Aging Clin Exp Res (2017) 29 (Suppl 1):S29–S33
DOI 10.1007/s40520-016-0665-8

ORIGINAL ARTICLE

# Management of concomitant hyperparathyroidism and thyroid diseases in the elderly patients: a retrospective cohort study

**Alessandra Panarese[1] · Vito D'Andrea[1] · Stefano Pontone[1] · Pasqualino Favoriti[1] · Daniele Pironi[1] · Stefano Arcieri[1] · Angelo Filippini[1] · Salvatore Sorrenti[1]**

Received: 29 August 2016 / Accepted: 26 October 2016 / Published online: 10 November 2016


**Abstract**

*Background* Thyroid disease and hyperparathyroidism are the most common endocrine disorders. The incidence of thyroid disease in patients with hyperparathyroidism ranges in the different series from 17 to 84%, and thyroid cancer occurs with an incidence ranging from 2 to 15%.

*Aim* The aim of our study was to analyze the management of elderly patients with concomitant thyroid and parathyroid disease in order to define the best surgical therapeutic strategy and avoid reoperations associated with a higher risk of complications.

*Methods* All consecutive patients (64 patients, age range 60–75 years), undergoing surgery for hyperparathyroidism, from January 2011 to June 2014, were retrospectively evaluated. Enrolled patients were divided into two study groups of patients affected by hyperparathyroidism with or without a concomitant thyroid disease.

*Results* Out of 64 patients enrolled in our study (24 men, age range 60–75 years), affected by hyperparathyroidism, 34 had an associated thyroid disease and were treated with total thyroidectomy and parathyroidectomy. The group, who underwent parathyroidectomy associated with thyroidectomy, had no greater complications than the group receiving only parathyroidectomy.

*Conclusions* Thyroid disease must be excluded in patients affected by hyperparathyroidism. It is difficult to determine whether hyperparathyroidism can be considered a risk factor for thyroid disease, but an accurate preoperative study is essential for a surgery able to treat both thyroid and parathyroid disease. In this way, we avoid the elderly patient, with associated morbidity and increased surgical risk, to undergo a reoperation for thyroid disease, burdened with major complications.

**Keywords** Hyperparathyroidism · Thyroid disease · Parathyroidectomy · Thyroidectomy

**Abbreviations**

| | |
|---|---|
| PHPT | Primary hyperparathyroidism |
| QPTH | Intraoperative parathyroid hormone assay |
| PH | Parathyroid hormone |
| US | Ultrasonography |
| CT | Computer tomography |
| MEN | Multiendocrine neoplasia |
| FNA | Fine-needle aspiration biopsy |

## Background

Thyroid disease and hyperparathyroidism are the most common endocrine disorders [1]. The association between the two diseases was first described by Kissin et al. in 1947 [2]. The incidence of thyroid disease in patients with hyperparathyroidism ranges in the different series from 17 to 84%, and thyroid cancer occurs with an incidence ranging from 2 to 15% [3–13].

Murray et al. [14], on the contrary, evaluated with a retrospective study the incidence of hyperparathyroidism in patients with thyroid disease requiring surgery. The incidence observed was significant at 5%, and this result was consistent with previously studies reporting 2–6% [15–17].

On the basis of their study, Wagner et al. [18] state that the incidence of primary hyperparathyroidism in patients

✉ Alessandra Panarese
sandrapana78@gmail.com

[1] Department of Surgical Sciences, Policlinico Umberto I, "Sapienza" University of Rome, V.le Regina Elena n.324, 00161 Rome, Italy

with thyroid disease is three times the frequency found in patients without thyroid disease. The variability of these case studies could be due to geographical variation, selection of patients or different methods of examination. However, this association leads to a greater attention in the preoperative and surgical management of patients with thyroid and parathyroid disease.

## Aim

The aim of our study was to analyze the management of elderly patients with concomitant thyroid and parathyroid disease in order to define the best surgical therapeutic strategy and avoid reoperations associated with a higher risk of local and general complications.

## Patients and methods

All consecutive patients (age range 60–75 years) undergoing surgery for hyperparathyroidism, from January 2011 to June 2014, at the Department of Surgical Sciences, "Sapienza" University of Rome, were retrospectively evaluated in a cohort study.

Enrolled patients were divided into two study groups: a group affected by hyperparathyroidism (Group H) and a group affected by hyperparathyroidism in association with thyroid disease (Group HT). We included all patients with complete clinical data, who agreed to undergo the medical evaluation. The patients who refused to undergo medical check and follow-up and patients with recurrent thyroid disease were excluded.

All patients were preoperatively investigated by a clinical evaluation, blood tests, neck ultrasonography (US), a scintigraphy with sestamibi 99mTc, chest computer tomography (CT) and indirect laryngoscopy for evaluation of the vocal cords' motility. The indication for surgery has been decided in case of primary hyperparathyroidism (PHPT) with the endocrinologist and in case of secondary and tertiary hyperparathyroidism with nephrologists.

The bilateral neck exploration was the surgical approach for parathyroidectomy and total thyroidectomy for thyroid disease.

Intraoperative parathyroid hormone assay (QPTH) was performed in all parathyroidectomy in order to predict the complete removal of all hyperfunctional parathyroid glands [19, 20].

In PHPT, the decrease in serum parathyroid hormone (PTH) 5 min after the removal of the parathyroid pathologic must have a cutoff $\geq$50% [21, 22]. In the secondary hyperparathyroidism, the decrease in serum PTH 10 min after the removal of the last pathologic parathyroid must have a cutoff $\geq$60% [23]. During the follow-up, patients were subjected to a medical check at our department, providing a neck US and blood tests (serum calcium, phosphorus and postoperative PTH).

## Results

Sixty-four patients (24 men, age range 60–75 years) were enrolled in our study (Table 1). In the Group H, nine patients were affected by PHPT, caused by a parathyroid hyperplasia in one case and by an adenoma in the other cases. In case of hyperplasia, all the hyperplastic parathyroid glands were completely removed. In case of parathyroid adenoma, the surgical treatment was the excision of parathyroid adenoma. Twenty-one patients were affected by secondary hyperparathyroidism, supported by parathyroid hyperplasia. The surgical treatment was a total parathyroidectomy.

In the Group HT, 20 patients were affected by primary hyperparathyroidism, caused by an adenoma, with associated thyroid disease (three papillary thyroid carcinomas and 17 multinodular thyroid diseases). The surgical treatment was, therefore, the excision of the parathyroid adenoma, associated with total thyroidectomy. Thirteen patients were affected by secondary hyperparathyroidism, supported by parathyroid hyperplasia with an associated thyroid disease (one papillary thyroid carcinoma and 12 multinodular thyroid diseases). The surgical treatment was a subtotal parathyroidectomy, associated with total thyroidectomy. Only one patient had tertiary hyperparathyroidism and had an associated multinodular thyroid disease. The surgical treatment was parathyroidectomy, associated with total thyroidectomy.

Intraoperative parathyroid hormone assay (QPTH) was performed in all parathyroidectomy. The decrease in intraoperative parathyroid in primary hyperparathyroidism respected the cutoff of $\geq$50%. The decrease in intraoperative parathyroid in secondary hyperparathyroidism respected the cutoff of $\geq$70% in 10 min.

The thyroid disease was always identified preoperatively. In some patients, we performed a quantitative ultrasound elastography (Q-USE), because of its diagnostic utility in the differential diagnosis of thyroid nodules [24]. We never decided to perform a thyroidectomy during the operation. No incidental thyroid pathology was found during operation. No cases of patients present with thyroid disease and incidental finding of hyperparathyroidism.

Three patients had thyroid lesion in ipsilateral thyroid lobe, four patients in the contralateral lobe and 57 in the bilateral side of thyroid.

After surgery, all patients were treated with calcitriol and calcium salts intravenous or per os. This treatment

**Table 1** Type of hyperparathyroidism and type of thyroid-associated disease

| No of patients | Type of hyperparathyroidism | No of thyroid-associated disease | No of associated multinodular thyroid disease | No of associated papillary thyroid disease |
|---|---|---|---|---|
| 64 | 29 primary hyperparathyroidism | 20 (68.9 %) | 17 (85 %) | 3 (15 %) |
| | 34 secondary hyperparathyroidism | 13 (38.2 %) | 12 (92 %) | 1 (8 %) |
| | 1 tertiary hyperparathyroidism | 1 (100 %) | | 1 (100 %) |

proved successful in reducing the rate of patients with asymptomatic hypocalcemia and in cutting out the cases of tetanic crisis, thus shortening hospital stay. All patients were discharged between the third and fourth postoperative day.

We did not have in any of the two groups neither postoperative bleeding nor recurrent nerve injury nor definitive hypocalcemia. In Group H, we had four cases (13.3%) of patients with PHPT with transient hypocalcemia. In the Group HT, we had five cases (14.7%) of patients with PHPT, returned to normal value with medical therapy. We observed no significant differences between the two groups. The mean follow-up was two years (range 6–48 months).

## Discussion

Excluding the multiendocrine neoplasia 1 (MEN 1) and MEN 2A in which the syndromic association between thyroid disease and parathyroid is due to genetic mutations, inherited in an autosomal dominant manner, respectively, of a gene located on chromosome 11 and of a proto-oncogene c-RET, the association remains unclear. A role seems to have the increased calcium concentrations, growth factor or iodine deficiency (10), or other authors suggest only simple coincidence.

Smith et al. [25] carried out a study to explain the correlation between thyroid disease and PHPT. They found elevated serum levels of 1,25-dihydroxyvitamin D3 in some patients with PHPT. In addition, the presence of a specific binding site for the vitamin D in the anterior pituitary thyrotropic cells indicates that vitamin D has a role in the modulation and secretion of TSH. In the secondary HPT, on the contrary, chronic renal failure determines numerous alterations of the thyroid, including reduced levels of the hormone in serum and tissues and accumulation of iodine in the thyroid with a volume increase [26].

In addition, if the thyroid cancer occurs after the age of 70, the neoplasm displays features of greater biological aggressiveness (greater incidence of undifferentiated forms, presence of lymph nodes at diagnosis and vascular invasion, locally advanced forms, greater incidence of stage IV) [27], but we do not have prognostic biomarker in thyroid cancers [28].

Lin et al. [29] investigated on the relationship between secondary HPT and thyroid cancer in end-stage renal disease and demonstrated a considerable higher incidence of thyroid cancer in patients affected by a secondary HPT.

However, despite this frequent association, there are no guidelines for the treatment of thyroid disease when diagnosed preoperatively in patients with hyperparathyroidism.

An important survey of the American Association of Endocrine Surgeons, conducted by Wang et al. [30], demonstrated that for thyroid nodules <1 cm identified preoperatively, low-volume parathyroid surgeons were more likely to perform thyroid resection than high-volume parathyroid surgeons (78 vs. 59%, $P < 0.05$). Eighty-nine percent of surgeons would perform preoperative fine-needle aspiration biopsy (FNAB) of a thyroid nodule >1 cm; 16% would plan for elective thyroidectomy regardless of nodule size.

Gul et al. [10] emphasize the importance of evaluation with preoperative ultrasonography and FNAB to detect thyroid disease, especially malignancy in patients with primary hyperparathyroidism, but they may not be sufficient. Intraoperative evaluation of the thyroid by the surgeon is also necessary.

Murray et al. [14] recommend the detection of concurrent hyperparathyroidism in patients with thyroid disease, because it allows to treat both diseases with a single definitive surgery. This avoids a second neck operation. Reoperative neck surgery is challenging, and dense scar tissue and distorted tissue plans are often encountered with greater complications rates [14, 31]. However, there is no uniformity of management among the various surgeons, and it depends on their own experience.

Performing a parathyroidectomy and a thyroidectomy at the same time may expose the patient to greater complications, including injury of recurrent nerve. A skilled and dedicated surgeon can minimize these risks. However, in high-risk thyroidectomies the surgeon can rely on adjunctive reassuring techniques, as a preoperative duplex ultrasound, a noninvasive method with high diagnostic sensitivity that can easily complete the preoperative thyroid ultrasonography and detect a nonrecurrent inferior laryngeal nerve or an intraoperative recurrent laryngeal nerve monitoring [32, 33].

We do not believe feasible to apply the selective embolization of thyroid arteries (SETA) in the case of cervico-mediastinal goiter, associated with hyperparathyroidism, as it is always necessary a bilateral neck exploration [34].

In our cohort study, we found no differences between the two groups. This result shows that combining a thyroidectomy with a parathyroidectomy does not expose the patient to greater risks, as long as the intervention is performed by an experienced and dedicated surgeon. Possible limitations of our study are the not numerous samples and the short follow-up in same patient.

## Conclusions

In patients with hyperparathyroidism is crucial to exclude thyroid disease. It is difficult to determine whether hyperparathyroidism can be considered a risk factor for thyroid disease, but it is important an accurate preoperative study in order to perform a surgery able to treat both thyroid and parathyroid disease and avoid the risk of a reoperation, associated with greater complications.

In this way, we avoid the geriatric patient, with associated morbidity and increased surgical risk, to undergo a reoperation for thyroid disease, burdened with major complications and a further operation.

#### Compliance with ethical standards

**Conflict of interest** All authors listed have contributed sufficiently to the project to be included as authors, and to the best of our knowledge, no conflict of interest, financial or other exists.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

## References


1. Golden SH, Robinson KA, Saldanha I et al (2009) Clinical review: prevalence and incidence of endocrine and metabolic disorders in the United States: a comprehensive review. J Clin Endocrinol Metab 94:1853
2. Kissin M, Bakst H (1947) Coexisting myxedema and hyperparathyroidism. J Clin Endocrinol Metab 7:152–158
3. Ryan S, Courtney D, Timon C (2015) Co-existent thyroid disease in patients treated for primary hyperparathyroidism: implications for clinical management. Eur Arch Otorhinolaryngol 272:419–423
4. Bentrem DJ, Angelos P, Talamonti MS et al (2002) Is preoperative investigation of the thyroid justified in patients undergoing parathyroidectomy for hyperparathyroidism. Thyroid 12:1109–1112
5. Strichartz SD, Guiliano AE (1990) The operative management of coexisting thyroid and parathyroid disease. Arch Surg 125:1327–1331
6. Heizmann O, Viehl CT, Schmid R et al (2009) Impact of concomitant thyroid pathology on preoperative workup for primary hyperparathyroidism. Eur J Med Res 14:37–41
7. Prinz RA, Barbato AL, Braithwaite SS et al (1982) Simultaneous primary hyperparathyroidism and nodular thyroid disease. Surgery 92:454–458
8. Monroe DP, Edeiken-Monroe BS, Lee JE et al (2008) Impact of preoperative thyroid ultrasonography on the surgical management of primary hyperparathyroidism. Br J Surg 95:957–960
9. Zheng YX, Xu SM, Wang P et al (2007) Preoperative localization and minimally invasive management of primary hyperparathyroidism concomitant with thyroid disease. J Zhejiang Univ Sci B 8:626–631
10. Gul K, Ozdemir D, Korukluoglu B et al (2010) Preoperative and postoperative evaluation of thyroid disease in patients undergoing surgical treatment of primary hyperparathyroidism. Endocr Pract 16:7–13
11. Sidhu S, Campbell P (2000) Thyroid pathology associated with primary hyperparathyroidism. Aust N Z J Surg 70:285–287
12. Kösem M, Algün E, Kotan C et al (2004) Coexistent thyroid pathologies and high rate of papillary cancer in patients with primary hyperparathyroidism: controversies about minimal invasive parathyroid surgery. Acta Chir Belg 104:568–571
13. Masatsugu T, Yamashita H, Noguchi S et al (2005) Significant clinical differences in primary hyperparathyroidism between patients with and those without concomitant thyroid disease. Surg Today 35:351–356
14. Murray SE, Sippel RS, Chen H (2012) Incidence of concomitant hyperparathyroidism in patients with thyroid disease requiring surgery. J Surg Res 178:264–267
15. Sianesi M, Del Rio P, Arcuri MF et al (2003) Hyperparathyroidism associated with thyroid pathology. Am J Surg 185:58–60
16. Del Rio P, Arcuri MF, Bezer L et al (2009) Association between primary hyperparathyroidism and thyroid disease. Role of preoperative PTH. Ann Ital Chir 80:435–438
17. Katz AD, Kong LB (1992) Incidental preclinical hyperparathyroidism identified during thyroid operations. Am Surg 58:747–749
18. Wagner B, Begic-Karup S, Raber W et al (1999) Prevalence of primary hyperparathyroidism in 13387 patients with thyroid diseases, newly diagnosed by screening of serum calcium. Exp Clin Endocrinol Diabetes 107:457–461
19. Catania A, Sorrenti S, Falvo L et al (2002) Validity and limits of intraoperative rapid parathyroid hormone assay in primary hyperparathyroidism treated by traditional and mini-invasive surgery. Int Surg 87:226–232

20. Romani AM, Panarese A, La Torre V et al (2007) The role of intraoperative parathyroid hormone assay in the surgical management of hyperparathyroidism. Ann Ital Chir 78:91–96
21. Irvin GL, Deriso GT (1994) A new, practical intraoperative parathyroid hormone assay. Am J Surg 168:466–468
22. Thompson GB, Grant CS, Perrier ND et al (1999) Reoperative parathyroid surgery in the era of sestamibi scanning and intraoperative parathyroid hormone monitoring. Arch Surg 134:699–704; discussion 704–5
23. Chou F-F, Lee C-H, Chen J-B et al (2002) Intraoperative parathyroid hormone measurement in patients with secondary hyperparathyroidism. Arch Surg 137:341–344
24. Cantisani V, Grazhdani H, Ricci P et al (2014) Q-elastosonography of solid thyroid nodules: assessment of diagnostic efficacy and interobserver variability in a large patient cohort. Eur Radiol 24:143–150
25. Smith MA, Mc Henry C, Oslapas R et al (1989) Altered TSH levels associated with increased serum 1,25-dihydroxyvitamin D3: a possible link between thyroid and parathyroid disease. Surgery 106:987–991
26. Kutlay S, Atli T, Koseogullari O et al (2005) Thyroid disorders in hemodialysis patients in an iodine-deficient community. Artif Organs 29:329–332
27. Falvo L, Catania A, Sorrenti S et al (2004) Prognostic significance of the age factor in the thyroid cancer: statistical analysis. J Surg Oncol 88:217–222
28. Baldini E, Tuccilli C, Prinzi N et al (2015) Deregulated expression of aurora kinases is not a prognostic biomarker in papillary thyroid cancer patients. PLoS ONE 10:25
29. Lin SY, Lin WM, Lin CL et al (2014) The relationship between secondary hyperparathyroidism and thyroid cancer in end stage renal disease: a population based cohort study. Eur J Intern Med 25:276–280
30. Wang TS, Roman SA, Cox H et al (2009) The management of thyroid nodules in patients with primary hyperparathyroidism. J Surg Res 154:317–323
31. Pironi D, Pontone S, Vendettuoli M et al (2014) Prevention of complications during reoperative thyroid surgery. Clin Ter 165:e285–e290
32. Tartaglia F, Blasi S, Tromba L et al (2011) Duplex ultrasound and magnetic resonance imaging of the supra-aortic arches in patients with non recurrent inferior laryngeal nerve: a comparative study. G Chir 32:245–250
33. Calò PG, Pisano G, Medas F et al (2013) Intraoperative recurrent laryngeal nerve monitoring in thyroid surgery: is it really useful? Clin Ter 164:e193–e198
34. Tartaglia F, Salvatori FM, Russo G et al (2011) Selective embolization of thyroid arteries for preresection or palliative treatment of large cervicomediastinal goiters. Surg Innov 18:70–78