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Original research

Differentiated thyroid cancer in patients ≥75 years: Histopathological features and results of surgical treatment

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HIGHLIGHTS

- Age as prognostic factor for thyroid cancer is a matter of debate.
- Differentiated thyroid carcinoma is more aggressive in elderly patients.
- Surgery is the treatment of choice for differentiated thyroid carcinoma in all ages when performed by skilled surgeons.

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ABSTRACT

Introduction: The aim of this retrospective study was to investigate clinical and pathologic characteristics of differentiated thyroid cancer (DTC) in patients ≥75 years and to analyze results of surgical treatment in this age group.

Methods: The clinical records of patients submitted to total thyroidectomy between 2009 and 2014 with histopathological diagnosis of DTC were analyzed. Patients were divided into 3 groups: patients ≤64 years were included in group A, those between 65 and 74 in B and those ≥75 years in C.

Results: Classic papillary thyroid cancer was more frequent in group A, whereas follicular variant of papillary carcinoma, tall cell and follicular carcinoma were more frequent in C. Multicentric and locally invasive tumors were more frequent in group C; younger patients (group A) showed higher incidence of node metastases (12.54% in group A, 6.33% in B and 7.89% in C). Postoperative stay was significantly longer in group C (3.13 ± 1.28 days vs 2.55 ± 1.27 vs 2.89 ± 1.27; $p < 0.001$). Transient hypoparathyroidism was more frequent in groups A and B compared with C (29.26% vs 19.71% vs 18.42%; p 0.033) whereas transient recurrent laryngeal nerve palsy was more frequent in group C compared with A and B (2.63% vs 0.16% vs 2.11% p 0.009).

Conclusions: In aging patients DTC show a worse prognosis compared with younger patients due to higher incidence of more aggressive histotypes but also to a significant diagnostic delay. Total thyroidectomy is safe when surgical operation is performed by skilled surgeons. Age alone does not exclude surgical option.

1. Introduction

Thyroid neoplasms account for 2.5% of all malignancies, representing the most common endocrine tumors. Differentiated thyroid cancers (DTC) makes up 90% of all thyroid cancers [1]. In recent years there has been a constant increase in the incidence of malignant DTC [2,3], which is most likely due to the spread of diagnostic methods such as ultrasound and needle aspiration cytology. DTC typically progresses slowly with a favorable prognosis, nevertheless, some reports suggest that tumor characteristics and clinical course are more aggressive in older patients affected by thyroid cancer [4,5]: neoplasms tend to be larger, with more extrathyroidal disease and distant metastases [4–6]. Impact of age on thyroid cancer prognosis is matter of debate: patient age greater than 45 years has been recognized as a poor prognostic factor by

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various reports [7], in agreement with risk stratification promoted by American Joint Commission on Cancer (AJCC), whereas other authors suggested alternative age cutoffs ranging from 40 to 60 years [8–10]. In a previous report [11] we reported our results regarding impact of age in DTC characteristics and prognosis, at the time we chose a cutoff age at 65 years. In this report we extend our contribution by analyzing the clinical and pathologic characteristics of DTC in elderly patients and the results of surgical treatment, by using a more complex age stratification.

2. Materials and methods

The clinical records of patients who underwent total thyroidectomy between 2009 and 2014 in our Surgical Department at University of Cagliari with histopathological diagnosis of DTC, including microcarcinoma, were analyzed. Patients with incomplete data or those lost at follow up were excluded from our retrospective study. 778 patients were included in this study. For each patient preoperative assessment consisted of FT3-FT4 and TSH blood measurements, high resolution ultrasound (US) of the neck and fibrolaryngoscopy for assessment of vocal fold motility. In case of suspicious nodules US-guided fine-needle aspiration cytology was performed. All surgical operations were performed by three skilled endocrine surgeons. Serum calcium and intact parathyroid hormone (PTH) were essayed on first postoperative day and then on the basis of clinical course and evaluation. Patient demographic data and postoperative complications were recorded, including postoperative hematoma, recurrent laryngeal nerve injury, hypoparathyroidism, wound infection and chylous fistula. Hypoparathyroidism (defined as a PTH level < 10 pg/ml) and recurrent laryngeal nerve palsy (defined as vocal fold paralysis assessed by postoperative fibrolaryngoscopy) were considered permanent if lasting for more than 6 months after surgical operation. Postoperative radioablation iodine therapy was administered, according to guidelines, in case of gross extra-thyroidal extension, primary tumor size greater than 4 cm, distant metastases or selected patients with primary tumor ranging from 1 to 4 cm confined to the thyroid gland but with significant risk of recurrence. Follow up consisted of neck US examination and dosage of Tg and TgAb levels every six months during suppressive L-thyroxine treatment (a serum Tg level of 0.2 ng/ml was considered as undetectable). In patients with suspicious recurrence a whole-body ^{131}I scanning after recombinant human thyrotropin (rhTSH) was performed. Diagnosis of disease recurrence in the cervical lymph nodes was based on serum Tg level monitoring, US-guided FNAC and Tg washing of FNAC aspirates. Patients were divided into 3 groups: patients up to the age of 64 were included in group A, those aged between 65 and 74 were included in group B and those 75 years old and older were included in group C. To assess factors influencing patients' outcomes, analysis of variance (ANOVA) was used for continuous variables and Chi-squared test for categorical data. The p-value of less than 0.05 was considered statistically significant.

3. Results

As reported in Table 1, 778 patients were included in our study; 598 (76.86%) were included in group A (younger patients), 142 (18.25%) in group B and 38 (4.88%) in group C (older patients); women were more numerous than men in all age groups. FNAC was performed in 387 patients: an indeterminate or suspicious nodule was identified in 271 patients (34.83%), whereas a carcinoma was diagnosed in 64 (8.22%). In 249 patients (32%) thyroid cancer was suspected on the basis of physical examination and characteristics of the nodule at ultrasound. In 229 patients (29.43%) thyroid cancer was diagnosed accidentally after surgical operation for benign thyroid disease (multinodular goiter, hyperthyroidism).

All the patients underwent total thyroidectomy; central neck compartment lymphadenectomy was associated in 116 (14.91%) cases (100 in group A, 13 in group B and 3 in group C), whereas modified lateral neck dissection was performed in 47 (6.04%) cases (40 in group A, 4 in group B and 3 in group C). The mean surgical time was 100 ± 26.97 min in group A, 96.92 ± 26.91 min in group B and 100.15 ± 27.17 min in group C; postoperative stay was 2.55 ± 1.27 days in group A, 2.89 ± 1.27 in group B and 3.13 ± 1.28 in group C (Table 2). Classic papillary carcinoma was more frequent in group A, whereas follicular variant of papillary carcinoma, tall cell carcinoma and follicular carcinoma were more frequent in group C (Table 3); in Group C the incidence of multicentric and locally invasive carcinoma was higher. By the other side, younger patients (group A) demonstrated higher incidence of node metastases compared with other age groups (12.54% in group A, 6.33% in group B and 7.89% in group C). In all groups mortality rate was 0%. In group A postoperative hematoma occurred in 6 patients (1%), wound infection in 1 (0.16%), transient recurrent laryngeal nerve palsy in 1 (0.16%), transient hypoparathyroidism in 175 (29.26%), permanent hypoparathyroidism in 10 (1.67%) and chylous fistula in 1 (0.16%); in group B postoperative hematoma occurred in 1 patient (0.7%), transient recurrent laryngeal nerve palsy in 3 (2.11%), transient hypoparathyroidism in 28 (19.71%), permanent hypoparathyroidism in 1 (0.7%), whereas wound infection and chylous fistula did not occur; in group C transient recurrent laryngeal nerve palsy occurred in 1 patient (2.63%), transient hypoparathyroidism in 7 (18.42%), whereas postoperative hematoma, wound infection, permanent hypoparathyroidism and chylous fistula did not occur. There weren't permanent recurrent laryngeal nerve palsy. Local recurrence affected 9 patients (1.5%) in group A, 2 (1.4%) in group B, and none in group C developed (Table 4).

4. Discussion

DTC mainly affects young adults: the highest incidence occurs in patients aged from 25 to 54 years [12]; however, DTC can affect all age groups, from youth to old age. Between 2.5 and 12% of all DTC occur in patients older than 65 years [13], which represent a considerable part of population: from 2000 to 2050 the number of people aged 85 and older is estimated to increase 350% [14]. DTC is the only human cancer in which age is included as a part of the staging criteria; different age cutoffs have been used in several predictive models for risk of malignancy and prognostic tools (AMES, DAMES, MACIS, TNM) [15,16]. At present, age as a prognostic factor for thyroid cancer is still a matter of debate and literature data are discordant. First of all, a precise definition of “old age” does not exist and it is difficult to compare results of literature reports; we chose our age cutoffs with the aim of obtaining a larger series. Furthermore, the association of age with worse prognosis in DTC does not reach consensus: some authors showed a correlation between worse prognosis and age 45 years or older [17–20], whereas other authors did not find a correlation between age and prognosis in thyroid cancer [21]. Nevertheless, patient age greater than 45 years has been recognized as a poor prognostic factor by various reports [7] and recent literature shows that particularly poor prognosis is associated with age greater than 60 years [22,23]. In older adults DTC are more advanced and mortality and recurrence rates are higher [5,24]; more aggressive histopathological patterns, poorer general physical condition and delayed diagnosis are the major reasons to explain the worse prognosis in elderly patients [25,26]. In his report [6] Lin showed that in patients aged 60 years old and older mortality rate of DTC was higher than in the general population; in his series, ratio of follicular to papillary