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PhD THESIS

**THE ROLE OF ELASTOGRAPHY IN THE LOCALISATION
OF PARATHYROID DISEASE**

A B S T R A C T

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**Timișoara
2022**

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GENERAL PART

Hyperparathyroidism is a disease of the parathyroid glands, characterized by high parathyroid hormone levels (PTH). The disorder can be categorized as primary, secondary, or tertiary.

Primary hyperparathyroidism is defined as the most common cause of hypercalcemia, most commonly asymptomatic or with complications such as nephrolithiasis, bone disease, or neuromuscular illness.

Secondary hyperparathyroidism (sHPT) is due to chronic hypocalcemia caused by multiple disruptions in the calcium metabolism, such as chronic kidney disease or digestive causes: vitamin D deficiency, gastrointestinal malabsorption, Crohn's disease, celiac disease, inpatient after bariatric surgery, hyperphosphatemia, or drug-induced.

Secondary hyperparathyroidism (sHPT) is the most prevailing complication of chronic kidney disease (CKD).

The clinical diagnosis of PTHP is mainly based on biochemical screening, as patients are most often asymptomatic. Given that approximately 90% of the cases of PTHP are determined by a single parathyroid adenoma [68], cervical ultrasonography is considered the first line morphologic tool as it is non-invasive, repetitive, and cost-efficient.

Parathyroidectomy is considered the definitive treatment for the symptomatic disease; preoperative radiologic imaging identification and localization of the hyperfunctioning parathyroid gland has better outcomes turning to elective surgical excision. Scintigraphy and ultrasonography are the imaging modalities most often used for preoperative localization.

Elastographic techniques, especially shear wave elastography, can be a valuable tool in diagnosing parathyroid adenomas. Elastography does not offer a decisive diagnosis of parathyroid lesions, but as an additional tool, it can add significant value to the ultrasound examination. When considering a therapeutic method, the final decision should consider conventional ultrasound and elastography.

SPECIFIC PART

1. GENERAL OBJECTIVES

The present thesis is composed of multiple studies that are gradually and consecutively meant to reach the final aim: ***to assess the role of elastography in the localizing of the parathyroid adenoma or hyperplasia and its role in preoperative diagnosis.***

The five consecutive studies have the following objectives:

1. Firstly, to establish the clinical settings of ultrasonography and elastography in the field of hyperparathyroidism and to identify the targeted parathyroid dysfunctions

2. To evaluate the value of elastography in the presurgical localization of secondary renal hyperparathyroidism and primary hyperparathyroidism.
3. To identify the other misleading factors in the elastographic evaluation of hyperparathyroidism.
4. To identify which elastographic method is more reliable and valid in clinical practice.
5. To evaluate the differences between the types of hyperparathyroidism and establish a cut-off value in the elastographic evaluation for each one.
6. Furthermore, to try to determine an algorithm in the evaluation of hyperparathyroidism.

2. STUDY I: HYPERPARATHYROIDISM ASSOCIATED WITH CHRONIC KIDNEY DISEASE – AN OVERVIEWED CONDITION

2.1. AIMS OF THE RESEARCH

This study aimed to identify by using 2D shear wave elastography the characteristics of hyperplastic parathyroid glands in patients with chronic kidney disease and determine the technique can add information in order to improve the preoperative localization of these glands by determining threshold values suggestive for parathyroid tissues and comparing them to the surrounding tissues.

2.2. MATERIALS AND METHODS

This first study was a prospective study conducted from May 2019 to July 2019 (3 months) in the Dialysis Medical Center B Braun Avitum Timisoara, Romania, one of the most important dialysis centers in Timisoara. The study included 120 patients over 18 years of age presenting stage five chronic kidney disease undergoing hemodialysis therapy three times per week. Of the 120 patients examined from the dialysis center, 59 patients presented parathyroid disease by clinical, biochemical assessment and scintigraphy scan or MRI scan.

Ultrasound cervical evaluation was conducted firstly in conventional B- mode in all cases on the Aixplorer Mach 30 (SuperSonic Imagine, France) using a high-resolution linear transducer of 15-4 MHz, with the patient maintaining a supine position with normal breathing, applying an adequate amount of ultrasound gel to the transducer. The elastographic evaluation was performed right after the grey ultrasound and color Doppler exam, with the Aixplorer system (SuperSonic Imagine, France) using two high-resolution multifrequency linear transducers of 15-4 and 18-5 MHz.

2.3. RESULTS

A total number of 59 patients (male to female ratio 27/32) with a mean age of 56.95 +/- 10.92, mostly above 65 years old, with confirmed terminal chronic kidney disease, registered on ERSD (end-stage renal disease) program, on hemodialysis three times a week.

The most accurate quantitative measurement of the parathyroid EI found in our study was mean SWE. When comparing the mean elasticity index of the hyperplastic parathyroid glands (7.83 ± 2.94 kPa) with the thyroid parenchyma (13.780 ± 4.039 kPa) and surrounding muscle (15.788 ± 4.409 kPa), we found that the elasticity of parathyroid hyperplasia was significantly lower than both thyroid and muscle tissue. The cut-off value below 9.74 kPa had a sensitivity and specificity of 94%, respectively 90% of identifying parathyroid using thyroid

tissue as standard. A cut-off value below 9.98 kPa had a specificity and sensitivity of 90%, respectively 93% in identifying parathyroid tissue using muscle tissue as standard.

2.4. DISCUSSION

Elastography does not define a role in the international guidelines for secondary hyperparathyroidism. There is no "when and why" applied for the parathyroid ultrasound to manage secondary renal hyperparathyroidism. Because nodular thyroid disease is persistent in ERDS cases, the diagnosis, identification, and localization of hyperplastic parathyroid are mandatory.

Several literature studies have cited elastographic measurement on parathyroid hyperplasia. However, the measurements were not done in patients admitted to the dialysis centers or end-stage renal disease patients. The literature studies used several elastographic methods and determined multiple cut-off values for parathyroid hyperplasia: 1.46 m/s (shear wave elastography), 1.35 +/- 0.61 (Elasticity contrast index value determined with Elastoscanner Score Index). The studies included parathyroid hyperplasia determined by chronic kidney disease or vitamin D deficiency but did not include patients with end-stage renal disease on hemodialysis.

Multiple research studies were performed on ultrasound characteristics of hyperplastic parathyroid glands from secondary hyperparathyroidism from end-stage renal disease and concluded that parathyroid enlargement is present in more than one parathyroid gland, especially in patients following hemodialysis for more than three years. Also, they found that the parathyroid gland increase in size is directly proportional to the duration of dialysis. Other studies have not found any correlation between parathyroid hyperplasia and clinical or biochemical features in CKD patients.

2.5. CONCLUSIONS

This prospective study aimed to quantify the value of 2D Shear Wave Elastography in localizing and treating secondary hyperparathyroidism. Elastography can be an excellent qualitative and quantitative tool and can offer a better differentiation on tissue elasticity when diagnosing parathyroid hyperplasia. Using this elastographic technique, a cut-off value below 9.98 kPa has been established for the mean elasticity index for parathyroid tissue in patients with secondary hyperparathyroidism.

3. Study II: THE FREQUENCY OF THYROID PATHOLOGY IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND ITS INTERFERENCE IN THE PARATHYROID ELASTOGRAPHIC EVALUATION

3.1. AIMS OF THE RESEARCH

The purpose of this study was to evaluate the prevalence of thyroid morphological changes and hormonal dysfunction in hemodialysis patients and to investigate the possible associations between the total duration of the dialysis, age of the patient, sex, body mass index, or biochemical serum changes and the prevalence of thyroid disease.

3.2. MATERIALS AND METHODS

A cross-sectional observational single-center study was performed in the B Braun Dialysis Center Timisoara from May 2019- to June 2019. One hundred twenty-three patients were enrolled in the cohort. All patients presented end-stage renal disease and were registered on chronic hemodialysis treatment with various primary causes of renal failure, with a total mean duration of hemodialysis therapy of 5.6 ± 4.89 years old. The study cohort

comprised adult patients with clinical, biochemical, and imagistic confirmed end-stage renal disease on renal replacement therapy with previous or no history of thyroid disorders.

3.3. RESULTS

The total cohort included 122 patients, most with a normal thyroid function - euthyroid (72.4%); however, hypothyroidism was quite frequent (24.4%).

In concordance with the ultrasound results, 48.7% of patients had a normal thyroid ultrasound appearance, 51.2% had a nodular goiter, defined as a minimum of one thyroid nodule in any thyroid lobe, and 17.8% had autoimmune thyroiditis with positive antibodies.

Out of the subgroup with nodular thyroid goiter, seven patients underwent total thyroidectomy, and 3 had papillary thyroid carcinoma on histopathology report after surgery. Thirty-one patients had one thyroid nodule (49.2%), 16 patients had two thyroid nodules on cervical ultrasound evaluation (25.3%), and 16 patients, including those who underwent surgery, had a minimum of three thyroid nodules on cervical ultrasound evaluation (25.3%). The male/female ratio in the thyroid goiter group was 34 females (53.9%) and 29 male patients (46.03%), and in the autoimmune group, 12 females (54.4%) and ten males (45.4%).

Concerning the laboratory results, we have found that a high number of patients (46.34%) presented low levels of T3. Low T3 syndrome or "euthyroid sick syndrome" is a consequence of chronic nonthyroidal illness caused by uremia and protein malnutrition.

3.4. DISCUSSIONS

In this cross-sectional study, our primary endpoint was to determine the total prevalence of thyroid disease, nodular thyroid goiter, and autoimmune thyroid disease among patients with chronic kidney disease on hemodialysis. The study included all patients with ERSD on renal replacement therapy from one dialysis center with a slightly increased number of male subjects.

Various studies have proven a strong correlation between chronic kidney disease and thyroid disorders. CKD affects the metabolism of thyroid hormones and, by that means, influences thyroid morphology. Literature studies have shown that hemodialysis can cause thyroid abnormalities in both functions and morphology in patients with end-stage renal disease.

The total prevalence of thyroid disease was 61.8%, including nodular thyroid goiter and autoimmune thyroid disease. A total of 57 patients (46.34%) from the cohort presented low T3 syndrome, but only 40 patients showed thyroid disease. The absolute risk of developing thyroid disease is 3.41 x times higher for women with ERSD on hemodialysis than men. Our findings are similar to other results reported in the literature.

3.5. CONCLUSION

In conclusion, we established that thyroid disorders have a higher incidence among patients with end-stage renal disease on hemodialysis therapy. Female patients with chronic kidney disease and hemodialysis have a 3.41 times higher chance of developing thyroid disease. Interestingly, the body mass index presented a critical role, establishing that an increase of BMI with one unit or more increases the risk of developing thyroid disease by 1.083 times in patients with end-stage renal disease. The euthyroid sick syndrome was well represented in our cohort, accounting for 46.34%.

The prevalence of thyroid disease is estimated at 61.3% among the cohort of studied patients with end-stage renal disease on chronic hemodialysis.

Clinical surveillance, dietary counseling, and routine screening for thyroid disorders are essential to improving these patients' life quality and life expectancy.

4. Study III: THE VALUE OF ELASTOGRAPHY IN PRIMARY HYPERPARATHYROIDISM

4.1. AIMS OF THE RESEARCH

This prospective study aimed to determine the characteristics of parathyroid adenomas by shear wave elastography (SWE) and real-time elastography (RTE) and to evaluate further whether these techniques add information in the preoperative diagnosis of primary hyperparathyroidism.

4.2. MATERIALS AND METHODS

This prospective study evaluated 20 patients diagnosed with primary hyperparathyroidism from October 2018 to June 2019. Primary hyperparathyroidism was confirmed by biochemical evaluation, localization with Technetium Sestamibi scintigraphy (MIBI), and certified by pathology report after surgery (parathyroid adenoma excision).

The study cohort consisted of adult patients with confirmed primary hyperparathyroidism. After performing all measurements, we divided our study group into two subgroups to determine significant differences between patients with primary hyperparathyroidism and autoimmune thyroid disease. The first group included patients with parathyroid adenoma and autoimmune thyroid disease (11 patients) and the second group with parathyroid adenoma but without thyroid disease (9 patients).

Conventional B-mode parathyroid ultrasound was done in all cases on two different ultrasound systems, with Aixplorer SuperSonic System (SuperSonic Imagine, France) using a high-resolution linear transducer of 15-4 MHz and also with Hitachi Preirus Machine (Hitachi Medical Corporation, Tokyo, Japan) machine with a 6-13 MHz linear probe.

After performing conventional greyscale ultrasound, elastographic measurements using the shear wave elastography software were conducted with an Aixplorer system (SuperSonic Imagine, France) with a high-resolution multifrequency linear transducer 15-4 MHz. Real-time elastography (RTE) was performed after conventional ultrasound evaluation using Hitachi Preirus (Hitachi Medical Corporation, Tokyo, Japan) with a 6-13 MHz linear probe.

4.3. RESULTS

Twenty consecutive patients (male to female ratio 1/19) with mean age 57.3 ± 13.33 , primarily postmenopausal women with confirmed primary hyperparathyroidism, were examined. Each patient had a greyscale ultrasound and elastographic examination using shear wave and strain methods.

Parathyroid tissue stiffness was best determined by measuring mean SWE, providing valuable quantitative information in identifying and localizing the parathyroid adenomas. The mean (\pm SD) SWE value determined was 4.74 ± 2.745 kPa for all adenomas enrolled in the study.

Compared with thyroid parenchyma - mean SWE value 11.718 ± 4.206 kPa and surrounding muscle - mean SWE value 16.362 ± 3.829 kPa, the elasticity of parathyroid adenoma had a significantly lower value than both thyroid and muscle tissue. Considering that our study included a finite number of patients, we assessed using cross-tabulation on the receiver operating curves that the best mean SWE cut-off value for predicting parathyroid adenomas has been identified below 7 kPa.

We observed that 2D-SWE evaluation had better results in identifying parathyroid adenomas. The best diagnosis performance was documented using the mean SWE parathyroid/muscle (AUROC = 0.997, Sn = 100%, Sp = 95%), followed by the mean SWE

parathyroid/thyroid (AUROC = 0.950, Sn =95% Sp =90%) RTE retains lower diagnosis performance (AUROC= 0.646, Sn=75%, Sp=66.7%).

4.4. DISCUSSIONS

This prospective study compared elastographic features, both in shear wave elastography and strain elastography of clinically and biochemically confirmed parathyroid adenomas with surrounding thyroid tissue and sternocleidomastoid muscle. The study included only solitary parathyroid adenomas initially localized in conventional B-mode ultrasonography. Our study mainly included female patients, empowering that single parathyroid adenoma is typical among women above 55 years of age.

The role of elastographic evaluations in the parathyroid field is advancing, as several studies have demonstrated that elastography can be a helpful technique in differentiating parathyroid pathology. Literature studies conducted by Polat et al. examined parathyroid lesions using the SWE VTIQ method and compared the shear wave velocity (SWV) of parathyroid adenomas and/or parathyroid hyperplasia with benign cervical lymph nodes, establishing a cut-off value greater than 1.92 m/s for diagnosing parathyroid adenoma. Batur et al. measured parathyroid adenomas elasticity using ARFI imaging 2D-SWE and compared it to benign and malignant thyroid pathology. The final results demonstrated that the adenomas with a mean SWV value of 3.09 ± 0.75 m/s present a lower elasticity than benign thyroid nodules with a mean of 2.20 ± 0.39 m/s and a higher elasticity compared to malignant thyroid lesions with a mean of 3.59 ± 0.43 m/s.

4.5. CONCLUSION

To conclude, this prospective study aimed to quantify the value of strain elastography and 2D- shear wave elastography in identifying and localizing parathyroid adenomas. Strain elastography has proven to be a useful qualitative tool using a color mapping. 2D-SWE elastography can better differentiate tissue elasticity if diagnosing parathyroid adenomas. Using this elastographic technique, a cut-off value of less than 7 kPa for the mean elasticity index suggests parathyroid adenoma.

5. Study IV: PRIMARY VERSUS SECONDARY HYPERPARATHYROIDISM – ELASTOGRAPHIC DIFFERENCES

5.1. BACKGROUND AND AIMS OF THE RESEARCH

This prospective study aims to determine the characteristics of parathyroid adenomas and hyperplastic parathyroid glands from patients with end-stage renal disease on hemodialysis by using shear wave elastography to determine the elastographic differences and identify a cut-off value for the parathyroid tissue, adding value to the presurgical identification and differential diagnosis.

5.2. MATERIALS AND METHODS

This study evaluated a total number of 68 patients and divided them into two groups - primary and secondary hyperparathyroidism.

The first group enrolled from October 2018 to December 2019 comprised twenty-seven patients diagnosed with primary hyperparathyroidism. Primary hyperparathyroidism was identified by biochemical evaluation, Technetium Sestamibi scintigraphy (MIBI), and 2B-ultrasound examination and confirmed by pathology report, considered the gold standard for diagnosis.

The second group evaluated 41 patients from the B Braun Dialysis Center from May 2019 to June 2019. All patients presented end-stage renal disease and were on chronic

hemodialysis treatment, clinically stable, and without acute intercurrent. Haemodialysis was done three times a week, with the meantime of hemodialysis therapy being 5.6 +/- 4.89 years.

Of 59 patients identified with secondary hyperparathyroidism, 25 presented multiple hyperplastic parathyroid glands (2-4 parathyroid hyperplasia). We selected only the gland with the most oversized diameter from these twenty-five patients, the gland with the maximal elasticity index for the statistical analysis.

After conducting a conventional ultrasound, two-dimensional shear wave elastography (2D-SWE) with an Aixplorer system (SuperSonic Imagine, France) was performed using the identical linear, high-resolution transducers, patient maintaining the supine position and neck hyperextension.

5.3. RESULTS

A total of sixty-eight patients were included in the final analysis – divided into two groups, one consisting of 27 patients with primary hyperparathyroidism and forty-one patients with secondary renal hyperparathyroidism.

The results are structured into two parts. The first results section evaluated the elastographic measurements results by dividing them into primary hyperparathyroidism and secondary hyperparathyroidism. We further compared the results with thyroid and muscle elastographic results.

In the second results section, we have evaluated the entire study group to determine the contrasts between the parathyroid, thyroid, and muscle tissue to gain a final cut-off value for each studied tissue. The first group of parathyroid adenomas comprises 25 women and two men, as primary hyperparathyroidism is more prevalent among postmenopausal women.

We evaluated the differences amid the two subgroups primary and secondary hyperparathyroidism, highlighting the significant statistical differences among mean SWE and minimum shear wave elastographic ($p < 0.001$). Comparing the two entities of hyperparathyroidism, the best cut-off value determined for parathyroid adenoma is a mean SWE valued below 5.96 kPa, thus accentuating differences between primary and secondary hyperparathyroidism is ever in doubt.

Keeping in mind these significant differences, even when we adjusted our PTH values for age, the difference of PTH serum levels remains substantial, resulting in that age does not influence parathormone values.

5.4. DISCUSSIONS

The endpoint of this current study was to establish the elastographic characteristics of parathyroid tissue in primary and secondary hyperparathyroidism and to determine the differences between them, even if adjusted to the non-parametric criterion. It also attempts to assess the differences between thyroid and muscle tissue to identify the parathyroid tissue better, adding value to the presurgical identification and diagnostic. The role of elastographic techniques in the parathyroid field has been evaluated but not established in the literature. The frequency of this endocrine disease and the mandatory discriminative diagnostic, identification, and localization before definitive treatment is compulsory.

Research studies are trying to determine the best cut-off value for primary hyperparathyroidism in the literature, but this method is less studied for secondary hyperparathyroidism.

Based on the elastographic techniques, literature studies on primary hyperparathyroidism have determined different threshold values for parathyroid adenomas. By using shear wave virtual touch imaging quantification, higher levels for parathyroid adenomas were established - 2.16 ± 0.33 m/s than for parathyroid hyperplasia - 1.75 ± 0.28 m/s,

establishing a cut-off value greater than 1.92 m/s for parathyroid adenomas [79], by using the identical elastography technique, another study compared parathyroid adenomas with thyroid tissue concluding that parathyroid adenoma presented low shear wave velocity value than thyroid tissue (2.01 m/s, respectively 2.77 m/s).

Using 2D SWE elastography, similar results, a study conducted on parathyroid adenomas and benign thyroid nodules has concluded that parathyroid adenomas, with a mean SWE 5.2 ± 7.2 kPa, presented a significantly lower plasticity index benign thyroid nodules with a mean SWE of 24.3 ± 33.8 kPa.

Other studies could help establish the elastographic differences between pathological parathyroid tissue and thyroid nodules. We must keep in mind that literature studies have concluded that the elastography index of benign and malignant thyroid nodules is higher than the elasticity index of healthy thyroid tissue.

5.5. CONCLUSIONS

In conclusion, this study aimed to identify and quantify the value of two-dimensional shear wave elastography in identifying, localizing, and diagnosing hyperparathyroidism. Identifying the elastographic differences between primary and secondary hyperparathyroidism was the secondary goal of this study. A mean SWE cut-off value below 5.96 kPa was specific to primary hyperparathyroidism. If considering both parathyroid adenomas and parathyroid hyperplasia, we can establish a mean SWE cut-off value for parathyroid tissue below 9.58 kPa, a significant difference between thyroid tissue and muscle tissue.

6. Study V: PARATHYROID ELASTOGRAPHIC AND ITS ROLE IN THE CURRENT CLINICAL SETTING

6.1. BACKGROUND AND AIMS OF THE RESEARCH

This prospective study aims to determine, using elastographic methods, shear wave elastography (SWE) attributes of parathyroid adenomas and secondary hyperplastic parathyroid glands from secondary hyperparathyroidism and determine whether the technique adds information in the preoperative diagnostic.

6.2. MATERIALS AND METHODS

We firstly evaluated 20 consecutive patients diagnosed with primary hyperparathyroidism from November 2018 to June 2019. All cases were patients over 18 years old that presented solitary parathyroid adenoma, confirmed by biochemical evaluation, localization with Technetium Sestamibi scintigraphy (MIBI), and certified by pathology report after surgery (parathyroid adenoma excision).

Secondly, we evaluated 120 patients from the B Braun dialysis center, over 18 years of age, with stage 5 CKD, three times per week under hemodialysis therapy. Fifty-nine patients had parathyroid disorders by clinical, biochemical evaluation, and scintigraphy scan or MRI scan.

After performing the conventional ultrasound, 2D-SWE was performed with an Aixplorer system (SuperSonic Imagine, France) utilizing a multifrequency linear transducer of 15-4 or 18-5 MHz in function the depth of the parathyroid lesion.

6.3. RESULTS

The statistical analysis found that tissue inelasticity of parathyroid adenoma was best confirmed by measuring the mean shear wave elastography index, giving quantitative information that may be useful in identifying parathyroid tissue. The mean (\pm SD) shear wave elasticity index value was 4.74 ± 2.745 kPa for all parathyroid adenomas enrolled in the study. In

comparison with thyroid parenchyma (mean SWE value 11.718 ± 4.206 kPa) and surrounding muscle (mean SWE value 16.362 ± 3.829 kPa), the measured elasticity index of parathyroid tissue was significantly lower than both thyroid and muscle tissue. After analyzing all measured data, we concluded that the most useful elastographic index is mean SWE, with a cut-off value for predicting parathyroid adenomas below 7 kPa [5].

Tissue stiffness of parathyroid hyperplasia measured by SWE means provided quantitative information that may be useful in diagnosing and treating parathyroid hyperplasia and preventing tertiary hyperparathyroidism. The mean (\pm SD) SWE was 7.83 ± 2.94 kPa for all parathyroid glands enrolled in the study. When compared the elasticity index of the hyperplastic parathyroid glands with the thyroid parenchyma mean SWE (13.780 ± 4.039 kPa) and surrounding muscle (15.788 ± 4.409 kPa), the elasticity of parathyroid hyperplasia was significantly lower than both thyroid and muscle tissue. The cut-off value below 9.74 kPa had a sensitivity and specificity of 94%, respectively 90% of identifying parathyroid tissue compared with thyroid tissue. A value below 9.98 kPa had a specificity and sensitivity of 90%, respectively 93% of identifying parathyroid tissue compared to surrounding muscle tissue.

6.4. DISCUSSION

This study evaluated and compared the determined elastographic features using shear wave elastography of confirmed parathyroid adenomas and parathyroid hyperplasia secondary to end-stage renal disease. The elastographic values of pathological parathyroid glands were compared to the elastographic features of thyroid and sternocleidomastoid muscle tissues. In the cases of primary hyperparathyroidism, we had confirmation by biological evaluation, confirmation by Technetium Sestamibi scintigraphy (MIBI), and finally certification by pathology report after surgery (parathyroid adenoma excision). We incorporated hyperplastic parathyroid glands, confirmed by biochemical means, initially localized with conventional B-mode ultrasonography, and confirmed by scintigraphy for the secondary hyperparathyroidism lot.

There are clinical implications regarding the use of elastography in localizing and influencing treatment decisions in patients with both primary and secondary hyperparathyroidism. This is a simple, operator-independent, repeatable and reproducible method that can be used complementary to conventional ultrasound, correctly distinguishing between thyroid and muscle tissue. Elastography could bring important information regarding parathyroid elasticity and be valuable in localizing and studying hyperparathyroidism.

6.5. CONCLUSIONS

To conclude, this study aimed to quantify the value of 2D Shear Wave Elastography in both primary and secondary hyperparathyroidism and determine whether it can be used to identify parathyroid tissue correctly. Elastography can be a useful qualitative and quantitative tool and can offer a better differentiation on tissue elasticity when diagnosing parathyroid disease. Using this elastographic technique, an elastographic value measured with shear wave elastography less than 7 kPa is highly suggestive for parathyroid adenoma, and an elastographic value less than 9.98 kPa is highly suggestive for parathyroid tissue in patients with secondary renal hyperparathyroidism.

FINAL CONCLUSIONS

1. Hyperparathyroidism Associated With End-Stage Renal Disease with/under Renal Replacement Therapy – An Overlooked Condition

Our findings highlight that elastography; predominantly two-dimensional shear-wave elastography can have a decisive role in evaluating secondary hyperparathyroidism in patients with end-stage renal disease on hemodialysis therapy.

Elastography, used as a complementary technique to conventional ultrasound, can add value to the localization of the hyperplastic parathyroid glands and thus improving preoperative diagnostic and localization of the targeted gland. It is a very convenient, operator-independent, repeatable and reproducible method, complementary to conventional ultrasound, cost, and time-efficient method for evaluating hyperparathyroidism.

Shear wave elastography has shown a discriminative diagnostic power in identifying the parathyroid glands and in the differential diagnostic in case of coexistence of thyroid disease or total thyroidectomy, in the latter case using the discriminative power between the muscle and parathyroid gland.

2. The Frequency Of Thyroid Pathology In Patients With Chronic Kidney Disease And Its Interference In The Parathyroid Elastographic Evaluation

As previously known, thyroid disease has a higher prevalence among patients with chronic kidney disease, and the exact pathophysiological mechanism is not well known.

Our second cross-sectional study evaluated the prevalence of thyroid disorders among the cohort of patients with end-stage disease on renal replacement therapy.

The total prevalence of thyroid disease among the evaluated patients was 61.8%, including nodular thyroid goiter and autoimmune thyroid disease. The euthyroid sick syndrome was considered in the total prevalence, but it was present at 46.34% of the evaluated patients.

The absolute risk of developing thyroid disorders calculated from our studied cohort was 3.41 times higher for women with ERSD on hemodialysis than in men, adding that an increase of BMI with one unit or more increases the risk of developing thyroid disease by 1.083 times. Our findings were concordant with the literature results.

3. The Place And Value Of Elastography In Primary Hyperparathyroidism

The second prospective study evaluated elastography's role in primary hyperparathyroidism, respectively parathyroid adenomas.

The elastographic index measured in shear wave elastography of the parathyroid adenoma tissue was significantly lower than the thyroid and muscle elastographic index. The results were in concordance with the literature results.

The cut-off values of the mean measured elasticity index in 2D- shear wave elastography for parathyroid adenomas was established at a value below 7 kPa.

By comparing the two elastographic methods, shear wave elastography and strain elastography, we concluded that although strain elastography can be a useful qualitative tool by using color mapping, 2D-SWE elastography can offer a better differentiation on tissue elasticity when localizing parathyroid adenomas.

4. Primary Versus Secondary Hyperparathyroidism – Elastographic Differences

The most challenging and exciting study was our third prospective study that aimed to determine the elastographic characteristics of primary and secondary hyperparathyroidism and evaluate the differences between them.

The study was divided into two parts, and the patient cohort was evaluated firstly by comparing the elastographic values of parathyroid adenomas with the elastographic values of parathyroid hyperplasia. In the second part, we evaluated the entire study group to assess the differences between the parathyroid, thyroid, and muscle tissue to obtain a final cut-off value for each studied tissue.

In the first part of the results, we concluded that there are significant differences between elastographic values for primary and elastographic values for secondary hyperparathyroidism. We determined a mean SWE cut-off value below 5.96 kPa to be specific for primary hyperparathyroidism.

When both elastographic values of parathyroid adenomas and parathyroid hyperplasia were considered, we established a mean SWE cut-off value for parathyroid tissue below 9.58 kPa, with a significant difference between thyroid tissue and muscle tissue.

5. Parathyroid Elastography And Its Role In The Current Clinical Setting

In conclusion, this thesis aimed to identify and quantify the value of two-dimensional shear wave elastography in identifying, localizing, and diagnosing hyperparathyroidism and the elastographic differences between primary and secondary hyperparathyroidism. Elastography has been proven and validated in many clinical areas, including thyroid disease, and it presents an essential role in the localization of parathyroid disease. It can be a helpful tool, qualitative, but mainly quantitative, in offering a better differentiation of parathyroid tissue. We must keep in mind that there are significant elastographic differences between parathyroid adenoma and parathyroid hyperplasia. However, the parathyroid tissue is significantly lower than the healthy thyroid tissue and the surrounding muscle tissue in either case.

To conclude, the clinical implications regarding the role of elastography in evaluating hyperparathyroidism, wheatear it is primary or secondary hyperparathyroidism is unequivocal. Complementary to conventional ultrasonography, elastography is a simple, non-invasive, repeatable, and reproducible method that can improve localization and preoperative evaluation of the patient with either primary or secondary hyperparathyroidism.