the 6-month follow-up.

Statistical analysis

Data analysis was performed by SPSS software, version 20 (SPSS, Chicago, IL). Non-skewed data are presented as the mean ± standard deviation (SD). Skewed data were analyzed by using the Anderson-Darling Normality Test and are presented as median values. As appropriate for the presented data, the Wilcoxon Matched-Pairs Signed-Ranks Test for paired observations, independent sample t-tests, paired sample t-tests, and the Pearson chi2 test were used to identify any correlations between the clinical data, laboratory values, SF-36 scores and surgery responses. A conservative alpha for any correlation was set at $p < 0.01$.

Results

From July 2013 to December 2018, 201 patients with SHPT and ESRD were prospectively enrolled in the study. All patients were enrolled in a dialysis protocol at admission.

Patient history and demographic data are listed in Table 1. The male/female ratio was almost 2:1. The median patient age at dialysis was 78 months. Except for ESRD, which was significant, the most common causes of SHPT were hypertension, coronary heart disease, anemia, diabetes and chronic viral hepatitis. Three patients received a kidney transplant, but all were placed back on dialysis years later.

Table 1
Preoperative patient characteristics

Variables	No. of pts.	Percentage %	Mean ± SD
Sex (male/female)	134/67		
Age (years)			46 ± 12
Duration of dialysis (months)			78 ± 34
Diabetes	13	6.5	
Hypertension	178	88.8	
Stroke history	50	25.2	
Drinking history	48	24.3	
Renal transplant history	4	2.0	

The most common indication for PTX was failure to control PTH levels; 197 patients (98.0%) had a preoperative PTH level > 800 pg/ml. The median preoperative value of PTH was 2033 pg/ml. The preoperative blood calcium level was 3.62 mmol/L (Table 2). All patients underwent total PTX with autotransplantation.

Table 2
Laboratory data before and after surgery

Variables	Preoperative	Postoperative	6 months
Calcium (mg/dl)	3.62	1.84	1.99
Phosphorus (mg/dl)	2.30	1.60	1.43
PTH (pg/ml) (months)	2033.6	62.5	149.68

However, in only 186 (92.5%) patients, the PTH levels decreased to normal 7 days postoperatively. Thirteen patients still had PTH levels > 200 pg/ml. Five patients underwent reoperation months later, and PTH levels finally decreased to normal. The rest of the patients are currently under observation.

In 162 (80.60%) patients, 4 glands were found, and 3 glands were found in 21 (10.45%) patients. Four of the patients underwent reoperation, and the left gland was found. In 11 (5.47%) patients, 5 glands were found. There was only 1 patient who had 6 glands. However, 2 glands were found in 2 (0.9%) patients, and 1 gland was found in 5 (2.49%) patients, whose PTH levels decreased to normal after the operation (Fig. 1).

The anatomic locations of the parathyroid glands also varied. Glands were found in the thoracic cavity in 4 (2.3%) patients, the thyroid gland in 4 (2.3%) patients, the posterior esophagus in 3 (1.72%) patients and the carotid sheath in 1 (0.57%) patient (Fig. 2).

As expected, the PTH levels decreased significantly after surgery to a median of 62.5 pg/ml, with 186 patients having PTH levels within normal limits 7 days postoperatively and 191 patients 6 months postoperatively (Table 2). All patients required calcium supplementation after surgery, and normalization occurred in 2 to 7 days. Three patients received emergency dialysis because of hyperkalemia. There were no other postoperative complications reported, such as bleeding or recurrent laryngeal nerve injury.

The responses to the SF-36 health survey are shown in Table 3. The surveys completed prior to surgery showed that SHPT patients had lower scores than the general population in all 8 individual and 2 component summary scales, with a more significant decrease in the physical health scales. Six months after surgery, patients improved significantly on 8 scales: PF, RP, BP, GH, VT, PCS, MH, MCS ($p < 0.001$), and SF ($p = 0.002$). RE was also improved, but not significant ($p = 0.087$).

Table 3
SF-36 health survey results

SF-36 scale	Preoperative	Postoperative 6 months	p
Physical functioning (PF)	48.57 ± 15.06	76.55 ± 17.43	< 0.001
Role physical (RP)	53.24 ± 30.44	84.74 ± 18.20	< 0.001
Pain (BP)	41.31 ± 20.21	74.50 ± 17.95	< 0.001
General health (GH)	11.10 ± 5.70	17.46 ± 6.42	< 0.001
Role emotional (RE)	51.23 ± 4.80	52.40 ± 3.49	.087
Social functioning (SF)	48.86 ± 7.36	54.38 ± 13.71	.002
Vitality (VT)	29.43 ± 24.76	84.84 ± 18.37	< 0.001
Emotional well-being (MH)	49.71 ± 4.17	64.00 ± 10.84	< 0.001
Physical component summary (PCS)	38.56 ± 25.80	63.32 ± 31.06	< 0.001
Mental component summary (MCS)	46.19 ± 17.47	62.53 ± 17.26	< 0.001

Significant progress at the 6-month follow-up was obtained on the following SF-36 scales: pain, role-physical, and physical functioning. The most commonly reported symptoms preoperatively were joint pain, bone pain, pruritus, weakness, and difficulty standing, which were all significantly decreased 7 days postoperatively, and the decrease continued 6 months postoperatively.

Discussion

Most patients on dialysis with SHPT have multiple enlarged parathyroid glands, for which the definitive treatment is surgery. PTX is required in approximately 15% of patients after 10 years and 38% of patients after 20 years of ongoing dialysis therapy.[12] The surgical options are subtotal and total PTX. Subtotal PTX is preferred if there is a single or double adenoma causing tertiary HPT after kidney transplantation, for which the incidence of recurrent SHPT is low. Conversely, total PTX with autotransplantation is preferred for patients with compelling reasons to avoid reoperative neck surgery.[13]

In our center, we performed total PTX with autotransplantation in all ESRD patients with SHPT. No deaths occurred among patients suffering from SHPT during the perioperative period. We also demonstrated that total PTX with autotransplantation was a safe, feasible, and effective surgical option for SHPT patients because no deaths occurred among the 47 study subjects.[14] When total PTX with autotransplantation is performed, a fragment of parathyroid tissue is placed into the sternocleidomastoid or forearm muscle or into the subcutaneous abdominal adipose tissue.[13] In our center, a fragment of parathyroid tissue was placed into the deltoid or forearm muscle. There were no significant differences in

the levels of PTH postoperatively between the two groups. However, placement into the deltoid could shorten the operation time and improve convenience.

The number of parathyroid glands found in our center varied from 2 to 6. Four glands were found in most of the patients (80.6%). In 11 (5.47%) patients, 5 glands were found. There was only 1 patient who had 6 glands. However, 2 glands were found in 2 (0.9%) patients whose PTH levels decreased to normal after the operation. In only 186 (92.5%) patients, the PTH levels decreased to normal 7 days postoperatively. The anatomic location of the parathyroid glands also varied. Glands were found in the thoracic cavity in 4 (2.3%) patients, the thyroid gland in 4 (2.3%) patients, the posterior esophagus in 3 (1.72%) patients and the carotid sheath in 1 (0.57%) patient. 99mTc-MIBI is the most important imaging technique for these patients, especially for those with glands found in the thoracic cavity.

In addition, the present study provides evidence of significant improvements in QoL in patients undergoing total PTX with autotransplantation. Patients with ESRD have important physical, mental, emotional, and psychosocial limitations that can have a major impact on QoL. In the present study, we prospectively evaluated data from 201 patients undergoing total PTX, and the data were analyzed preoperatively and postoperatively. We chose the SF-36 health survey to evaluate QoL. The SF-36 is a measure of health status and an abbreviated variant, and it is commonly used in health economics as a variable in the quality-adjusted life year calculation to determine the cost-effectiveness of a health treatment. There are two limitations of the survey. One is that it does not take into consideration a sleep variable, and the other is that it has a low response rate in the population of patients > 65 years of age.[15]

In our series, we observed significant improvements in the PCS and MCS when compared between the preoperative and postoperative periods. Similar to previous research, there were also significant improvements in almost all eight SF-36 dimensions before and after surgery. The only exception was RE. However, a possible explanation for the less pronounced increase in our study may be the tendency for better REQoL at baseline. In our study, the median RE score at the time of diagnosis was higher (51.23 ± 4.80) than that in the previous study and did not improve to the same magnitude following PTX.[16] Another explanation may be that more than half of the patients were asymptomatic. In four randomized controlled trials (RCTs) that included only asymptomatic SHPT patients and used the SF-36 health survey, three of the studies observed a modest improvement in two to four of the domains (emotional, social functioning, general health, and vitality) in the PTX group compared to the medical observation group.[17–19] However, the fourth RCT showed ambiguous results with a slight but significant difference in scores in favor of surgery in the RE and physical domains, while the mental health subdomain showed higher (better) scores at the 2-year follow-up in favor of the medical observation group.[20]

Conclusions

Elevated PTH levels are associated with many complications, which can severely compromise the QoL of already impaired SHPT patients. This study provides evidence of significant improvements in QoL in

patients undergoing total PTX with autotransplantation. Significant improvements were observed in the PCS and MCS when compared between the preoperative and postoperative periods.

List Of Abbreviations

ESRD end-stage renal disease

QoL quality of life

SHPT secondary hyperparathyroidism

PTX parathyroidectomy

PTH parathyroid hormone

ALP alkaline phosphatase

SF-36 36-item short-form

KDIGO Kidney Disease Improving Global Outcomes

PF physical functioning

SF social functioning

RE role functioning emotional

RP role functioning physical

VT vitality

BP pain

MH mental health

GH general health

PCS physical component summary

MCS mental component summary

Declarations

Ethics approval and consent to participate

The ethics committee reviewed and discussed the research. The research is in accordance with the Helsinki Declaration of the World Medical Congress and approved by the Ethics Committee for its implementation.

Consent for publication

This manuscript does not contain any individual person's data. Informed consent was obtained from all parents or legal guardians.

Data availability statement

Materials, data and associated protocols promptly are available to readers without undue qualifications in material transfer agreements.

Competing Interests

The authors declare no competing interests.The results presented in this paper have not been published previously in whole or part.

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Contributions

Conception and design of the work: YuL Wang;Jia Xu;RongZ Fu. Acquisition of data: Jia Xu;DongS Zhou. Analysis of data: Jia Xu. Interpretation of data:Jia Xu;DongS Zhou. Drafting of the work: YuL Wang.All authors read and approved the final manuscript.

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Figures

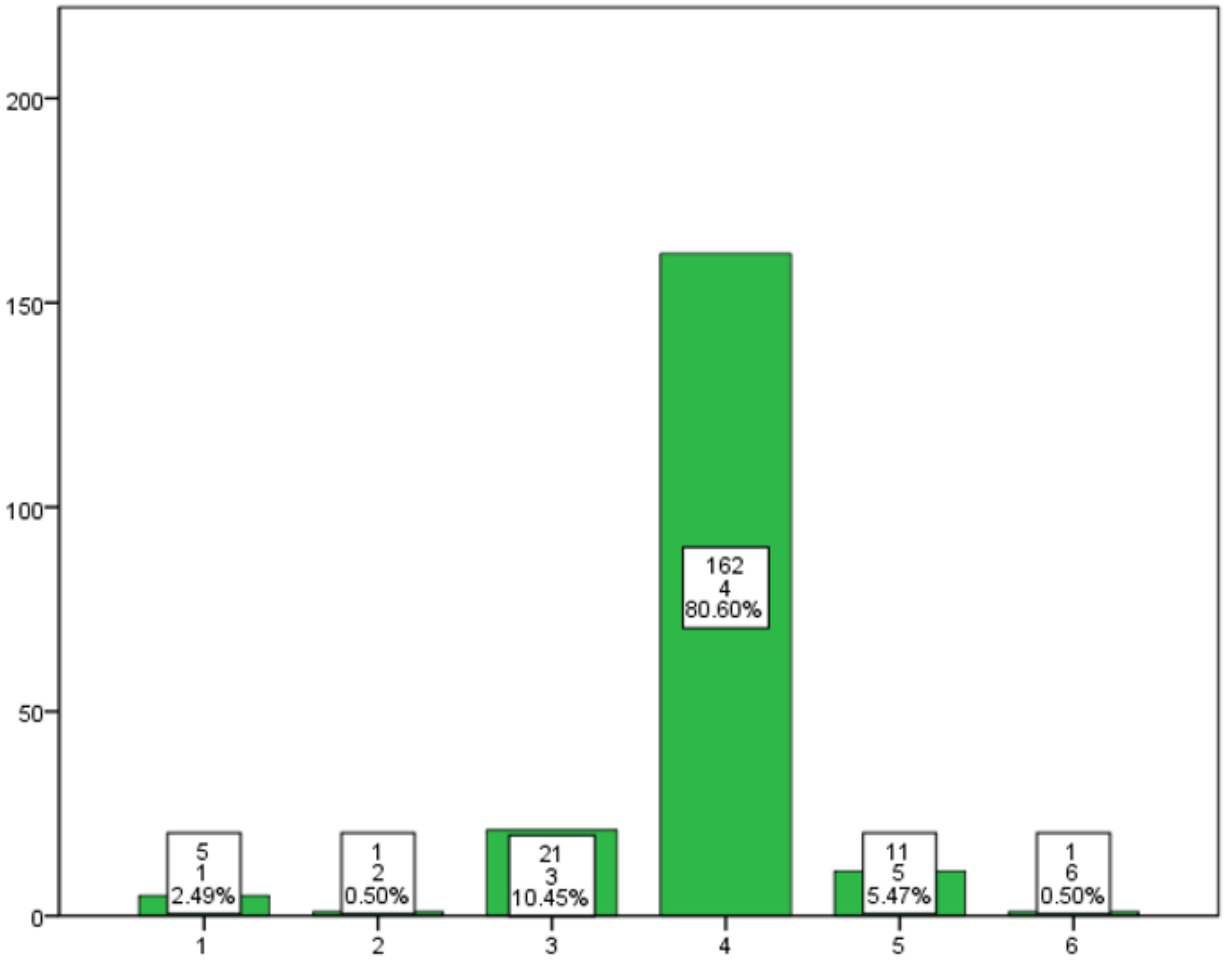
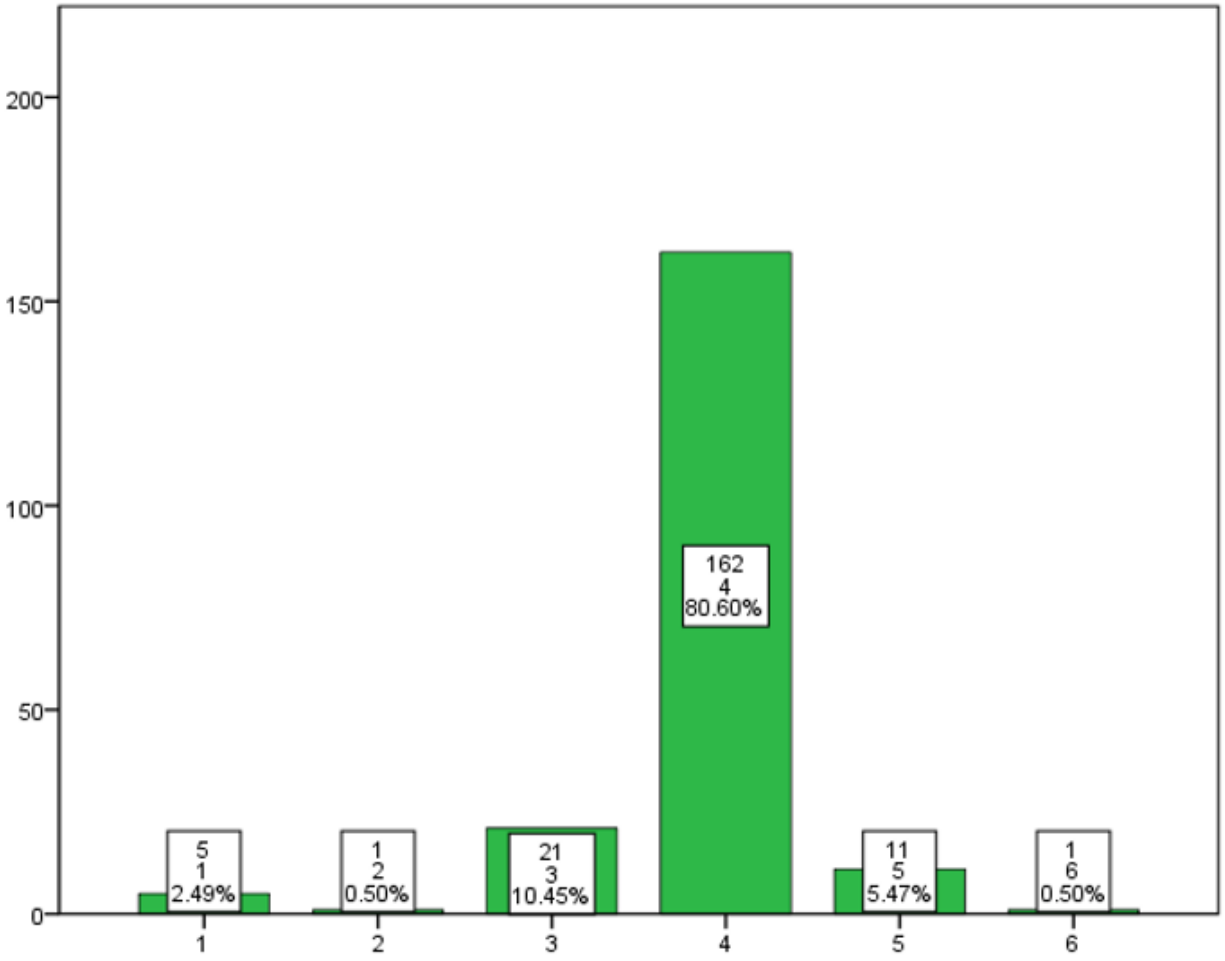


Figure 1

Number of glands



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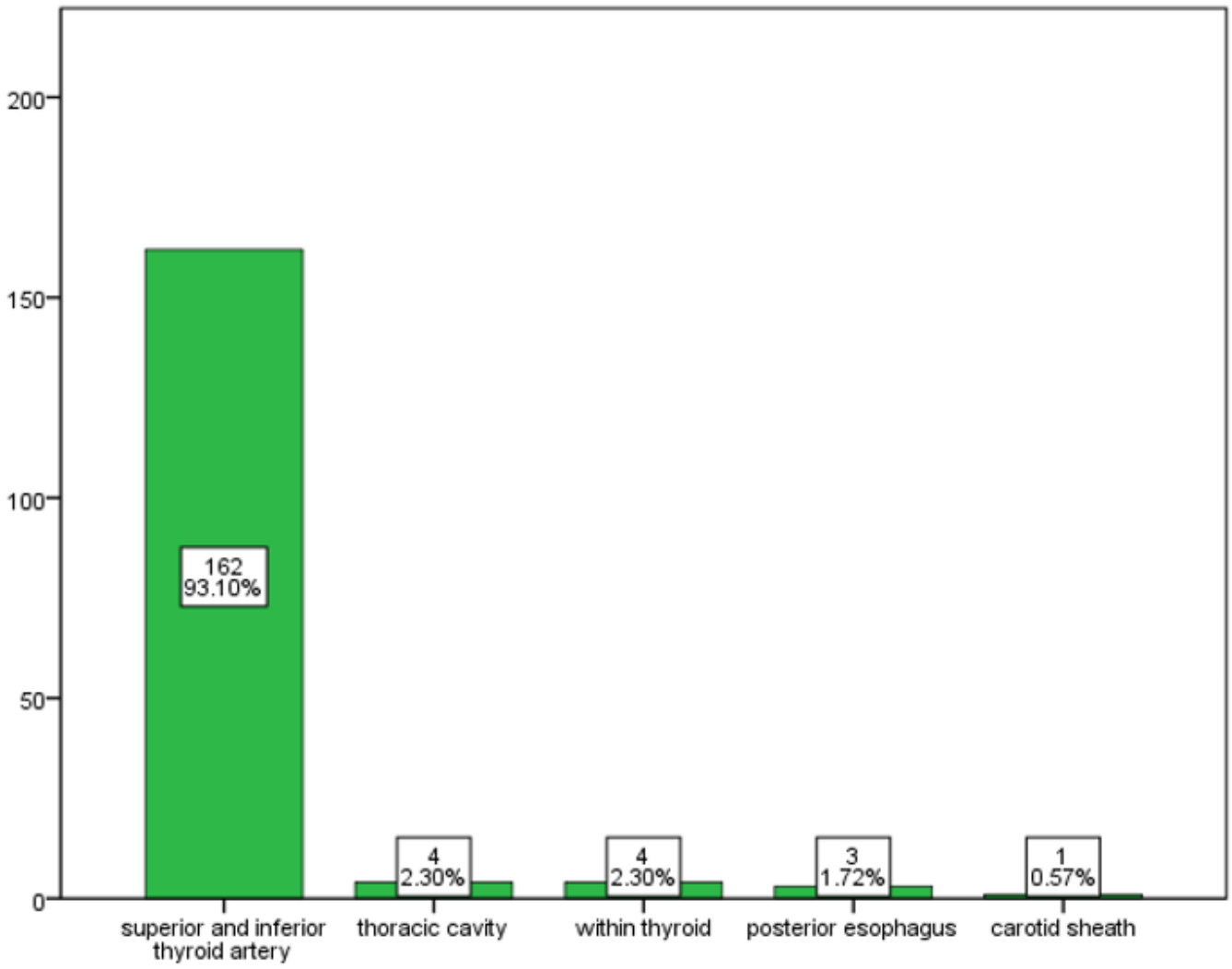
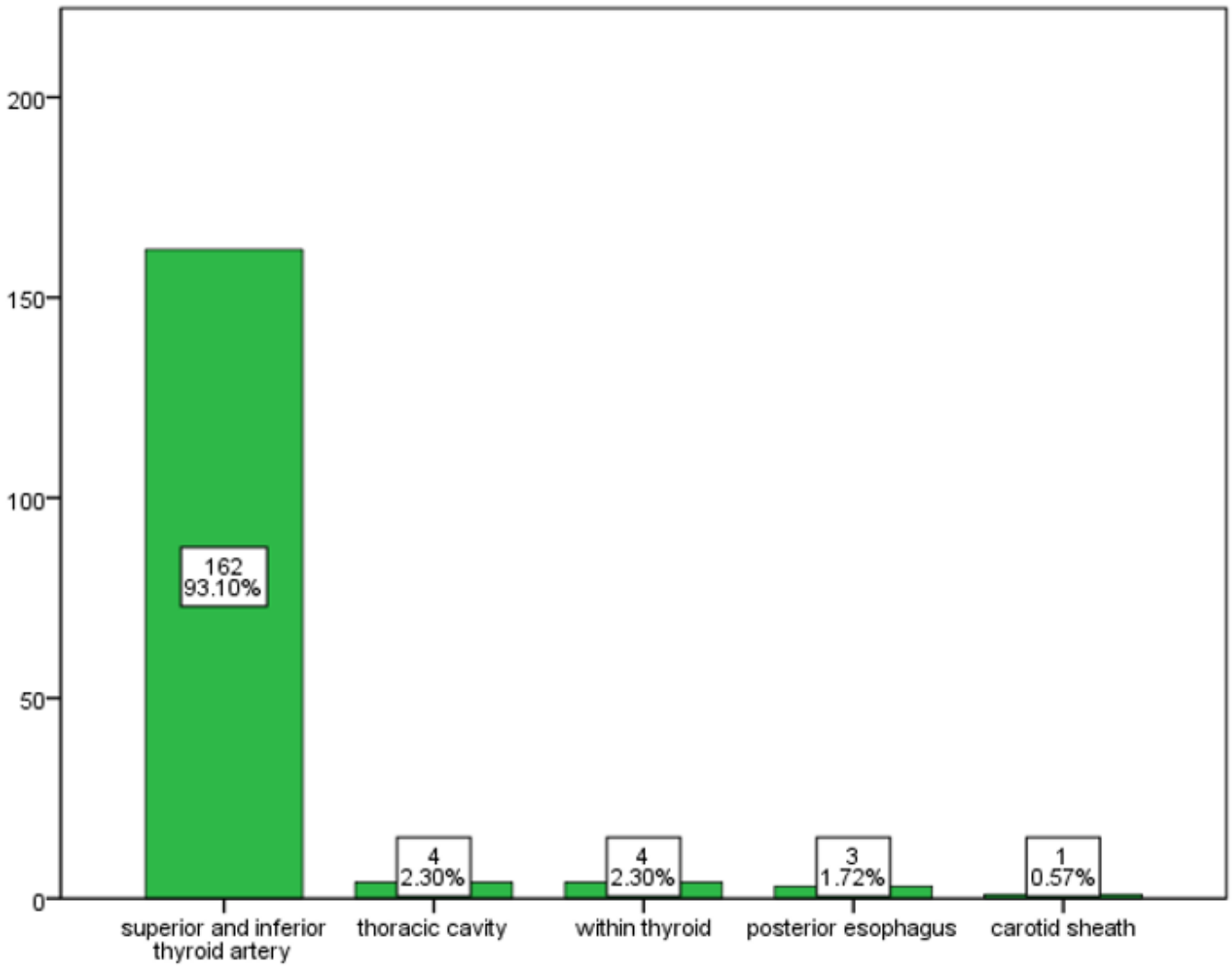


Figure 2

Anatomic location of glands



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