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RESEARCH ARTICLE

Percutaneous Microwave Ablation of Benign Thyroid Nodules: Prognostic Value of Pre-Ablative ^{99m}tc-Scintigraphy and Ultrasound Imaging

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Abstract

Purpose

Percutaneous microwave ablation (MWA) poses a new, minimal-invasive therapeutic approach to thyroid nodules. The goal of this retrospective study is to find out about the prognostic value of different pre-ablative diagnostic results concerning the outcome of benign thyroid nodules treated with MWA at a 3-month follow-up.

Materials and Methods

Twenty-four patients with 26 nodules were treated. Pre-ablative assessment contained different sonographical modalities as well as functional imaging with ^{99m}Tc-pertechnetate and ^{99m}Tc-MIBI. At a 3-month follow-up, ultrasound examination was performed to assess the nodular volume reduction. Correlation of pre-ablative diagnostic parameters and nodular volume reduction was assessed by calculating Pearson's r and Spearman's rank correlation coefficient ρ.

Results

Mean relative nodular volume reduction at follow-up was 50.9 ± 19.8 %. The surveyed diagnostic parameters showed the following results concerning correlation with nodular volume reduction: $r = -0.53$ for baseline volume, $r = -0.40$ and $r = 0.32$ for ^{99m}Tc-MIBI-scintigraphy and ^{99m}Tc-pertechnetate-scintigraphy, $\rho = 0.21$ for nodular vascularity, $\rho = -0.07$ for stiffness and $\rho = -0.33$ for nodular composition.

Conclusions

Except baseline nodular volume, none of the sonographic findings presented a good correlation with nodular volume reduction. After all, ^{99m}Tc-scintigraphy still represents an important tool when dealing with thyroid nodules, although a prognostic significance relating to this procedure could not be validated.

Introduction

Thyroid nodules pose a common clinical issue, ranking amongst the most frequent transformations of the thyroid. The prevalence in Germany, until 2005 representative for a region of relative iodine deficiency [1], is estimated to be up to 68%, depending on age and the way of detection [2,3], with the incidence increasing with continuous improvement of sonographical imaging [4]. Those nodules tend to be benign in most cases; the incidence of thyroid cancer in Europe is reported to be 2.2/100,000 – 12.4/100,000 [5], making it a relatively rare malignant event. Still, benign thyroid nodules may require treatment due to cosmetic issues or subjective symptoms.

In the last years, minimally invasive techniques of treating thyroid nodules have emerged, representing a promising alternative to the well-established methods, i.e. surgical intervention and radioiodine therapy [6]. Amongst these, radiofrequency ablation

(RFA) [7,8], percutaneous ethanol injection [9], ultrasound-guided laser therapy [10,11] as well as high-intensity focused ultrasound (HIFU) [12] are to be mentioned. Percutaneous microwave ablation (MWA) is a thermal ablative technique [13] that has already been successfully put to use in order to treat malignancies in other organs such as the liver [14]. The limited number of clinical and experimental studies dealing with the use of MWA in the treatment of thyroid nodules [15-19] has presented encouraging results featuring a favorable profile of adverse effects [20-23]. In this context, thyroid scintigraphy represents a useful diagnostic tool in terms of assessing the consistency and function of thyroid tissue [24], furthermore allowing a rapid post-ablative prognostic evaluation considering the later outcome [23]. Other diagnostic approaches based on the principle of sonography can be used in pre-ablative examination of thyroid nodules: While duplex ultrasound (DU) poses a widespread and well-known sonographic modality for the detection of blood flow [25], ultrasound elastography (UE), sometimes referred to as a "virtual palpation", is used to image tissue elasticity [26-28]. The prognostic value of these sonographic modalities in the given context has so far not been explored. With ^{99m}Tc-scintigraphy being a significant and efficient, yet comparatively wearing (radiation exposure) diagnostic method, the aim of this retrospective study is to find out in what extent findings of pre-ablative sonography and ^{99m}Tc-scintigraphy correlate with nodular volume reduction at a 3-month follow-up and therefore deliver a prognostic statement about the clinical outcome of MWA of thyroid nodules.

Materials and Methods

Patients

This study evaluates data collected from 24 patients with a total of 26 nodules who were treated with MWA (11 men, 13 women; mean age 52.4 years; median age 54 years; range 31 – 75 years). Patients met the criteria for treatment if there were (a) cosmetic problems, (b) symptomatic nodules (e.g. swallowing problems, hoarseness, distress) or (c) refusal of surgery or contraindications against it, respectively. Exclusion criteria for treatment were (a) excessive thyroid volume with retrosternal growth, (b) lack of symptoms, (c) histological evidence for follicular proliferation in terms of a malignant dysplasia or (d) critical position of adjacent structures such as vessels or nerves.

Patients were treated on a compassionate use basis; written informed consent, clarifying possible risks and the experimental nature of the treatment, was obtained from all patients. Local ethics committee approved the study protocol and the retrospective evaluation of gathered data, respectively.

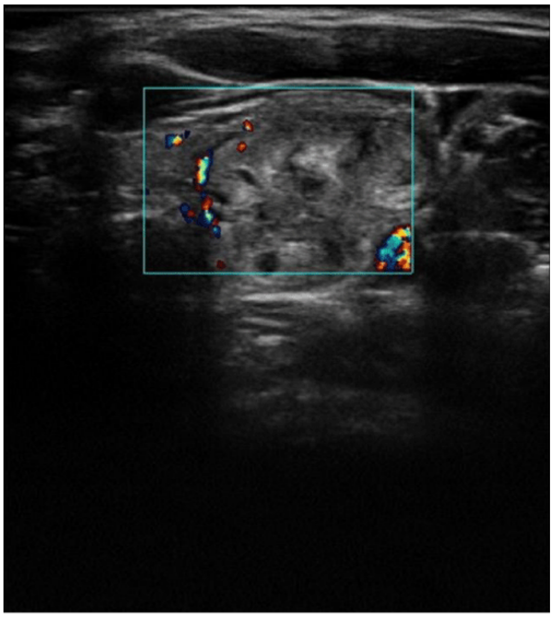

Figure 1: Duplex ultrasound image of thyroid. In this case the nodule presents minimal blood flow.

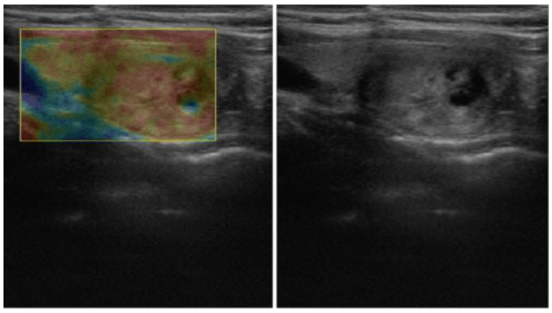

Figure 2: Ultrasound elastography image of the thyroid. Note: Red areas represent tissue of hard consistency, blue areas represent tissue of soft consistency. On the right : The same nodule imaged in regular 2D/B-Mode.

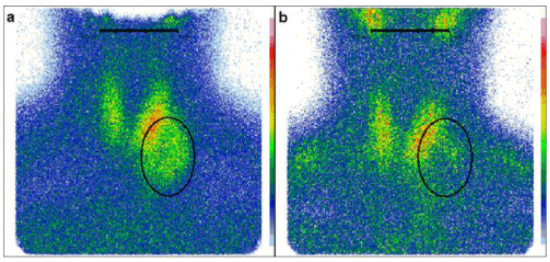

Figure 3: Scintigraphy of the thyroid with 99mTc-pertechnetate before (A) and after (B) ablation. Note the encircled areas, hinting at the location of the treated nodule.

Equipment

The microwave system used in this study (Avecure MWG881, MedWaves, Inc., San Diego, CA) works in a frequency range of 902–928 MHz generating maximum temperatures of approximately 140°C. According to individual needs and the

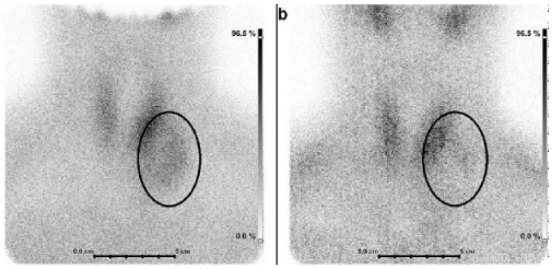

Figure 4: Scintigraphy of the thyroid with 99mTc-MIBI before (A) and after (B) ablation. Note the encircled areas, hinting at the location of the treated nodule.

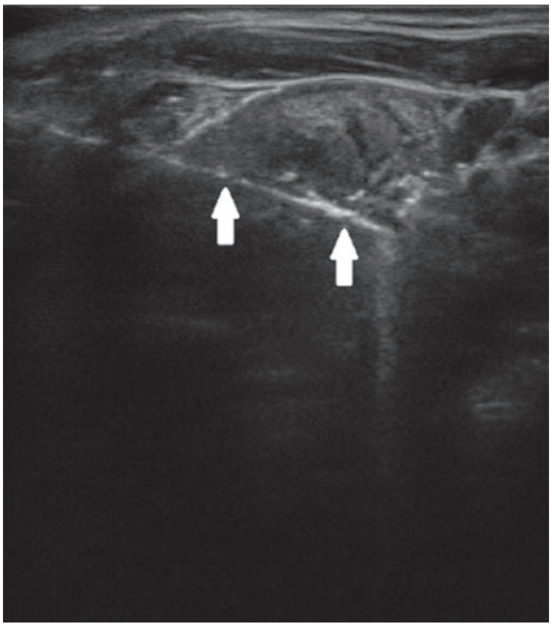

Figure 5: Sonographical imaging of the thyroid during ablation. Note how the microwave probe, white arrows marking its position, is completely visualized in order to ensure its correct placement and to avoid damage of adjacent structures.

size of the area to be ablated, three different probes (uncooled tip, 14–16 G) with diverging ablation radii are available. The field size varies from 1 – 4 cm, all probes feature integrated temperature sensors. The target temperature was 60–95°C with an output of 24–36 W. The device was operated in power control mode with the microwave generator periodically delivering pre-adjusted peak energy.

All sonographic examinations were performed using a SonixTOUCH Ultrasound system (Ultrasonix Medical Corporation, Richmond, BC, Canada), ran in 2D/B-Mode for regular ultrasound imaging of the thyroid, in Power Color Doppler mode in order to display nodular vascularity and in Elastography mode, respectively. A linear transducer was used for all sonographic modalities.

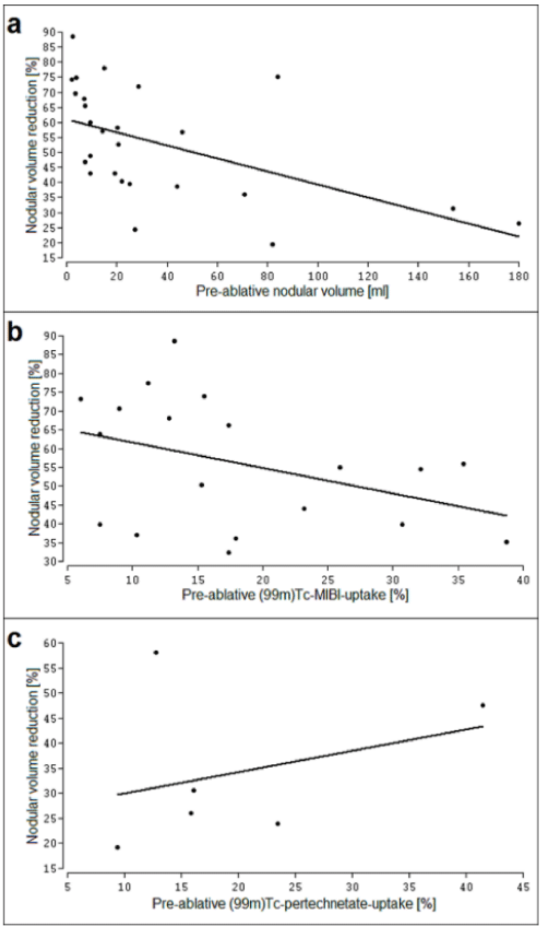

Figure 6: a) Correlation the mean pre-ablative nodular volume with r = -0.53 (p = 0.005) which strongly indicates a better effect of MWA on smaller nodules, b) shows the correlating relative volume reduction with pre-ablative 99mTc-uptake, Pearson's r was found to be - 0.40 (p = 0.088) and 0.32 (p = 0.532) and c) for nodules imaged with 99mTc-MIBI and 99mTc-pertechnetatestructures.

Pre-ablative assessment

Before ablation all patients underwent ultrasound examination, laboratory tests and scintigraphic thyroid imaging. Ultrasound examination was performed in order to evaluate volume, number and composition of the nodules. Volume was calculated using the following equation:

$$Volume\,[cm^3] = \frac{height\,[cm] \times width\,[cm] \times depth\,[cm]}{2}$$

Duplex ultrasound examination [Figure 1] and ultrasound elastography [Figure 2] were performed in order to determine vascularity and stiffness of each nodule. Vascularity was graduated as following: 1 – no blood flow; 2 – minimal blood flow; 3 – marked blood flow. Nodular stiffness was graduated in the following way: 1 – soft; 2 – rather soft; 3 – rather hard; 4 – hard. Additionally, nodules were classified by their composition, as imaged by sonography, depending on their relation of solid and cystic portion: 1 – cystic; 2 – rather cystic; 3 – equally cystic and solid; 4 – rather solid; 5 – solid. The type of vagus nerve location [29] was identified in order to avoid irritation or lesion of the vagus nerve during ablation. Laboratory tests included a complete thyroid hormone status, blood count, coagulation diagnostic, C-reactive protein and blood glucose.

Patients with known "hot" or "indifferent" nodules, according to earlier scintigraphy, received a thyroid scan with averagely 75 MBq ^{99m}Tc-pertechnetate [Figure 3a]. Patients presenting "cold" nodules in earlier scintigraphic examinations underwent a thyroid scintigraphy with 500 – 557 MBq ^{99m}Tc-MIBI [Figure 4a] and additionally fine needle aspiration biopsy (FNAB), which has proven to be a safe method of excluding malignancy, especially when combined [30]. In patients with both "cold" and "indifferent" thyroid nodules both of the mentioned scintigraphy modalities were performed. Acquisition was conducted 20 minutes after administration of ^{99m}Tc-pertechnetate or, in case of ^{99m}Tc-MIBI scans, 10 and 60 minutes after, respectively. For this purpose a scintillation camera (Nucline TH/22, Mediso Medical Imaging Systems, Budapest, Hungary) equipped with a low energy collimator was used.

Procedure

The intervention was performed during local anesthesia and under aseptic conditions. If realizable an access via transisthmic approach was chosen, hereby permitting the display of the microwave probe in its entire length and its current location in reference to vascular or nerval structures via ultrasound imaging. If transisthmic approach was not accomplishable, a craniocaudal access path was chosen. After correct identification of vagus and recurrent laryngeal nerve the probe was placed in the nodule under sonographical guidance [Figure 5]. If nodules were found to be mainly cystic, fluid contents were aspirated before ablation in order to minimize the pre-procedural ablation volume and to exclude possible heat-sink effects resulting from cystic fluids [31].

During ablation the operating physician had to pay attention to the occurrence of so-called "microbubbles" and hypoechogenic areas, sonographical signs indicating the direct effects of heat development in the ablation area [32]. If required, the probe was repositioned and other parts of the nodule were treated equally.

Twenty-four hours after intervention each patient received a second thyroid scan using the same tracer as before ablation [Figures 3b, 4b] and ultrasound control was conducted to exclude focal complications. Additionally, laboratory blood tests were performed again to ensure no thyroid dysfunction had occurred. Three months after treatment patients underwent another ultrasound examination of the ablation site in order to evaluate post-ablative nodular volume reduction. No patients were re-treated.

Statistical analysis

Statistical results were obtained using "BIAS.", version 10.04 (epsilon Verlag, 1989 – 2013). Values were tested for normality of distribution and t-tests as well as Wilcoxon-matched-pairs-test were performed to evaluate nodular volume and functional imaging findings. Pearson's r was calculated in order to find a possible correlation between nodular volume reduction and pre-ablative nodular volume and ^{99m}Tc-uptake, respectively. Additionally, Spearman's rank correlation coefficient ρ was determined to correlate nodular volume reduction with nodules' vascularity, stiffness and composition, respectively. All data are reported as mean ± standard deviation.

Results

MWA

Mean pre-ablative nodular volume was 35.2 ± 45.4 ml, post-ablative volume was 21.9 ± 34.7 ml. This equals a mean absolute volume reduction of 13.3 ± 14.7 ml and a relative reduction of 50.9 ± 19.8 % ($p < 0.001$). Duplex ultrasound examination showed 1 nodule with no relevant blood flow, 12 with minimal and 13 nodules with marked blood flow. Ultrasound elastography imaged 2 nodule of soft, 14 of rather soft, 7 of rather hard and 3 of hard consistency. Furthermore, regarding nodular composition, 3 nodules presented as rather cystic, 12 as equally cystic and solid, 4 as rather solid and 7 as solid. Mean pre-ablative nodular ^{99m}Tc-uptake was 18.3 ± 10.0 % (^{99m}Tc-MIBI) and 16.7 ± 13.0 % (^{99m}Tc-pertechnetate).

Correlating relative volume reduction with nodular baseline volume and ^{99m}Tc-uptake, Pearson's r was found to be - 0.53 ($p = 0.005$) for baseline volume and - 0.40 ($p = 0.088$) and 0.32 ($p = 0.532$) for nodules imaged with ^{99m}Tc-MIBI and ^{99m}Tc-pertechnetate, respectively. One nodule, rather forming a conglomerate of 4 single nodules imaged partly with ^{99m}Tc-MIBI and ^{99m}Tc-pertechnetate, could not be separately distinguished by sonographic means and therefore was not taken into consideration in terms of correlating volume reduction and ^{99m}Tc-uptake. Correlating nodular volume reduction with the other pre-ablative findings, the calculation of Spearman's rank correlation coefficient showed the following results: $\rho = 0.21$ ($p = 0.293$) for vascularity, as displayed with DU, $\rho = - 0.07$ ($p = 0.718$) for stiffness, as found by UE, and $\rho = - 0.33$ ($p = 0.097$) for nodular composition.

Complications

Slight pain and a feeling of pressure during the ablation were reported by all patients, yet the pain could be easily decreased by just reducing the temperature. No further treatment was required; the pain rapidly vanished after ablation. All patients developed first-degree skin burns at the puncture site which did not require any specific treatment either and disappeared within days. One patient developed a cervical hematoma, yet an active hemorrhage could be ruled out by color duplex sonography. Three patients reported dragging pain towards the mandibular angle and ear during the treatment. No swallowing difficulties, vagal reactions or voice changes were observed.

Serious complications like secondary hemorrhage, infections, nodule ruptures, deep hematomas or injuries of nerval structures did not occur. In one patient a slight hyperthyreosis with a T4 level of 207 nmol/l (normal range: 55 – 170 nmol/l) without elevated T3 was discovered after ablation, yet the thyroid function normalized within one week without occurrence of any further complications. Another patient with known diabetes mellitus presented a slightly increased blood glucose level of 118 mg/dl. All other patients presented a proper thyroid function after ablation. In the post-procedural observation period one patient who had received radioiodine therapy in addition to MWA developed Graves' disease. Although self-limiting immunogenic hyperthyreosis is known to rarely occur in patients after radioiodine therapy it is not possible to definitely exclude MWA as a potential (co-) factor.

Discussion

The goal of this study was to explore whether there are sufficient ultrasound-based alternatives to ^{99m}Tc-scintigraphy in the prognostic evaluation of thyroid nodules treated with MWA. For this purpose nodular volume reduction at a 3-month follow-up, which was averagely 50.9 ± 19.8 % ($p < 0.001$), was correlated with pre-ablative diagnostic parameters.

Considering the mean pre-ablative nodular volume, an appreciable correlation could be found, with r = - 0.53 (p = 0.005), which strongly indicates a better effect of MWA on smaller nodules [Figure 6a]. Yue et al. [21] propose that the final clinical outcome considerably depends on nodular baseline volume, with a significant inverse correlation between baseline volume and volume reduction ratio. The results of this study support this thesis, even presenting a stronger correlation, as Yue et al. found that the correlation was r = - 0.24, which might actually be considered as rather weak. A significant prognostic value of the baseline nodular volume might be deduced from these findings; hence smaller nodules might be expected to respond to the treatment better as bigger ones. This circumstance might be based on the overall difficulty of delivering an adequate dose of microwave energy to the entire node if the microwave probe needs to be relocated due to the nodule's size [33]. In this case overlapping microwave fields are thinkable as well as the deficient covering of marginal areas by MWA, both leading to a less desirable outcome than in nodules requiring only a single shot ablation.

Pre-ablative sonographic examinations also included the rating of nodular vascularity by duplex ultrasound and stiffness of nodular tissue by qualitative ultrasound elastography. No strong correlation of nodular volume reduction and nodular blood flow could be discovered, with Spearman's ρ = 0.21 (p = 0.293) tending to indicate better results in well perfused nodules. While the diagnostic advantages of DU are hardly deniable in various medical fields, one may attribute a rather negligible role to DU in terms of this particular context. Apart from the lacking diagnostic value there was no apparent therapeutic consequence for the treatment with MWA coming from DU findings, as Happel et al. [24] pointed out that DU cannot replace scintigraphy in the diagnosis of functional thyroid autonomy, while Algin et al. [34] interpreted DU as not useful for distinguishing malignant from benign thyroid nodules. Nodular stiffness, as detected by UE, showed a correlation of ρ = - 0.07 (p = 0.718), hence not indicating a prognostic advantage of soft nodules over nodules of rather hard structure or vice versa. These findings do not support UE as a potential replacement for scintigraphy in the detection or evaluation of thyroid nodules. Etzel et al. [35] concluded that UE might deliver additional information about nodular consistency compared to manual palpation, yet that it could not replace scintigraphy in diagnostic terms. As for DU, there were no therapeutic consequences for MWA coming from UE findings, for the important question of malignancy cannot be clarified by UE alone [36]. After all, neither DU or UE seem to deliver reliable predications in the field of thermal ablation of thyroid nodules [37]. This, as well as the lacking therapeutic consequence of DU and UE findings, respectively, does not allow assessing these sonographic modalities as useful tools in the field of MWA of thyroid nodules.

As another aspect of ultrasound-based diagnostic nodules were classified by their composition in terms of the relation of cystic and solid portion. Compared to the results of DU and UE, there was a better, yet still mediocre, correlation with nodular volume reduction detectable, with ρ = - 0.33 (p = 0.097) hinting at cystic nodules to have a better prognosis than solid ones. Feng et al. [20] and Yue et al. [21] both found a significant better outcome of MWA treated nodules, which were of predominantly cystic composition compared to mixed or solid nodules. In this context, the role of a more homogenous conduction of heat and removal of cystic components were discussed as possible explanations for the more effective nodular volume reduction. Lim et al.[38] declared a similar correlation in the radiofrequency ablation of thyroid nodules at a 4-year follow-up. Bearing in mind, that there were no nodules of mainly cystic composition in this collective and that the overall distribution of different compositional types was fairly homogenous, with the majority of treated nodules being of mixed solid-cystic composition, nodular composition cannot explicitly negated as a prognostic factor for the morphological outcome. Yet, it remains unclear whether the assumed better response to MWA comes only from the pre-ablative aspiration of the cystic portion, resulting in a more or less striking loss of volume itself, or if there are further factors, which may lead to an improvement of prognosis.

Correlating relative volume reduction with pre-ablative ^{99m}Tc-uptake, Pearson's *r* was found to be - 0.40 (p = 0.088) [Figure 6b] and 0.32 (p = 0.532) [Figure 6c] for nodules imaged with ^{99m}Tc-MIBI and ^{99m}Tc-pertechnetate, respectively. Korkusuz et al. [23], using a center specific functional imaging score (CSFIS), found a significant decrease of nodular ^{99m}Tc-uptake 24 hours after ablation for both scintigraphic modalities, suggesting a statistical correlation of ^{99m}Tc-uptake reduction and nodular volume reduction. Viewing at the results of this study, single pre-ablative scintigraphy with ^{99m}Tc-MIBI presented a good and significant correlation with nodular volume reduction at a 3-month follow-up. Here, the negative correlation (r = - 0.40) indicates a better prognosis for nodules with rather little ^{99m}Tc-MIBI-uptake. This circumstance seems to be not transferable to ^{99m}Tc-pertechnetate-scintigraphy (r = 0.32), with the positive correlation indicating a contrary interpretation compared to the findings of ^{99m}Tc-MIBI-scintigraphy, thus nodules with high ^{99m}Tc-pertechnetate-uptake potentially showing rather appreciable results. The reason for this circumstance is not apparent and requires further analyses, with higher case numbers possibly allowing a more comprehensive interpretation.

The comparatively small number of examined cases surely poses a major limitation to this retrospective study, as well as its retrospective nature itself, with higher case numbers maybe allowing a more reliable statement about the prognostic value of the different diagnostic tools in the context of microwave ablation of thyroid nodules. Future endeavors should imply prospective randomized studies to define the role of MWA in the field of minimal-invasive treatment of thyroid nodules.

Conclusions

MWA appears to be a sufficient minimal-invasive approach to benign nodules of the thyroid, with a mean nodular volume reduction of 50.9 ± 19.8 % at a 3-month follow-up. Neither ultrasound elastography (ρ = - 0.07) or duplex ultrasound (ρ = 0.21) seem to bear the potential of delivering a reliable statement about the final morphological and thereby clinical outcome. Although the correlation of nodular composition and nodular volume reduction (ρ = - 0.33) could not be explicitly confirmed, based on the collective of nodules examined, it might serve as a prognostic factor with a negative correlation. Nodular baseline volume occurred to be of appreciable prognostic value (r = - 0.53), with smaller nodules presenting a more favorable outcome than bigger ones. Single pre-ablative ^{99m}Tc-scintigraphy (r = - 0.40 for ^{99m}Tc-MIBI; r = 0.32 for ^{99m}Tc-pertechnetate) might potentially obviate a second post-ablative scan, considering the prognostic value. Yet, the results appear somewhat dubious, since scintigraphy with ^{99m}Tc-MIBI suggests a negative correlation in contrast to the positive correlation of nodular volume reduction and ^{99m}Tc-pertechnetate-scintigraphy. After all, ^{99m}Tc-scintigraphy still remains an important diagnostic tool in the field of the treatment of thyroid nodules, for example with MWA, that may be sufficiently complemented by sonographic tools.

References

1. Hampel R, Bennöhr G, Gordalla A, Below H. Urinary iodide excretion in adults in germany 2005 meets WHO target. Exp Clin Endocrinol Diabetes. 2010; 118: 254–257
2. Vanderpump MPJ. The epidemiology of thyroid diseases. Br Med Bull. 2011; 99: 39–51
3. Guth S, Theune U, Aberle J, Galach A, et al. Very high prevalence of thyroid nodules detected by high frequency (13 MHz) ultrasound examination. Eur J Clin Invest. 2009; 39: 699–706
4. Ross DS. Non-palpable Thyroid Nodules – Managing an Epidemic. J Clin Endocrinol Metab. 2002; 87: 1938–1940
5. European Age-Standardized rates calculated by the Cancer Research UK Statistical Information Team, 2011, using data from GLOBOCAN 2008 v1.2, IARC, version 1.2. Accessed June 3, 2014.
6. Gharib H, Hegedüs L, Pacella CM, Baek JH, et al. Nonsurgical, image-guided, minimally invasive therapy for thyroid nodules. J Clin Endocrinol Metab. 2013; 98: 3949–3957
7. Dong Gyu Na, Jeong Hyun Lee, So Lyung Jung, Ji-hoon Kim, et al. Radiofrequency Ablation of Benign Thyroid Nodules and Recurrent Thyroid Cancers: Consensus Statement and Recommendations. Korean J Radiol. 2012; 13: 117–125
8. Spiezia S, Garberoglio R, Milone F, Ramundo V, et al. Thyroid Nodules and Related Symptoms Are Stably Controlled Two Years After Radiofrequency Thermal Ablation. Thyroid. 2009; 19: 219–225
9. Kim YJ, Baek JH, Ha EJ, Lim HK, et al. Cystic versus predominantly cystic thyroid nodules: efficacy of ethanol ablation and analysis of related factors. Eur Radiol. 2012; 22: 1573–1578
10. Valcavi R, Riganti F, Bertani A, Formisano D, et al. Percutaneous laser ablation of cold benign thyroid nodules: a 3-year follow-up study in 122 patients. Thyroid. 2012; 20: 1253–1261
11. Døssing H, Bennedbæk FN, Hegedüs L. Interstitial laser photocoagulation (ILP) of benign cystic thyroid nodules-a prospective randomized trial. J Clin Endocrinol Metab. 2013; 98: 1213–1217
12. Korkusuz H, Fehre N, Sennert M, Happel C, et al. Early assessment of high-intensity focused ultrasound treatment of benign thyroid nodules by scintigraphic means. J Ther Ultrasound. 2014; 2: 18
13. Korkusuz Y, Gröner D, Raczynski N, Relin O. Thermal ablation of thyroid nodules: are radiofrequency ablation, microwave ablation and high intensity focused ultrasound equally safe and effective methods? Eur Radiol. 2018; 28: 929-935
14. Ratanaprasatporn L, Charpentier KP, Resnick M, Lu S, et al. Intra-operative microwave ablation of liver malignancies with tumour permittivity feedback control: a prospective ablate and resect study. HPB (Oxford). 2013; 15: 997–1001

15. Vorländer C, David Kohlhase K, Korkusuz Y et al. Comparison between microwave ablation and bipolar radiofrequency ablation in benign thyroid nodules: differences in energy transmission, duration of application and applied shots. Int J Hyperthermia. 2018; 35: 216-225.

16. Teng D, Sui G, Liu C, Wang Y, et al. Long-term efficacy of ultrasound-guided low power microwave ablation for the treatment of primary papillary thyroid microcarcinoma: a 3-year follow-up study. J Cancer Res Clin Oncol. 2018; 144: 771-779

17. Wenjun Wu, Xiaohua Gong, Qi Zhou, Xiong Chen, et al. Ultrasound-Guided Percutaneous Microwave Ablation for Solid Benign Thyroid Nodules: Comparison of MWA versus Control Group. Int J Endocrinol. 2017; 9724090

18. Wu W, Gong X, Zhou Q et al. US-guided percutaneous microwave ablation for the treatment of benign thyroid nodules. Endocr J. 2017; 64: 1079-1085.

19. Liu YJ, Qian LX, Liu D, Zhao JF. Ultrasound-guided microwave ablation in the treatment of benign thyroid nodules in 435 patients. Exp Biol Med (Maywood). 2017; 242: 1515-1523.

20. Feng B, Liang P, Cheng Z, Yu X, et al. Ultrasound-guided percutaneous microwave ablation of benign thyroid nodules: experimental and clinical studies. Eur J Endocrinol. 2012; 166: 1031–1037

21. Yue W, Wang S, Wang B, Xu Q, et al. Ultrasound guided percutaneous microwave ablation of benign thyroid nodules: Safety and imaging follow-up in 222 patients. Eur J Radiol. 2012; 82: 11–16

22. Korkusuz H, Happel C, Grünwald F. Ultrasound guided percutaneous microwave ablation of hypofunctional thyroid nodules: evaluation by scintigraphic 99mTc-MIBI imaging. Nuklearmedizin. 2013; 52: N68

23. Korkusuz H, Happel C, Heck K, Ackermann H, et al. Percutaneous Thermal Microwave Ablation of Thyroid Nodules: Preparation, Feasibility and Efficiency. Nuklearmedizin. 2014; 53: 123–130

24. Happel C, Truong PN, Bockisch B, Zaplatnikov K, et al. Colour-coded duplex-sonography versus scintigraphy. Can scintigraphy be replaced by sonography for diagnosis of functional thyroid autonomy? Nuklearmedizin. 2013; 52: 186–191

25. Aslan A, Sancak S, Aslan M, Ayaz E, et al. DIAGNOSTIC VALUE OF DUPLEX DOPPLER ULTRASOUND PARAMETERS IN PAPILLARY THYROID CARCINOMA. Acta Endocrinol (Buchar). 2018; 14: 43-48

26. Dewall RJ. Ultrasound elastography: principles, techniques, and clinical applications. Crit Rev Biomed Eng 2013; 41:1–19

27. Andrioli M, Persani L. Elastographic techniques of thyroid gland: current status. Endocrine. 2014; 46: 455–461

28. Paredes-Manjarrez C, Magdalena-Buitrago A, Meza-Hernández G, Camacho-Zarco E, et al. Elastography in the evaluation of thyroid nodules Rev Med Inst Mex Seguro Soc. 2017; 55: S402-S407

29. Ha EJ, Baek JH, Lee JH, Kim JK, et al. Clinical Significance of vagus nerve variation in radiofrequency ablation of thyroid nodules. Eur Radiol. 2011; 21: 2151–2157

30. Leidig-Bruckner G, Cichorowski G, Sattler P, Bruckner T, et al. Evaluation of thyroid nodules-combined use of 99mTc-methylisobutylnitrile scintigraphy and aspiration cytology to assess risk of malignancy and stratify patients for surgical or nonsurgical therapy-a restrospective cohort study. Clin Endocrinol. 2012; 76: 749–758.

31. Kim YS, Rhim H, Tae K, Park DW, et al. Radiofrequency Ablation of Benign Cold Thyroid Nodules: Initial Clinical Experience. Thyroid. 2006; 16: 361–366.

32. Wood MA, Shaffer KM, Ellenbogen AL, Ownby ED. Microbubbles during radiofrequency catheter ablation: composition and formation. Heart rhythm. 2005; 2: 397–403

33. Korkusuz Y, Kohlhase K, Gröner D, Erbelding C, et al. Microwave Ablation of Symptomatic Benign Thyroid Nodules: Energy Requirement per ml Volume Reduction. Rofo. 2016; 188: 1054-1060

34. Oktay Algin, Efnan Algin, Gokhan Gokalp, Gokhan Ocakoğlu, et al. Role of duplex power Doppler ultrasound in differentiation between malignant and benign thyroid nodules. Korean J Radiol. 2010; 11: 594–602

35. Etzel M, Happel C, von Müller F, Ackermann H, et al. Palpation and elastography of thyroid nodules in comparison. Nuklearmedizin. 2013; 52: 97–100

36. Unlütürk U, Erdoğan MF, Demir O, Güllü S, et al. Ultrasound elastography is not superior to grayscale ultrasound in predicting malignancy in thyroid nodules. Thyroid. 2012; 22: 1031–1038

37. Andrioli M, Valcavi R. The peculiar ultrasonographic and elastographic features of thyroid nodules after treatment with laser or radiofrequency: similarities and differences. Endocrine. 2014; 47: 967–968

38. Lim HK, Lee JH, Ha EJ, Sung JY, et al. Radiofrequency ablation of benign non-functioning thyroid nodules: 4-year follow-up results for 111 patients. Eur Radiol. 2013; 23: 1044–1049