**Key Points**

* The incidence of papillary thyroid microcarcinoma (PTMC) (<1cm) is increasing globally secondary to screening programmes
* Experts are suggesting adopting a more conservative approach by actively surveilling these tumours.
* The role of active surveillance of (PTMC) in the United Kingdom (UK) population remain unclear.
* Active surveillance may only be suitable for a minority (<4 %) of patients with differentiated thyroid cancer in the UK as most PTMC are diagnosed incidentally following thyroidectomy.
* A selective approach to investigation of incidental thyroid nodules is relevant to the UK population for optimal use of healthcare resources.

**Abstract**

**Background**

The incidence of thyroid cancer is increasing globally due to the increase in detection of subclinical, low volume papillary thyroid microcarcinomas (PTMC) (<1cm). Several international groups have recommended an active surveillance approach for this low-risk disease. In contrast to many other countries, the UK’s approach to thyroid nodules is to avoid detection of incidental lesions where appropriate.

**Objective**

This study aims to establish the proportion of patients with thyroid cancer in the UK that would benefit from active surveillance.

**Design, participants, and outcome measures:**

Individuals with PTMC in NHS Lothian from 2009-2020 were reviewed from a local thyroid cancer database. The mode of detection of PTMC and proportion of patients who might benefit from active surveillance were established.

**Results**

From 651 individuals with differentiated thyroid cancer managed over 12-year period, 185 individuals with PTMC were identified (28.4%). The majority of PTMC 151/185 (81.6%) were either diagnosed post-operatively following thyroidectomy for benign disease or with nodal disease. Only 24 individuals with PTMC were identified following palpable thyroid nodule, incidental finding on imaging and surveillance screening. Therefore, when the indication for surgery was considered, only 24/651 (3.7%) patients were identified pre-operatively and would therefore be realistic candidates for active surveillance.

**Conclusion**

Less than 4% of patients with thyroid cancer in the UK would be appropriate for active surveillance. Rather than developing programs to deal with this minority of patients, focus should be maintained on minimizing detection of these low-risk cases.

**Key words:**

Active surveillance, differentiated thyroid cancer, micropapillary thyroid cancer

**Introduction**

The incidence of differentiated thyroid cancer (DTC) is increasing internationally (1-5), with a particularly marked rise in small (<1cm), low-risk papillary thyroid microcarcinoma (PTMC) (6). Over the past decade, a significant shift towards a more conservative approach to managing differentiated thyroid cancers has been expressed through influential international guidelines (7). For the first time, experts are now recommending an active surveillance approach be considered in the lowest-risk cases of papillary thyroid cancer (PTC) (7, 8). Such an approach involves identification and diagnosis of the disease, counselling of the patient and subsequent serial ultrasound imaging to follow disease progression. Such an approach, in the hands of an expert, has been shown to result in excellent outcomes and a low conversion rate to surgery without compromising survival (9, 10).

At present, a number of guideline groups are working in the United Kingdom (UK) to update documents which shape national practice patterns for years to come. However, no evidence relating to active surveillance has been drawn from the UK population.

The aim of this study was to analyse a large cohort of patients with DTC and consider how a strategy of active surveillance would impact teams managing this patient group within the UK.

**Materials and Methods**

Individuals with papillary thyroid microcarcinoma (PTMC) diagnosed from 2009-2020 at NHS Lothian were identified from a prospectively collected regional thyroid cancer database. Individuals with non-papillary cancers, recurrent disease and those treated with a palliative approach were excluded. Patient demographic details (e.g., age and gender), mode of presentation, type of treatment (e.g., hemithyroidectomy or total thyroidectomy), lymph node surgery, radio-active iodine treatment, tumour-node-metastasis (TNM), size of tumour, perineural invasion, lympovascular invasion, extra-thyroidal extension, and type of recurrence (e.g., local, regional, and distant) were recorded.

PTMC was defined as tumours with size less than 1cm on final pathology results (pT1a). Individuals who had completion thyroidectomy had pathology results collected from primary and completion surgery. All pathology slides were analyzed by pathologists with sub-specialty interest in thyroid disease.

All PTMC in this study was staged were staged according to the 7th TNM staging of the American Joint Committee of Cancer (AJCC) (7). Individuals were clinically managed as per contemporary British Thyroid Association (BTA) guidelines after multidisciplinary team discussion and taking into account patient’s preferences. The primary outcome was mode of detection of PTMC to determine the percentage of PTMC eligible for active surveillance.

**Ethical Consideration**

This study was reviewed by NHS Lothian Caldicott and ethics committee and full ethical approval was waived for this study by the ethics committee (study number: 16113).

**Statistical Analysis**

Data was collected using Microsoft Excel and analysed using SPSS (version 19.0).

**Results**

From January 2009 to December 2020, 651 individuals with differentiated thyroid cancer were identified in Southeast Scotland (Table 1)**.** A total of 192 of 651 (29%) individuals had a diagnosis of papillary thyroid microcarcinoma with a size of less than 1cm (Table 1). Seven of these patients had confirmed PTMC but no further clinical details were available. 147 of the remaining 185 (79%) were female with a median age disease presentation of 50 years (range 16-80 years). Patient demographics and clinicopathological details of the tumour are shown in Table 1. All patients with PTMC were T1N0MO or T1N1MO in accordance with AJCC staging (7th edition). No local or distant recurrence was identified during follow-up. One individual developed incidental nodal recurrence of papillary microcarcinoma during squamous head and neck cancer resection.

**Mode of detection of PTMC**

The mode of detection of PTMC in Southeast Scotland is shown in Table 2. The majority of PTMC in this cohort were identified incidentally following thyroidectomy for benign disease 151/185 (81.6 %). Benign disease includes multinodular goitre, Graves’ disease, follicular adenoma, thyrotoxicosis, thyroid hyperplasia, parathyroid adenoma, Hashimoto, hyperparathyroidism and benign cysts. A total of 10/185 (5.4%) patients with PMTC presented with a positive neck lymph node on presentation who subsequently had total thyroidectomy. Only 10/185 (5.4%) of patients presented with palpable thyroid nodules which was subsequently diagnosed with PTMC. 3/185 individuals (1.6%) were imaged abroad and subsequently had PTMC diagnosed whereas 11/185 (5.9%) individuals had PTMC diagnosed incidentally on radiological imaging e.g., MRI, CT scan, PET scan and carotid ultrasound.

**Discussion**

The concept of “overdiagnosis” is accepted in a number of malignancies, including thyroid cancer (4, 5, 11). This phenomenon is the diagnosis of a medical condition that would never have caused any symptoms or problems. PTMC is a good example of this in the majority of cases. Autopsy studies confirm high rates of occult thyroid malignancy in patients who dies of other causes (12) and screening programs have been shown to result in huge increases in disease incidence without impacting on survival (13-16). As a result, such attempts to identify sub clinical disease have largely been abandoned (14, 17). Nonetheless with increasing access to highly accurate medical imaging, the identification of otherwise occult thyroid nodules and therefore malignancies remain a significant problem worldwide.

The National Cancer Institute defines active surveillance as “A treatment plan that involves closely watching a patient’s condition but not giving any treatment unless there are changes in test results that show the condition is getting worse.” (<https://www.cancer.gov/publications/dictionaries/cancer-terms/def/active-surveillance>).

This approach has been in use in papillary microcarcinoma for over 25 years in Japan and has been adopted by a number of international units with great success (18-22). The experience of these units confirms the fact that the majority of patients identified as harboring PTMC will not show significant disease progression while under surveillance. Indeed, although some patients will show an increasing volume of primary disease and others may even demonstrate nodal metastasis while under surveillance, a small group will demonstrate regression of primary disease volume (23). As such, active surveillance represents a promising approach to minimize the potential over-treatment of PTMC which rarely represents a risk to the patient, in contrast to thyroidectomy with the associated risks of bleeding, recurrent laryngeal nerve injury, hypocalcaemia and hypothyroidism, not to mention the healthcare associated costs of surgery.

However, active surveillance has not gained widespread popularity in the UK. Although a small number of patients with comorbidities which preclude general anaesthesia or concurrent malignances of higher clinical urgency may be followed rather than actively treated, the overwhelming majority of patients who present with DTC in the UK undergo primary surgery.

Our group has previously demonstrated that the population of patients who present to our multi-disciplinary teams is significantly different from those presenting internationally (24). A higher rate of male patients, more follicular carcinomas and larger primary tumours characterize the cohort of patients presenting in the UK. Here we analyse our cohort with a specific focus on who would be suitable for an active surveillance approach should it be adopted in upcoming UK guidelines. We found that of 651 patients managed over 12-year period, only 192/651 (29.5%) would be potential candidates for active surveillance based on pathological variables. However, when the indication for surgery was considered, only 24/651 (3.7%) patients were pre-operatively identified and would therefore be realistic candidates; the remaining 168 were diagnosed post operatively, or with nodal disease and therefore would not be suitable for active surveillance.

The reasons for the differences in the UK population of DTC to that seen internationally are not fully understood. However, it is likely that international differences in the patterns of imaging differences in terms of potential screening programs and access to imaging for asymptomatic patients have a role. In contrast to countries where imaging rates are high, or screening programs exist, guidelines recommend against over-investigation of small, incidental thyroid nodules in the UK.

In 2014, the British Thyroid Association Guidelines recommended that small (<1cm) nodules which are found incidentally on ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI) could be managed in primary care. It went on to state that only incidental nodules with worrying features such as extra thyroidal extension, nodal metastasis or uptake on fluorodeoxyglucose positron emission tomography (FDG-PET) scanning warranted further investigation (25). This advice was recommended to avoid significant resource implications. Additionally, and perhaps more importantly, it also serves to protect against over diagnosis and over treatment of patients with incidental thyroid nodules, which contrasts to approaches in other developed countries.

In the US it is projected that over 50,000 patients in the next 5 years will be candidates for active surveillance (26). Our results, in contrast, suggest that in UK practice very few patients are suitable. Only a small group present with <1cm PTC and of those that do, almost none are diagnosed pre-operatively. Active surveillance has been found to be extremely effective in selected populations when performed by groups with high levels of experience. Whether such an approach would translate to UK centers and whether such an approach would be acceptable to a UK population remains to be seen (27). However, even more critical is that during a time where practice guidelines are increasingly influential, updated iterations of such documents continue to support an approach to incidental thyroid nodules which minimizes the requirement to further investigate patients who have an extremely low risk of harbouring clinically significant disease.

This study is limited by generalising the patterns of a single UK multidisciplinary team as representation of the nation’s standard, it may thus not be replicable across different centres across the UK. It is important to stress that we have not attempted to report the success of active surveillance for PTMC here, as this was not the aim of the study. It is also possible that some PTMC cases were not discussed in the multidisciplinary team meetings, although it is institutional practice to discuss all malignant thyroid cases irrespective of mode of presentation, which is monitored by both surgical and pathological disciplines.

**Conclusion**

Our results suggest that, in contrast to the situation in USA, active surveillance for papillary thyroid microcarcinoma may only be suitable for a tiny minority of cases presenting to thyroid multi-disciplinary teams in the UK. Although the merits of active surveillance in a UK population warrant consideration, continuation of the UK’s selective approach to investigation of incidental thyroid nodules should be prioritised to ensure optimal use of healthcare resources.

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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