SUMMARY

Objective: The authors review anatomical, clinical characteristics and prevalence of thyroid microcarcinoma. Diagnostic procedures and risk factors of aggressiveness at diagnosis and during follow-up are also reviewed. The possible clinical, pathologic and therapeutic risk factors are scrutinized by meta-analysis. Treatment procedures by different authors and guidelines suggested by societies are reported.

Conclusions: Papillary thyroid microcarcinoma (PTMC) is diagnosed with increased frequency, mainly due to the widespread use of ultrasound-guided FNAB, and an increased percentage of all thyroid cancers are PTMC.

COMMENT

The authors carried out a key word search (Medline & Pubmed databases), between 1966 & 2008. From a total of 243 abstracts retrieved, 76 articles were used to describe the characteristics of papillary thyroid microcarcinoma (PTMC). The authors selected further 17 articles (English/Italian) that met the inclusion/exclusion criteria for the meta-analysis part of the study.

Descriptive characteristics of PTMC were as follows: mean size of 4.1-8 mm; papillary type most often found (65-99%) with other less common histological types such as follicular variant (10-31%) and follicular cancer (0.3-23.6%), oncocytic & tall cell variant (0.8%), & sclerosing variant (5-11.7%). Mean age at diagnosis was 42-55 years, with a range between 4 and 85 years. The female/male sex ratio was 5/1. Familial PTMC had an overall prevalence of 4.5%, not different from the 5-10% familial prevalence of all thyroid carcinoma.

Concerning epidemiology, the increased accuracy in clinical & laboratory evaluation, especially since the introduction of US-guided fine needle aspiration biopsy (FNAB), has led to a dramatic increase in the incidence of thyroid cancer and also PTMC which is often diagnosed during thyroidectomy for benign thyroid (and parathyroid) diseases. In a total of 5,035 PTMC patients, 71% were discovered incidentally at surgery.

Concerning preoperative diagnosis, US features such as micro-calcifications within malignant nodules was found in 7.5-59% and irregular nodule margins in 21.5-77% of PTMC patients. Concerning FNAB specifically, the smaller the nodule size the less accurate the FNA results. However, there has been no systematic study of FNA diagnostic precision in nodules with a diameter ≤1 cm. Among the relevant
questions pertaining to final diagnosis (after surgery) are issues such as the frequency of bilateral and/or multiple foci (from 3% to 57%), extracapsular invasion and lymph node metastases (from 2% to 64%), risk of associated distant metastases (<0.4%). These highly variable frequency data clearly indicate that PTMC represents a very heterogeneous disease, depending upon the conditions leading to its suspicion and diagnosis.

Concerning initial treatment, the authors pooled together data from different studies that reported clearly the extent of surgery. Among 9,259 PTMC patients, total thyroidectomy was performed in 72%, subtotal thyroidectomy in 11%, and lobectomy in 17% of the cases. Additional ablation using radioiodine was carried out in 17% of the patients following surgery.

Concerning risk factors for recurrence, the meta-analysis study showed that cancer recurrence was significantly associated with younger age (<45 years), conditions of diagnosis (overt disease versus incidental discovery), and multifocality or lymph node involvement at diagnosis.

Finally, the authors discuss specific recommendations made by scientific societies for the treatment of patients with PTMC and showed that there is no real consensus between the ATA, ETA, BTA, and AACE: diagnosis and treatment reported in the different studies are, in general, increased in contrast to the guidelines suggested by scientific societies. In some studies, a more aggressive treatment than that recommended has been adopted. Present meta-analysis showed some clinical & pathologic characteristics associated with increased aggressiveness. A more aggressive treatment should probably be reserved to PTMC showing such characteristics. Despite the increased PTMC prevalence, thyroid cancer-related mortality did not change over the years. This finding suggests that PTMC has, in general, a benign clinical course; therefore, increasingly sophisticated diagnostic procedures and aggressive treatment procedures appear unnecessary. However, the scientific perception and the patient perception of the problem are different. (Daniel Glinoer, M.D.; Ph.D.)

**See Figures below**

![Figure 1](image1.png)  
**Figure 1** Pooled data for the association of tumor recurrence and age. OR in patients aged <45 years was 1.846 (95% CI 1.096–3.291; \(P=0.039\)). There was no statistical heterogeneity (\(P=0.783\)). Tumor recurrence was significantly associated to younger age (<45 years).

![Figure 3](image3.png)  
**Figure 3** Pooled data for the association of tumor recurrence and tumor focality at diagnosis. OR in patients with unilocular tumor was 0.174 (95% CI 0.105–0.290; \(P=0.006\)). There was no statistical heterogeneity (\(P=0.535\)). Positive association was found between tumor recurrence and multifocal tumors at diagnosis.