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Thyroid Doppler parameters association with coronary atherosclerosis burden

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SOUHRN

Kontext: Dosud se toho ví málo o možné spojitosti mezi cévním zásobením štítné žlázy a aterosklerotickou zátěží koronárních tepen u pacientů s podezřením na ischemickou chorobu srdeční.
Cíle: Posoudit možnou spojitost mezi dopplerovskými parametry horní štítné tepny a markery aterosklerózy koronárních tepen včetně závažnosti stenózy, kalcifikace koronárních tepen (CAC) a rozsahu plátu zjištěného koronarografickým vyšetřením pacientů s podezřením na ischemickou chorobu srdeční (ICHS) metodou multidetektorové výpočetní tomografie (MDCT).
Pacienti a metody: Do této průřezové studie bylo zařazeno 100 pacientů s bolestí na hrudi, u nichž byla pro vyloučení okluzivní ischemické choroby srdeční provedena koronarografie MDCT. Všichni zařazení pacienti byli z klinického hlediska eutyreoidní, bez klinických známek hypotyreózy nebo hypertyreózy. U zařazených pacientů byla pro stanovení cévních parametrů včetně indexu rezistence (RI), maximální rychlosti proudění krve v systole (PSV), rychlosti proudění krve na konci diastoly (EDV) a indexu pulsatility (pulsatility index, PI) sonograficky vyšetřena horní štítná tepna.
Výsledky: Byla nalezena statisticky významná spojitost mezi sníženými hodnotami PSV (16 cm/s vs. 15 cm/s; $p = 0{,}03$) a CAC ≥ 400, a to i po další adjustaci na rizikové faktory koronárních příhod (OR [CI] = 0,3 [0,1–0,8]; $p = 0{,}03$). Pacienti s významnou koronární stenózou (≥ 50%) vykazovali vyšší hodnoty RI (0,58 vs. 0,54; $p = 0{,}04$) než jedinci bez významné koronární stenózy (< 50%). Po adjustaci na jiné rizikové faktory koronárních příhod však již tato spojitost nepřetrvávala. Nebyla pozorována spojitost mezi parametry vyšetření štítné žlázy dopplerovským ultrazvukem včetně PSV, EDV, RI a PI na jedné straně, a přítomností koronárních plátů na straně druhé.
Závěr: Hodnoty PSV a RI v horní štítné tepně vykazovaly statisticky významnou spojitost se zátěží CAC a s významnou koronární stenózou. Tyto výsledky mohou naznačovat možné spojení mezi parametry rezistence cév štítné žlázy a zátěží aterosklerózou koronárních tepen.

Keywords:
Atherosclerosis
Coronary
CT angiography
Doppler ultrasonography
Thyroid

ABSTRACT

Background: Little is known about the potential association between thyroid vascular parameters and coronary atherosclerotic burden in patients with suspected coronary artery disease.
Objectives: To assess the potential association between superior thyroid artery Doppler parameters and coronary atherosclerotic markers, including stenosis severity, coronary artery calcification (CAC), and plaque assessed by multi-detector CT (MDCT) coronary angiography among patients with suspected coronary artery disease (CAD).
Patients and methods: This cross-sectional study included 100 patients with chest pain who underwent MDCT coronary angiography to exclude the presence of occlusive coronary artery disease. All of the enrolled patients were clinically euthyroid, with no clinical features of hypothyroidism or hyperthyroidism. The superior thyroid artery in enrolled patients was examined using ultrasound to assess vascular parameters, including resistive index (RI), peak systolic velocity (PSV), end-diastolic velocity (EDV), and pulsatility index (PI).
Results: There was a significant association between decreased PSV values (16 cm/s vs. 15 cm/s, $p = 0.03$) and CAC ≥400, even after further adjustment for coronary risk factors (OR (CI) = 0.3 (0.1–0.8. $p = 0.03$). Patients with significant coronary stenosis severity ≥50% had higher RI values (0.58 vs. 0.54, $p = 0.04$) than those with

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a non-significant coronary stenosis <50%. However, this association did not persist after adjustment for other coronary risk factors. No significant association was observed between thyroid Doppler parameters, including PSV, EDV, RI, and PI, and coronary plaque presence.
Conclusion: PSV and RI of the superior thyroid artery showed a significant association with CAC burden and significant coronary stenosis. These results may suggest a possible link between thyroid vascular resistance parameters and coronary atherosclerosis burden.

Introduction

The thyroid gland is a highly vascular tissue located in close proximity to carotid arteries. Superior thyroid artery, which is the chief artery supplying blood to the thyroid tissue arising from external carotid artery, is superficial and easily assessed by Doppler sonography in comparison to inferior thyroid artery. Assessing thyroid gland vascularity during carotid ultrasound examination is not time consuming and may have diagnostic implications.[1,2] Clinical and pathological studies have reported altered thyroid gland vascularity in clinically euthyroid individuals secondary to various diseases, including coronary artery disease (CAD).[3]

Vascular resistance parameters of thyroid arteries measured by pulsed-wave Doppler sonography, such as resistive index (RI), peak systolic velocity (PSV), end-diastolic velocity (EDV), and pulsatility index (PI) may reflect not only local vascular resistance or hemodynamic changes but also systemic arterial stuffiness or endothelial dysfunction.[4] Results from previous studies suggest that parameters of vascular resistance of renal or retinal arteries can estimate the severity of systemic atherosclerosis, particularly among persons with coronary risk factors.[4,5]

Thyroid hormones affect the heart and coronary vessels through different pathophysiological mechanisms, including endothelial dysfunction, increased intima-media thickness, and increased vascular resistance. Moreover, several clinical studies have reported an increased risk of all-cause mortality morbidity in patients with thyroid disorders, even after accounting for coronary risk factors such as dyslipidemia, diabetes, and hypertension.[6–8] Other studies have found a significant link between thyroid gland dysfunction and coronary calcification, even in patients with normal thyroid function.[9,10]

In contrast to primary thyroid disorders, peripheral thyroid hormone metabolism is impaired, as part of the non-thyroidal illness syndrome, in a variety of cardiovascular diseases such as myocardial infarction and heart failure. This abnormal alteration in thyroid hormone balance is proportional to the severity of the underlying heart disease and serves as a predictor of poor cardiovascular outcomes.[11]

In the literature, little is known about the possible link between thyroid vascular parameters and coronary atherosclerotic burden in patients with suspected CAD. The main aim of the present study was to assess the potential association between the superior thyroid artery Doppler parameters, including RI, PSV, EDV, and PI, and coronary atherosclerotic markers, including stenosis severity, coronary artery calcification (CAC), and plaque assessed by multi-detector CT (MDCT) coronary angiography among patients with suspected CAD.

Patients and methods

A cross-sectional study was conducted between January 2023 and October 2023. It included a sample of 100 patients with chest pain who underwent 64-MDCT coronary angiography at the Al-Sader teaching hospital in Al-Najaf city, Iraq, to exclude the presence of occlusive CAD. As described in detail in our previous study, each patient provided a thorough history at the time of the MDCT angiography examination regarding coronary risk factors such as sex, age, diabetes mellitus, hypertension, smoking, dyslipidemia, family history of premature CAD, and BMI.[12] All of the enrolled patients were clinically euthyroid, with no clinical features of hypothyroidism or hyperthyroidism. The exclusion criteria were as follows: (1) a history of hypothyroidism or hyperthyroidism or prior treatment with radioiodine; (2) use of medications that could interfere with thyroid function; (3) previous thyroid or neck surgery; and (4) thyroid nodules or altered parenchymal echo pattern identified during Doppler sonography examination.

MDCT examination

CT coronary angiography examination was conducted using a 64-slice scanner (Aquilon 64, v. 4.51 ER 010; Toshiba Medical Systems, Tochigi, Japan), with retrospective electrocardiography gating, and a non-contrast CT was acquired to measure the calcium score according to the Agatston method using a sequence scan with a slice thickness of 3 mm, as previously described in detail.[12] Coronary stenosis severity was graded as normal to non-significant stenosis (a mean lumen diameter reduction of <50%) and significant coronary stenosis as a mean lumen diameter reduction of ≥50% in a single vessel by comparing the lumen diameter of the narrowest segment with that of a more proximal or distal normal segment in two orthogonal projections. Coronary plaques were identified as thickening ≥1 mm in thickness within or adjacent to the coronary artery wall. Plaques were categorized into calcified plaques (plaques consisting of only calcium or containing both calcified and non-calcified components) and non-calcified plaques (plaques that were free of calcium). All CT angiography data analyses were assessed independently by two radiologists with over five years of expertise in coronary MDCT angiography interpretation. Verbal, informed consent was obtained from all enrolled participants. The study was approved by our medical college board.

Superior thyroid Doppler ultrasonography

The color Doppler ultrasound examination of the superior thyroid artery was performed by an experienced radiologist for all included patients before MDCT examination

using a ML probe (frequency 6–15 MHz) of the GE LOGIC E9 XD Clear ultrasound system (GE Healthcare, 2019, USA). The ultrasonography examination was conducted while the patient was in the supine position with a cushion under his shoulder and his neck extended. The superior thyroid artery was identified as the first branch of external carotid artery that arises anteriorly at the level of the hyoid bone and is traced up to the upper pole of the thyroid gland. The Doppler parameters of the left and right superior thyroid arteries measured were RI, PSV, EDV, and PI. RI was calculated according to the following formula: RI = PSV – EDV / PSV of the superior thyroid artery. The right and left superior thyroid artery-related Doppler parameter values were averaged to obtain a single mean for each parameter.

Statistical analysis

The statistical analysis of the data was conducted using SPSS version 23.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD). Categorical variables were expressed as numbers (%). The significance of the differences among groups was analyzed using a two-tailed Student t-test. A p-value <0.05 was considered statistically significant in all analyses. Binary logistic regression was used to assess the association between superior thyroid artery Doppler parameters and coronary risk factors, including age, sex, BMI, diabetes mellitus, hypertension, family history, and smoking with CAC ≥400 and significant coronary stenosis.

Results

A total of 100 patients (age = 59 ±5 years, male sex 46%) with suspected CAD and clinically euthyroid state who underwent 64 multi-slice MDCT coronary angiography to rule out the presence of occlusive coronary artery disease were enrolled in the present study. The prevalence of coronary risk factors was as follows: hypertension (55%), smoking (45%), obesity (42%), diabetes mellitus (39%), family history (30%), and dyslipidemia (30%). Eleven patients had CAC ≥400, whereas 15 patients had significant coronary artery stenosis (stenosis severity ≥50%). Coronary plaque was detected in 68 patients. Calcified plaque was detected in 66 patients, while only two patients had non-calcified plaque. The mean values of Doppler parameters of the superior thyroid artery were as follows: RI = 0.55 ± 0.09; PSV = 16 ± 0.78; EDV = 7 ± 0.89; PI = 0.89 ± 0.13. Clinical characteristics, as well as coronary atherosclerotic markers assessed by MDCT and Doppler parameters of the superior thyroid artery, are displayed in **Table 1**. There was a significant association between decreased PSV values (16 cm/s vs. 15 cm/s, p = 0.03) and CAC ≥400, even after further adjustment for coronary risk factors (OR (CI) = 0.3(0.1–0.8. p = 0.03). No significant association was found between other Doppler parameters and CAC ≥400, as in **Tables 2** and **3**. **Table 2** shows that patients with significant coronary stenosis severity ≥50% had higher RI values (0.58 vs. 0.54, p = 0.04) than those with non-significant coronary stenosis <50%. However, this association did not persist after adjustment for other coronary risk factors, as seen in **Table 3**. Other Doppler parameters, as shown in **Table 2**, showed no significant differences between coronary stenosis severity groups. No significant association was observed between thyroid Doppler parameters and coronary plaque presence, as seen in **Table 2**.

Discussion

In the literature, thyroid dysfunction is associated with accelerated coronary atherosclerosis and an increased risk of adverse cardiovascular events. This association can be explained by the effect of thyroid hormones on endothelial dysfunction, vascular resistance, and the higher prevalence of hypertension and lipid abnormalities in patients with thyroid dysfunction.7 Furthermore, evidence from clinical studies suggests that thyroid disorders when thyroid hormones are within the euthyroid range may be associated with significant coronary stenosis and carotid atherosclerosis, even in young people with low overall cardiovascular risk.[10]

Pulsed-wave Doppler parameters of thyroid arteries are quantitative and qualitative markers of arterial compliance and endothelial dysfunction, representing an early and reversible feature of atherosclerosis. PSV and RI indices of the superior thyroid artery measured by Doppler ultrasonography are affected by both vascular wall

Table 1 – Patients characteristics

Variables	Mean ± SD or n (%) or median (IQR)
Age (years)	59 ± 5
Male sex	46 (46)
Family history	30 (30)
BMI	27 ± 5
Obesity (BMI ≥30)	42 (42)
Diabetes mellitus	39 (39)
Hypertension	54 (55)
Smoking	45 (45)
Dyslipidemia	30 (30)
Coronary atherosclerosis markers	
Coronary artery calcium score	280 (160–350)
CAC ≥400	11 (11)
Significant coronary stenosis >50%	15 (15)
Coronary plaque presence	68 (69)
Non-calcified plaque	2 (2)
Calcified plaque	66 (67)
Multiple coronary plaques	25 (25)
Thyroid Doppler parameters	
Resistive index (RI)	0.55 ± 0.09
Peak systolic velocity (PSV), cm/s	16 ± 0.78
End-diastolic velocity (EDV), cm/s	7 ± 0.89
Pulsatility index (PI)	0.89 ± 0.13

Table 2 – Association of coronary atherosclerotic markers with thyroid Doppler parameters

CAC			
	CAC <400	**CAC ≥400**	***p*-value**
RI	0.54 ± 0.0	0.58 ± 0.1	0.25
PSV	16 ± 0.7	15 ± 0.6	0.03
EDV	7 ± 0.8	7 ± 1	0.63
PI	0.9 ± 0.1	0.8 ± 0.1	0.07
Coronary stenosis severity			
	Stenosis <50%	**Stenosis ≥50%**	***p*-value**
RI	0.54 ± 0.0	0.60 ± 0.1	0.04
PSV	16 ± 0.7	15 ± 0.8	0.38
EDV	7 ± 0.8	7 ± 1	0.48
PI	0.9 ± 0.1	0.8 ± 0.1	0.09
Coronary plaque presence			
	Without plaque	**Plaque presence**	***p*-value**
RI	0.54 ± 0.0	0.55 ± 0.0	0.71
PSV	16 ± 0.8	16 ± 0.7	0.39
EDV	7 ± 0.8	7 ± 0.9	0.92
PI	0.8 ± 0.1	0.8 ± 0.1	0.88

Table 3 – Regression analysis*

CAC ≥400			
	Odd ratio	**Confidence interval**	***p*-value**
PSV	0.3	0.1–0.8	0.03
Diabetes mellitus	5	1.3–15	0.01
Significant coronary stenosis >50%			
Age	1.3	1–1.6	<0.01
Diabetes mellitus	4	1–10	<0.01
Hypertension	5	2–12	<0.01

* Only variables with statistically significant associations are displayed in the **Table**.

disorders, such as atherosclerosis, and parenchymal thyroid dysfunction, such as inflammation or fibrosis.[13] Furthermore, PSV is widely used in the differential diagnosis of thyrotoxicosis and can provide valuable data about underlying thyroid functional status.[1,14,15] In the present study, the significant and independent association of superior thyroid artery PSV with CAC ≥400 may suggest that thyroid vascular resistance, as measured by Doppler ultrasound, may reflect the systemic atherosclerosis burden such as significant coronary calcification, particularly among patients with suspected coronary artery disease.

Studies of the association between thyroid vascular parameters and coronary atherosclerosis markers are sparse and have been inconsistent in the literature.

A significant positive association has been reported between thyroid hormones, even in the euthyroid range, and coronary calcification burden.[9,16] A study conducted by Y. Zhang et al. enrolled an apparently healthy young and middle-aged euthyroid population and reported a significant association between thyroid hormones and a higher prevalence of subclinical coronary artery disease and a greater degree of coronary calcification.[10] Furthermore, Gunduz et al. conducted a prospective study to assess the impact of internal carotid angioplasty and stenting on the superior thyroid artery Doppler parameters. They found that there was no significant correlation between superior thyroid artery Doppler flow parameters and the presence of coronary artery disease and other coronary risk factors such as increased age, hypertension, diabetes mellitus, smoking, or dyslipidemia.[1]

Another study conducted by Chekalina et al. found that PSV and RI of thyroid arteries were considerably higher among euthyroid patients with autoimmune thyroiditis and coronary artery disease than in healthy persons, suggesting that high values of thyroid Doppler parameters in patients with thyroiditis and CAD have been linked to endothelial dysfunction secondary to pro-inflammatory cytokines overproduction.[17]

Several limitations should be addressed when interpreting the findings of the present study. First, this was a single-center cross-sectional study including patients with suspected CAD. As a result, the findings may not be generalizable, and the causal relationship between thyroid vascular parameters and coronary atherosclerotic markers cannot be determined. Second, the possibility of residual confounding in an observational cross-sectional study design cannot be entirely excluded. Third, thyroid hormone measurements were not performed, and the likelihood of some patients having subclinical thyroid functional changes cannot be ruled out, despite a normal thyroid appearance on ultrasound examination. Also, the potential effect of thyroid hormones on the association between thyroid vascular parameters and coronary calcification cannot be adjusted. Fourth, we enrolled a relatively small sample size of the study population, which may limit the power of the study to detect a statistically significant association between some Doppler parameters and coronary atherosclerosis markers. Further large prospective studies are required to establish a causal relationship between coronary atherosclerotic markers and thyroid vascular resistance and explore the potential mechanism.

Conclusion

PSV and RI of the superior thyroid artery showed a significant association with CAC burden and significant coronary stenosis. These results may suggest a possible link between thyroid vascular resistance parameters assessed by Doppler ultrasonography and coronary atherosclerosis burden among patients with suspected CAD.

Conflict of interest
The authors declare that they have no conflict of interest.

Funding
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Ethical approval
Not applicable.

Informed consent
Verbal informed consent was obtained from all enrolled participants.

Availability of supporting data
The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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