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Article

Diagnostic Value of Thyroid Physical Examination in the Elderly and Comparison with Ultrasonography

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Abstract: This study is part of the health project called "Health screening for the elderly in Ankara" for patients aged 65 and over, with 1200 participants. Patients with missing laboratory tests (n = 59), movement disorders and/or bedridden (n = 54) were excluded from the study. PE was performed by a geriatrician or an ear, nose, and throat surgeon, and ultrasonographic evaluation was performed by a radiologist. PE and USG findings were compared. We aimed to investigate the diagnostic accuracy of physical examination (PE) of the thyroid gland (TG) in patients over 65 years of age and to assess the reliability by comparing PE with ultrasonographic (USG) examination. The median age of the patients participating in the study was 71.17. When the differences between thyroid nodules (TN), the number of TN size, and goiter detection were compared in terms of PE and USG, all values were statistically significant, and *P* values were < 0.001. The sensitivity of PE of TG was calculated as 31.0%. In our study, the sensitivity of PE of TG in terms of TN and goiter was found to be low. The diagnostic accuracy of PE of TG is low, and therefore, its impact on clinical decision-making is limited. Furthermore, detected nodules rarely progress to clinically relevant disease, leading to overdiagnosis and overtreatment. Especially in groups at risk for nodules and malignancy, PE must be combined with imaging methods and, if necessary, pathological examination, even if nodules or goiter are not palpable in PE.

Highlights:

- The clinical features of thyroid disease are altered in older people, so that the symptoms and physical findings may be different and less prominent than in younger people, or may even be absent.
- TNs have a prevalence of 4% in the general population based on PE and ≤ 50% based on USG or direct visualisation during surgery, and ≤ 100% in autopsy series.
- An important finding of the present study is that as the size of the thyroid increases, the ability to palpate TNs also increases.
- Thyroid PE should always be combined with imaging and, if necessary, histopathology in those at risk of TNs and malignancy, even when TNs or goiters are not palpable.

Keywords: Thyroid Nodule; Ultrasonography; Physical Examination; Elderly

1. Introduction

The thyroid gland is one of the primary determinants of the development and metabolism of almost every organ system. Thyroid disorders can occur in all age groups, but their prevalence increases with age. The clinical features of thyroid disease are altered in older people, so that the symptoms and physical findings may be different and less prominent than in younger people, or may even be absent. Normally, ageing is associated with changes in the gross appearance and histological and microscopic findings of the thyroid gland, but some studies report that ageing results in little change in the size of the thyroid gland as measured by ultrasound [1].

The rate of adults with palpable TN on PE is less than 5%. Although the rate is low, the number of people who need to be assessed is quite high. The majority (> 95%) of TNs are the result of benign disease processes. However, the possibility of thyroid cancer should always be considered. In patients with TN, the medical history includes gender, age, history of low-dose head and neck irradiation, family history of thyroid or endocrine disease, hypermetabolism, and recent symptoms of hoarseness and dysphagia. The physical examination (PE) will mainly assess the size and location of the thyroid abnormality, the presence and degree of stiffness of the TNs, vocal cord paresis or paralysis, palpable cervical lymph nodes, tachycardia, and tremor. Important thyroid abnormalities in these patients include adenomas, cysts, thyroiditis, and cancer [2]. Thyroid disorders are common in the elderly and can cause serious morbidity if left untreated. The typical symptoms mentioned may not be present and may be attributed to normal ageing or comorbidities. A PE of the thyroid gland in the elderly is not always helpful, as the gland often shrinks and becomes difficult to palpate.

TNs have a prevalence of 4% in the general population based on PE and ≤ 50% based on USG or direct visualisation during surgery, and ≤ 100% in autopsy series. PE can detect almost 10% of TNs, and in general < 5% of TNs are cancerous [3]. Clearly, there is a significant gap in the frequency of TNs detected by PE and other modalities. The world's population is ageing, and by 2050, 1.6 billion of the world's population will be aged ≥ 65 years or older. If incidental TNs and patients with thyroid pain are excluded, US of the thyroid is performed whenever there is a PE abnormality, such as a goiter or nodule. This raises the possibility that, in elderly patients with normal PE findings, PE is not a sufficiently sensitive or reliable method for clinical decision-making to show that they have TNs and are goiter-free. This is because TNs and thyroid cancer are clinically silent in most cases, and PE may lead to a lack of early detection of TNs with malignant potential and early intervention. The aim of the present study was to determine the diagnostic accuracy of PE of the thyroid gland in the elderly and whether PE is a reliable method by comparing PE and US findings. We hypothesised that the diagnostic accuracy of thyroid palpation is low.

2. Materials and Methods

This study was part of the Health Screening in the Elderly in Ankara Mamak Region project, which included 1200 participants aged ≥ 65 years. The main objective of the study was to determine the prevalence of thyroid disorders and iodine status of the population after 10 years of mandatory iodisation. Participants were invited through announcements in the community. Of the 1200 participants, those with communication difficulties (n = 108), those who did not give consent for thyroid US (n = 81), those with incomplete laboratory tests (n = 59), and those with mobility problems and/or bedridden (n = 54) were excluded from the study. A total of 898 participants were included in the study.

The PE was performed by a geriatrician or an otorhinolaryngologist with 9 years of experience, and the radiological evaluation was performed by a radiologist with 11 years of experience. Thyroid glands > 4–4.8 x 1 cm–1.8 x 0.8–1.6 cm were accepted as goiter [4]. The US was performed using a General Electric Logic 200 unit with a 7.5 MHz linear probe. The US was used to measure three dimensions of each thyroid lobe and the TN/TNs detected. Thyroid and TN volumes were calculated using the ellipsoid body formula proposed by Brunn et al.: 18 mL for females and 25 mL for males were accepted as goiter [5,6].

Venous blood samples were taken for thyroid function tests [7]. Thyroid fine-needle aspiration biopsy (FNAB) was performed by the same physician who performed the US for TNs > 1 cm and with non-suppressed TSH levels. Samples were evaluated by a cytologist. Data were analysed using IBM SPSS Statistics for Windows v.20.0 (IBM Corp., Armonk, NY). Results are presented as mean ± SD and percentage. The chi-squared test was used to examine statistical associations between independent categorical variables. Correlations between categorical variables were assessed using the Spearman test. The level of statistical significance was set at $P < 0.05$. The study was ethically approved by the Ethical Committee of Ankara University under number 124-3368. All participants were enrolled with informed consent.

3. Results

Demographic characteristics and thyroid disorders are shown in **Table 1**, and PE and US findings are shown in **Table 2**. Based on the US, 235 participants had TNs, of which 104 (31.0%) were found to have TNs by PE palpation. Of the 121 participants who had TNs based on palpation, 104 also had TNs based on US. Of the 777 participants who did not have TNs based on PE palpation, 546 did not have TNs based on US, and the difference was significant (*P* < 0.001) (**Table 3**).

Table 1. Participant Characteristics.

Age (years) ± Standard Deviation	71.17 ± 6.01
Sex	Number (%)
Female	603 (67.1)
Male	295 (32.9)
TSH Level µIU/mL	2.36 ± 6.88
sT3 Level pmol/L	16.34 ± 3.56
sT4 Level pmol/L	4.73 ± 1.19
Thyroid Hormone Replacement Users Number(%)	45 (5%)
Antithyroid Medication Users Number(%)	11 (1.2 %)

Table 2. Examination of the Thyroid Gland.

	Physical Examination Number (%)	Ultrasonographic Examination Number (%)	Ultrasonographic Nodule Size	
Goiter present	240 (26.7)	258 (28.7)	< 1 cm	72 (21.5)
Goiter absent	658 (73.27)	640 (71.3)	1–2 cm	142 (42.4)
No nodule	777 (86.5)	563 (62.7)	≥ 2 cm	121 (36.1)
Solitary nodule	86 (9.6)	155 (17.3)		
Two nodules	35 (3.9)	180 (20.0)		

Table 3. Comparison of Thyroid Nodule Detection Between Physical and Ultrasonographic Examination.

	Cases TN + in PE, n(%)	Cases TN - in PE, n(%)	Total n (%)	*P*-value
Cases TN + in USG, n	104 (31.0)	231 (69.0)	235(100)	
Cases TN - in USG, n	17 (3.0)	546 (97.0)	563(100)	< 0.001
Total n	121	777	898	

Notes: TN: thyroid nodule, PE: physical examination, USG: ultrasonography, n: number.

Overall, of the 777 participants found to have no TNs based on PE palpation, 129 had a solitary TN and 102 had ≥ 2 TNs based on US. Of the 86 participants with a solitary TN based on PE palpation, 16 had no TN, and 47 had ≥ 2 TNs based on US. Of the 35 participants with 2 TNs based on PE palpation, 1 had no TN and 3 had 3 TNs based on US; the differences were significant (*P* < 0.001) (**Table 4**).

Table 4. Compatibility of Physical and Ultrasonographic Examination of Thyroid Gland Regarding Nodule Number.

		Nodule Number in PE, n(%)			Total n(%)	
		0	1	2		*P*-value
Nodule number in USG	**0**	546 (97.0)	16 (2.8)	1 (0.2)	563(100)	< 0.001
	1	129 (83.2)	23 (14.8)	3 (1.9)	155(100)	
	≥ 2	102 (56.7)	47 (26.1)	31 (17.2)	180(100)	
Total n		777	86	35		

Notes: PE: physical examination, USG: ultrasonography, n: number.

Of the 72 TNs < 1 cm in diameter based on US, 4 were palpated by PE, of the 142 TNs ≥ 1–2 cm in diameter based on US, 33 were palpated by PE, and of the 121 TNs ≥ 2 cm in diameter based on US, 67 were palpated by PE; the differences were significant (*P* < 0.001) (**Table 5**). Of the 240 participants found to have a goiter by PE palpation, 134 had a goiter based on US. Of the 658 participants with normal thyroid size, 124 had a goiter, and the difference was significant (*P* < 0.001).

Table 5. Comparison of Palpability of Thyroid Nodules Regarding Size.

		Palpable Nodules in PE, n(%)	Impalpable Nodules in PE, n(%)	Total n(%)	*P*-value
Nodule size in USG	< 1 cm	4 (5.6)	68 (94.4)	72 (100)	< 0.001
	1-2cm	33 (23.2)	109 (76.8)	142(100)	
	≥ 2cm	67 (55.4)	54 (44.6)	121(100)	
Total n		104	231	335	

Notes: PE: physical examination, USG: ultrasonography, n: number.

Of the 235 participants with TNs based on US, 76 had TNs based on PE palpation, and 177 had a goiter based on US. Of the 158 participants with a goiter based on US, 28 had TNs based on PE palpation, and the difference was significant ($P < 0.001$). Thyroid PE had a positive predictive value of 86.0%, a negative predictive value of 70.3%, a sensitivity of 31.0%, and a specificity of 97.0%. No malignant pathology was detected by FNAB cytology in the 60 participants who agreed to undergo FNAB.

4. Discussion

Our results suggest that TNs are missed in most cases of PE in the elderly and are in agreement with Detweiler et al. [8]. Tunbridge et al. reported a TN frequency of 1% in patients aged 18–75 years by palpation, Bruenton et al. found a TN rate of almost 35% in an adult population based on the USA, and Oertel and Click observed a TN rate of 94% in autopsies of adults aged 18–39 years [9–11]. Taken together, these studies suggest that TN detection in PE is not a reliable method. Age is a risk factor for mortality in patients with thyroid cancer. Cady et al. [12] reported a 26-fold increase in clinical mortality risk based on age, distant metastases, and extent of primary cancer. In addition, Belfiore et al. [13] showed that the frequency of malignant TNs was higher in patients aged > 60 years and that the frequency of malignancy did not differ between single and multiple TNs, concluding that the risk of malignancy is related to iodine intake, gender, and age. As palpation of TNs in the elderly has a sensitivity of 31%, clinicians should be aware that failure to detect TNs by palpation in the elderly does not always mean that TNs are not present, and that there should be a lower threshold for confirming PE findings by imaging.

TN growth has been shown to increase the risk of malignancy; therefore, detection of TNs prior to malignant transformation is essential for both follow-up and early diagnosis. Recently, O'Connell et al. [14] reported that a minimum 2 mm increase in TN size is associated with the risk of malignancy; TNs double in size in 463 days, and if diagnosed early, there is sufficient time for TN intervention. The number of TNs is another important parameter for clinical decision-making. None of the participants in the present study had > 2 TNs based on PE, but some were found to have up to 5 TNs based on US. Castro et al. [15] studied 462 patients with TNs and concluded that patients with cytologically suspicious TNs, multiple TNs, or TNs > 2 cm have an increased risk of malignancy. The present results show that, in addition to being unreliable, PE may also be misleading, as TNs ≥ 2cm were not palpated in 45% of cases and TNs < 1cm were missed in > 95% of cases, suggesting that TNs are rarely palpated when silent.

The size of the TN is also clinically relevant. Although TNs ≥ 2 cm in diameter have a higher risk of malignancy, this does not mean that smaller TNs have no risk of malignancy. TNs 1.0–1.9 cm in diameter have a malignant potential of almost 10%, compared to 14% for those ≥ 2 cm [16]. Khalife et al. [17] reported that TNs 1–1.9 mm and 2–29 mm have the same risk of malignancy. Kizilgul et al. [18] recently reported that TNs ≥ 4 cm in diameter have a higher rate of malignancy or a higher rate of false-negative benign cytology. Unsurprisingly, the present results show that as TN size increases, the likelihood of being palpable also increases. In the present study, TNs ≥ 2 cm were detected more frequently than those < 2 cm. The present results show that 76.8% of TNs ≥ 1-2 cm had a 10% risk of malignancy, and 44.6% of TNs ≥ 2 cm had an almost 15% risk of malignancy and were missed by palpation. As prevention and early detection of cancer are the mainstays of oncology practice, alternative methods for detecting TNs can be used in clinical practice.

We believe that although PE is free, quick, and presumably harmless, there are cases where PE can be dangerous to the patient by giving the clinician a false sense of security when nothing is palpated. Whether or not to screen for TN is controversial. According to the United States Preventive Task Force, the incidence rate of thyroid cancer is 15.3 cases per 100,000 persons, the 5-year survival rate of thyroid cancer is 98.1%–99.9% for localised cancer and 55.3% for distant metastatic disease, there is no health improving effect of screening for thyroid cancer using PE or US, and after the introduction of population-based screening there is no difference in mortality rates between patients treated and those only monitored. In addition, it was concluded that the detection of TNs/cancer after population-based screening could lead to harm from overtreatment and overdiagnosis [19]. The prevalence of thyroid cancer is close to 0.1% in the elderly, which is clinically evident, and the prevalence of TNs is up to 100% in autopsy series [20]. Similarly, in the present study, 29.77% of TNs were not palpable, and no malignancy was noted in any of the biopsy results. A subgroup analysis of the Framingham study supports this, as more than 5000 patients were followed for 15 years, with a 1.4% incidence of new TNs, none of which showed evidence of malignancy [21]. The American Thyroid Association recommends the use of serum thyrotropin, incidental findings, and US parameters to assess the risk of TN [22]. The McGill TN Score System uses 8 clinical or laboratory parameters (15 points), 8 imaging findings (17 points), 6 cytological or molecular findings (31 points), and only 1 PE finding (1 point), which is the presence of a palpable TN, and gives a 27% risk of malignancy to 1–3 points, which the geriatric population already has at age > 65 years [23].

5. Conclusions

Up to 95% of TNs < 1 cm are missed by PE; therefore, PE misses TNs with a 27% risk of malignancy. If clinical decision-making is to be based on published guidelines, an alternative method to PE must be used in clinical practice to detect TNs, especially in the elderly. Therefore, we strongly recommend the definition of a specific target population for further clinical evaluation of TNs, especially in the elderly who have a limited life expectancy compared to younger adults, as there is a high probability that the patient will die before any complications of the TN. In the present study, 14% of palpated TNs were not detected by US, and none of the TNs were malignant. In the light of our findings, we believe that for the specific group of elderly people who are at high risk of thyroid malignancy - those with a family history of medullary thyroid cancer, familial adenomatosis polyposis, Cowden's disease, Carney's complex, and a first-degree relative with thyroid cancer - and for those who live in an iodine deficient diet, US may be a useful tool, and those living in an iodine-deficient region, with radiation exposure, a high BMI, non-smokers, non-drinkers, and those with a low monthly household income - PE findings should be confirmed with the most appropriate imaging modality for each patient, regardless of PE findings [24,25].

Another important finding of the present study is that as the size of the thyroid increases, the ability to palpate TNs also increases. To the best of our knowledge, there is no study to support or refute this finding, but we believe that as the thyroid increases, it becomes easier to palpate, both because of the increase in size and because of its more superficial location, and that this increase in size may lead clinicians to pay more attention during PE; however, this needs to be supported by further studies. Despite the increase in thyroid size, only about 50% of goiters are detected by palpation.

The present study has several strengths: it is the first study with the primary aim of determining the correlation between PE and US of the thyroid gland in the elderly; the study population was sufficiently large; the elderly participants - both healthy and unhealthy - lived in the community; the study used a double-blind design. The study also has limitations, including the fact that it was not known whether the TNs detected by US were the same TNs that had been palpated or whether there was chance, leading us to believe that the sensitivity of PE was lower than that of US; the accuracy of both PE and US depends on the skill of the clinician; and each participant underwent PE and US only once. Also, echogenicity, irregular border, and shape of TNs were not detected in this study. PE of the thyroid in the elderly has low sensitivity for detecting TNs and goiters, with minimal impact on clinical decision making, leading to overdiagnosis and overtreatment, and in certain circumstances, such as suspicious cytology results, PE findings may also be misleading. Thyroid PE should always be combined with imaging and, if necessary, histopathology in those at risk of TNs and malignancy, even when TNs or goiters are not palpated.

Author Contributions

Conceptualization, M.I.G.; methodology, M.I.G. and C.A.; software, M.I.G.; validation, M.I.G. and C.A.; formal analysis, M.I.G.; investigation, C.A.; resources, C.A.; data curation, M.I.G.; writing—original draft preparation, C.A.; writing—review and editing, M.I.G.; visualization, M.I.G.; supervision, M.I.G.; project administration, C.A.; funding acquisition, C.A. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of Ankara University (protocol code 124-3368 and date of approval).

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

This study was part of the Health Screening in the Elderly in Ankara Mamak Region project.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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