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Differentiated thyroid cancer in patients over 60 years of age at presentation: A retrospective study of 438 patients

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ABSTRACT

Objectives: The aim of this study is to identify the prognostic factors predicting remission and subsequent disease relapse in patients with differentiated thyroid cancer (DTC) greater than 60 years of age.

Materials and Methods: The institute thyroid cancer database had 4370 patients with DTC, of which 447 (10%) were aged > 60. However, 9 patients were excluded due to follow-up less than 1 year. The prognostic factors in the remaining 438 patients were studied.

Results: Among the 438 patients, 311 (71%) had only loco-regional disease (M_0) and 127 (29%) had distant metastases (M_1) at the time of initial presentation. The host factors predictive of distant metastases at presentation were female gender, primary tumor size (>4 cm), follicular histology, and extra-thyroidal extension. Among M_o patients, 195 (63%) achieved complete remission while only 12 (9%) M_1 patients did so. Average number of radioactive iodine (^{131}I) doses administered to achieve complete remission was 2.3 (range, 1–6) and the mean cumulative dose was 3404 MBq (range, 925–46,250 MBq). In multivariate logistic regression among M_0 patients, follicular histology, nodal metastases, and surgical treatment lesser than total/near-total thyroidectomy and among M_1 patients, site of distant metastases (skeletal and multiple sites) were independent factors predicting non-remission. Among the patients (both M_0 and M_1) who achieved remission, factors associated with disease recurrence were primary tumor size (>4 cm), nodal metastases, pulmonary metastases, and non-remission after first dose of radioactive iodine and were associated with greater chances of disease relapse.

Conclusion: This study highlights that DTC in older patients behaves more aggressively than in adults age < 60 years, and identifies several prognostic factors for remission and subsequent relapse.

1. Introduction

Thyroid cancer accounts for only 1% of all human cancers, but it is the most common endocrine malignancy [1]. Differentiated thyroid cancer (DTC) comprising of papillary and follicular histology, makes up 90% of all thyroid cancers [2]. Unlike other cancers, DTC has been shown to have favourable overall prognosis with 10-year survival rates as high as 93% in papillary thyroid cancer (PTC) and 85% in follicular thyroid cancer (FTC) [3]. Maximum disease-related mortality has been attributed to distant metastases [4]. American Joint Commission on Cancer (AJCC) staging system stratifies the risk in

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patients with thyroid cancer according to tumor-related factors, nodal status, and distant spread in age less than and greater than 45 years. Patient age greater than 45 years has been recognised as a poor prognostic factor by various reports [5]. However, recent literature suggests that among the patients greater than 45 years, particularly poor prognosis is associated with age greater than 60 years [6,7]. Literature on prognostic factors and long term outcome of DTC in patients greater than 60 years of age is scarce.

This study aimed at identifying the factors associated with remission and subsequent disease relapse in patients > 60 years of age.

2. Materials and Methods

2.1. Patients

From the medical records of 4370 patients treated for differentiated thyroid carcinoma at All India Institute of Medical Sciences (AIIMS), New Delhi from 1970 to 2012, 447 (10%) patients were age ≥ 60 years. Nine patients who had total follow-up duration of less than 12 months were excluded. Therefore, 438 patients were finally enrolled in the analysis. The study protocol was approved by the institutional review board.

2.2. Diagnosis and Treatment Protocol

The standard treatment of DTC at our institution was surgical tumor resection followed by radioactive iodine ^{131}I (RAI) therapy. As per the surgical indication, thyroidectomy with or without nodal dissection was performed. The completeness of surgical resection was assessed by the diagnostic whole body scan (WBS) [74–111 MBq], performed 30–40 days after surgery without thyroxine supplementation. All patients showing scintigraphic evidence of disease were treated with RAI (1110–9250 MBq) after an informed consent. RAI dose was calculated on the basis of residual thyroid bed activity. A larger dose was administered to the patients with distant metastases. After administration of RAI, all patients were admitted to the radio-iodine therapy ward. The post-therapeutic scan was performed at the time of discharge to look for the additional sites of disease. All patients were prescribed once daily 2 μg/kg of levo-thyroxine.

Follow-up was performed at 6 months interval according to the standard protocol, involving WBS and serum thyroglobulin (Tg) levels after one month thyroxine withdrawal. Serum anti-Tg antibody (ATA) and thyroid stimulating hormone (TSH) levels were also assayed. After the patients became radiologically and biochemically disease-free, regular follow-ups were conducted annually for the detection of disease relapse through thorough clinical examinations, serum Tg, ATA and TSH levels. If necessary, radiological evaluations like neck ultrasonography, chest X-ray, and computerized tomography (CT) scan were also performed. Any patient who was lost to follow-up before 12 months was excluded from analysis. So the minimum duration of follow-up was 12 months while the maximum duration was 216 months. The mean follow-up duration in our patient cohort was 67 months.

2.3. Final Outcome

Disease status was classified based on the scintigraphic and radiologic findings and serum Tg levels as disease-free, recurrent disease, stable disease, and progressive disease. Remission was defined as stimulated Tg levels < 10 ng/ml along with ^{131}I uptake ≤ 0.2% in 24-hour WBS. A minimum period of six months was necessary to classify disease status as in remission. A patient was considered as disease-free if he/she stayed in remission till the last follow-up. Recurrence accounted for the reappearance of disease (elevation in Tg levels and/or appearance of new lesions in WBS/radiological investigation) at least 12 months after remission. Persistently elevated, though static, serum Tg levels and/or persistence of disease in WBS without appearance of any new lesions was taken as stable disease. Progression was defined as rising serum Tg levels (two-fold rise from the baseline) and/or appearance of new lesions in WBS/radiological investigation in a patient who had never achieved remission.

2.4. Statistical Methods

Disease-free and recurrent disease status patients, who had achieved remission at least once during their follow-up, were taken as group I while patients with stable disease and progressive disease, who did not achieve remission in their follow-up were taken as group II. Variables predicting non-remission/persistence of disease were analysed using chi square/Fisher's exact test. Stepwise multivariate logistic regression was used to identify the independent predictors of non-remission. Within group I, factors predicting recurrence were analysed using the Cox proportional hazard model. The disease-free survival plots were constructed using the Kaplan–Meier method. P values ≤ 0.05 were considered as significant. Stata 11.2 (StataCorp, College Station, Texas) was used for the analysis.

3. Results

Table 1 shows the clinico-pathologic characteristics and final disease outcome of patients stratified by the presence/absence of distant metastases. The median age at diagnosis was 65 years. Among the 438 patients, 173 (39%) were males and 265 (61%) were females with a female to male ratio of 1.5:1. Only 2 patients had a family history of DTC. History of prior radiation exposure was absent in all patients. The initial clinical presentation was solitary thyroid nodule in 123 (28%) patients, cervical lymphadenopathy in 45 (10%) patients, and both thyroid nodule and cervical lymphadenopathy in 267 (61%) patients. Three patients presented with a multinodular goitre. All patients were euthyroid before surgery.

Thyroid surgery was performed in 425 (97%) patients. Among these, total/near total thyroidectomy was carried out in 295 (69%) patients and subtotal/hemithyroidectomy in 130 (31%) patients. Among the 13 patients who did not undergo surgery, 9 were inoperable either due to extensive spread of the tumor or due to presence of comorbidities and 4 patients refused surgery. Among the 220 patients in whom nodal