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Research Article

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Microwave ablation of thyroid nodules: effects on recurrence and outcome

Abstract

Background: Microwave ablation developed into an accepted treatment for benign thyroid nodules. Definition and risk factors for recurrence are under discussion. We assumed recurrence in case of a second procedure for the same reason or if clinical symptoms reappear after initial relief, and analyzed our prospectively collected data for risk factors and outcome.

Methods: Indications included benign thyroid nodules (n=24), cystic nodules (n=9), autonomous functioning nodules (n=9), recurrent cancer (n=3) and Basedow's disease (n=2). For microwave ablation, a CE certified generator was used. All procedures were conducted under ultrasound control and with general anesthesia or mild sedation. Follow-up included ultrasound, laboratory parameters and a standardized questionnaire.

Results: A total of 47 patients were enrolled into the study. Among them were 19 cases with risk factors for recurrence which were defined as nodule size exceeding 4 cm with or without cystic appearance. Recurrence occurred in 9 cases leading to conventional hemithyreoidectomy (n=1), reablation (n=5) or sclerotherapy (n=1). The association of recurrence with the presence of a risk factor was statistically significant (p<0,001, Chi square test). In case of recurrence, statistically significant less energy was deployed in comparison to successful MCT (0,39 +/- 0,31 kJ/mL vs. 1,57 +/- 2,37 kJ/mL, p< 0,005, t-test).

Conclusion: Recurrence is a common problem following microwave ablation of thyroid nodules. Nodules > 4 cm and cystic disease seem to predispose for treatment failure. Further studies are required to define recurrence and the best indications for microwave ablation of thyroid nodules.

Keywords: thyroid ablation, microwave ablation, recurrence

Volume 10 Issue 1 - 2022

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Received: July 19, 2022 | **Published:** July 26, 2022

Introduction

Local ablation has emerged as a valuable treatment option for benign thyroid nodules during recent years. Among others, microwave coagulation therapy (MCT) has become popular because of its safety and effeciency.[1–4] Moreover, some theoretical advantages seem to predestine MCT for the purpose of treating particularly larger benign thyroid nodules,[5] because it enables faster heating in a shorter period of time[6] than radiofrequency ablation. MCT creates an in-situ ablation, which means the heated tissue remains in the site of the ablation as long as it is not completely resorbed. This leads to a typical time frame of six to nine months required for assessing the eventual treatment success. Wang et al. suggest a definition for treatment success if more than 50 % volume decrease is achieved at the end of the follow-up schedule of 12 months.[7]

The ablation area is occasionally still visible in ultrasound scans during a longer follow-up period. This has early been observed following laser ablation of thyroid nodules.[8,9] As long as the treated nodules do not show any signs of metabolic activity or vascularization, they are supposed to be considered successfully treated. Consequently, Wang et al. define recurrence as revascularization in the ablation area and/or regrowth of > 50 % volume increase within 3 months.[7]Numerous guidelines recommend local ablation for benign thyroid nodules in case of symptomatic disease consisting in dysphagia, pressure or cosmetic disturbances.[10–12] Therefore, disappeared symptoms apparently indicate successful treatment, regardless of the volume reduction rate. The decrease of nodule volume which is sufficient to relief symptoms in such cases, depends on individual factors like the site and initial size of the causative nodule. Therefore, data on patient reported outcomes (PROM) seem paramount to determine the role of local ablative treatment modalities in thyroidology.

We intended to analyze our experience in microwave ablation of thyroid nodules with regard to treatment success and recurrence. The aim of our investigation is to find risk factors for unsatisfying outcome summarized under the term "recurrence" and to define the influence recurrence exerts on the outcome parameters of our patients.

Patients and methods

The general setup and technique adopted have already been described elsewhere.[13] In brief, the indications were chosen according to generally accepted international guidelines[10,11] and patient preferences. In case of benign disease, malignancy was excluded by aspiration cytology, histology or ^{99m}Tc MIBI scintigraphy. Coagulation disorders and uncontrolled hyperthyreoidism had to be excluded within a week prior to the procedures. The technical execution followed the published recommendations of the European Federation of Societies for Ultrasound in Medicine and Biology.[14] The procedures were offered under local anesthesia with or without mild sedation or under general anesthesia. No upfront size limit was set, though in large goiters (> 30 mL), no bilateral treatments were performed. Thermoablation was performed using the microwave ablation (MWA) system MedWaves AveCure® (SanDiego, CA, U.S.A.). Treatment data like energy deployment, duration of the ablation and temperatures were recorded. Temperature was controlled in a range of 70°C to 80°C, whereas the maximum power output was limited to 16 W.

The first 9 patients stayed one night in the hospital, all the other procedures were performed as outpatient treatments. Follow-up included ultrasound, laboratory parameters and a clinical examination after 1, 3, 6 and 12 months and annually thereafter. A standardized questionnaire was requested after one year.

Definitions:

Treatment success: – 50 % or more volume decrease after 6 months

Treatment failure: – less than 50% volume decrease after 6 months

Recurrence: - second procedure required to achieve treatment success later than 6 months

- regrowth of the target volume after initial volume decrease

- recurring vascularization in the ablation area

- reoccurring symptoms after initial relief

Risk factor: – nodule size larger than 4 cm max. diameter

The results are presented as a descriptive analysis with mean +/- standard deviation in case of standard normal distribution and median and range in case of non-standard normal distribution. Parametric data were compared using Student's t-test, categorical data with the Chi square test.

Results

A total of 47 patients were included, 34 female and 13 male. The average age was 53±12 years. Indications were benign nodules (n= 24, 51 %), cysts (n= 9, 19 %), recurrent carcinoma (n= 3, 6 %), autonomous adenoma (n= 9, 19 %) and M. Basedow (n= 2, 4 %). 16 procedures were conducted under general anesthesia, whereas in 31 procedures, local anesthesia with or without mild sedation was used. Average maximum nodule size was 35,3 +/- 16,3 mm, average nodule volume 17,7 +/- 18,9 mL. Duration of the procedure was 24±13 min.

In the average, 1,34 +/- 2,17 kJ energy was applied per ml nodule volume. In case of recurrence, the deployed energy was 0,39 +/- 0,31 kJ/mL, whereas in successful ablations, 1,57 +/- 2,37 kJ/mL were applied (p< 0,005, t-test). One skin burn accounts for a complication rate of 2 %. Postoperative temporary hoarseness was found in one patient (2 %). All patients except for four reported an improvement of complaints following the procedure (91,5 %).

One patient underwent uneventful hemithyreoidectomy one year after local ablation for a recurrent cystic lesion. Five reablations were scheduled for recurrence of solid nodules. Two patients meet the criteria for recurrence, denied however undergoing follow-on treatment due to asymptomatic condition. In one case, a cyst had to be treated twice. Lost to follow-up was one patient (2%). The follow-up period was 25 months in the average.

Recurrence or treatment failure was recorded in nine cases (19%). Risk factors for recurrence as defined before were found in 19 of our patients (40,4%). In Chi square test, a statistically significant association of the presence of one or more risk factors and unsatisfactorily outcome (recurrence or failure) was found (p< 0,01) besides the above-mentioned association with insufficient energy deployment.

Discussion

Reasons for unsatisfying results following MCT are not frequently reported in the current literature. Wang et al. found 16 recurrencies in their series of 94 patients representing a recurrence rate of 17 %,[7] resembling our own results of 19 % on a per-patient basis. In a more recently published paper, Xia et al. found a recurrence rate of only 2,3 % using the same definition for recurrence as Wang et al.[15] Under the term "recurrence", we summarized all unsatisfying outcomes of our patients, including regrowth of the treated nodule during ultrasound follow-up, recurrent symptoms and failure of reducing the nodule volume > 50 % within 6 months. This liberal definition led to a comparably large part of patients experiencing recurrence.

The energy needed to treat per mL nodule volume has been an object of investigation for years. Korkusuz et al. found an average of 1,5 kJ sufficient for 1 mL volume reduction.[16] Our patients without recurrence confirm these statement since they received 1,57 kJ/mL. Likewise, Wang et al. report on 1,58 kJ/mL in the non-recurrence group.[7] Xia et al. report contradictory data with a higher energy to volume ratio in the recurrence group (p<0,05) in his retrospective case series.[15] The energy deployment in our patients with recurrence might have been underestimated: Cysts are recorded with the volume prior to evacuation, which takes part at the beginning of the procedure. Once evacuated, the target volume has become smaller requiring a respectively smaller amount of energy for sufficient treatment of the remaining wall. However, only two of our patients with recurrence suffered from recurring cysts.

Thyroid cysts are generally considered good indications for thermoablation. Success rates are rather high with rarely reported recurrencies,[7,15,17] even though the Korean guidelines recommend ethanol ablation as a first line treatment in cystic and predominantly cystic nodules.[11] Thermoablation is recommended as the next step in cases with incompletely resolved symptoms or recurrence. Ethanol ablation is regarded as simple and less expensive with a fewer number of treatment sessions, indicating that repeated thermoablation has occasionally been required to treat cystic nodules completely.

Deandrea et al. identified the three categories solid, cystic and spongiform as influencing factors for the energy required to treat a nodule with radiofrequency ablation.[17] The amounts of energy were generally much higher when compared to findings obtained with microwave ablation. The authors found microcystic and spongiform ultrasound pattern as well as intense peripheral and intranodular vascularity to be favorable prognostic factors. We did not examine distinct ultrasound patterns nor did we quantify vascularization. The main risk factor in our study was nodule size, endorsing Wang et al., who found significantly larger initial nodule volumes in the recurrence group (24 vs. 12 mL, p< 0,01).[7]

The sonomorphologic changes after MCT have been described by Wei et al.[18] The nodules following MCT seem to be characterized by a marked volume decrease within the first three months following the procedure, whereas further alterations affect much more the shape rather than the size of the nodules. These findings make it difficult to define recurrence or relate recurring symptoms to still visible residual nodule masses present in up to 15 % of all patients.[18] In such cases, we offered a redo ablation to the patients. An ambitious network meta-analysis comparing different thyroid ablation modalities found two subsequent treatment sessions with radiofrequency ablation most effective in the treatment of benign thyoid nodules.[19] This suggests upfront planning two procedures to treat larger nodules an accepted recommendation.

From a value-based point of view, two ablation treatment sessions are more expensive than a single conventional surgical procedure. Jin et al. call approximately 1.600, - $ as the cost of a local ablative treatment in China,[20] whereas Che et al. report approximately 2.500, -

Citation: Eisele RM. Microwave ablation of thyroid nodules: effects on recurrence and outcome. *Endocrinol Metab Int J.* 2022;10(1):36–39.
DOI: 10.15406/emij.2022.10.00316

$ for conventional surgery in China.[21] In Germany, at date the Figures 1&2 are circling around 3.200, - € for conventional surgery and 2.000, - € for thermal ablation. These figures render a two-step therapy schedule with MCT economically inferior to conventional surgery. Thus, recurrence following thermoablation of thyroid nodules turns out to be a socio-economic factor which is not neglectable.

Figure 1 Microwave ablation system in use.

Above: Generator

Below: Antenna

Figure 2 Example of a patient treated with MCT for benign thyroid nodule.

a) Before, b) after treatment

Recurrence does not seem to impair quality of life in our patients. Recurrence rate according to our definition was 19 %, whereas satisfaction with the treatment reaches 91,5 %. Two of the patients with recurrence (22 %) refused to undergo further treatment. In an earlier publication, we presented data of our first 30 patients describing high degrees of satisfaction in various items screened using a standardized questionnaire.[13] This corroborates previously published data of 92 % of patients satisfied with the cosmetic results following radiofrequency ablation ,[22] a similar figure obtained in our cohort.

The shortcomings of this work are evident: highly selected patients, a debatable definition of recurrence and risk factors and a comparably small number of patients might lead to a certain bias in the interpretation of the results. However, our analysis shows that recurrence in terms of our definition seems to be rather common following MCT for benign thyroid nodules and is more probable in case of larger solid and cystic nodules. In addition, the required energy per nodule volume is at least 1,5 kJ/mL.

Funding

None

Acknowledgments

None.

Conflicts of interest

The authors declared no potential conflict of interest.

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Citation: Eisele RM. Microwave ablation of thyroid nodules: effects on recurrence and outcome. *Endocrinol Metab Int J.* 2022;10(1):36–39.
DOI: 10.15406/emij.2022.10.00316