Research Article

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Abstract

Aim: Aim of this study was to document the sustainable effect of bipolar Radiofrequency Ablation (bRFA) in the therapy of parathyroid adenoma. For this purpose, Calcium- and Parathyroid Hormone (PTH) serum levels as well as node volumes were evaluated in a three-month follow-up investigation.

Material and Methods: Seven patients with primary parathyroid adenoma were treated using bRFA in one single session. Serum levels for Calcium and PTH were determined prior to and three months following the intervention. Volume reduction was established using sonography, prior to and three months following bRFA.

Results: It was found that bRFA led to a significant (p<0.05) reduction of Calcium serum levels (median 0.2 mmol/l). PTH levels also showed a significant (p<0.05) reduction (median 87 ng/l). Furthermore, bRFA led to a significant (p<0.05) reduction of the node volumes (delta v), in median 0.56ml. In the three-month follow-up investigation, there were no signs of any complications or side effects such as infections, persisting pain, bleedings, nerve lesions or immunogenic stimulation, nor did any patient report any of these.

Conclusion: The utilization of bRFA is an effective, safe, precise, controllable and appropriate thermoablative technique for the treatment of parathyroid adenoma. Its therapeutic success was verified in a three-month follow-up investigation.

Introduction

In the western world, Primary Hyperparathyroidism (pHPT) is a relatively common disorder diagnosed in 2.1% of post-menopausal women and 0.7% of the general population [1,2]. Pathogenetically, pHPT is the result of a lack of feedback of ionized blood calcium on the production of parathyroid hormone. Excess PTH initiates the mobilization of calcium from the bones as well as its absorption from the intestine, leading to hypercalcemia and increased PTH levels. In most cases (>90%), pHPT occurs sporadically and is caused by a solitary adenoma of the parathyroid gland (85-90%), only rarely by parathyroid carcinoma (<1%) [3].

Current reference standard in the therapy of parathyroid adenoma is the surgical parathyroidectomy. In individual cases, a temporary therapy with calcimimetic medications is feasible until surgery can be carried out [4]. This procedure is especially beneficial for cases when patients are temporarily in a physical condition where general anesthesia would be contraindicated or the strain of the surgery itself might be too high. A parathyroidectomy...

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is typically a surgery that last for several hours under general anesthesia. Especially the patients’ suitability for general anesthesia and the associated risks, respectively, can be problematic for some, especially elderly and morbid patients [5].

Over the last years, some minimally invasive methods have gained attention as viable alternatives for the treatment of parathyroid adenoma. Worth mentioning in this context are especially various thermoablative therapeutic options, such as High Intensity Focused Ultrasound (HIFU), Microwave Ablation (MWA), Laser-Induced Thermotherapy (LITT), Monopolar RFA (mRFA), Laserablation (LA) and Bipolar RFA (bRFA) [6-10]. These treatment methods can be regarded as feasible alternatives to the classical parathyroidectomy. In some countries (China, USA, Italy) some of these new, minimally invasive treatment methods have already been incorporated in the treatment guidelines [11-13].

The history of radiofrequency ablation (RFA) as a thermal procedure in medicine is characterized by several developmental stages. Its fields of application are versatile and applicable to various organs [14-21].

A further development of mRFA, namely bRFA, has already been used in the treatment of benign thyroid nodes. Several studies with relatively high case numbers and low complication rates (merely 3.3%) have documented its therapeutic success, thus establishing it as a feasible treatment alternative [22, 23].

Regarding the treatment of parathyroid adenoma, the establishment of RFA as a therapeutic option may still rank behind that of the treatment of benign thyroid nodes in terms of case numbers as well as documented long-term success. However, there are very promising prospects. Some studies have already described both mRFA as well as bRFA as feasible treatment methods for parathyroid adenoma [20-23]. Furthermore, concerning the treatment of thyroid nodes, evidence has been provided that bRFA is superior over mRFA regarding volume reduction of the nodes as well as tolerability of the therapy implementation [24].

The usage of bRFA has some important advantages over that of mRFA, especially with regards to the safety of the procedure. The main advantage of bRFA over mRFA arises from the fact that in bRFA, the energy flow only takes place within the adenoma [22]. Thus, the energy can be ideally distributed within the desired tissue and an unnecessary electrical flow towards the neutral electrode, as taking place in mRFA, can be avoided [25,26] as it might result in a higher risk for interferences with cardiac pacemakers and skin burns because of the electrical flow through most of the thorax [27,28]. Bipolar systems are capable of avoiding these side effects, because anode and cathode arecombined within the same probe [25].

It shall be demonstrated that bRFA is a good, precise and safe therapeutic option for the treatment of parathyroid adenoma by investigating its success in a three-month follow-up investigation, in order to further establish bRFA as a feasible treatment method of parathyroid adenoma.

Material and Methods

Study population

A total of seven patients (five female, two male) aged between 47 and 74 years (median age: 56 years) took part in the study, all of which were diagnosed with a parathyroid adenoma. All patients rejected, for various reasons, surgical treatment. All patients consented to the collection and analysis of data for the purpose of this study. Exclusion criteria were evidence of malignancy and patients under the age of eighteen.

Methods

Measurement parameters of this study were serum levels of Calcium and PTH and sonographic parameters (volumes of the parathyroid adenoma). Additionally, critical observation was used in order to detect possible complications and side effects of the treatment.

Radiofrequency system

The bRFA device used in this study was made by Olympus Hamburg (Germany), utilizing a generator (POWER system), with an output of 9-40 W (max 250 W) at a frequency of 470 ± 10 kHz. The utilized probes were either cooled 15 gauge electrodes (active tip 20-40mm; CelonProSurge) or uncooled 18 gauge electrodes (active tip 9-15mm; CelonProSurge). If desired, patients received a 0.9% NaCl infusion with 2mg Metamizole (Novaminsulfon-ratiopharm, Ulm, Germany). Following the reconfirmation of the localization of the adenoma, a local anesthetic (Mepivacainhydrochloride 1%; AstraZeneca,Wedel, Germany) was injected, ultrasound-guided, followed by a small skin incision through which the probe was then inserted. The parathyroid glands were at all times (pre-ablative, post-ablative and in the three-month follow-up) examined using the same ultrasonic device (LogIQ5, GE Healthcare, UK).

Measurement parameters

Calcium and PTH serum levels were determined prior to and three months flowing bRFA. Sonographic measurement of node volumes was carried out directly before the intervention and three months following the treatment. Sonography was performed by the same physician at all times, using the same ultrasonic device. The occurrence of side effects and complications was also documented during the three months following bRFA. Measurement intervals
were chosen in accordance with similar follow-up studies [7,22,29].

Anticoagulation

Two of the seven patients stated the use of anticoagulants in their medical history (1x Marcumar, 1x ASS 100). The management of these during this study was in accordance with current guidelines: the patient under Marcumar therapy was temporarily bridged with heparin, ASS was discontinued for seven days prior to the bRFA treatment [30]. Irrespective of their anamnesis, coagulation parameters (blood count, INR and aPTT) were determined for all patients.

Ethical principles

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all patients for being included in the study.

Statistical analysis

Statistical significance was assessed using the biometric-statistics analysis software “BIAS” (software version 10.04, epsilon Verlag, 1989-2013 Hochheim, Darmstadt, Germany), utilising the Wilcoxon matched pairs test (non-parametric test). P-values below 0.05 were rated as statistically significant.

Results

The three-month follow-up examination showed a significant (p=0.03125) median decrease of the calcium serum levels of 0.2 mmol/l (range: 0.0-0.45 mmol/l) in comparison to the ones prior to bRFA. This corresponds to a median reduction of 7%. The median calcium serum level prior to bRFA was 2.76 mmol/l (range: 2.3-3.23 mmol/l). Three months following bRFA, median calcium serum level was 2.67 mmol/l (range: 2.2-2.9 mmol/l).

For the same time range, PTH serum values also showed a significant (p=0.015625) median decrease of 87 ng/l (range: 1-310 ng/l). The median reduction was 41%. The median PTH serum level prior to bRFA was 199 ng/l (range: 75-976 ng/l). Three months following bRFA, median PTH levels had fallen to 68 ng/l (range: 44-889 ng/l).

In the three-month follow-up, bRFA also lead to a significant (p=0.015625) reduction of the node volumes (delta v), in median 0.56ml (reduction range: 0.05-1.09ml), which represents a decrease of 55,3%. The median start volume was 0.73ml (range:0.66-1.97ml), three months following bRFA, the median volume was 0.48ml (range: 0.1-0.88ml).

None of the patients were found to have or report any complications such as infections, persisting pain, bleedings, nerve lesions or immunogenic stimulation in the three months following bRFA and all patients were able to receive outpatient treatment.

Discussion

The aim of this study was to determine whether bRFA, as a minimally invasive therapeutic method for the treatment of parathyroid adenoma, can provide successful results in a three-month follow-up setting. For this purpose, Ca and PTH serum levels as well as node volumes were documented and analyzed.

The comparison of pre- and three-month post-ablative Ca and PTH serum levels lead to the conclusion that bRFA can be regarded as a successful therapeutic option for the treatment of parathyroid adenoma. For both parameters, a significant reduction following bRFA was documented, proving its success in the treatment of parathyroid adenoma.

Similarly, the statistically significant volume reduction also underlines the successful therapy of parathyroid adenoma using bRFA, showing a median reduction of 41% three months following the intervention. It is likely that the volume reduction of the adenoma is at least partly responsible for the Ca and PTH reduction. Furthermore, it reduces the risks associated with displacing adenoma growth, thus protecting sensitive structures such as vessels and nerves.

The three-month follow-up examination showed that Ca serum levels in two of our seven patients had fallen to levels within the standard value range (2.2-2.6 mmol/l). For the PTH serum levels, all patients showed a decrease, the levels of four patients had also fallen to ones
within the standard value range (12-72 ng/l). Even though not all parameters had normalized completely, there appears to be a clear tendency towards a considerable reduction.

The uncomplicated implementation of bRFA as well as the lack of complications or side effects in any of the follow-up examinations of our patients, stress the safety of this therapeutic approach. Thus, bRFA can be regarded as a feasible method for high-risk patients, e.g. where general anesthesia is contraindicated or declined for whatever reasons. Largely responsible for this development is the improvement of thermoablative procedures from mRFA to bRFA, since collateral damage is substantially reduced due to the more precisely controllable energy flow [22,25,26]. This might also be a possible starting point for further investigation concerning adenoma in close proximity to crucial anatomical structures such as vessels or nerves.

In order to decide on the best, possibly minimally invasive, treatment method for each and every patient, all individual aspects of the case have to be taken into account. Considering different, minimally invasive treatment options for parathyroid adenoma, it can be stated that HIFU, MWA and RFA have already been established as feasible alternatives. Regarding volume reduction, however, RFA appears to offer the most promising prospects [31]. Comparing only the feasibility, volume reduction and patient friendliness of the different RFA methods, bRFA can be regarded as superior to Mrfa [24]. Comparing bRFA an LA, therapy recommendations will even, at least partly, be based upon node volumes, since both procedures can generally be regarded as effective and safe alternatives [27,28]. However, research has shown that LA appears to be slightly superior to bRFA in the treatment of larger nodes and vice versa [10,32]. Additionally, specific procedures such as sono-elastography might complement the therapy decision, possibly providing more information about the node histology [33].

Thus, one of the forthcoming challenges will be, to carefully weigh the risks and benefits of the many available therapeutic options in order to come to an evidence-based recommendation in every individual case. Differentiated analyses and comparisons of the above-stated methods are mandatory.

Shortcomings of the present study are especially its small number of cases and the relatively short follow-up period of three months. Nevertheless, it has produced promising results in the treatment of parathyroid adenoma with bRFA concerning the feasibility [21] and success in the three-month follow-up examination of our patients. These results should, however, be investigated further in studies with higher case numbers as well as longer follow-up periods in order to really establish bRFA for this indication. The individual advantages or disadvantages of the different existing new methods are also at present quite vague and should be evaluated further and under long-term aspects in order to enable a scientifically based treatment recommendation.

**Conclusion**

From the pool of thermoablative treatment methods of parathyroid adenoma, bRFA represents a viable new therapy option. Its feasibility has been shown utilizing both laboratory (Calcium and PTH serum levels) as well as sonographic (node volumes) criteria. The treatment results were documented in a three-month follow-up

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**Figure 2: PTH reduction.** Median reduction of PTH serum level in three-month follow-up was 87ng/l. The asterisk indicated a significant reduction (p<0.05).

**Figure 3: Volume reduction.** Median reduction of node volume in three-month follow-up was 0.56ml. The asterisk indicated a significant reduction (p<0.05).
setting, proving the successful treatment of parathyroid adenoma by means of bRFA. All three objective parameters of this study showed a statistically significant reduction. Furthermore, none of the patients in this present study reported any complications or side effects at any time.

Thus, bRFA may be considered a viable option for the treatment of parathyroid adenoma, especially for high-risk patients where general anesthesia is contraindicated.

References


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