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Shear wave elastography of adrenal masses is feasible and may help to differentiate between solid and cystic lesions — an initial report

Elastografia fali poprzecznej guzów nadnerczy jest możliwa do wykonania i może pomóc w różnicowaniu zmian litych z torbielowatymi — doniesienie wstępne

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Abstract

Introduction: The aim of this study was to evaluate the feasibility and usefulness of supersonic shear wave elastography (SSWE) in the diagnosis of nonmalignant adrenal masses.
Material and methods: 13 patients with a total number of 16 adrenal masses were enrolled in the study. In each case, both conventional ultrasound imaging and SSWE for stiffness assessment were performed. The final diagnosis was based on CT, MRI, biochemical studies, surgery or more than one year of follow up.
Results: The final diagnosis: nodular hyperplasia in six masses, six adenomas, three cysts, and one myelolipoma. All solid adrenal masses presented the elastography signal in contrast to cystic lesions that were devoid of it, as shear waves do not propagate through fluids.
Conclusions: SSWE is a feasible technique that can be applied during ultrasound of the abdomen and retroperitoneum. SSWE presents potential for the differentiation of solid and cystic adrenal lesions. Further large scale studies evaluating the possibility of differentiation of adrenal and other retroperitoneal masses with SSWE are warranted. **(Endokrynol Pol 2014; 65 (2): 119–124)**

Key words: *adrenal gland diseases; cyst; diagnostic imaging; ultrasound; elastography*

Streszczenie

Wstęp: Celem badania była ocena wykonalności i przydatności naddźwiękowej elastografii fali poprzecznej (SSWE) w diagnostyce łagodnych zmian ogniskowych nadnerczy.
Materiał i metody: U 13 pacjentów wykonano badania ultrasonograficzne, oceniając 16 zmian ogniskowych nadnerczy z oceną ich spoistości z wykorzystaniem naddźwiękowej elastografii fali poprzecznej. Ostateczne rozpoznanie ustalono na podstawie wyników badań CT i MR, badań biochemicznych, operacji lub monitorowania ponad rok.
Wyniki: Ostateczne rozpoznania: 6 zmian o typie guzkowego rozrostu kory nadnercza, 6 gruczolaków, 3 torbiele, 1 myelolipoma. Sygnał elastograficzny zarejestrowano we wszystkich litych guzach nadnerczy w przeciwieństwie do zmian torbielowatych, które nie wykazywały sygnału elastograficznego, zgodnie z zasadą, że fale poprzeczne nie rozchodzą się w płynach.
Wnioski: Badanie z użyciem SSWE jest możliwe do wykonania i może być zastosowane w trakcie badań ultrasonograficznych jamy brzusznej i przestrzeni zaotrzewnowej. Metoda ta wykazała potencjał dla różnicowania litych i torbielowatych zmian ogniskowych nadnerczy. Uzasadnione są dalsze szerokie badania oceniające możliwość różnicowania guzów nadnerczy i innych zmian ogniskowych przestrzeni zaotrzewnowej. **(Endokrynol Pol 2014; 65 (2): 119–124)**

Słowa kluczowe: *choroby nadnerczy; torbiele; diagnostyka obrazowa; ultrasonografia; elastografia*

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Introduction

Ultrasound is a high resolution, real time, non-invasive, cheap and easily accessible modality frequently used for the evaluation of patients with neoplastic diseases, arterial hypertension and endocrine dysfunction in whom an adrenal lesion may be expected. Abdominal ultrasound can also incidentally detect adrenal masses known as incidentalomas. Ultrasound may be applied for follow up of quite a large group of patients with adrenal incidentalomas that are not referred for surgery. Moreover, endoscopic ultrasound is a prime method for the evaluation of left adrenal gland masses. Ultrasound may visualise normal adrenal glands and, more importantly, enlarged adrenal glands (wings of glands > 2–5 cm long and 6–10 mm thick) are detectable

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in a high percentage of cases [1–4]. Among many new ultrasound techniques for the evaluation of adrenal masses, elastography is an emerging one that deserves exploration [5, 6].

The estimation of tissue hardness is a very ancient diagnostic tool in medicine. Palpation – the earliest and most common form of tissue hardness estimation — was practiced by Egyptian physicians as early as 2600 BCE [7].

A more recent and sophisticated method of imaging tissue hardness is the technique known as elastography. A new generation of elasticity imaging called supersonic shear wave elastography (SSWE) has already been introduced to imaging of such superficial organs as the breast and the thyroid with high frequency linear probes [8-13]. This type of elastography does not require the compression of the tissues during their elasticity examination and may be applied with lower frequency convex probes for the examination of deep laying organs and tissues.

The aim of this study was to evaluate the feasibility and usefulness of SSWE in studies on incidentally found adrenal tumours (adrenal incidentalomas), which have been a true challenge for clinicians and radiologists because of the rapid growth in their numbers. For 20 years, we have observed a significantly increased number of such tumours [14–18], as a result of wider access to diagnostic imaging modalities, and have tried to differentiate benign masses from malignant ones. There is an urgent necessity to look for modern methods which could facilitate differential diagnosis of such tumours [6, 19].

Material and methods

During a few weeks' trial time in 2010, 13 consecutive outpatients with adrenal masses visible on B-mode ultrasound were evaluated (Table I). Approval for this study was obtained from the Ethics Committee of the Medical University of Warsaw, and all the patients provided informed consent. The B-mode ultrasound revealed 16 adrenal masses that were examined with SSWE quantitatively, with an Aixplorer ultrasound scanner (Supersonic, Aix-en-Provence, France) with convex abdominal transducer 1–6 MHz. The patients stayed supine during ultrasound examination. Depending on the constitution of the patient, different settings for SSWE penetration were applied: from a high resolution low penetration one, to a lower resolution deep penetration one.

The stiffness in kilo-Pascal (kPa) of the masses was evaluated qualitatively by visual inspection of elastographic map (with different settings of the scale range, that could be freely changed within acquired data gathered in the scanner) and quantitatively with a circular region of interest (ROI) placed over the elasticity signal within the mass with measurement of the mean stiffness on two images. The mean stiffness of such neighbouring organs as liver, kidney or spleen was also measured for calculation of adrenal/neighbouring organ ratio.

Table I. *Patient data*

Tabela I. *Dane pacjentów*

Women : 9	Men: 4
Mean age: 58.9 years	Range of age: 27–77 years
Right adrenal masses: 9	Left adrenal masses: 7
Mean maximal diameter: 41 mm	Range of maximal diameter: 17–103 mm

Table II. *The stiffness in kilo-Pascals (kPa) of nonmalignant adrenal masses*

Tabela II. *Twardość w kilopaskalach (kPa) ładgodnych guzów nadnerczy*

Adrenal mass	Average of mean stiffness (kPa)	Range of mean stiffness (kPa)
Myelolipoma	29.4	20–38.7
Adenomas	6.8	0.4–27
Hyperplastic nodules	6.3	2.4–18
Cysts	0	0

The final diagnosis was based on CT, MRI, biochemical studies, surgery or more than one year follow up.

Statistical analysis included Statistica 10 (StatSoft Inc.,USA) with W Shapiro-Wilk and U Mann-Whitney tests. Statistical significance was set at $\alpha \leq 0.05$.

Results

Final diagnosis (in six cases established on the basis of histopathological studies of the removed adrenal tumours) revealed: nodular hyperplasia in six masses, six adenomas, three cysts, and one myelolipoma.

All the solid lesions presented the elastography signal and measurements of their hardness in kPa were possible (Table II).

Myelolipoma (Fig. 1) was harder than adenomas (Fig. 2) and hyperplastic nodules.

All three cysts (one not obvious on B-mode imaging) (Fig. 3) did not show elasticity signal, as shear waves do not propagate through liquids.

There was no significant statistical difference $\alpha = 0.33$ between hardness in kPa of adenomas and hyperplastic nodules (Fig. 4). Also the ratios of adrenal gland hardness to hardness of neighbouring organs was not significant $\alpha = 0.51$ in differentiating between adenomas and hyperplastic nodules.

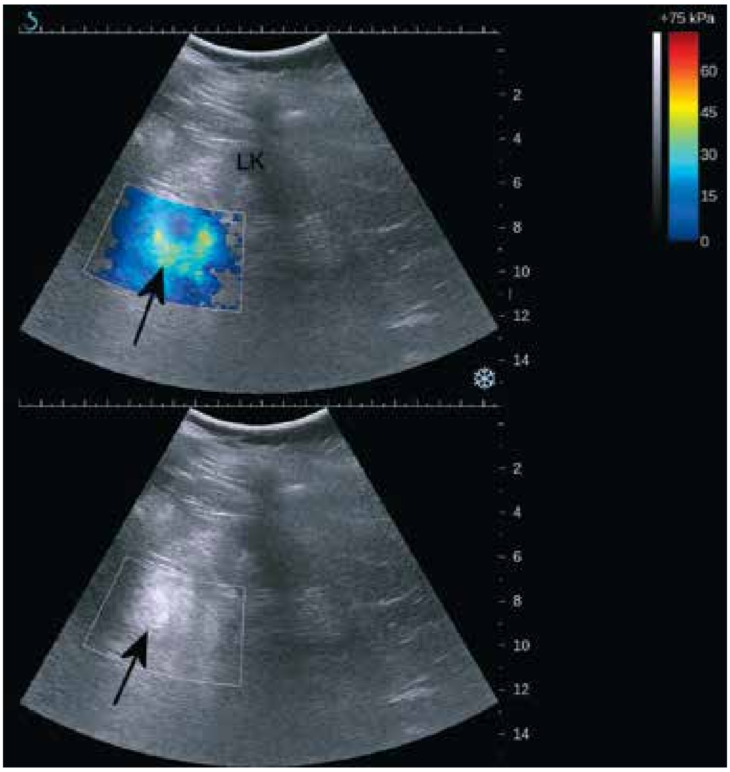

Figure 1. *Myelolipoma of the left adrenal gland (arrows). LK — left kidney. On the upper elastographic image, myelolipoma is harder (circa 40 kPa) than adenoma (next figure). On B-mode presentation (lower image), myelolipoma is distinctively hyperechoic*

Rycina 1. *Myelolipoma lewego nadnercza (strzałki). LK — lewa nerka. Na obrazie elastografii (górny) myelolipoma jest twardszy (około 40 kPa) niż gruczolak (ryc. 2). W prezentacji B (dolny obraz) myelolipoma jest charakterystycznie hyperechogeniczny*

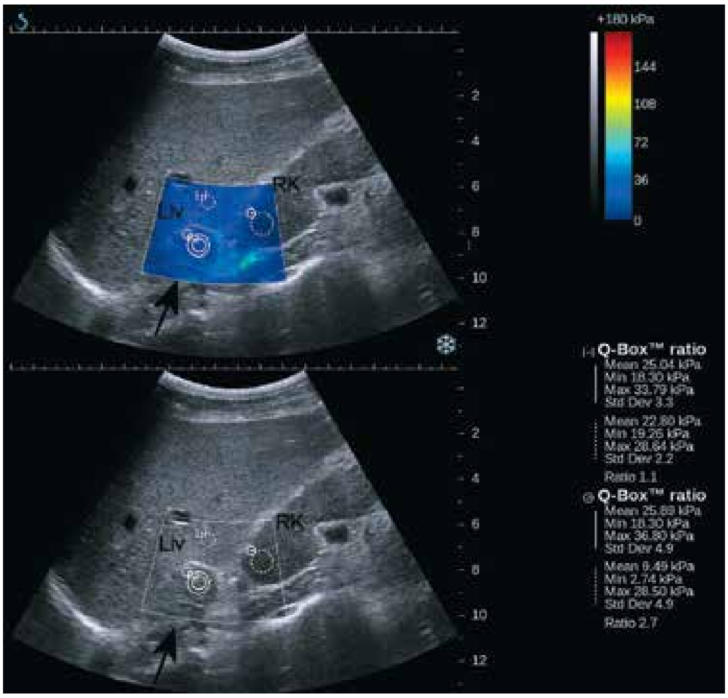

Figure 2. *Non-hyperfunctioning adenoma (incidentaloma) of the right adrenal gland (arrows). RK — right kidney; Liv —liver. On the elastographic image (upper), the measurements of adenoma hardness (circa 25 kPa) and hardness of liver and kidney parenchyma are marked with a circle region of interest. The respective ratios of the hardness are also calculated. On B-mode presentation (lower image), adrenal adenoma is isoechoic to liver*

Rycina 2. *Gruczolak prawego nadnercza bez nadmiernej czynności hormonalnej (incydentaloma) (strzałki). RK — prawa nerka; Liv — wątroba. Na obrazie elastografii (górny) pomiary twardości gruczolaka (około 25 kPa) i twardości wątroby i miąższu nerki są zaznaczone okrągłymi obszarami zainteresowania (pomiarowymi). Wyliczono również wartości odpowiednich proporcji twardości. W prezentacji B (dolny obraz) gruczolak nadnercza jest izoechogeniczny z wątrobą*

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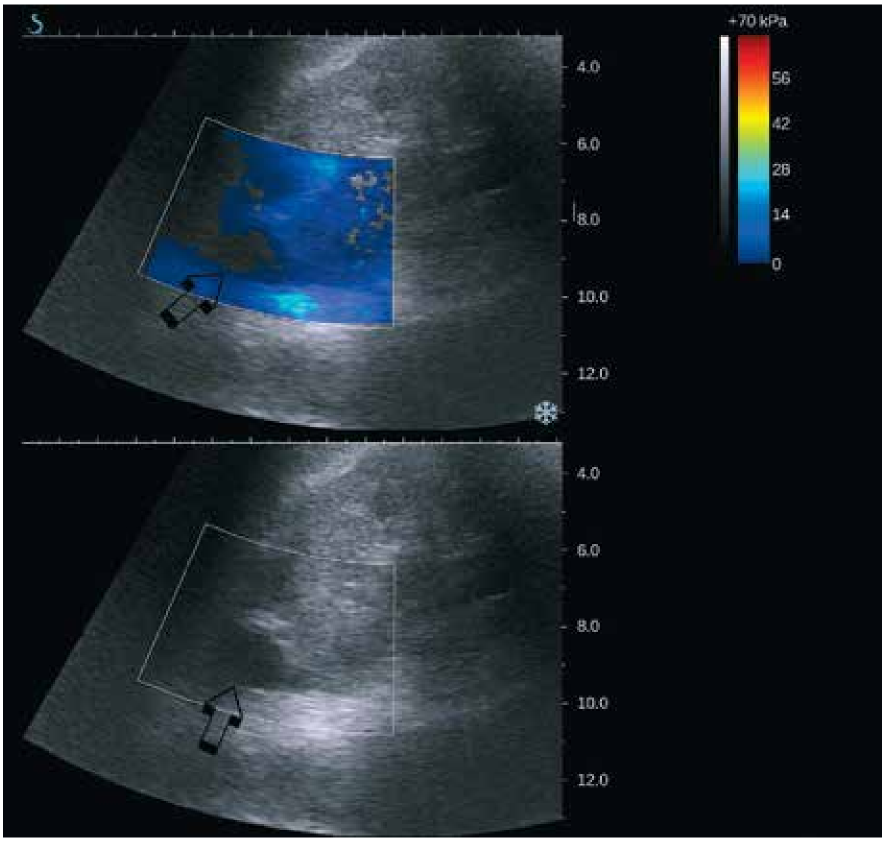

Figure 3. *Recurrent cyst of left adrenal gland (arrows). On the upper elastographic image, cyst is devoid of elastographic signal as shear waves do not propagate through liquids. On B-mode presentation (lower image), the mass is hypoechoic, without posterior enhancement, thus not presenting features of simple cyst*

Rycina 3. *Nawracająca torbiel lewego nadnercza (strzałki). Na obrazie elastografii (górny) torbiel jest pozbawiona sygnału elastograficznego, zgodnie z zasadą, że fale poprzeczne nie przechodzą przez płyny. W prezenacji B (dolny obraz) zmiana jest hipoechogeniczna, bez wzmocnienia poza zmianą, czyli nie wykazuje cech torbieli prostej*

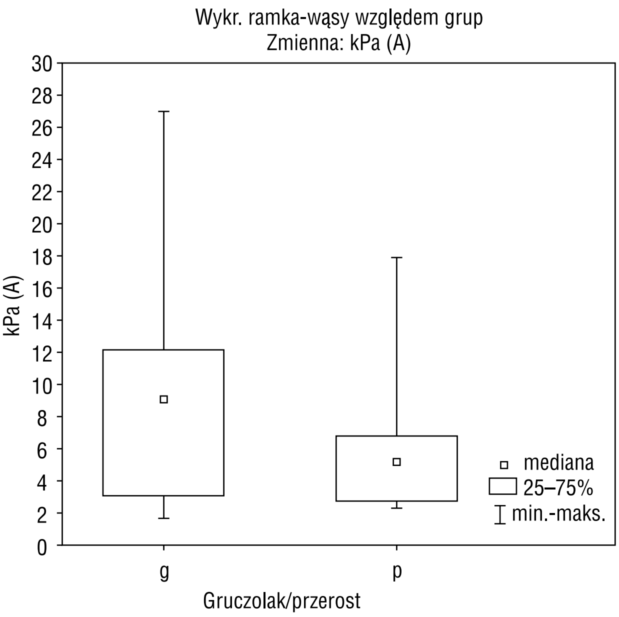

Figure 4. *Hardness in kPa of adenomas (g) and hyperplastic nodules (p)*

Rycina 4. *Twardość w kPa gryczolaków (g) i guzków rozrostu kory nadnercza (p)*

The calculation of ratios to different neighbouring organs, where appropriate, could contribute to non-significance of the result.

Discussion

A more recent and sophisticated method of imaging of tissue hardness is the technique known as elastography. The term 'elastography' was coined by Ophir et al. [20] to refer to an ultrasound based imaging technique where local axial strains were estimated by computing the gradient of axial shifts in echo arrival times along the ultrasound beam direction following quasi-static tissue deformation. Elastography, however, is now used as a more general term to identify methods that image tissue stiffness, using different imaging modalities e.g. ultrasound, magnetic resonance imaging, optical coherence tomography, different perturbation techniques to deform tissue and based on the elasticity parameter being measured or imaged [21]. Roughly 20 years have elapsed since the first images depicting the local elastic properties of tissues were obtained. The first decade of development produced a remarkable proliferation of techniques and optimisation strategies. In the second decade, this trend continued, but with an important extension to dedicated platforms for conducting clinical trials in the hands of radiologists and skilled clinicians [22].

There are three main types of ultrasound elasticity imaging: elastography that tracks tissue movement during compression to obtain an estimate of strain (quasi-static elastography); sonoelastography that uses colour Doppler to generate an image of tissue movement in response to external vibrations (harmonic elastography); and a technique tracking shear wave propagation through tissue to obtain the elastic modulus (transient elastography) [7], which includes among others SSWE.

Supersonic shear wave elastography consists of the generation of remote radiation force by focused ultrasonic beams, the so-called 'pushing beams', a patented technology called 'SonicTouch' [11]. Using SonicTouch, ultrasound beams are successively focused at different depths in tissues. The source is moved at a speed that is higher than the speed of the shear waves that are generated. In this supersonic regime, shear waves are coherently summed in a 'Mach cone' shape, which increases their amplitude and improves their propagation distance. For a fixed acoustic power at a given location, SonicTouch increases shear wave generation efficiency by a factor of 4–8 compared to a non supersonic source [23]. After generation of this shear wave, an ultrafast echographic imaging sequence is performed to acquire successive raw radiofrequency dots at a very high frame rate (up to 20,000 frames per second). Based on Young's modulus formula, the assessment of tissue elasticity can be derived from shear wave propagation speed. A colour-coded image is displayed, which shows softer tissue in blue and stiffer tissue in red. Quantitative information is delivered; elasticity is expressed in kPa [11].

This preliminary report based on a group of consecutive outpatients indicates that SSWE with a convex ultrasound probe is a feasible technique for the evaluation of adrenal masses. Shear wave elastography showed some potential for the differentiation of non-malignant adrenal masses, indicating the liquid content of adrenal cystic lesions, even these that do not present simple cyst features on B-mode ultrasound.

B-mode ultrasound is not always optimal in the confirmation of all features of simple cyst in the retroperitoneal region (well known examples are some kidney cysts), and thus additional simple and noninvasive proof would be of great importance. To the contemporary armoury of new ultrasound techniques such as tissue harmonic imaging and compound ultrasound the new technique called SSWE can be added and applied for this purpose.

One has to bear in mind that cysts with SSWE may present diverse findings: non-viscous fluids do not support shear waves and so they appear as colour voids, usually seen as black regions where the anechoic B-mode layer shows. However, when the fluid is viscous, shear wave signals may be seen as soft regions [24]. Apparently, all three adrenal cysts presented here contained non-viscous fluids.

However, the absence of an SSWE signal may be related to other circumstances than liquid composition. When the elasticity cannot be estimated, the colour display is switched off so that the underlying B-mode image (usually black) is revealed. This should not be mistaken for a low value that signifies a soft region. Biological conditions where the shear wave cannot be imaged are also encountered, such as when the shear wave speed is too high to be captured (e. g. in extremely stiff breast cancers), and when the interrogating beam cannot penetrate e. g. in regions that are shadowed-out, typically in the deeper parts [25] of the image. The problem of penetration range may be partly solved with penetration setting of SSWE examination.

Patients with incidentally discovered adrenal masses measuring greater than 4 cm, who do not have a history of malignancy, usually undergo surgery if the lesions cannot be characterised as cysts or myelolipomas. For lesions measuring 1 to 4 cm that are characterised as adenomas, and if autonomous function is not present on the initial study, imaging and hormonal follow-up is usually recommended [26].

Thus, though adrenal cysts are a rare condition, constituting in a large series approximately 1% of adrenal incidentalomas [27], SSWE could possibly increase interest in ultrasound of adrenal masses as an adjunct to the differentiation of commonly encountered adrenal adenomas that often present similarly to adrenal cysts density on plain CT (without contrast agent administration) [28].

If contrast CT is not performed for various reasons (e.g. allergy to iodine contrast agents, kidney insufficiency, thyroid disease, X-ray dose limitations, CT scanner time limitations), ultrasound together with supersonic shear wave imaging could be the option to follow. Additionally, unlike CT, elastography is a radiation-free method and no contrast agent is needed.

Conclusions

SSWE is a feasible technique that can be applied during ultrasound of the abdomen and retroperitoneum. SSWE presents potential for the differentiation of solid and cystic adrenal lesions. Further large scale studies evaluating the possibility of differentiation of adrenal and other retroperitoneal masses with SSWE are warranted.

Acknowledgements

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