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ORIGINAL ARTICLE

Comparison of clinical characteristics of patients with follicular thyroid carcinoma and Hürthle cell carcinoma☆

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KEYWORDS
Follicular thyroid carcinoma;
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Abstract
Introduction: Hürthle cell carcinoma (HCC) is an uncommon thyroid cancer historically considered to be a variant of follicular thyroid carcinoma (FTC). The aim of this study was to assess the differences between these groups in terms of clinical factors and prognoses.
Patients and methods: A total of 230 patients (153 with FTC and 77 with HCC) with a median follow-up of 13.4 years were studied. The different characteristics were compared using SPSS version 20 statistical software.
Results: Patients with HCC were older (57.3 ± 13.8 years versus 44.6 ± 15.2 years; $p < 0.001$). More advanced TNM stages were also seen in patients with HCC and a greater trend to distant metastases were also seen in patients with HCC (7.8% versus 2.7%, $p = 0.078$). The persistence/recurrence rate at the end of follow-up was higher in patients with HCC (13% versus 3.9%, $p = 0.011$). However, in a multivariate analysis, only age (hazard ratio [HR] 1.10, confidence interval [CI] 1.04–1.17; $p = 0.001$), size (HR 1.43, CI 1.05–1.94; $p = 0.021$), and histological subtype (HR 9.79, CI 2.35–40.81; $p = 0.002$), but not presence of HCC, were significantly associated to prognosis.
Conclusion: HCC is diagnosed in older patients and in more advanced stages as compared to FTC. However, when age, size, and histological subtype are similar, disease-free survival is also similar in both groups.

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PALABRAS CLAVE
Carcinoma folicular de tiroides;
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Supervivencia libre de enfermedad;
Tiroidectomía

Comparación de las características clínicas en pacientes con carcinoma folicular de tiroides y carcinoma de células de Hürthle

Resumen
Introducción: El carcinoma de células de Hürthle (CCH) es un tipo de cáncer de tiroides infrecuente considerado históricamente una variante del carcinoma folicular de tiroides (CFT). El objetivo de este estudio fue conocer las diferencias que existen entre estos grupos en cuanto a los factores clínicos y pronósticos.
Pacientes y métodos: Se incluyeron 230 pacientes (153 CFT y 77 CCH) con un seguimiento mediano de 13,4 años. Se compararon las diferentes características utilizando el programa estadístico SPSS versión 20.
Resultados: Los pacientes con CCH tenían mayor edad (57,3 ± 13,8 años vs. 44,6 ± 15,2 años; p < 0,001). También se observaron estadios TNM más avanzados en los CCH, con una mayor tendencia a presentar metástasis a distancia (7,8% vs. 2,7%; p = 0,078). El porcentaje de persistencia/recurrencia al finalizar el seguimiento del estudio fue mayor entre los pacientes con CCH (13% vs. 3,9%; p = 0,011). Sin embargo, en el análisis multivariante, solo la edad (*hazard ratio* [HR]: 1,10; intervalo de confianza [IC]: 1,04-1,17; p = 0,001), el tamaño (HR: 1,43; IC: 1,05-1,94; p = 0,021) y el subtipo histológico (HR: 9,79; IC: 2,35-40,81; p = 0,002) se asociaron de forma significativa con el pronóstico, pero no el presentar un CCH.
Conclusión: El CCH se diagnostica en pacientes de mayor edad y en estadios más avanzados que el CFT. Sin embargo, si la edad, el tamaño y el subtipo histológico son similares, la supervivencia libre de enfermedad no difiere en ambos grupos.

Introduction

Thyroid cancer is the most common endocrine neoplasm and accounts for 1% of all tumors. Differentiated thyroid carcinoma or differentiated follicular line carcinoma, which includes papillary carcinoma and follicular carcinoma, accounts for over 90% of all thyroid gland neoplasms.[1]

Follicular thyroid carcinoma (FTC) is the second most frequent thyroid cancer, after papillary carcinoma, representing 10–15% of all thyroid carcinomas in iodine-sufficient areas.[2,3] It is a malignant epithelial tumor with evidence of follicular differentiation, but lacks the nuclear features that characterize papillary carcinoma (i.e., a large pale nucleus, the absence of a nucleolus, and the presence of notches and pseudoinclusions). Follicular thyroid carcinoma is more common in women, and the mean age at the time of diagnosis is 45–55 years (older than in other differentiated thyroid carcinomas).

Two histopathological categories have been established for the effects of prognosis: minimally invasive and extensively invasive follicular carcinoma.[4] The minimally invasive subtype is characterized by a complete capsule with microscopic capsular or vascular invasion foci (<4 foci), while the extensively invasive variant presents more than four foci corresponding to vascular and/or capsular invasion and/or extrathyroid spread.[5] The extensively invasive presentations can infiltrate adjacent tissues, though regional lymph node involvement is rare, since spread is usually via the hematogenous route.[6]

Hürthle cell carcinoma (HCC) accounts for 3% of all thyroid gland tumors.[7,8] Hürthle cells are large polygonal cells derived from the thyroid follicular epithelium, and exhibit an eosinophilic granular cytoplasm due to the presence of abundant mitochondria, a large nucleus, and a prominent nucleolus. These cells can be observed in both benign and malignant thyroid gland disease. The diagnosis of HCC is defined by the presence of a nodule with the characteristics of FTC, a prevalence of Hürthle cells (at least 75% of all the cells) and capsular and/or vascular invasion. These tumors can also be classified as minimally invasive or extensively invasive.[5]

The latest thyroid tumor classification of the World Health Organization (WHO) of 2017 defines HCC as an independent type of thyroid carcinoma, whereas it had previously been regarded as a variant of FTC.[5,9] Recent studies suggest that HCC has clinical features that differentiate it from FTC. These tumors are characterized by a certain male predominance; the patients are older on average; and in some studies the tumor size is greater.[10–14] Furthermore, recent molecular studies also suggest that HCC is different from FTC.[15,16] With regard to the prognosis, HCC has been considered more aggressive than FTC, among other reasons due to a higher incidence of distant metastases at the time of diagnosis.[12,14] However, doubts have been raised concerning the extent to which this is due to the diagnosis of HCC at older ages than other differentiated thyroid carcinomas, the higher male frequency, and the presentation of the disease in more advanced stages.

In the same way as in FTC, the treatment of patients with HCC comprises surgery with ablative I^{131} therapy. However, there is controversy regarding the usefulness of I^{131} treatment in HCC, since iodine uptake appears to be lower than in the other differentiated thyroid carcinomas. Most studies that have evaluated this aspect are retrospective