



Thyroid Embolization for Nonsurgical Treatment of Nodular Goiter: A Single-Center Experience in 56 Consecutive Patients

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ABSTRACT

Purpose: To investigate the safety and efficacy of thyroid artery embolization (TAE) in the treatment of nodular goiter (NG).

Methods: During a 5.5-year period, 56 consecutive patients with a NG underwent TAE. In Group A, there were 20 patients with a solitary/dominant 5–11-cm nodule, and in Group B, there were 36 patients with numerous nodules. Of the 56 patients, 47 (84%) had a retrosternal goiter and 25 had hyperthyroidism. In all patients, clinical and radiological evaluations were made at baseline and 6 months after TAE, and these parameters were statistically compared.

Results: In 56 patients, 145 of the 146 thyroid arteries were successfully embolized. The 30-day mortality rate was 1.8%. Minor and major complications occurred in 25 and 2 patients, respectively. Six months after the TAE, the mean nodule volume was reduced from 80.2 mL to 25.0 mL, the mean thyroid volume was reduced from 147.0 mL to 62.6 mL, and the mean intrathoracic extension was reduced from 31.7 mm to 15.9 mm ($P < .001$). Of the 22 patients with non-Graves hyperthyroidism, 19 (86%) became euthyroid. The mean thyroid-related patient-reported outcome scores improved from 155.4 to 70.4 ($P < .001$). Of the 51 patients, 50 (98%) declared that they would recommend TAE to other patients with NG.

Conclusions: TAE is safe and effective for the treatment of NG, with a significant volume reduction of the nodule(s) and thyroid gland.

ABBREVIATIONS

FNAB = fine-needle aspiration biopsy, HRQoL = health-related quality of life, MR = magnetic resonance, NG = nodular goiter, PVA = polyvinyl alcohol, RAI = radioactive iodine, TAE = thyroid artery embolization, ThyPRO = thyroid-related patient-reported outcome

Nodular goiter (NG) is a common disorder affecting approximately 3%–6% of the population in endemic areas. Since the risk of malignancy is only approximately 5%, therapy is generally performed to relieve compressive or cosmetic complaints. Hemithyroidectomy or total

thyroidectomy is currently the standard therapy. However, thyroidectomy may result in complications such as recurrent laryngeal nerve palsy, hypoparathyroidism, and permanent hypothyroidism that require lifelong hormone therapy. Considering that more than 100,000 thyroidectomies are performed in the United States each year and approximately half of them are done for NG, a less invasive and safer alternative may be necessary for this otherwise benign disorder (1–3).

In the literature, thyroid artery embolization (TAE) was reportedly used in several series in a limited number of patients. The main indication was toxic diffuse goiter (Graves disease) (4–7). Embolization was successful in more than two-thirds of patients with Graves disease, but in all patients after embolization, there was also a marked volume reduction in the thyroid gland. Interestingly, this secondary effect did not receive enough attention, and thyroid embolization has not been used for this indication, except as noted in some case reports (8,9). The purpose of

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RESEARCH HIGHLIGHTS

- This single-center retrospective cohort study investigated safety and efficacy of thyroid artery embolization (TAE) in 56 patients with nodular goiter (NG).
- Six months after TAE, the mean nodule volume and thyroid volume were reduced from 80.2 mL to 25.0 mL and from 147.0 mL to 62.6 mL respectively. Of the 22 patients with hyperthyroidism, 19 (86%) became euthyroid. The mean thyroid-related patient-reported outcome (ThyPRO) score improved from 155.4 to 70.4.
- TAE is safe and effective for the treatment of NG, with a significant volume reduction of the goiter and improvement of the quality of life.

this study is to report a 5-year, single-center experience with thyroid embolization for the nonsurgical treatment of NG.

MATERIALS AND METHODS

Between May 2015 and October 2020, 56 consecutive patients who underwent TAE for NG were retrospectively reviewed. Inclusion criteria were single nodules that were not eligible for percutaneous laser or radiofrequency ablation (>5 cm in size, intrathoracic extension) and multiple nodules that caused compressive or cosmetic symptoms, with a Bethesda category 2–3 (benign, or atypia or follicular lesion of undetermined significance) fine-needle aspiration biopsy (FNAB) result. Exclusion criteria were renal insufficiency, inability to tolerate angiography, and a Bethesda 4–6 FNAB result (suspicious for follicular neoplasm, suspicious for malignancy, or malignant). In 25 patients, the thyroid-stimulating hormone levels were below normal; 3 patients were diagnosed with Graves disease with NG. In the remaining 22 patients, there was no specific etiology, and hyperthyroidism was attributed to NG. In 47 (84%) patients, there was some degree of intrathoracic extension, which was the main reason for preferring embolization over other treatments. The degree of intrathoracic extension was defined as the distance from the cranial border of the clavicle to the lowermost border of the thyroid. All patients in the present study were previously offered surgery, but they either refused or were not suitable candidates for surgical resection. The characteristics of the patients are presented in **Table 1**.

Before embolization, all patients were examined with ultrasound, computed tomography, or magnetic resonance (MR) imaging to determine the size, location, and number of the nodules, and they were divided into 2 groups. Group A comprised 20 patients who had a solitary/dominant nodule (maximum diameter, 5–11 cm) with or without several subcentimeter nodules. In these patients, only the size and

STUDY DETAILS

Study type: Retrospective, observational, cohort study

Table 1. Demographic, Clinical, and Radiologic Characteristics of 56 Patients Who Underwent Thyroid Artery Embolization

Characteristics	Values
Age, y, median	51.2 (range: 23–86)
Sex	
Female	33 (59)
Male	23 (41)
Goiter location	
Cervical	9 (16)
Substernal	47 (84)
Nodules	
Solitary*	20 (36)
Multiple (MNG)	36 (64)
Hormonal status	
Euthyroid	28 (50)
Hyperthyroid	25 (45)
Hypothyroid	3 (5)
Previous treatment	
Levothyroxine	11
Antithyroid drugs	9
Cyst aspiration	1
Laser/radiofrequency ablation	3
Radioactive iodine	7
Thyroidectomy	5
No. of embolized arteries	
2	23 (41)
3	33 (59)
Embolized arteries (n = 145)	
Left superior thyroid	42 (29)
Left inferior thyroid	46 (32)
Right superior thyroid	14 (9)
Right inferior thyroid	42 (29)
Thyroidea ima	1 (1)
Complications (SIR)	
Minor	25 (45)
Major	2 (4)

Note—Values are n (%).

MNG = multiple, often numerous, thyroid nodules; SIR = Society of Interventional Radiology.

*With or without several subcentimeter nodules.

volume of the dominant nodule were evaluated since the target of the therapy was the dominant nodule. Group B comprised 36 patients who had multiple, often numerous, thyroid nodules. In these patients, the size and volume of the thyroid were evaluated, since embolization was targeted to the whole gland (**Table 2**). Prior to the embolization, all patients had at least 1 FNAB from the dominant/suspicious nodules (1–3,10–12). The results were benign

Table 2. Characteristics of Group A and Group B Patients Who Underwent Thyroid Artery Embolization

Characteristics	Group A (n = 20)	Group B (n = 36)
Hormonal status		
Euthyroid	19 (95)	9 (25)
Hyperthyroid	0	25 (69)
Hypothyroid	1 (5)	2 (6)
Intrathoracic extension		
Yes	14 (70)	33 (92)
No	6 (30)	3 (8)
No. of embolized feeders		
2 feeders	18 (90)	5 (14)
3 feeders	2 (10)	31 (86)
Follow-up imaging		
(Available in 51 patients)	(n = 19)	(n = 32)
Ultrasound	6 (32)	3 (10)
CT	5 (26)	11 (34)
MR imaging	8 (42)	18 (56)

Note—Values are n (%).

in 53 patients (Bethesda category 2), and atypia of undetermined significance/follicular lesion of undetermined significance was reported in 3 patients (Bethesda category 3). Of the 56 patients, 25 (45%) underwent previous medical, interventional, or surgical therapy (Table 1). Before embolization, all patients were informed about the risks and potential benefits of the embolization as well as alternative treatments, and they signed a dedicated informed consent form. The study, being retrospective in nature, was exempted from approval by the institutional review board of Akdeniz University. All procedures in the present study were in accordance with the ethical standards of the national research committee and with the 1964 Helsinki Declaration.

All TAE procedures were performed via a femoral arterial approach using a 5-F sheath. After a 5-F angled vertebral catheter was advanced over a hydrophilic guide wire and supra-aortic vessels were selectively catheterized, the thyroid arteries that fed the nodule(s) and the healthy parenchyma (if present) were identified (Fig 1a–e). Based on the angiography results, a decision was made to embolize 2 or 3 of the thyroid arteries that supply the nodule(s) most, leaving another artery (or arteries) intact to avoid the potential risk of hypoparathyroidism. In general, single large nodules with or without subcentimeter nodules (Group A) were supplied by 2 arteries, and multiple nodules (Group B) were supplied by 3 arteries. After the feeding arteries were identified, a 2.2–2.7-F microcatheter was selectively advanced into these vessels and placed in a secure position. After a superselective digital subtraction angiography was performed, the artery was embolized with 355–500- μ m polyvinyl alcohol (PVA) particles (Contour; Boston Scientific, Natick, Massachusetts). To ensure distal embolization and to avoid PVA aggregation, the particles were diluted in an 80–100-mL 1-to-1 contrast-saline mixture

for a vial, a vasodilator (papaverine, 5 mg) was added, and the mixture was very slowly injected into the target artery until stagnation. Early on, the proximal part of the feeding arteries was also occluded with coils in 4 patients, a procedure that was later abandoned owing to its cost and a belief that it may hinder repeated embolization in case of insufficient treatment. Subsequently, the target arteries were embolized, the procedure was completed, and the patient was observed overnight.

The postprocedural medication included intravenous dexamethasone (8 mg) and a nonsteroidal anti-inflammatory drug to reduce the postoperative edema and inflammation, as well as a prophylactic antibiotic (cefuroxime axetil, 500 mg, twice daily) for 1 day. After discharge, the patient was prescribed an oral nonsteroidal anti-inflammatory drug (dexketoprofen, 25 mg, twice daily) and continued the antibiotic for 5–10 days. The thyroid hormones were studied at intervals according to the hormone levels of the patients. In patients with postembolization hyperthyroidism, the intervals were every 2–4 days, and in euthyroid patients, they were every 2–4 weeks for approximately 3 months. In patients who developed postembolization hyperthyroidism, antithyroid drugs (methimazole, propylthiouracil) and intestinal thyroid hormone binders (cholestyramine) were also given, when necessary, until the thyroid hormone levels returned to normal. At 6 months, follow-up ultrasound, computed tomography, or MR imaging was performed, and the images were compared with the pre-embolization images. On these images, the solitary/dominant nodule, both thyroid lobes, and isthmus were measured in the 3 perpendicular planes, and their volumes were calculated. The degree of thoracic extension was also measured and compared in patients with retrosternal goiter.

All patients were requested to fill in a health-related quality of life (HRQoL) questionnaire before and 6 months after the TAE. This questionnaire was a reduced version of thyroid-related patient-reported outcome (ThyPRO), which is the most widely used quality of life measurement instrument in thyroid disorders (13). The subgroups of ThyPRO can be selected to evaluate specific areas of interest. In this study, the Goiter Symptoms, Hyperthyroid Symptoms, and Appearance subgroups were selected for evaluation. In this reduced version of the ThyPRO questionnaire, there were 25 questions, and answers were evaluated with a 5-point scale from 0 (not at all) to 4 (very much). At 6 months, patients were also asked whether or not they would recommend TAE to other patients with NG.

Data analyses were conducted using SPSS Windows 22.0 (IBM Inc., Armonk, New York). A paired *t* test was used to evaluate the changes before and after TAE for the following parameters: dominant/single thyroid volume in Group A, total thyroid volume in Group B, thoracic extension in patients with substernal goiter, and the ThyPRO questionnaire including its subgroups (Goiter Symptoms, Hyperthyroid Symptoms, and Appearance). A *P* value of <.05 was considered statistically significant.

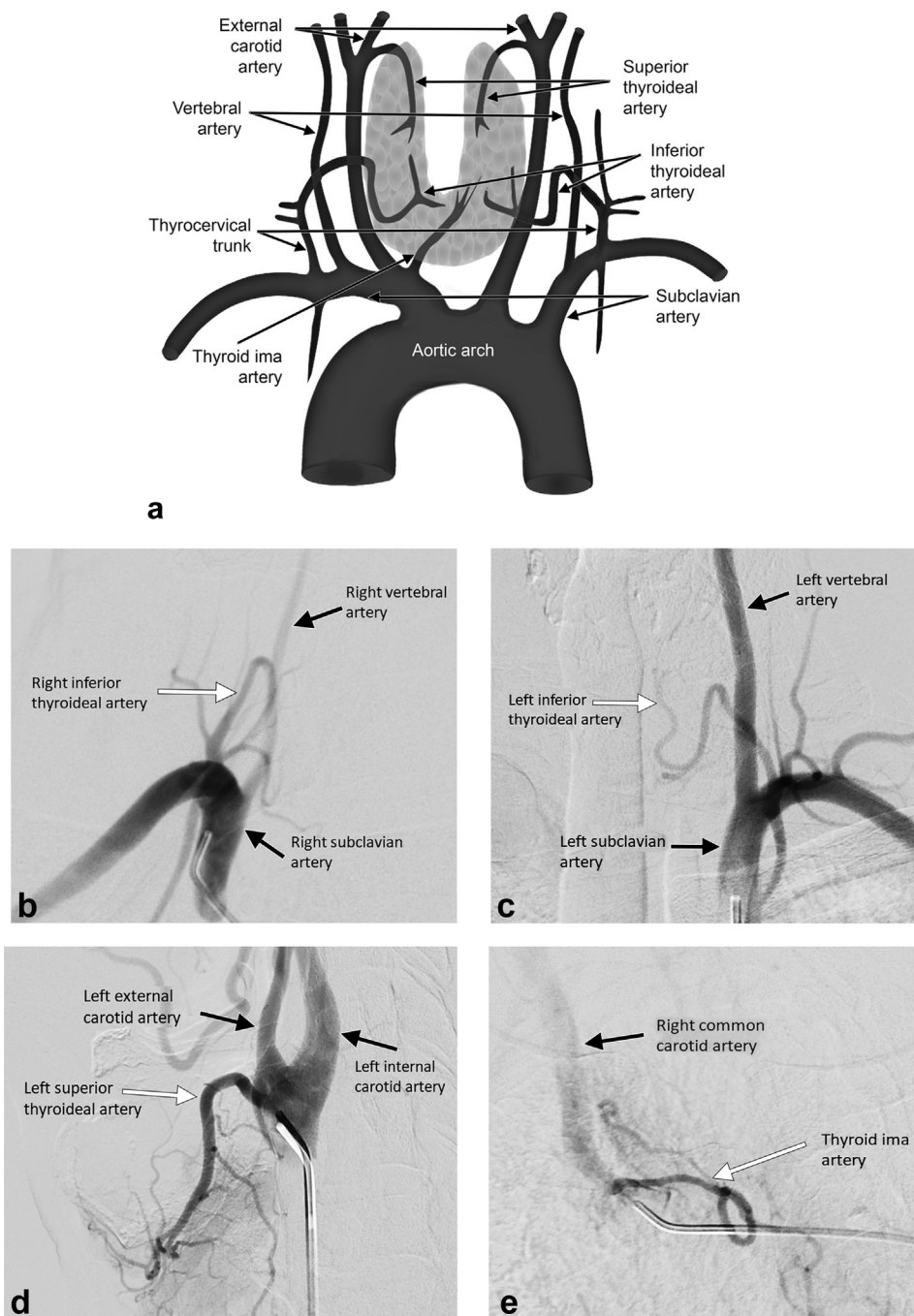


Figure 1. Anatomy of the thyroid arteries. The diagram (a) shows the origin and course of the bilateral superior and inferior thyroid arteries, which are the usual feeders of the thyroid. Thyroid ima artery can be seen in approximately 10% of patients and is usually a branch of the right common carotid artery or innominate artery. Selective anteroposterior subclavian angiograms (b, c) show the right and left inferior thyroid arteries (white arrows), which originate from the thyrocervical trunks slightly distal to the vertebral arteries. A selective lateral common carotid angiogram (d) shows the left superior thyroid artery (white arrow), which may originate from the external or common carotid arteries. Because of the close proximity of the origin of thyroid arteries to the internal carotid and vertebral arteries, the risk of nontarget embolization to cerebral vessels may be high in case of reflux. A selective innominate artery angiogram (e) shows the thyroid ima artery (white arrow), which originates from the proximal part of the common carotid artery. The thyroid ima artery is a small branch but may become a dominant feeder in the absence or atrophy of one of the inferior thyroid arteries.

RESULTS

In 56 patients, 146 thyroid arteries were planned for embolization based on initial angiographic findings. In 1 patient (an 86-year-old woman), the right inferior thyroid

artery could not be catheterized owing to severe tortuosity of the supra-aortic vessels. Thus, 145 of the 146 targeted arteries were successfully embolized. According to the Society of Interventional Radiology adverse events classification system (14), 25 patients developed minor complications,

Table 3. Volume and Score Changes in Group A and Group B Patients Following Thyroid Artery Embolization

Volume and score	Value before treatment	Value after treatment	P value
Thyroid volume in 32 Group B patients (mL)	147.0 ± 85.9 (50–635)	62.6 ± 31.9 (20–180)	<.001
Single/dominant nodule volume in 19 Group A patients (mL)	80.2 ± 46.7 (40–220)	25.0 ± 15.3 (9–70)	<.001
Intrathoracic extension (mm) in 45 patients	31.7 ± 19.8 (12–90)	15.9 ± 10.3 (5–50)	<.001
ThyPRO scores (51 patients)	155.4 ± 47.3 (45–246)	70.4 ± 21.2 (27–130)	<.001
Goiter scores (51 patients)	155.7 ± 46.8 (56–246)	70.3 ± 21.3 (28–129)	<.001
Hyperthyroid scores (51 patients)	73.1 ± 40.2 (23–210)	49.2 ± 22.4 (23–120)	<.001
Appearance scores (51 patients)	173.8 ± 56.9 (43–289)	75.4 ± 22.9 (33–120)	<.001

Note—Values are n (%), mean ± SD (range).

ThyPRO = thyroid-related patient-reported outcome.

and 1 patient had blurred vision during the procedure that resolved spontaneously within several hours. Two patients had significant hoarseness following TAE that resolved after oral corticosteroid treatment for 4 days. Other minor complications occurred in 22 patients and included neck pain and subclinical hyperthyroidism. Major complications occurred in 2 patients; 1 patient developed groin hematoma, and 1 patient developed symptomatic hyperthyroidism that required extended (>48 hour) hospitalization. There were no grade E or F adverse events; notably no patient developed neurologic sequela and permanent hypoparathyroidism or de novo hypothyroidism. The 30-day mortality rate was 1.8%. A 76-year-old woman died 2 weeks after the TAE presumed to be from myocardial infarction, which was possibly procedure related.

The 6-month clinical, radiological, and HRQoL evaluations were available in 51 of the 56 patients. Imaging findings showed statistically significant changes in the nodules and thyroid gland at 6 months (Table 3). In Group A patients, the mean volume of the single/dominant nodule was reduced from 80.2 mL to 25.0 mL ($P < .001$) (Fig 2a–e). In Group B patients, the mean volume of the thyroid gland was reduced from 147.0 mL to 62.6 mL ($P < .001$) (Fig 3a, b). In 46 patients with substernal goiter, the mean intrathoracic extension was reduced from 31.7 mm to 15.9 mm ($P < .001$). At 6 months, there were also significant findings in the hormonal status of the patients. In 28 euthyroid patients, none developed hypothyroidism after TAE and no hormone replacement therapy was needed. The 3 hypothyroid patients remained hypothyroid after TAE and maintained levothyroxine treatment. In 3 of the 25 hyperthyroid patients who had Graves disease, the hormone levels improved but did not return to normal. These patients reported a marked improvement of their symptoms and reduced their antithyroid medications. In the remaining 22 patients with non-Graves hyperthyroidism, 19 patients (86%) became euthyroid and stopped antithyroid medication after TAE, whereas 3 patients remained hyperthyroid.

At the 6-month follow-up, there were also statistically significant changes in the ThyPRO scores (Table 3). The overall mean ThyPRO scores improved from 155.4 to

70.4 ($P < .001$). The goiter symptoms improved from 155.7 to 70.3 ($P < .001$), the hyperthyroid symptoms improved from 73.1 to 49.2 ($P < .001$), and the appearance improved from 173.8 to 75.4 ($P < .001$). Of the 51 patients, 50 (98%) declared that they would recommend the TAE treatment to other patients with NG.

DISCUSSION

The results of the present study show that TAE may significantly decrease the volumes of solitary/dominant nodules and goiters with multiple nodules, which may result in a significant improvement in the quality of life and hormonal status of patients with NG. The procedure is well tolerated by the patients and is associated with a low complication rate. Therefore, TAE may be a good alternative to surgery or percutaneous ablation in selected patients with NG.

Because of the disadvantages of thyroidectomy, percutaneous ablation has been introduced as a minimally invasive therapeutic option in NG (15–20). Ideal patients for percutaneous ablation are those with a single or a few thyroid nodules of small to medium size. It is generally accepted that percutaneous ablation is less effective in nodules with a volume of >30 mL than in the smaller ones (19,20). If the nodules are numerous, very large, or extend into the thoracic cavity, then ablation is technically challenging, time consuming, and probably less effective (15,18–20).

Unfortunately, in many patients with NG, thyroid nodules are multiple, large-sized, or extend into the thoracic cavity (1,2). These cases are more likely to have compressive symptoms such as dyspnea, dysphagia, and hoarseness. Apart from being unsuitable for percutaneous ablation, surgical operation may also be difficult in such patients, especially in those with intrathoracic extension, as an additional chest incision is frequently necessary (21,22). Quite commonly, patients refuse to undergo surgery, and the nodules may grow larger, causing further tracheal compression and making future resection even more risky (21). Although radioactive iodine (RAI) was proposed as an alternative to surgery in these cases, it often results in permanent hypothyroidism, requiring lifelong levothyroxine treatment. Additionally, compared with toxic nodules and

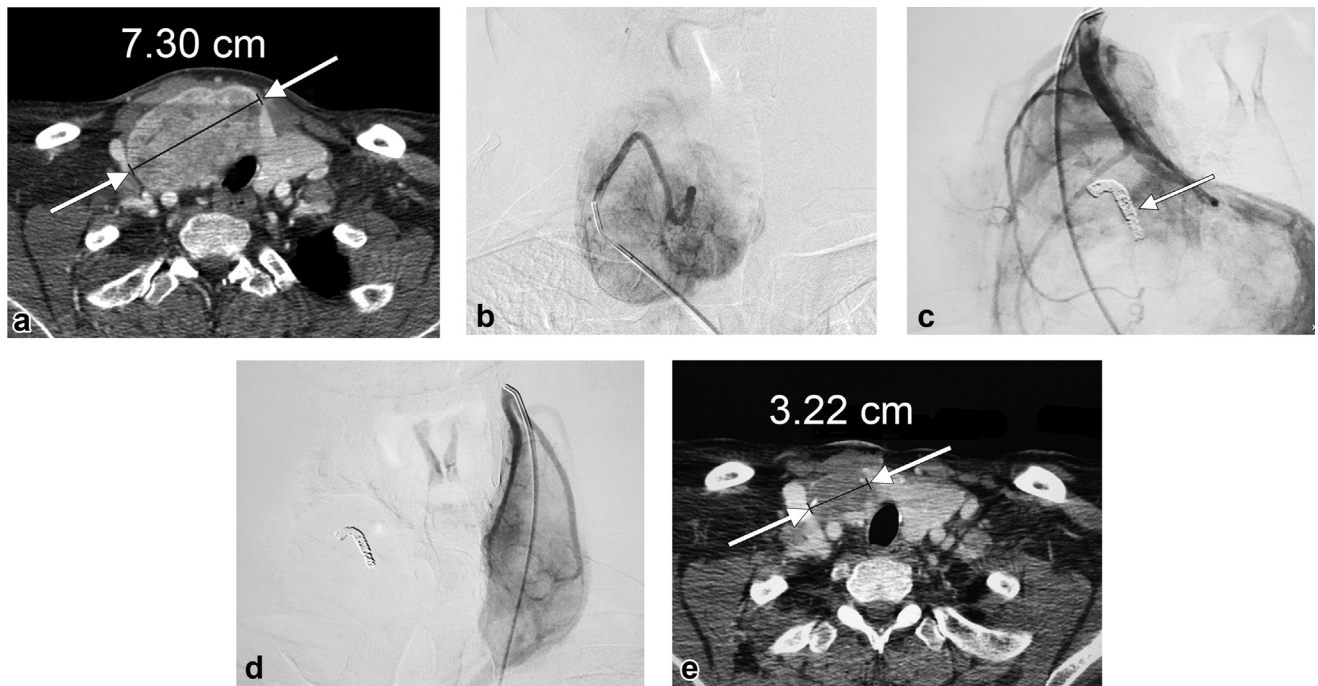


Figure 2. In a 45-year-old man with a large solitary cervical nodule in the right thyroid lobe, the axial image (a) shows the nodule (arrows) that measures $7.3 \times 7 \times 4.5$ cm (volume, 115 mL). The patient underwent particle and coil (arrow) embolization of the right inferior thyroid artery (the main supplier) and the right superior thyroid artery (b, c) while the arteries of the left lobe (d) were left intact. At 6 months, the follow-up axial computed tomography image (e) shows a marked shrinkage of the nodule in the right lobe measuring $4.5 \times 3.2 \times 2.1$ cm (volume, 15.1 mL; volume reduction, 87%) and compensatory hypertrophy of the healthy left lobe. The patient was asymptomatic and very satisfied with the cosmetic result.

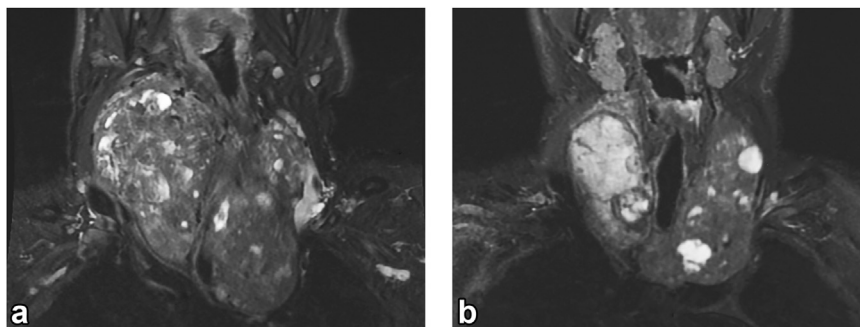


Figure 3. In a 55-year-old man with a large retrosternal goiter and hyperthyroidism (thyroid-stimulating hormone [TSH], 0.008 mIU/L), the T2-weighted coronal magnetic resonance image (a) shows the retrosternal goiter (right lobe = $15.5 \times 9.1 \times 6.8$ cm [volume, 479 mL]; left lobe = $12.4 \times 6.3 \times 4.0$ cm [volume, 156 mL]). The patient underwent embolization of the right superior and bilateral inferior thyroid arteries. He developed temporary hyperthyroidism for several weeks, but at 3 months, his TSH levels became normal (1.7 mIU/L). At 6 months, the coronal T2-weighted image (b) demonstrated a marked shrinkage of the goiter mass (right lobe = $9.24 \times 3.9 \times 4.7$ cm [volume, 84 mL]; left lobe = $9.8 \times 3.0 \times 4.7$ cm [volume, 69 mL]). The volume reduction was 82.5% in the right lobe and 56% in the left lobe. The intrathoracic extension was also reduced from 8 cm to 5 cm (37.5% reduction). After the embolization, the patient became asymptomatic and remained euthyroid throughout the follow-up.

goiters, it requires a substantially higher radiation dose in nontoxic and voluminous goiters, and yet the outcome is frequently suboptimal (23).

In the present study, TAE resulted in a mean volume reduction of 69% in large single/dominant nodules, which is comparable to that obtained after percutaneous ablation in small/medium thyroid nodules (18–20). Since there are scarce published data on percutaneous ablation of large thyroid nodules, it is not possible to compare the TAE results with those of ablation. However, percutaneous ablation

is not recommended in large (>30 mL) nodules, and the mean volume of the embolized nodules in this series was much higher (80.2 mL) than the threshold. Yet the outcome was as favorable as that of percutaneous ablation. These findings suggest that embolization is probably a better option than percutaneous ablation in large thyroid nodules. In the present study, the mean total thyroid volume was reduced by 56% after TAE. This rate compares favorably with those reported after RAI treatment (23), suggesting that TAE is at least as effective as RAI in reducing the size of

voluminous goiters, although only 2 or 3 of the 4 thyroid arteries were embolized depending on the number and location of the nodules. Owing to this patient-specific embolization, it was possible to treat the thyroid nodules more aggressively while leaving the normal or less affected lobe fully or partially intact. It is probable that, unlike RAI, which destroys the whole thyroid gland progressively and results in hypothyroidism in most patients, TAE allows a personalized treatment that affects the nodules to a greater extent and spares or even enlarges the relatively healthy thyroid parenchyma, reducing the risk of hypothyroidism.

In patients with retrosternal goiter, levothyroxine and RAI are not typically successful, and surgery is the only effective treatment (1,2). However, in such patients, surgery is associated with a higher complication rate (recurrent laryngeal nerve palsy, hypoparathyroidism, tracheomalacia) and mortality rate compared with standard surgery for cervical goiter (21,22). In the present study, after TAE, the mean intrathoracic extension was reduced from 31.7 mm to 15.9 mm, corresponding to a 50% decrease, and all patients reported a significant relief of symptoms. These results suggest that TAE may be a viable alternative to surgery in patients with retrosternal goiter.

After TAE, temporary hyperthyroidism may occur, especially in patients with previous hyperthyroidism. This phenomenon was reported in the previous TAE series and after RAI in the literature (4,5,22), and it is probably due to excessive release of thyroid hormones from the necrotic tissue into the circulation following these treatments. In the present study, after TAE, most patients had low thyroid-stimulating hormone levels but no symptoms. Even in the patients with an additional elevation of triiodothyronine and thyroxine hormones, hyperthyroidism symptoms were surprisingly mild, and no medication was needed in most patients. In symptomatic patients, besides antithyroid drugs (methimazole, propylthiouracil), cholestyramine was also given to inhibit the intestinal reabsorption of thyroid hormones. Since temporary hyperthyroidism is caused by the excessive release of stored hormones and not by excessive hormone production, drugs such as cholestyramine may be more effective than antithyroid medications after TAE (24).

In the literature, TAE has been used for the treatment of Graves disease in several studies (4,5) with successful outcomes. In the series of Xiao et al (4), 14 of 22 patients (63.6%) became euthyroid after TAE and remained in this state for the duration of the study. These findings were later confirmed by Zhao et al (5). However, for non-Graves hyperthyroid goiters, there are no data in the literature on the efficacy of TAE. In the present study, 3 of the 25 hyperthyroid patients had Graves disease. After TAE, although the hormone levels were reduced in all 3, none of the patients became euthyroid, which is in contrast to the reported literature data. However, in the remaining 22 patients with non-Graves hyperthyroidism, 19 (86%) became euthyroid at 6 months after TAE, and the remaining 3 reduced their antithyroid medications. None of these patients became hypothyroid and needed levothyroxine substitution. These

results suggest that, in patients with non-Graves hyperthyroid goiters, TAE not only reduces the thyroid volume substantially but also normalizes or improves thyroid hormone levels without causing hypothyroidism. If confirmed by further studies with long-term data, these results suggest that TAE may be a good alternative to surgery and RAI in the treatment of non-Graves hyperthyroidism associated with NG.

In the present study, the HRQoL was also markedly improved after TAE. In the literature, there are some studies that report the HRQoL after thyroidectomy and RAI in patients with NG (25,26). In this study, there was a significant improvement in all 3 groups of parameters (goiter symptoms, hyperthyroid symptoms, and appearance) at 6 months. Interestingly, many patients described the relief of compressive goiter symptoms even on the first day after embolization, much before the volume reduction occurred. This early improvement may be due to the sudden cessation of pulsatile arterial flow of the goiter mass. The improvement in hyperthyroid symptoms started several months after the TAE and was generally preceded by temporary hyperthyroidism that lasted for several weeks. In the present study, the improvement in appearance was also described by many patients after several months, but it was more evident at 6 months. The overall HRQoL improvement in patients compares favorably with that reported following thyroidectomy and RAI administration (25,26). The high satisfaction rate reported by these patients at 6 months is also reflected by the fact that 98% of them declared they would recommend the TAE treatment to another patient with NG.

In a previous series, thyroid embolization was performed mainly with 150–500- μ m PVA particles (7). In a histologic analysis by Xiao et al (7), the average diameter of the capillary network within the body of the thyroid adjacent to the superior and inferior artery was 0.12–0.25 mm, with the smallest ones ranging from 0.04–0.11 mm. Therefore, they recommended 150–300- μ m PVA particles for TAE. Although smaller particles and liquid materials may produce a more profound ischemia and necrosis, the risk of complications may be higher because of the increased probability of too distal or nontarget embolization. Because of this concern, in the present study, 355–500- μ m particles were preferred to smaller particles. It is possible, however, that smaller particles and liquid agents such as glue or onyx may produce better results without increased complications. This issue may be clarified in the future series.

The limitations of the current study include its retrospective design and the unavailability of the long-term results. However, although this was a retrospective study, most data were complete, and except for 1 death, there were no missing cases. The 6-month follow-up was also available in a high percentage of patients (91%). Although only 6-month clinical and radiological data are presented in the current study, none of the previously treated patients have presented with any evidence of recurrence so far. Despite that, the long-term results of TAE may be different and should be determined by

continued follow up or in a separate study. Another limitation of the present study may be the use of different modalities such as ultrasound, computed tomography, or MR imaging for volume calculation. This heterogeneity may have compromised the consistency of preoperative and postoperative comparisons. Finally, the absence of any comparison with other treatment options such as surgery and RAI may be another limitation. However, this study reported only a single-center experience with TAE in a relatively large number of patients with NG, and these results should be confirmed first by further series before any comparative studies with alternative treatments are performed.

Despite these limitations, the current study shows that TAE is safe and effective for the treatment of NG, with a significant volume reduction of the nodule(s) and the thyroid gland. These findings should be considered when offering the treatment options to patients with NG.

REFERENCES

- Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association Guidelines Task Force on thyroid nodules and differentiated thyroid cancer. *Thyroid* 2016; 26:1–133.
- De Martino E, Pirola I, Gandossi E, Delbarba A, Cappelli C. Thyroid nodular disease: an emerging problem. *Minerva Endocrinol* 2008; 33:15–25.
- Brito JP, Yarur AJ, Prokop LJ, McIver B, Murad MH, Montori VM. Prevalence of thyroid cancer in multinodular goiter versus single nodule: a systematic review and meta-analysis. *Thyroid* 2013; 23:449–455.
- Xiao H, Zhuang W, Wang S, et al. Arterial embolization: a novel approach to thyroid ablative therapy for Graves' disease. *J Clin Endocrinol Metab* 2002; 87:3583–3589.
- Zhao W, Gao BL, Yang HY, et al. Thyroid arterial embolization to treat Graves' disease. *Acta Radiol* 2007; 48:186–192.
- Kaminski G, Jaroszk A, Zybek A, et al. The calcium-phosphate balance, modulation of thyroid autoimmune processes and other adverse effects connected with thyroid arterial embolization. *Endocrine* 2014; 46:292–299.
- Dedecjus M, Tazbir J, Kaurzel Z, et al. Evaluation of selective embolization of thyroid arteries (SETA) as a preresective treatment in selected cases of toxic goitre. *Thyroid Res* 2009; 2:7.
- Ducloux R, Sapoval M, Russ G. Embolization of thyroid arteries in a patient with compressive intrathoracic goiter ineligible to surgery or radioiodine therapy. *Ann Endocrinol (Paris)* 2016; 77:670–674.
- Tartaglia F, Salvatori FM, Russo G, et al. Selective embolization of thyroid arteries for preresection or palliative treatment of large cervicomedial goiters. *Surg Innov* 2011; 18:70–78.
- van Overhagen H, Reekers JA. Uterine artery embolization for symptomatic leiomyomata. *Cardiovasc Intervent Radiol* 2015; 38:536–542.
- Laughlin-Tommaso SK. Alternatives to hysterectomy: management of uterine fibroids. *Obstet Gynecol Clin North Am* 2016; 43:397–413.
- van der Kooij SM, Bipat S, Hehenkamp WJ, Ankum WM, Reekers JA. Uterine artery embolization versus surgery in the treatment of symptomatic fibroids: a systematic review and meta-analysis. *Am J Obstet Gynecol* 2011; 205:317.e1–317.e18.
- Wong CK, Lang BH, Lam CL. A systematic review of quality of thyroid-specific health-related quality-of-life instruments recommends ThyPRO for patients with benign thyroid diseases. *J Clin Epidemiol* 2016; 78: 63–72.
- Khalilzadeh O, Baerlocher MO, Shyn PB, et al. Proposal of a new adverse event classification by the Society of Interventional Radiology Standards of Practice Committee. *J Vasc Interv Radiol* 2017; 28:1432–1437.e3.
- Guan SH, Wang H, Teng DK. Comparison of ultrasound-guided thermal ablation and conventional thyroidectomy for benign thyroid nodules: a systematic review and meta-analysis. *Int J Hyperthermia* 2020; 37: 442–449.
- Livraghi T, Paracchi A, Ferrari C, et al. Treatment of autonomous thyroid nodules with percutaneous ethanol injection: preliminary results. *Work in progress. Radiology* 1990; 175:827–829.
- Hahn SY, Shin JH, Na DG, et al. Ethanol ablation of the thyroid nodules: 2018 consensus statement by the Korean Society of Thyroid Radiology. *Korean J Radiol* 2019; 20:609–620.
- Trimboli P, Castellana M, Sconfienza LM, et al. Efficacy of thermal ablation in benign non-functioning solid thyroid nodule: a systematic review and meta-analysis. *Endocrine* 2020; 67:35–43.
- Pacella CM, Mauri G, Achille G, et al. Outcomes and risk factors for complications of laser ablation for thyroid nodules: a multicenter study on 1531 patients. *J Clin Endocrinol Metab* 2015; 100:3903–3910.
- Lim HK, Lee JH, Ha EJ, Sung JY, Kim JK, Baek JH. Radiofrequency ablation of benign non-functioning thyroid nodules: 4-year follow-up results for 111 patients. *Eur Radiol* 2013; 23:1044–1049.
- Pieracci FM, Fahey TJ 3rd. Substernal thyroidectomy is associated with increased morbidity and mortality as compared with conventional cervical thyroidectomy. *J Am Coll Surg* 2007; 205:1–7.
- Khan MN, Goljo E, Owen R, Park RCW, Yao M, Miles BA. Retrosternal goiter: 30-day morbidity and mortality in the transcervical and trans-thoracic approaches. *Otolaryngol Head Neck Surg* 2016; 155:568–574.
- Bonnema SJ, Hegedüs L. Radioiodine therapy in benign thyroid diseases: effects, side effects, and factors affecting therapeutic outcome. *Endocr Rev* 2012; 33:920–980.
- Mercado M, Mendoza-Zubieta V, Bautista-Osorio R, Espinoza-de los Monteros AL. Treatment of hyperthyroidism with a combination of methimazole and cholestyramine. *J Clin Endocrinol Metab* 1996; 81: 3191–3193.
- Törring O, Watt T, Sjölin G, et al. Impaired quality of life after radioiodine therapy compared to antithyroid drugs or surgical treatment for Graves' hyperthyroidism: a long-term follow-up with the thyroid-related patient-reported outcome questionnaire and 36-item short form health status survey. *Thyroid* 2019; 29:322–331.
- Sorensen JR, Watt T, Cramon P, et al. Quality of life after thyroidectomy in patients with nontoxic nodular goiter: a prospective cohort study. *Head Neck* 2017; 39:2232–2240.