Multiparametric US-US Methodological Standards

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Testicular lesions (TLs) are challenging clinical or ultrasound findings. When large, hard palpable lumps, TL management is mainly clinical, requiring conventional color-Doppler ultrasound (CDUS) to confirm that they are solid, vascularized lesions suggesting malignancy. However, when their CDUS characteristics are uncertain or when nonpalpable, multiparametric US (mp-US) (i.e., the combination of CDUS and more recent US techniques such as contrast-enhanced US and sonoelastography) plays a key role in their characterization, aimed at differentiating benign from malignant TL. This is relevant, since TLs are frequent, testicular tumors are the most common malignancies in young men, and the accurate assessment of a TL is critical to define its correct management including testicular salvage and US follow-up or orchiectomy.

ultrasound (US) multi-parametric ultrasound (mp-US) gray-scale ultrasound (GSUS) color-Doppler ultrasound (CDUS) contrast-enhanced ultrasound (CEUS)

1. Introduction

Ultrasonography (US) represents the gold standard imaging method for scrotal investigation and is widely used to assess a variety of scrotal diseases [1][2][3]. It is a simple, rapid, and harmless diagnostic tool that is able to provide live images of the scrotal content and, among the imaging techniques, it is the least expensive [1][2][3]. Over time, the use of US has progressively expanded since it is useful to assess scrotal features related to reproductive health, scrotal pain, masses, and trauma [1][2][3].

Currently, conventional gray-scale US (GSUS), supplemented by color-Doppler US (CDUS), is considered as being highly sensitive in detecting testicular lesions, however, it has limits in delineating their nature [3]. If performed by an expert operator, scrotal US, together with clinical history and physical examination, may suggest a differential diagnosis among benign and malignant testicular lesions [4]. However, in some cases, it is difficult to discriminate the benign or malignant origin of a testicular lesion, and in case of a “likely” malignant lesion, it is challenging to suggest a possible cancer type. Hence, to date, histology remains the only certain diagnostic tool to define the nature of a testicular lesion [2].

Recently, the use of contrast-enhanced US (CEUS) and sonoelastography (SE) have led to improvements in the differential diagnosis of testicular lesions [2]. This led to a new diagnostic paradigm, the so called “multiparametric

US" (mp-US) [5][6], combining conventional techniques (i.e., GSUS and CDUS) with CEUS [7] and SE [8]. Although not entirely diagnostic, mp-US is able to provide a detailed characterization of testicular lesions [4][9][10]. This is relevant in clinical practice, since an accurate mp-US evaluation of a testicular lesion, beside and along with clinical assessment, is critical to define its correct management including testicular US follow-up or orchiectomy [11]. On the one hand, when "palpable" testicular masses are found, they can be malignant in more than 90% of cases, making radical orchiectomy the standard treatment [12]. On the other hand, when nonpalpable testicular lesions are detected, often incidentally during a scrotal US performed for different reasons (e.g., male infertility, varicocele, history of cryptorchidism, scrotal pain or trauma), the clinical management is more cautious. In fact, these lesions are small and mostly benign [13][14], so unnecessary orchiectomy must be avoided, however, they can also be malignant and can grow over time. In this scenario, US is crucial in the follow-up of small lesions, suggesting surgery in the case of growth/modification of small nodules, especially if testicular tumor-related risk factors (e.g., age 15 to 40 years old, family history of testicular tumors, history of contralateral testicular tumor, cryptorchidism or oligo-/azoospermia) are present [1][15]. Hence, either in the case of palpable testicular masses or, especially, in the case of small testicular lesions, US is useful. In particular, mp-US can help in distinguishing benign and malignant lesions with good accuracy, providing a more detailed characterization than CDUS, CEUS, or SE alone.

Mp-US is increasingly recognized as a valuable problem-solving technique in scrotal pathologies, particularly in differential diagnosis of testicular lesions [9][16]. Mp-US combines conventional techniques (GSUS and CDUS) with CEUS, and SE [9][16], which are relatively recent in evaluating scrotal organs, particularly testicular lesions [2][17].

2. Scrotal/Testicular Color-Doppler Ultrasonography (CDUS)

The standardization of the methodology used to perform scrotal color-Doppler ultrasonography (CDUS) is relatively new. A detailed description of the standard operating procedures (SOPs) for performing scrotal CDUS have been reported by the European Academy of Andrology for the entire male genital tract [17][18][19][20]. The EAA-proposed SOPs to assess scrotal CDUS and, in particular, testicular lesions, have been reported elsewhere [2][17][19] (see https://www.andrologyacademy.net/eaa-studies (accessed on 20 October 2023)). In particular, testicular US should be performed with a high frequency linear transducer, with the patient in the supine position. A US scan of both testicles should be performed including longitudinal, oblique, and transverse scans, with slow, continuous side-to-side movements that allow for the assessment of the entire parenchyma. The operator should evaluate at GSUS the volume of the testes (using the "ellipsoid" formula [height × width × length × 0.52] for adult testes [21] and the Lambert's empirical formula [height × width × length × 0.71] for pre-pubertal testes [3]), the echogenicity, the echotexture, the possible presence of testicular calcifications or microlithiasis, and vascularization by CDUS, comparing the two sides. Testicular lesions should be accurately evaluated in longitudinal, oblique, and transverse scans. A complete evaluation should include: (1) diameters (length × height × width); (2) position and extension; (3) type (solid, cystic, mixed), homogeneity (homogeneous/inhomogeneous), and echogenicity (hypoechoic, hyperechoic, anechoic); (4) presence of intralesional calcifications; (5) shape (regular or irregular) and margins (clean-cut, smooth, multi-lobed, infiltrating); (6) vascularization pattern (absent, peripheral, intranodular). The images must be stored to be used for the comparison during follow-up. The report must also describe, besides the

lesion, the US characteristics of both testicles and must specify the absence of lesions in the contralateral testicle [1][2][3][17][19].

3. Contrast-Enhanced US (CEUS)

The methodological standards for the clinical practice of contrast-enhanced US (CEUS) in non-hepatic applications including scrotum investigation have been reported by the EFSUMB Guidelines [21]. As a result, the assessment of some pathological conditions using CEUS has improved [7][21]. Using time–intensity curves, evaluating the wash-in and wash-out curves may help to distinguish malignant from benign tumors, although CEUS analyses still overlap between different histological types [7]. In addition, CEUS can discriminate non-viable regions in testicular trauma and can identify segmental testicular infarction [7][21].

For CEUS, a dedicated machine-setting with a low mechanical index (0.05–0.08) is needed to avoid early microbubble destruction. US contrast medium (very small-sized organic shells filled with gas with high impedance) should be injected as intravenous bolus and followed immediately by 10 mL of 0.9% saline solution. The entire examination needs to be recorded to perform qualitative and quantitative analyses [7].

4. Sonoelastography (SE)

The methodological standards for the clinical practice of sonoelastography (SE) in non-hepatic applications including testicular investigation have been reported by the EFSUMB Guidelines and Recommendations [22]. So far, strain elastography and shear wave elastography, which includes acoustic radiation force impulse-based techniques, and transient elastography are available. The basic principles of SE have been extensively described in previous EFSUMB Guidelines [23], while methodological standardization for different organs including the testis are reported in the updated EFSUMB guidelines [22]. From a methodological point of view, the use of SE to investigate focal testicular lesions can only be recommended in conjunction with other US techniques as there is overlap between benign and malignant neoplasms [22][24].

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