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ORIGINAL ARTICLE

Ethanol Ablation for the Treatment of Cystic and Predominantly Cystic Thyroid Nodules

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Abstract

Objective: To determine the efficacy and safety of percutaneous ethanol injection (PEI) for the treatment of symptomatic cystic thyroid nodules.

Patients and Methods: Retrospective analysis of patients with benign cystic thyroid nodules treated with PEI from February 1, 2000, through October 31, 2016. The main outcomes were efficacy, defined as symptom relief or reduction in nodule volume of 50% or more, and safety, defined as no or minor adverse events.

Results: Twenty patients had PEI. Mean age at the time of PEI was 50 years, and 13 (65%) were women; all patients were euthyroid. Twelve patients (60%) had complex cystic thyroid nodules (>50% cystic component), with the rest being purely cystic. The median largest diameter of the thyroid cyst was 4.5 cm (interquartile range [IQR], 3.2-5.3 cm; range, 2.3-8.0 cm); the median volume pre-PEI was 19.6 mL (IQR, 10.4-48.5 mL; range, 2.8-118.1 mL). The median amount of cystic fluid drained before PEI was 13.5 mL (IQR, 6.8-32.3 mL), and the median amount of ethanol administered was 3 mL (IQR, 2-5 mL; range, 0.5-20 mL). After median follow-up of 2 years, 17 of 19 patients (89%) were asymptomatic. Of 10 patients with available imaging on follow-up, 7 (70%) had a 50% or greater reduction in nodule volume (median volume decrease, 75.64% [IQR, 41.40%-91.99%]). Adverse effects occurred in 4 patients (20%) and were mild and temporary (slight pain, vagal reaction, and bleeding into the cyst).

Conclusion: Percutaneous ethanol injection seems to be a safe and effective alternative to surgical resection for patients with purely or predominantly cystic thyroid nodules and compressive symptoms who decline surgery or are not good surgical candidates.

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Thyroid nodules are common in clinical practice, and their incidence has increased with the use of high-resolution ultrasonography.[1,2] The management of thyroid nodules is complex as clinicians need to take into consideration patient features (age, comorbidities, and fitness for surgery), the presence or absence of compressive symptoms, the ultrasonography "imaging phenotype" and risk of malignancy, and patient preference. Ruling out malignancy is a priority in all patients, and imaging phenotype plus cytologic examination of fine-needle aspiration (FNA) biopsy are useful for this.[3] The American Thyroid Association (ATA) thyroid nodule sonographic patterns[4] consider pure cysts to be of negligible malignancy risk (benign), with a risk of malignancy of less than 1%; partially cystic nodules with no suspicious features to be of very low suspicion (<3% risk of malignancy); and partially cystic nodules with eccentric solid areas to be of low suspicion for malignancy (5%-10% risk). Once malignancy has been ruled out, further treatment usually depends on the presence of compressive symptoms because some patients with benign nodules may require surgery for symptomatic relief.[5,6] In the case of patients with symptomatic thyroid cystic nodules, treatment options include simple nodule aspiration, minimally invasive techniques, or surgical resection. Aspiration can be performed, but recurrence rates are high, observed in approximately 60% to 90% of patients.[7] Surgical treatment is more definitive but may be associated with potential complications.[8] As a result, some patients are not interested in surgery, and others may sometimes be too sick due to existing comorbidities so that surgery is contraindicated. In such patients, minimally

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invasive therapeutic procedures, such as percutaneous ethanol injection (PEI), have become a good treatment option.[9]

Percutaneous ethanol injection was first evaluated at the end of the 1980s,[10] and in the 1990s for the treatment of autonomous thyroid nodules as an alternative to surgery and radioiodine.[11] Percutaneous ethanol injection of benign thyroid cysts is performed under ultrasound guidance. Ethanol causes permanent tissue damage by cellular dehydration and protein denaturation, with subsequent necrosis, fibrosis, and thrombosis of small cyst wall blood vessels.[12,13]

The procedure is currently described as effective and safe for the treatment of benign thyroid cysts and complex nodules with a predominant cystic component.[14-16] In controlled studies, the remission rate after 1 to 3 PEI sessions is approximately 75% to 85%, compared with 7% to 38% after aspiration only or treatment with isotonic saline.[14,16,17]

There is limited information on the use of PEI for the treatment of thyroid cysts in the American literature. Therefore, the aim of this study was to determine the efficacy and safety of this technique and to delineate the clinicopathologic outcomes of patients with thyroid cysts treated with PEI at Mayo Clinic's campus in Rochester, Minnesota.

PATIENTS AND METHODS

Study Design and Search Strategy

A retrospective review of medical records of all patients with a diagnosis of thyroid nodules treated with PEI at Mayo Clinic from February 1, 2000, through October 31, 2016, was performed. Eligible patients were identified by using the Mayo Clinic Life Sciences System Advanced Cohort Explorer search engine, which allows for rapid searching of the Mayo Clinic electronic record system, and the Radiology Information Management System.

Inclusion Criteria

Candidates for PEI included patients with purely or predominantly cystic (>50% cystic component) nodules, with a benign cytologic test result (in those with a solid component; for purely cystic nodules, a nondiagnostic result was acceptable) and with symptoms of compression or cosmetic concerns. Symptomatic nodules with persistent symptoms after simple drainage and symptotmatic nodules for which the primary intervention was PEI were included.

Efficacy and Safety

The efficacy of PEI was assessed by the degree of resolution of the patient's symptoms (based on documentation of symptoms on the medical record, no scale was used per the procedure's note report on the charts) and by the degree of volume reduction of the nodules during follow-up. A 50% or greater reduction in nodule volume from baseline was considered significant. Patients who had no follow-up at Mayo Clinic were contacted by telephone to evaluate for the presence of symptoms, thyroid nodule volume, and necessity of other therapies. If follow-up ultrasound imaging was performed at another institution, after proper authorization, the images (or radiology report, when images were not available) were submitted for review by our radiologist to assess objective response to therapy (R.A.L.).

Safety was assessed by review of the procedure note and postvisit follow-up. We specifically looked for bleeding, pain, hoarseness, or any other adverse effects described in the procedure note or during subsequent follow-up. We used the Society of Interventional Radiology classification system for complications by outcome.[18] The protocol was approved by Mayo Clinic Institutional Review Board.

PEI Procedure and Volume Calculations

Ethanol injection was performed under ultrasound guidance in all the patients using an 8- to 16-MHz probe with the General Electric Logiq E9 system (GE Healthcare) currently and the Acuson Sequioa system (Siemens) in the earlier years of the study and a 20- to 22-gauge needle. Four interventional radiologists performed the injections. Nodule volume and the percentage of volume reduction were calculated using the ellipsoid equation (length x width x depth x $\pi/6$) and the calculator available at the ATA website, and the percentage volume reduction was calculated using the following formula: [(initial volume − final volume) x 100%]/initial volume.[19] All the nodules were aspirated and drained as completely as possible immediately before