Sonography-Guided Ethanol Ablation of a Remnant Solid Component after Radio-Frequency Ablation of Benign Solid Thyroid Nodules: A Preliminary Study

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Sonography-Guided Ethanol Ablation of a Remnant Solid Component after Radio-Frequency Ablation of Benign Solid Thyroid Nodules: A Preliminary Study

BACKGROUND AND PURPOSE: No study has previously examined the feasibility of using EA to remove any peripherally located, solid components remaining after treatment of benign solid thyroid nodules by RFA. The aim of this study was to assess the efficacy of EA in removing remnant solid components following the incomplete ablation of benign solid thyroid nodules by RFA.

MATERIALS AND METHODS: During a 1-year period, RFA was performed in 18 benign solid thyroid nodules in 17 patients. EA was subsequently performed on 8 of these nodules. The success rate of EA, size and vascularity of the remaining solid components, amount of injected ethanol, degree of intranodular echo staining just after ethanol injection, and number of EA sessions were assessed.

RESULTS: Of 18 post-RFA nodules, 8 nodules were subsequently treated with EA because of incomplete ablation, as defined by the presence of peripherally located vascularized solid components. On follow-up US, 2 nodules showed marked hypoechochogenicity and no vascularity of the remaining solid components, while 3 nodules showed considerably decreased echogenicity and vascularity of the remaining solid components. Three nodules showed no significant decrease or mild decrease in the echogenicity and vascularity of the remaining solid components. No serious complications were observed during or after RFA or EA, with the exception of 1 patient who experienced diffuse glandular hemorrhage during these procedures.

CONCLUSIONS: EA was effectively used to remove incompletely ablated components of benign solid thyroid nodules remaining after RFA.

ABBREVIATIONS: EA = sonography-guided percutaneous ethanol ablation; RF = radio-frequency; RFA = sonography-guided percutaneous radio-frequency ablation; US = sonography
nODULES showed malignant US characteristics before RFA, and all
were confirmed to be benign following 1 or 2 sessions of US-guided
gene-needle aspiration. Serum thyroid hormone (total triiodothyro-
nine; normal range, 80–200 ng/dL), free thyroxine (normal range,
0.93–1.71 ng/dL), thyrotropin (normal range, 0.27–4.20 mIU/mL), and
thyroid peroxidase antibody (normal range, 0–35 IU/mL) levels were
also determined by chemiluminescent immunoassay (Modular E170;
Roche Diagnostics, Mannheim, Germany), both before RFA and EA
treatment and during follow-up. Routine scintiscans were not in-
cluded in this study. The ellipsoid formula (width \( \times \) length \( \times \)
height \( \times 0.52 \)) was used to calculate both the initial nodule volumes
and the volumes of vascularized solid components remaining follow-
ning RFA. In the case of multifocal remnant solid components, the sum
of the volumes of all calculated solid components was used.

**Thyroid US**

Each nodule was evaluated with real-time thyroid US, including a
color Doppler study both before and after RFA and EA treatments.
Thyroid US was performed by a single radiologist (D.W.K.) with a
high-resolution sonography instrument (iU22; Phillips Medical Sys-
tems, Andover, Maine) equipped with a 5- to 12-MHz linear probe.

During color Doppler US examination, a low value of pulse repet-
tion frequency, 700 Hz, was used for evaluation of the vascularity
of thyroid nodules. The vascularity of thyroid nodules was compared
with adjacent normal parenchymal vascularity on color Doppler US
and classified as follows: scant vascularity (no vascular signal intensity
or only a few vascular spots), low vascularity (the vascular signal in-
tensity is lower than that of adjacent normal parenchyma), iso-vascu-
ularity (the vascular signal intensity is the same as that of adjacent
normal parenchyma), mildly increased vascularity (the vascular sig-
nal intensity is greater than that of adjacent normal parenchyma and
covers \( \leq 30\% \) of the solid component), and markedly increased vas-
cularity (the vascular signal intensity covers at least \( 30\% \) of the solid
component).

**RFA Protocol**

Written informed consent was obtained from all patients before each
RFA. All RFAs were performed by the same operator (D.W.K.) with an
RF generator (Cool-tip RF System, Covidien, Boulder, Colorado;
SSP-2000, Taewoong Medical, Gimpo, Korea; M-1004, RF Medical,
Seoul, Korea), an internally cooled electrode (Cool-tip, Taewoong
Medical), and an active needle tip 1-, 1.5-, or 2-cm length, depending
on the nodule volume. RF power varied from 30 to 100 W, depending
on the size of the active needle tip, nodule vascularity, and nodule
volume. The position of a patient was different according to the loca-
tion of a nodule: A general position where an operator faced the pa-
tient’s face was used in RFA of the right thyroid nodule or right isth-
mic nodule, but a reverse position where an operator faced the pa-
tient’s feet was applied in RFA of the left thyroid nodule or left isthmic
nodule. After local anesthesia, all procedures were performed under
real-time US guidance. An electrode was placed in the thyroid
nodule by using a transisthmic approach, followed by an attempt to
achieve complete ablation while simultaneously minimizing thermal
injury to surrounding critical structures. Patients were not treated
with antibiotics before or after ablation.

**EA Protocol**

Written informed consent was obtained from all patients before each
EA. Eight patients required EA, which was performed on an outpa-
tient basis by the same operator (D.W.K.) at least 6 months after RFA
to remove the solid nodule components that remained following
treatment. During the entire procedure, the operator maneuvered the
US probe with his left hand and maneuvered a 10-mL plastic syringe
filled with 99.9% absolute ethanol attached to either a conventional
21- or 23-ga needle with his right hand. The US probe was adjusted to
center the target nodule on the US monitor, and a single-puncture
technique was used with no local anesthesia. The operator rapidly
inserted the needle almost perpendicular to the neck and applied
positive pressure to the syringe piston with the thumb of his right
hand to prevent an influx of blood into the needle lumen during
insertion. Adequate coverage of the target nodule, as indicated by its
echogenicity (called “intranodular echo staining”), was achieved by
injecting the injection of ethanol under US guidance. In all cases, the
amount of injected ethanol did not exceed 10 mL in 1 session.

Intranodular echo staining was roughly estimated on the basis of real-
time US and classified as follows: no staining (nearly complete
washout of injected ethanol), poor staining (\( \leq 10\% \) of the injected
area), mild staining (10%–50% of the injected area), and moderate
staining (\( \geq 50\% \) of the injected area).

One or 2 further EAs were performed at least 1 month following
the initial treatment if the outcome of the preliminary EA was deter-
mined to be unsuccessful on follow-up US. The amount of infused
ethanol, degree of intranodular echo staining just after ethanol injec-
tion, and the presence of pain or other complications during or after
the procedure were recorded for each patient. Any patients experienc-
ing a sensation of inebriation following EA were not allowed to drive
themselves home.

**Assessment of EA Outcomes**

All 8 nodules were sonographically followed up at 1 and 6 months
after EA. The decreased echogenicity and vascularity of solid compo-
nents were used as criteria to assess the ability of EA to remove any
components remaining after RFA. The nodule echogenicity was clas-
sified as follows according to the comparison with adjacent paren-
chyma and strap muscle: isoechogenicity (defined as the same echo-
genicity compared with the adjacent normal thyroid parenchyma),
hypoechochogenicity (defined as decreased echogenicity compared
with the adjacent normal thyroid parenchyma and the increased echoge-
nicity compared with the strap muscle), and marked hypoechochogenic-
ity (defined as the same or decreased echogenicity compared with the
strap muscle). The vascularity of solid components was assessed by
using real-time color Doppler US just before EA and following the
final EA. Cases in which the solid components showed marked hy-
poechochogenicity without vascularity on follow-up US were considered
successful. Nodule volumes and the volume of the remaining solid
components were calculated before RFA and EA, respectively, and at
the time of the final follow-up thyroid US following EA treatment;
and the change in volume was assessed.

**Results**

In this study, RFA of 18 benign solid thyroid nodules (mean of
the largest diameter, 3.3 cm; range of the largest diameter,
1.2–7.0 cm) was performed in 17 patients (Table 1). All pa-
tients had normal serum thyroid hormone levels before RFA
and EA and during the follow-up period (3–6 months after the
final session). One patient had a low serum level of thyrotro-
pin before RFA and EA; however, this low level was also ob-
served following EA. One patient had severe pain and anterior
neck swelling during the RFA because of severely diffuse gland-
ular hemorrhage. The procedure was therefore stopped, and
the patient was given oral analgesics for 3 days. However, diffuse glandular hemorrhage did not remain on follow-up US at 1 month after RFA. Three patients who experienced mild pain during and after RFA also took oral analgesics for 1 day following the procedure. On follow-up US, 10 nodules showed marked hypoechogenicity and scant or no vascularity, while 8 nodules had peripherally located solid components remaining following RFA.

Of the 18 nodules that were initially treated with RFA, 8 nodules subsequently underwent EA for complete ablation of peripherally located remaining solid components after RFA (Table 2 and Figs 1 and 2). The patient who experienced severely diffuse glandular hemorrhage at RFA also presented with the same symptom during EA, leading to discontinuation of the procedure. This patient again took oral analgesics for 3 days. Three of the 8 patients (37.5%) experienced mild pain either during or several minutes after the procedure; however, oral analgesics were not used for management of local pain. On follow-up US, 2 nodules showed marked hypoechogenicity and no vascularity of the previous remnant solid components, while 3 nodules showed considerably decreased echogenicity and vascularity of the previous remnant solid components after 1 EA session. The remaining 3 nodules showed no significant decrease or mild decrease in the echogenicity or vascularity of the remnant solid components following the first EA session; 1 of these was stopped with a single EA session and 2 were subsequently treated with 1 or 2 further procedures. Therefore, EA for 5 nodules (62.5%) was considered successful.

In the 3 failed cases, 1 showed a very large (volume, 71 cm³) highly vascularized remnant solid component remaining before EA and poor intranodal echo staining during and immediately after 1 session of EA, while another was found to have a large (volume, 25.3 cm³) peripherally located remnant solid component with mildly increased vascularity and poor intranodal echo staining during and immediately following 3 sessions of EA. In the final failed case, a small (volume, 3.2 cm³) highly vascularized remnant solid component was observed before EA, which maintained poor intranodal echo staining during and after 2 sessions of EA.
Discussion
The treatment of benign thyroid nodules by RFA has recently been accepted as a viable alternative to radioiodine therapy, surgery, and EA. In particular, RFA has proved to be a feasible and effective tool for treatment of benign solid thyroid nodules. Baek et al previously reported that the treatment of benign solid thyroid nodules by RFA had a high success rate (100%) and was effective in both reducing the volumes of benign solid thyroid nodules, with a mean volume reduction rate of 79.7%, and relieving nodule-related clinical problems.

Fig 1. An example of successful US-guided percutaneous EA for an eccentric peripherally located solid component remaining in a 20-year-old woman following RFA. A and B, Transverse gray-scale and color Doppler US images of a thyroid nodule (1.7 × 2.5 × 3.7 cm) in the left lobe show isoechogenicity and mildly increased vascularity, respectively. C, Longitudinal color Doppler follow-up US image obtained 6 months after the RFA session shows moderate shrinkage (1.0 × 1.4 × 2.2 cm, decrease in volume of 82.5%), while the presence of a vascularized solid component remaining in the upper portion of the nodule was also detected. D and E, Longitudinal gray-scale and power Doppler follow-up US images obtained 6 months after a single session of EA (total amount of injected ethanol, 1 mL) show no visualization of the solid component previously detected in the upper portion of the nodule, as well as a further decrease in nodule volume (0.7 × 1.1 × 2.0 cm, decrease in volume of 91.2%).

Fig 2. An example of successful US-guided percutaneous EA for a circumferential peripherally located solid component remaining in a 34-year-old woman following RFA. A and B, Transverse gray-scale and color Doppler US images of a thyroid nodule (1.5 × 2.3 × 2.4 cm) in the right lobe show isoechogenicity and mildly increased vascularity, respectively. C, Transverse color Doppler follow-up US image obtained 6 months after the RFA session shows mild shrinkage (1.1 × 1.5 × 1.5 cm, decrease in volume of 70.1%) and the presence of vascularized solid components in the peripheral regions of the nodule. D, Transverse gray-scale US images just after EA show complete replacement of the nodule with intranodular echo staining (arrows) due to injected ethanol (total amount of injected ethanol, 1 mL). E, Longitudinal gray-scale follow-up US image obtained 6 months after a single session of EA shows marked hypoechogenicity and no vascularity (0.5 × 0.8 × 1.1 cm, decrease in volume of 94.7%).
during a 6-month period of US follow-up. In the present study, the incidence of RFA success, defined as the absence of vascularized solid components remaining on follow-up US, was 55.6% (10/18). In the author’s opinion, an important factor that determines the success of RFA in the treatment of benign solid thyroid nodules is operator experience, in addition to nodule characteristics, such as vascularity, location, and volume.

In this study, 3 failed cases were found to have remnant solid components with high vascularity before EA and poor intranodular echo staining during and immediately following EA. This result corresponds with a previous study by this author that demonstrated that high vascularity and poor intranodular echo staining are significantly correlated with the success of EA in the treatment of benign solid thyroid nodules. Moreover, remnant solid components in 2 failed cases showed a volume of >5 cm³ before EA, while remnant solid components in 6 successful cases showed a volume of <5 cm³. Therefore, the author recommends the limited use of EA following incomplete RFA in cases in which the remaining component has a volume of <5 cm³ and is not highly vascularized.

The operator who performed all the procedures in this study had a low level of experience in using RFA to treat thyroid nodules (<20 RFA cases/year); this may have been a factor in the considerably high incidence of peripherally located nonablated components remaining after RFA treatment. In cases in which there is incomplete nodule ablation by RFA, resulting in peripherally located solid components remaining, additional RFA may not be recommended due to technical difficulty and cost. Indeed, RFA is significantly more expensive than EA and has been reported to cost approximately 3–6 times more than EA in South Korea.

The possible serious complication of EA is the direct damage of adjacent nerves or critical structures by leakage of ethyl alcohol following injection. However, substantial operator experience and a precise US-guided injection may help decrease the incidence of or avoid complications. With the exception of transient neck pain and diffuse glandular hemorrhage, no serious complications of EA occurred in this study. The author therefore recommends that EA be used to remove any nonablated components of benign solid thyroid nodules remaining after RFA treatment.

There were several limitations to this study, one of which is the small sample size. To address these issues, large-scale studies examining the treatment of solid thyroid nodules by RFA followed by EA are recommended. In addition, a single operator performed all of the RFA and EA procedures included in this report. Therefore, the author plans a multicenter study for further investigation into the efficacy of EA in the treatment of benign symptomatic thyroid nodule components remaining following RFA. Finally, thyroid scans were not performed before RFA or EA treatments, and long-term US follow-up of >12 months was not undertaken.

Conclusions
Despite the limitations of this study, the findings described in this report suggest that following incomplete RFA for benign symptomatic solid thyroid nodules, EA can be considered as a treatment, instead of a second round of RFA, when the solid components show peripheral localization, have a volume of <5 cm³, and are not highly vascularized.

References