The role of ethanol ablation during radiofrequency ablation of thyroid nodules: control of internal hemorrhage

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Purpose

Benign nodular thyroid disease is common and 15-25% of solitary nodules are cystic or predominantly cystic on ultrasound (US) examination [1]. Most cystic lesions are considered to be caused by the haemorrhage and subsequent degeneration of pre-existing nodules [2]. In patients with cosmetic or symptomatic problems, the initial procedure is the simple aspiration of the cystic portion; this serves not only to reduce the cyst volume, it also aids the diagnosis. However, this procedure is associated with a high recurrence rate of up to 80% [3, 4]. For recurrent cases after aspiration, ethanol ablation (EA) has been attempted, with good results [5, 6].

Recently, radiofrequency (RF) ablation was used to treat benign thyroid nodules that have a low complication rate [7-12], including thyroid nodules with a cystic portion [6, 8] and recurrent thyroid cancers [13]. When treating predominantly cystic nodules by thermal ablation, it is recommended that the internal fluid contents should be aspirated prior to RF or laser ablation [6, 14] because it is easier to treat decompressed small nodules than larger nodules [15]. However, internal haemorrhage can develop during the aspiration. This bleeding enlarges the nodule volume and has a heat sink effect, therefore bleeding could affect the efficacy of RF ablation.

In our clinic, predominantly cystic thyroid nodules that bled internally after aspiration were injected with ethanol, after which they were subjected to RF ablation. To the best of our knowledge, there are no reports on the efficacy of EA on internal bleeding before RF ablation. The aim of this study was to evaluate the feasibility and safety of EA in controlling internal bleeding during aspiration of the internal fluid of predominantly cystic thyroid nodules prior to RF ablation.

Methods and Materials

Patients

Between September, 2010, and August, 2011, 131 cases of RF ablation of benign thyroid nodules were performed in Asan medical Center. Forty of these cases involved patients with predominantly cystic nodules whose internal fluid was aspirated prior to RF ablation. In 11 of these patients, each of whom had one nodule, the cysts bled internally during the aspiration of internal fluid were enrolled in this study. They consisted of three males and eight females with a mean age of 47.1 years (range, 30-69 years). All patients fulfilled the following criteria: (1) the cystic portion of the nodule exceeded 50% of the nodule volume; (2) there were thyroid nodule-related pressure symptoms or cosmetic problems; (3) the serum thyroid hormone and thyrotropin levels were within normal limits; (4) two separate
US-guided fine needle aspirations led to a cytologically confirmed diagnosis of a benign lesion; and (5) there were no malignant features on the US examination [16-18].

Preablation assessment

The US and US-guided fine needle aspiration were performed by two radiologists. The US examinations were performed by using one of two US systems equipped with a linear high-frequency probe (5-14 MHz), namely, an iU22 unit (Philips Healthcare, Bothell, WA, USA) or an EUB-7500 unit (Hitachi Medical Systems, Tokyo, Japan). The size, characteristics, amount of solid component, and vascularity of each nodule was assessed. The three orthogonal diameters of each nodule were measured, and the volume of each nodule was calculated by using the following equation: volume = abc/6, where V is volume, a is the largest diameter, and b and c are the two perpendicular diameters [8, 13, 19]. Under US guidance, one of the two radiologists performed fine needle aspiration on the solid component of each nodule. At enrolment, the patients were asked to rate their symptom score on a 10-cm visual analogue scale (0-10). The physicians recorded a cosmetic grade (1, no palpable mass; 2, a palpable mass but no cosmetic problem; 3, cosmetic problem on swallowing only; and 4, readily detected cosmetic problem) [6, 20, 21].

Procedure (Figure 1)

All procedures were performed under US guidance. The patients were placed in a supine position with mild neck extension. After skin sterilisation and anaesthesia with 2% lidocaine at the puncture site, a 16- or 18-gauge needle was inserted into the cystic portion of the thyroid nodules through the isthmic area (this is the so-called trans-isthmic approach method) to prevent leakage of fluid or ethanol [6, 20, 22]. After the needle tip was placed into the cystic portion, as much of the internal fluid was aspirated as was possible. If active bleeding was detected during the aspiration of the internal fluid, the aspiration was stopped and 99% ethanol was injected slowly into the cystic space to control the bleeding. The injected volume of ethanol corresponded to about 50% of the aspirated fluid volume. After 2 minutes of ethanol retention, as much of the injected ethanol was removed as was possible [22]. After real-time US confirmed that the bleeding had stopped, RF ablation was initiated. Based on previous experience, the RF ablation was performed by using a trans-isthmic approach method and the moving shot technique [6-8, 10, 20, 21, 23-25]. For this, an 18-gauge, 7-cm long mono-polar modified internally cooled electrode (Well-Point RF electrode, Taewoong Medical, Kimpo, Korea; VIVA, STARmed, Gyeonggi, Korea), with a 1- or 1.5-cm active tip and a 200 watt RF generator (VIVA RF generator, STARmed, Gyeonggi, Korea), was employed. The moving shot technique used for thyroid RF ablation [7, 8, 10, 26-28] was first proposed by Baek et al. [21], who suggested that the thyroid nodule should be divided into multiple conceptual ablation units that would each undergo RF ablation; this was achieved by moving the electrode tip. As the conceptual units are smaller at the periphery of the nodule and larger in the centre of the nodule, the electrode tip was initially positioned in the deepest, most remote portion of the nodule where there were no disturbances caused by microbubbles;
this facilitated the monitoring of the electrode tip. RF ablation was terminated when all conceptual units of the targeted nodule had changed into a transient hyperechoic zone. Adverse events during and immediately after the procedure were recorded. After RF ablation, the patient was observed for 1-2 hours in the hospital.

![Procedure Diagram](image)

**Fig. 1**: Overall procedure

**References**: Radiology - Seoul/US

**Follow-up and analysis**

At 1, 6 and 12 month after RF ablation, and every 6-12 months thereafter, the clinical symptoms and cosmetic problems of all patients were re-evaluated. US examinations were also performed and changes in the amounts of the cystic portion, the internal vascularity, the echogenicity, the size, and the volume of the nodules were recorded. The efficacy of RF ablation was determined by measuring the volume reduction of the treated thyroid nodules and by assessing changes in the symptoms and cosmetic problems. Therapeutic success was defined as a nodule volume reduction > 50%. Adverse events during the follow-up period were also recorded. Recurrence was defined as an increase in nodule volume by > 50 % relative to the volume recorded by US previously [16].

**Statistical Analysis**
All statistical analyses were performed by using SPSS for Windows (version 18.0; SPSS, Chicago, IL). The Wilcoxon signed rank test was employed to evaluate the efficacy (changes in the largest diameter, the volume, and the cosmetic and symptom scores) of RF ablation at the 1 month, 6 month, and last follow-up visit.

Images for this section:

Fig. 1: Overall procedure
Results

After EA, the active bleeding stopped in all patients and it was confirmed that there was no blood collection within the thyroid nodule by US. The efficacy of RF ablation is summarised in Table 1.

Table 1: Efficacy of ethanol and RF ablation combination therapy

<table>
<thead>
<tr>
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<th>Initial</th>
<th>Last follow-up</th>
<th>P value</th>
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<tbody>
<tr>
<td>Largest diameter (cm)</td>
<td>4.1 ± 1.3</td>
<td>2.3 ± 0.6</td>
<td>0.003</td>
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<tr>
<td>Volume (mL)</td>
<td>17.1 ± 16.9</td>
<td>2.6 ± 2.1</td>
<td>0.005</td>
</tr>
<tr>
<td>Cosmetic score</td>
<td>4.0 ± 0</td>
<td>2.8 ± 1.0</td>
<td>0.01</td>
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<tr>
<td>Symptom score</td>
<td>2.7 ± 1.5</td>
<td>1.1 ± 1.0</td>
<td>0.011</td>
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<tr>
<td>Volume reduction (%)</td>
<td>-</td>
<td>81</td>
<td>-</td>
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<tr>
<td>Therapeutic success (%)</td>
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<td>100</td>
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Values are mane SD

Therapeutic success: volume reduction > 50%

Table 1: Table 1. Efficacy of ethanol and RF ablation combination therapy

References: Radiology - Seoul/US

The mean follow-up period was 11.4 ± 6.7 months (range, 6-24 months). The mean largest diameter decreased from 4.1 ± 1.3 cm (range, 2.4-7.1 cm) before treatment to 2.3 ± 0.6 cm (range, 1.3-3.0 cm) at the last follow-up (P = .003), and the mean volume dropped from 17.1 ± 16.9 ml (range, 2.9-59.0 ml) to 2.6 ± 2.1 ml (range, 0.2-6.9 ml) at the last follow-up (P = .005). At the 1 month, 6 month, and last follow-up visits, the mean volume reduction ratios were 52.9%, 75.6%, and 81.0%, respectively. Therapeutic success was achieved in all patients. The mean cosmetic score decreased from 4.0 before treatment to 2.8 ± 1.0 (range, 1-4) at the last follow-up (P = .01). The mean symptom score dropped from 2.7 ± 1.5 (range, 1-5) before treatment to 1.1 ± 1.0 (range, 0-4) at the last follow-up (P = .011). The follow-up US examinations indicated well-treated
nodules that no longer had a cystic portion and whose echogenicity of the solid portion and intra-nodular vascularity was decreasing (Fig. 2).

**Fig. 2**: Figure 2. A 59-year-old female patient who presented with a bulge in the neck. a Transverse US images at presentation show a thyroid nodule with a cystic portion in the right thyroid gland. The initial volume of the nodule was 11.4 ml. b On the Doppler US, increased vascularity in the solid portion of the nodule was also noted. c and d After active bleeding was controlled by EA, and RF ablation was performed, the volume of the ablated nodule decreased gradually to 2.8 ml and 0.9 ml at the 6 and 12 month follow-up US examinations, respectively. At the 12 month follow-up visit, the volume had been reduced by approximately 92%.

**References:** Radiology - Seoul/US
The mean number of ablation sessions was 1.2 ± 0.6 (range, 1-3): ten patients had one session, while the remaining patient had three sessions. The latter patient had a large initial thyroid nodule volume of 37.3 ml. The mean ablation time and power were 6.3 ± 3.0 min (range, 3-12 min) and 57.3 ± 24.9 watts (range, 30-120 watts), respectively. The mean total energy deposition was 21218.2 ± 11523.7 J (range, 7,800-36,000 J). The mean energy delivered per ml of pre-treatment nodule volume was 2013.3 ± 1228.3 J (range, 684.2-4230.8 J). The mean volume of aspirated internal fluid was 8.8 ± 9.3 ml.
(range, 2-35 ml), while the mean amount of ethanol that was injected was 5.1 ± 5.7 ml
(range, 1-20 ml).

There were no major complications, such as voice changes, skin burn, haematoma,
esophageal injury, tracheal injury, or infection, either during the procedure or in the follow-
up period. During RF ablation, most patients reported pain and a sensation of heat in the
neck that radiated to the head, shoulders, teeth, and chest. The symptoms were relieved
by reducing the RF power or stopping the ablation for several seconds. All patients
tolerated the RF ablation procedure well.

Images for this section:

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Therapeutic success: volume reduction > 50%
**Fig. 2:** Figure 2. A 59-year-old female patient who presented with a bulge in the neck. a Transverse US images at presentation show a thyroid nodule with a cystic portion in the right thyroid gland. The initial volume of the nodule was 11.4 ml. b On the Doppler US, increased vascularity in the solid portion of the nodule was also noted. c and d After active bleeding was controlled by EA, and RF ablation was performed, the volume of the ablated nodule decreased gradually to 2.8 ml and 0.9 ml at the 6 and 12 month follow-up US examinations, respectively. At the 12 month follow-up visit, the volume had been reduced by approximately 92%.
Conclusion

The present study showed that EA effectively controlled the bleeding of the nodule in all patients. The RF ablation, after the bleeding control was achieved, significantly reduced the nodule volume and relieved the symptomatic and cosmetic problems. In addition, 91% (10/11) of the patients could be treated by one RF session and there were no recurrences during the follow-up period. There were also no complications that related to the EA or RF ablation.

Initial nodule volume can be a risk factor for poor volume reduction by RF and the need for additional RF treatment sessions. Huh et al. [15] reported that an initial nodule volume larger than 20 ml required additional RF ablation to achieve satisfactory clinical results. Moreover, Jeong et al. [8] reported that thyroid nodules with a mean volume of 6.1 ml required an average of 1.4 treatment sessions while Lim et al. [29] reported that thyroid nodules with a mean volume of 9.8 ml required 2.2 treatment sessions on average. These results indicate that smaller thyroid nodules can be treated with fewer treatment sessions. In the present study, the mean nodule volume was larger (17.1 ml) than the mean volumes in the other RF studies (6.1-9.8 ml) [8, 29]. Nevertheless, 91% (10/11) of the patients could be treated in a single RF session; in addition, there were no recurrences during the mean follow-up period of 11.4 months. As a result, the mean treatment session number in this study was smaller (1.2) than the numbers in other studies (1.4-2.2). The present study differed from the preceding studies in that the internal fluid was aspirated to reduce the nodule volume with the aim of reducing the number of treatment sessions. The results indicate that this approach was successful. However, active bleeding can be triggered by the aspiration, and this can create an important technical problem: it can cause sudden enlargement of the thyroid nodule and the heat sink effect of the blood can make RF ablation ineffective. The present study showed that EA successfully controlled active bleeding during aspiration and that nodule volume was effectively reduced before RF ablation.

The reduction in nodule volume after RF ablation has been found to range from 33% to 58% at 1 month and from 51% to 92% at 6 months [21]. Jeong et al. [8] reported that after a mean follow-up period of 12 months, the mean volume reduction was 84.1% and that 70.2% of the nodules could be treated by a single treatment session. In the present study, the mean follow-up period was 11.4 ± 6.7 months, the mean volume reduction was 81.0%, and 91% (10/11) of the nodules could be treated by a single session. Therefore, our results are comparable to those of previous studies with fewer treatment sessions. In addition, there was 100% technical success and no major complications.

RF ablation combined with EA has been used for haemoptoma in high-risk locations and two studies have shown that this combination is more effective and safe than RF ablation alone [30, 31]. In these studies, the principle role of ethanol was to induce a larger necrotic area and to minimise complications [32, 33]. To our knowledge, the present study is...
the first to examine the efficacy of the combination of these two modalities in treating predominantly cystic thyroid nodules.

The present study has several limitations. First, it had a retrospective design. However, a standard technique was used to control active bleeding during the RF ablation. Second, the number of cases was small and the follow-up period was short. Third, there was no control group. Further prospective studies are required to verify the value of the current study.

In conclusion, EA is a feasible and safe technique for controlling the active bleeding of predominantly cystic thyroid nodules that can occur when internal fluid is aspirated prior to RF ablation. This combination therapy makes RF ablation both easy and effective.

References


Personal Information

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