

Clinical Features and Surgical Treatment of Thyroid Pathology in Patients Over 65 Years

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Rezumat

Manifestări clinice și tratamentul chirurgical al patologiei tiroidiene la pacienții peste 65 ani

Introducere: Creșterea semnificativă a duratei de viață a populației a condus la o semnificativă sporire a prevalenței condițiilor tiroidiene benigne și maligne și în egală măsură a intervențiilor chirurgicale pentru această patologie.

Pacienți și metodă: Într-o serie personală de 464 tireopatii tratate chirurgical într-un interval de două decade am înregistrat 51 cazuri (10.9%) peste 65 ani dintre care 11 (2.4%) depășind 75 ani. Sunt analizate caracteristicile demografice, clinice și diagnostice împreună cu indicațiile, tehnicile chirurgicale și rezultatele acestora în timp. Cercetarea statistică retrospectivă analizând raportul de risc și intervalul de încredere (95%) nu a identificat factori suplimentari de risc ai complicațiilor post-chirurgicale la această grupă de vârstă.

Rezultate: Am consemnat 33 femei și 18 bărbați (raport 1,8/1) confirmați clinic, paraclinic și histologic cu gușă (multi)nodulară 24 cazuri (47.0%), tirotxicoze 18 cazuri (35.2%) și respectiv carcinoame tiroidiene 9 cazuri (17.6%). Au fost practicate 34 tiroidectomii totale sau subtotale și 17 exereze conservatoare. Nu am înregistrat decese postoperatorii dar am notat câte trei cazuri de hipocalcemie prelungită și respectiv câte două paralizii recurențiale și recidive lezionale. În toate cazurile benigne am realizat vindecări stabile în timp ce în cancere am obținut supraviețuiri la 3-5 ani în 4 tumori papilare.

Concluzii: În pofida unor dificultăți de diagnostic și riscurilor

suplimentare legate de comorbidități, patologia tiroidiană benignă și malignă instalată la bolnavi peste 65 ani poate beneficia de toate tipurile de exereze glandulare conservatoare sau radicale în condițiile unei selecții riguroase a cazurilor.

Cuvinte cheie: patologie tiroidiană, vârstnici, tratament chirurgical

Abstract

Introduction: The significant increase in the average lifespan of the general population lead to a proportional enhancement in the prevalence of benign and malignant thyroid conditions and equally the number of surgeries for this pathology.

Patients and method: In a personal series of 464 thyroid disorders undergoing surgery over a two decades period we registered 51 patients (10.9%) aged over 65 years of which 11 (2.4%) having over 75 years. Demographic, clinical and diagnostic characteristics of these cases were analysed together with indications, management practice and outcome. Retrospective statistical analysis reaearching risk factor and confidence interval has not identified factors predicting higher risk of complication in this age group.

Results: There have been recorded 33 females and 18 males (R1=1,8/1) with clinically, laboratory and histologically confirmed diagnosis of 24 (multi)nodular goiters (47.0%), 18 thyrotoxicosis (35.2%) and also 9 (17.6%) thyroid carcinomas. Thirty-four total or near total thyroidectomies and 17 conservative exeresis were performed. There were not postoperative deaths but we recorded three cases of prolonged hypocalcemia, and two cases each of recurrent laryngeal nerve paresis and recurrences. In all benign cases we obtained a stable in time cure

while in carcinomas survivals of 3-5 years were obtained in only 4 papillary tumors.

Conclusions: Despite some difficulties in diagnostic and additional risks related to comorbidity benign and malignant pathology installed in patients over 65 years, may benefit of all types of conservative or radical thyroidectomies in terms of strict monitoring individualized in each case.

Key words: thyroid pathology, elderly, surgical treatment

Introduction

Although it is not universal agreement about a clear cut definition of "old age", conventionally the elderly has been considered as the chronological age of 65 years old or older while those over 75 years old are referred as "late elderly" (1,2,3).

The actual significant increase in the average lifespan of the general population lead to a proportional enhancement in the prevalence of benign and malignant thyroid, the most common endocrine pathology found among old population, reaching its highest rates in this age group. Epidemiological data are supported by clinical arguments, laboratory and imaging tests and necropsy studies. There are many similarities between thyroid disorders described in younger and the old people but due to atypical and reduced number of symptoms, increased susceptibility to adverse events related to non treated comorbidity and a greater likelihood of harm treatment, the diagnosis and therapy of this pathology in the last group can be challenging. (4,5)

However elective thyroid surgery and another complementary methods of treatment sustained by a careful preoperative preparation and an individual risk stratification can be

performed with good results and low morbidity and mortality than same procedures in youthful patients. (6,7,8,9,10,11,12)

Patients and Methods

A retrospective series of 464 consecutive patients with various thyroid disorders undergoing 479 different types of thyroid exeresis (including 15 own recurrences) for benign and malignant diseases performed in our unit in a two decades period is presented. (Table 1)

We registered 238 simple (multi)nodular goiters, 136 thyrotoxicosis, 72 thyroid carcinomas, 14 thyroiditis and 4 other lesions. (Table 2)

In our research we compared demographic and clinical data, including indications for surgery and operative procedures, pathology findings and final diagnosis, outcome and morbidity emphasizing significant differences between two groups based on their age.

The main group included 413 cases (89.0%) between 14-65 (mean age 42.5) years consisting 333 females and 80 males (female/male ratio 4/1). These included 214 (51.2%) simple euthyroid goiters i.e. 132 apparent isolated nodules and respectively 82 multinodular goiters. Likewise in the series of 136 cases of hyperthyroidism we registered 118 (86.8%) cases less than 65 years, 50 with Basedow disease, 30 with toxic multinodular goiters and 38 with toxic adenomas. Finally from 72 thyroid carcinomas 63 (87.5%) were discovered in patients having less than 65 years.

Thus our study group considered 51 (10.9%) "geriatric" cases aged over 65 (mean 68,3) years of which 11 surpassing 75 years of also predominating females – 33 cases and 18 males (female/male ratio 1,8/1) undergoing 53 thyroid procedures. This one gathers 24 simple euthyroid goiters (47.0%) toward 18 cases of hyperthyroidism (35.2%) (two Basedow disease, 7 multinodular toxic goiters 9 toxic adenomas together with 9 thyroid carcinomas) of the 3rd age. (Table 3)

Table 1. Patients characteristics

Patients characteristics:	total	< 65 years	≥ 65 years	
Cases (number, %)	464 (100%)	413 (89.0%)	51 (10.9%)	
			< 75years 40(78.4%)	≥ 75 years 11(21.6%)
Gender (number, %)	366 F / 98 M (78.9% / 21.1%)	333 F / 80 M (80.6% / 19.4%)	33 F / 18 M (64.7% / 35.3%)	

Table 2. Clinical forms of the patients who were operated; the "others" are more or less typical concomitant thyroid resections in surgery of hyperparathyroidism

nosology/surgical indications	Total number (%)	< 65 years number (%)	≥ 65 years number (%)
simple (multi)nodular goiter	238 (51.3%)	214 (51.8%)	24 (47.1%)
hyperthyroidism	136 (29.3%)	118 (28.6%)	18 (35.3%)
thyroid carcinoma	72 (15.5%)	63 (15.3%)	9 (17.6%)
thyroiditis	14 (3.0%)	14 (3.4%)	0 (0.0%)
others*	4 (0.9%)	4 (1.0%)	0 (0.0%)
total	464 (100.0%)	413 (100.0%)	51 (100.0%)

Table 3. The type of the 479 operations performed (15 reinterventions)

procedures performed 479 (including 15 own relapses, two cases having two prior surgeries) .				
	Performed procedures	Total number (%)	< 65 years number (%)	≥ 65 years number (%)
conservative	nodulectomies, biopsies, others	30 (13.9%)	27 (14.1%)	3 (12.0%)
	lobectomies	76 (35.2%)	66 (34.6%)	10 (40.0%)
	subtotal thyroidectomies	110 (50.9%)	98 (51.3%)	12 (48.0%)
	total	216 (100.0%)	191 (100.0%)	25 (100.0%)
extensive	lobectomies +- isthmus	134 (51.0%)	118 (50.2%)	16 (57.1%)
	near total/total thyroidectomies	129 (49.0%)	117 (49.8%)	12 (42.9%)
	total	263 (100.0%)	235 (100.0%)	28 (100.0%)
	+ lymphadenectomies*	27 (5.6%)	24 (88.9%)	3 (11.1%)
	reoperations**	15 (3.1%)	13 (86.7%)	2 (13.3%)

Results

Concerning the main clinical entities the most commonly encountered in our statistics representing about half of our patients registered 238 cases with benign thyroid (multi-)nodular diseases. One hundred and forty four of them (60,5%) were apparently isolated thyroid nodules while 94 (39,4%) were multinodular goiters.

Older people group recorded 24 cases from which 10 (41.6%) presented as isolated thyroid nodules and 14 as multinodular goiters (58.3%) most appearing as “dominant” nodules. Comparatively younger patients totalized 214 such cases, 134 (62.6%) presenting themselves as uninodular and 80 (37.3%) as multinodular lesions. From the clinical point of view most of nodular thyroid diseases in senescence are no different from subjects under 65 years associating presence of goiter often obvious and of varying sizes with atypical, elusive symptoms many of these depending on glandular volume and function together with varying time of evolution. In 6 of these subjects goiters was located substernal, half of them being asymptomatic and half presenting cough, chocking, dyspnea but no stridor or acute compressive phenomena. Chest plain film discovered these lesion but cross sectional imaging were the most useful study being an important component of the preoperative evaluation and surgical planning.

Regardless of age surgery has become the accepted therapy after the goiter get enough larger and symptomatic, another surgical indications including especially suspected malignancy but also large substernal component and cosmetic reasons. (13,14,15)

In the entire group of simple euthyroid goiters we performed four nodulectomies (two in recurrences), 12 lobectomies with-out or with isthmectomy and 8 underwent bilateral resections, most of them as “classical” subtotal thyroidectomy (three cases submitted to Hartley-Dunhill procedure). The histology showed colloid (hyperplastic) nodules (n=19), follicular adenomas (n=3), focal thyroiditis (n=2). However finally after paraffin

section malignancy in apparent “innocent” uninodular goiter was identified in two patients which imposed reoperations. Likewise in the series of 136 thyrotoxic patients who have undergone surgery, 18 (13.2%) were registered in subjects aged over 65 years, two cases (11.1%), with Basedow disease, 7 (38.8%) with toxic multinodular goiter and 9 (50.9%) with toxic adenoma, toward the 118 subjects aged 14 - 64 years, 50 (42.3%), cases with Basedow disease, 31 (26.2%) with toxic multinodular goiter and 37 (31.3%) with toxic adenomas. In elderly patients was not uncommon for thyrotoxicosis to present in an atypical manner, the classical “florid” manifestations described especially in Basedow disease being less pronounced or even absent. Therefore ocular signs, tremor, heat intolerance often lacked being replaced by unexplained weight loss, cardiovascular, respiratory and digestive isolated sufferings, myopathy, agitation and cognitive impairment, realizing in few cases the misleading picture of apathetic thyrotoxicosis. Even the goiter or thyroid nodule can be unapparent in a voluminous fat neck or retrosternal plunged lesions. In these condition imaging and hormonal dosages of fT3, fT4 and TSH highlighted abnormal glandular lesion and function. (16,17,18) Treatment of hyperthyroidism was difficult to choose between the three main therapies which dispute their indications, practical applications, advantages, risks, results and patient's choices. In these circumstances our option of surgery was been established in context of well-stipulated indications based on the evidence of a correct diagnostic, objective assessment of each therapeutic method, optimal preoperative preparation and best technical possibilities. However in elderly we were less prone to undergo extensive operations, these being applied preferential in the last period especially in young people. Thus in patients over 65 years we practiced two near total and 7 subtotal thyroidectomies in the cases of Basedow disease and multinodular toxic goiter and 3 adenomectomies and 6 lobectomies in toxic adenomas.

In both age groups, patients reviewed at 6-12 months from operation showed substantial regression or improvement of most

their clinical complaints. However younger patients presented a better remission at immediate and late follow-up.

Last category contained the 9 patients, 3 males and 6 females, (M/F ratio 1/3,) aging 65-72 years, representing 12.5% for all 72 cases with thyroid carcinomas. According to histological type 5 (55.5%) of tumors were papillary, one case (11.1%) was follicular and 3 patients (33.3%) were anaplastic. Comparatively in 63 young people the distribution of thyroid carcinomas was papillary 46.0% (n=34), follicular 22.2% (n=15), mixed 12.6% (n=8), medullary 3.1% (n=2), anaplastic 9.3% (n=6), and insular and Hürthle cell carcinomas, primary lymphoma and metastasis to the thyroid of a lung cancer 6.3% (n=4, one case each).

Patient distribution by the pTNM system were locally limited, stage I, T1-2 N0, 4 cases (two microcarcinomas), stage III, T3 N0 or T1-3 N1, two cases and stage IV (anaplastic tumors) 3 cases (one still limited to the gland, one have spread to lymph nodes and one spread to distant site). As in literature our patients often present with poor prognostic features such as large size, follicular or anaplastic subtype, extrathyroid growth and secondary deposits. (19,20,21)

Therefore an optimal therapeutical approach was attempted practicing four total/near total thyroidectomies (one completion procedure) and two lobisthmectomies. In two cases a modified neck dissection was done. In the last three patients only biopsy or abstention happened. Two cases with residual disease received radioiodine therapy. Moreover external beam radiotherapy, suppressive hormonal treatment and chemo-therapy was performed without results in inoperable tumors. Only four patients survived between 3-5 years.

Overall in our entire statistics postoperative results showed no mortality but general morbidity reported near percentages of both early and late complications in patients under 65 years and also in older group. Thus we noted 7 temporary vocal cord palsy (3 in elderly), 6 temporary hypocalcemia (3 in elderly) and three hematoma or wound infection in older group. Late follow up was incomplete however registering 33 unsatisfactory results: permanent vocal cord palsy in 6 cases (2 in elderly), permanent hypocalcemia in 7 cases (2 in elderly) and 15 cases of morphologic recurrences (2 in elderly). (Table 4)

Statistical analysis

In order to assess the risk of the cut age 65 years and morbidity

outcome we have applied the Chi square test with the Fisher approximation. Running the analysis we found text non-significant results: P immediate = 0.43, P late = 0.99 and P recurrences = 0.67.

The risk ratio and the confidence interval (95%) is presented next: RR immediate: 1,54, CI 95%=0,53-4,5; RR late= 1,01, CI=95%=0,26-3,8; RR recurrence: 1,22, CI 95=0,3-4,5. Therefore we conclude that the age 65 is not significant as a morbidity risk.

Discussions

Based upon literature survey and our personal experience the authors argue the existence of many similarities but also significant differences between clinical, therapeutic and prognostic features of thyroid diseases described in the young people and those in the 3rd age. (5,8,9)

For this purpose our series has been divided in three nosologic groups i.e.(multi)nodular euthyroid goiters, hyperthyroidism and thyroid carcinomas trying to define the main characteristics of each of these.

Primarily the incidence of thyroid "geriatric" subjects remains high, totalizing 11.0% from our casuistry, both because its endemic character in studied area including the existence /persistence of many cases evolving for numerous years and also growing overall length of age in general population. As well we found an overall increase with the age in the incidence of benign (multi)nodular goiters and of anaplastic carcinoma while in the cases of hyperthyroidism the number of toxic multinodular goiters and toxic adenomas is rising but that of the Basedow disease drops.

Additionally was confirmed the predominance of thyropathies in females but in a much lower ratio in elderly compared with younger patients (F/M ratio 4/1 toward 10/1). (22,23,24) Diagnostic approach included history, stating the setting of endemic or sporadic character of the lesion, approval of its clinical appearance (nodular, multinodular, diffuse, retrosternal extension, presence of lymph nodes, inflammatory phenomena), functional syndrome in cases of thyrotoxicosis or medullary carcinoma and complete inventory of associate sufferings.

However the thyroid size and growth together with functional consequences were the main factors influencing the surgical approach.

Thyroid hormone measurements have been limited to the

Table 4. Outcome, immediate and late morbidity and recurrences in our series

outcome		Total number (%)	< 65 years number (%)	≥ 65 years number (%)
morbidity	immediate	18 (3.9%)	15 (3.6%)	3 (5.9%)
	Late	18 (3.9%)	16 (3.9%)	2 (3.9%)
	recurrences	15 (3.2%)	13 (3.1%)	2 (3.9%)
mortality		0 (0.0%)	0 (0.0%)	0 (0.0%)
Total cases		464 (100.0%)	413 (100.0%)	51 (100.0%)

determination of T3, T4 and TSH confirming thyrotoxicosis which add dosage of thyrocalcitonin in cases of medullary carcinoma and of thyroglobulin which signals the presence of residual or recurrent malignant lesions.

Regarding imaging systematic ultrasound coupled with FNAB in the initial exploration of thyroid lesions providing most helpful morphologic and topographic data in most situations, particularly for (multi)nodular lesions assuring them solid guidance on strategy and extent of surgery. (8,10)

However we noted two false negative results which required a completing thyroidectomy and a false positive smear determining an abusive enlarged operation for a 2 cm Ø benign nodule.

The use of thyroid scan was significantly reduced, the method being recommended only to confirm the functioning nature when the serum thyrotropin is low or undetectable and in patients with multinodular goiters demonstrating the presence of an autonomous functioning nodule.

We still performed whole body scan in two cases for evidence of possible metastasis. CT and MRI remain indicated and useful to obtain data of eventually retrosternal goiters. (9,11)

Paraffin section established the final diagnostic in both dystrophic or hyperfunctioning processes and especially in glandular and lymph node components harboring malignant lesions.

Elderly subjects often present multiple complex comorbidities which interact with thyroid pathology including cardiovascular, respiratory troubles, disturbances of calcium metabolism, osteoporosis, diabetes, sensitivity to medications etc, all having a major impact on treatment. (5,7,8,22,23,24)

Adapted to our own philosophy indications for surgery in thyroid patients in the 3rd age are not much different to those formulated in younger individuals, grouping both benign disorders as simple (multi)nodular goiters of large size (> 4 cm or 50 g), without or with pressure symptoms, hyperthyroidism and also especially suspected or underlying glandular malignancies. (25,26,27,28)

Our operative strategy acquired in the spirit of the school in which we have formed reflected also the attitude toward elderly, including the respect for the healthy glandular tissue, assurance of a proper function closer to the euthyroid state but also an adapted oncologic resection in cases of thyroid carcinoma. Thereby in the early period of our activity a notable proportion of conservative operations i.e. enucleations, lobectomies and subtotal thyroidectomies were done. compared with extended techniques i.e. total/near total thyroidectomies.

However with the general tendency in literature as the changing spectrum and course of lesions together with the growth of our experience, our surgical attitude focused in the last many years by two main techniques i.e. total lobectomy with isthmectomy (hemithyroidectomy) and near total/total thyroidectomy whether is benign or malignant conditions. While remaining eclectic in indication and extension of thyroid surgery these main procedures were done both in young people and depending on lesional aspect also in patients older than 65 years.

Conclusions

Patients >65 years of age can undergo successful thyroid surgery but with challenging higher morbidity. From limited surgical indications of thyroid disorders in elderly, i.e. (multi)nodular disease with compressive phenomena, toxic multinodular goiters and thyroid carcinomas, actually after careful preoperative risk stratification and medical optimization extended to virtually all thyroid pathology, ablative therapy undertaking currently achieving similar good results as these obtained in young people. Nevertheless we plead for "supple" operative strategy adapted both to lesion but especially of hazards due to specific-age morbidity.

Conflict of interests

There are not conflicts of interest to declare.

Authors' contribution

MRD conceived and drafted the paper, IC and MC operative team, LB performed statistical analysis, SD revised the manuscript for intellectual content. All authors take full responsibility for the content of the article.

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