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# Safety and Efficacy of Ultrasound-Guided Thrombin Injection for Pseudoaneurysms Arising after Ultrasound-Guided Biopsy of Thyroid Nodules

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## ABSTRACT

**SUMMARY:** Iatrogenic pseudoaneurysm is a rare but potentially fatal complication of a thyroid biopsy. However, a standard management strategy has not yet been established. We aimed to evaluate the efficacy and safety of ultrasound (US)-guided thrombin injection (TI) for thyroid pseudoaneurysms. This retrospective study included 7256 patients who underwent thyroid biopsy and TI from January 2020 to January 2024. The technical success, clinical efficacy, and complication rates were evaluated. A total of 0.1% (7/7256) of pseudoaneurysms developed after thyroid biopsy. Except for 1 case that showed obliteration with manual compression, the remaining 6 refractory aneurysms (0.08%) were managed with US-guided TI. All cases (100%) were successfully occluded with US-guided TI. No major complications were observed. One patient (16.7%) developed transient loss of consciousness, which spontaneously resolved within a few seconds. US-guided TI is an effective, relatively safe, and minimally invasive method for managing pseudoaneurysms after thyroid biopsy.

**ABBREVIATIONS:** CNB = core-needle biopsy; FNA = fine-needle aspiration; TI = thrombin injection; US = ultrasound

Ultrasound (US)-guided fine-needle aspiration (FNA) and core-needle biopsy (CNB) are safe and effective; thus, they are currently recommended as the preferred diagnostic method for thyroid nodules. These biopsy methods are commonly well-tolerated, with a low complication incidence.<sup>1</sup>

Among the various complications, pseudoaneurysm is a rare but potentially life-threatening complication associated with the continued expansion of a perithyroidal hematoma. Unlike extremity pseudoaneurysms, perithyroidal pseudoaneurysms are closely associated with critical structures and potentially lead to patient morbidity of clinical significance. However, no standards have been established for managing perithyroidal pseudoaneurysms. Although there is substantial evidence regarding the efficacy and safety of thrombin injection (TI) in femoral pseudoaneurysms,<sup>2</sup> it has not been validated in perithyroidal pseudoaneurysms except for a few case reports.<sup>3,4</sup>

We aimed to evaluate the efficacy and safety of US-guided TI for pseudoaneurysms occurring after biopsy.

## MATERIALS AND METHODS

### Study Population

Between January 2020 and January 2024, 7256 consecutive patients underwent FNA or CNB at a single tertiary referral hospital to diagnose thyroid nodules. The medical records of patients with iatrogenic perithyroidal pseudoaneurysms were retrospectively reviewed. The Online Supplemental Data illustrate the patient inclusion flowchart.

### US Evaluation and US-Guided Biopsy

Before the procedure, patients taking antiplatelet agents or anticoagulants were asked to discontinue their medication per current guidelines.<sup>5</sup> Vascular mapping of the lesions was performed by checking nodule vascularity and the presence of large vessels along the expected needle trajectory on color Doppler before biopsy to prevent vascular injury.<sup>5,6</sup> Immediately after the biopsy, patients were instructed to firmly compress their necks at the biopsy site for at least 20 minutes. After compression, any patient with persistent tenderness, dysphagia, or neck swelling that seemed to aggravate upon continuous observation was rechecked by using US.<sup>6,7</sup>

When a persistent perithyroidal or intrathyroidal hemorrhage was suspected, meticulous US was performed to identify the presence of a pseudoaneurysm. US-guided compression was immediately attempted when a pseudoaneurysm was initially identified. Details of the US and US-guided biopsies are described in the Online Supplemental Data.

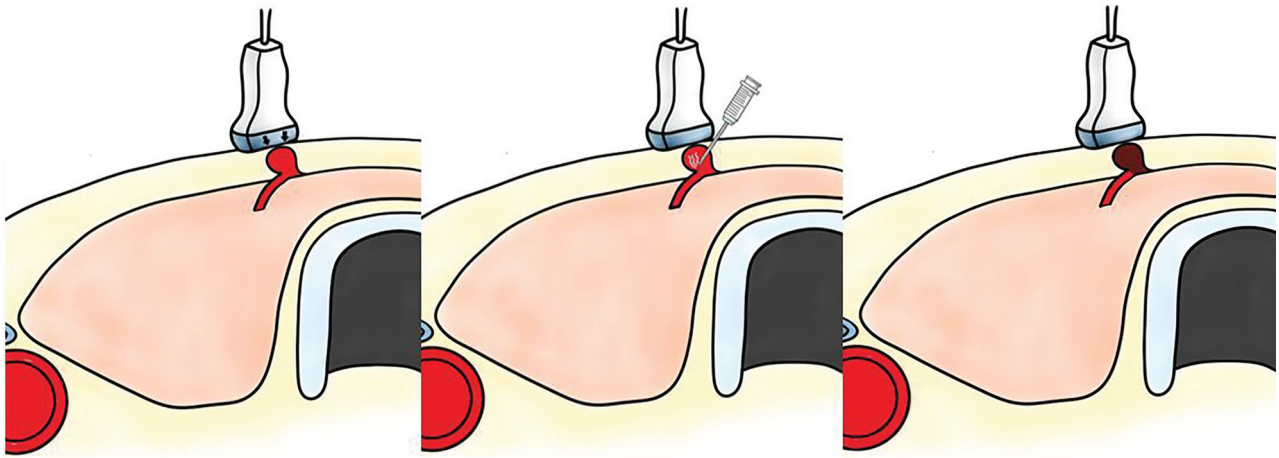
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**FIG 1.** Steps of US-guided thrombin injection. When the pseudoaneurysm was not obliterated by US-guided compression (*left*), the needle tip was positioned within the sac under US guidance, and thrombin solution was carefully and slowly injected into the aneurysm sac (*middle*). The procedure was continuously monitored in real-time during and after the injection to confirm thrombogenesis and complete obliteration of the pseudoaneurysm (*right*).

### Preparation and Injection of Thrombin

Percutaneous TI was planned when the aneurysm persisted despite >40 minutes of additional compression. Aneurysm geometry, including the sac and possible neck, was carefully evaluated in both transverse and longitudinal planes. A single vial of thrombin powder (5000 IU bovine-extracted thrombin; Reyon Pharmaceuticals), stored in a designated refrigerator, was prepared in advance. Thrombin was prepared by mixing thrombin powder with 5 mL of normal saline for dilution in a 5-mL syringe attached to a 23-gauge needle. The procedure was performed under continuous US guidance on an outpatient basis. After sterilization and skin puncture, the needle tip was advanced into the pseudoaneurysm sac via a parallel approach. Before injection, color and spectral Doppler were used to check for the presence of flow in the pseudoaneurysm, along with the intra-aneurysmal position of the needle tip. Subsequently, the prepared solution was carefully and slowly injected into the aneurysm sac to avoid leakage or distal embolization. The procedure was continuously monitored in real-time to confirm thrombogenesis and complete obliteration of the pseudoaneurysm on gray-scale, color Doppler, and spectral Doppler. Observation was continued for 20 min to confirm the resolution of the lesion and stability of the hematoma. Fig 1 illustrates the steps of US-guided TI.

### Outcome and Data Analysis

Technical success was defined as appropriate targeting and puncturing of the aneurysm sac, with thrombin delivery into the sac. Clinical efficacy was defined as the complete disappearance of the aneurysm sac along with improvement in patient-reported symptoms. Complications during the procedure were assessed in accordance with the reporting standards of the Society of Interventional Radiology.<sup>8</sup>

## RESULTS

### Baseline Demographics and Imaging Features of Pseudoaneurysms

A review of medical records identified 7 patients (0.1%) who presented with postbiopsy pseudoaneurysms among 7256 consecutive

patients (3928 FNA and 3328 CNB cases). One patient exhibited obliteration of the pseudoaneurysm sac after 20 minutes of manual compression. Six patients (0.08%) who were refractory to compression underwent US-guided TI for management. All cases were associated with CNB and multiple-site biopsies (median, 2; range 1–2). Except for 1 entirely calcified nodule, 5 nodules showed marked intranodular or perinodular vascularity. Five of the 6 patients had previously been taking antiplatelet agents or warfarin and discontinued their medications appropriately. Patient baseline characteristics and imaging features of pseudoaneurysms are summarized in the Online Supplemental Data.

### Outcome after TI

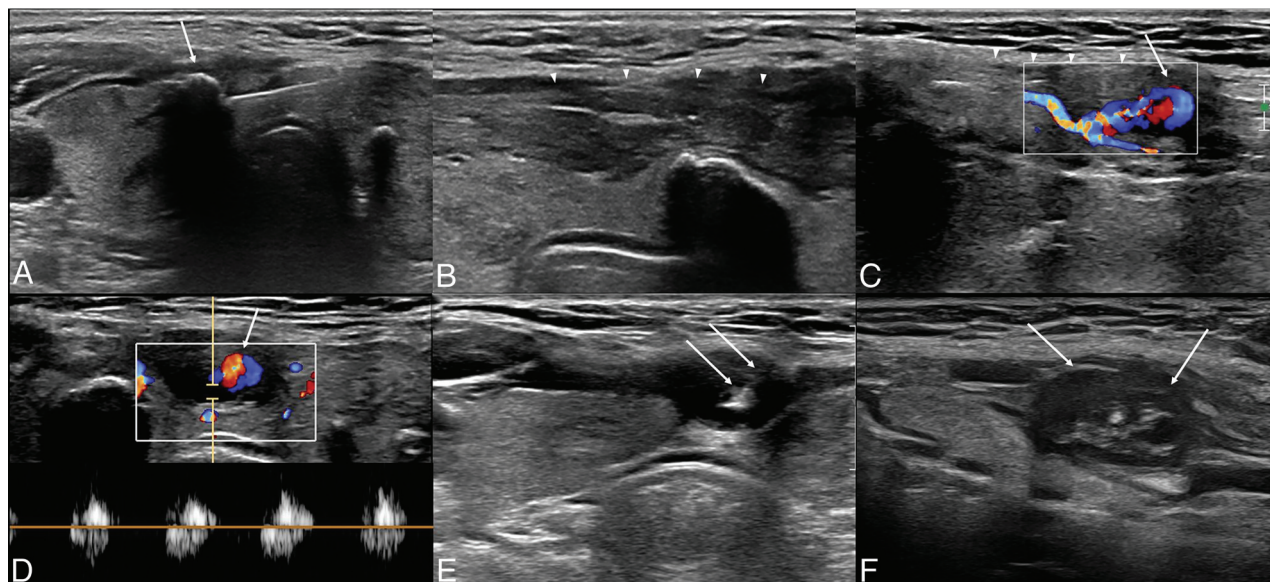
Technical success was achieved in 100% of the patients. All pseudoaneurysms showed complete obliteration on delayed US examination and symptom improvement, resulting in 100% clinical efficacy. No patients required further surgical repair after TI. All patients were treated in a single TI session, and the average TI cost was \$5.72. No long-term pseudoaneurysm recurrences were noted, as shown in Fig 2.

In 1 patient who received 200 IU of thrombin, loss of consciousness with involuntary movement of the upper extremities was observed immediately after TI. TI was promptly stopped, and the symptoms spontaneously improved within 5 seconds. No major complications were observed.

## DISCUSSION

This study presents the outcomes of patients who underwent TI for pseudoaneurysm management after thyroid nodule biopsy. Pseudoaneurysms refractory to manual compression occur infrequently but can result in significant hematomas; however, all were successfully treated with TI. These results suggest that TI may be a useful management option for pseudoaneurysms occurring after thyroid biopsy.

The management of pseudoaneurysms has evolved from traditional surgical repair to less invasive strategies, eg, US-guided compression and image-guided interventional methods. US-guided



**FIG 2.** A case of iatrogenic thyroid pseudoaneurysm in a 65-year-old woman. A, US-guided CNB was performed for an entirely calcified thyroid nodule (arrow). B, Following the biopsy, a perithyroidal hematoma developed (arrowheads). C, Color Doppler US study revealed a pseudoaneurysm in the anterior perithyroidal area (arrow) adjacent to the perithyroidal hematoma (arrowheads). The aneurysm persisted for 5 days of observation. D, Spectral Doppler demonstrated arterial flow within the sac (arrow). E, Thrombin was injected into the pseudoaneurysm sac under US guidance (arrows indicate the needle delivering thrombin). F, Postprocedural US shows obliteration of the lumen (arrows) with diminished internal flow.

compression induces spontaneous thrombogenesis; however, compression can be labor-intensive. Furthermore, several risk factors are linked to treatment failure during manual compression, including obesity, use of concurrent anticoagulant medication, and development of a large hematoma.<sup>9</sup> For refractory cases, interventional management, such as embolization and radiofrequency ablation, can be feasible for managing pseudoaneurysms;<sup>10</sup> however, both methods are costly and require dedicated equipment and experienced personnel.

Unlike pseudoaneurysms occurring in the extremities, most perithyroidal pseudoaneurysms are symptomatic, and persistent cases can lead to hematoma expansion<sup>4</sup> and airway compromise;<sup>11</sup> thus, immediate recognition and management are important. Thrombin has been used in various forms (Online Supplemental Data), and its efficacy in the femoral arteries has been proved; however, its effectiveness in the perithyroidal area is not well documented. Our study showed that TI is an immediate and effective treatment for perithyroidal pseudoaneurysms.

One patient in this study presented with severe headache and involuntary movement of the upper extremities immediately after TI. Previous studies reported similar systemic symptoms after TI.<sup>12</sup> In our patient, the symptoms disappeared within seconds without any sequelae, posing difficulty in pinpointing the cause of the occurrence. Considering that bovine thrombin was injected, it is plausible that thrombin escape into the systemic circulation caused a hypersensitivity reaction.<sup>13</sup>

In this study, most patients who developed refractory pseudoaneurysms had used anticoagulation or antiplatelet medication. In these patients, pseudoaneurysms occurred despite the discontinuation of medication according to guidelines. Considering that all nodules were hypervascular, caution is warranted during biopsy procedures for hypervascular

nodules in patients receiving such medications, as hemorrhagic complications may occur depending on nodule characteristics. Notably, certain nodule locations also warrant caution before performing a biopsy. The Online Supplemental Data illustrate the high-risk areas for hemorrhagic complications during thyroid biopsy.

There were multiple limitations to this study: First, the number of cases included in this study is limited, likely due to the low incidence of perithyroidal pseudoaneurysms. This study included all patients who underwent consecutive biopsies; therefore, we believe that the results are clinically relevant. Second, TI was performed for pseudoaneurysms that were refractory to manual compression; thus, the number of small pseudoaneurysms may have been underestimated because they may have been spontaneously obliterated. Pseudoaneurysms treated with manual compression alone are clinically insignificant; consequently, we believe that these results may be significant in practice. Future prospective studies might be helpful to determine the actual incidence of iatrogenic pseudoaneurysms. Lastly, no direct comparison was noted with manual compression or other management options regarding efficacy, safety, and cost in perithyroidal pseudoaneurysm treatment owing to their low incidence.

## CONCLUSIONS

US-guided percutaneous TI may be an effective, relatively safe, and cost-effective method for managing iatrogenic perithyroidal pseudoaneurysms that occur after thyroid biopsy.

**Disclosure forms** provided by the authors are available with the full text and PDF of this article at [www.ajnr.org](http://www.ajnr.org).



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