# Contrast-enhanced ultrasound in the differential diagnosis of small testicular masses

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| **Poster No.:** | C-2542 |
| **Congress:** | ECR 2015 |
| **Type:** | Scientific Exhibit |
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| **Keywords:** | Genital / Reproductive system male, Ultrasound, Contrast agent-intravenous, Neoplasia |
| **DOI:** | 10.1594/ecr2015/C-2542 |

## Aims and objectives

Small testicular masses (STMs), defined as non palpable, < 25mm diameter mass [1], are a growing problem, because many cases may be benign at final histology. Testicular cancer represents between 1% and 1.5% of male neoplasms and 5% of urological tumours in general, with 3-10 new cases occurring per 100,000 males/per year in Western countries [2-4]. Malignant germ cell neoplasms represent most of the palpable symptomatic testicular masses. Therefore, radical orchiectomy has been the standard of care for testicular masses. However the widespread use of high-frequency ultrasonography has led to an increasing number of incidentally STM detected, most of which have been shown to be benign [4]. Therefore Testis-Sparing Surgery (TSS) has been proposed as alternative to radical orchifunicolectomy [5].

The preoperative differential diagnosis of non-palpable testicular lesions by imaging methods (especially by ultrasound, US) has become crucial because it allows, in case of negativity of biochemical tumor markers, a conservative surgical approach (TSS).

Although Conventional ultrasonography has high sensibility (96.6%) for detection of small intra-testicular lesions, sonographic appearance of testicular lesions may be various and not specific and the technique cannot differentiate benign from malignant lesions [6].

Some advanced ultrasonography techniques, like contrast-enhanced ultrasonography (CEUS) have been proposed to increase diagnostic accuracy in characterization of testicular lesions [7]:

CEUS permits visualization of the microcirculation identifying avascular lesions without malignant potential [8]. This technique allows the study of enhancement pattern which could further assist in characterising lesions.

The aim of this study was to evaluate the role of Contrast Enhanced Ultrasound (CEUS) in the characterization of small testicular masses (STMs).

## Methods and materials

We evaluated 16 patients (pts) positive for STMs (lesion diameter <15 mm) to Ultrasound (US).

Scrotal US is performed with the use of high frequency broadband linear transducer (8-13 MHz) that can perform both power and spectral Doppler ultrasonography. Baseline gray scale and color Doppler sonographic examinations were performed using an MyLab™70 XVG system (Esaote, Genoa, Italy) with LA523 linear array contrast-enabled transducer.

The scrotum and its contents are evaluated in longitudinal and trasverse plans.

All images were stored on an external hard disk for review. The lesions were reviewed for morphologic characteristics (including size and shape) and sonographic appearances (including echogenicity, the presence of calcification, cystic areas or concentric rings). The presence or absence of vascular signals at color Doppler was noted.

In all cases further US with intravenous infusion of second-generation contrast agent (Contrast Enhanced Ultrasound, CEUS) was performed.

A low-mechanical index technique (Contrast tuned imaging, CnTI, Esaote) with mechanical index below 0.10 is applied. A bolus of 4.8 mL of sulfur hexafluoride microbubble contrast agent (SonoVue, Bracco SpA, Milan, Italy) is injected, followed by 10 mL of normal saline via an antecubital vein cannula. Split-screen technology is used and imaging is recorded on a cine loop for 180 seconds for later review.

On CEUS, note was made of if enhancement was present, and the pattern (hypo-, iso-, or hyper- enhancement) was noted.

The determination of the tumor markers such as alpha-fetoprotein (#FP), beta-human chorionic gonadotropion (#hCG) and lactate dehydrogenase (LDH) was assessed in all cases.

The patients underwent Testing sparing surgery (TSS) echoguided followed by eventual orchiectomy.

The selection criteria for TSS was the size of the mass (# 25 mm) and a safely distance of the mass from the rete testis, while advanced age of the patients was not considered an exclusion criteria.

All the patients underwent the exploration of the testis trough an inguinal access. After exteriorization of the testis, the small mass was identified by straight palpation of the testis or with intra operative ultrasonography (IUS), usually guided with a 30-g needle. In all patients we performed a cord clamping after the identification of the lesion in order to reduce the time of warm ischemia. After the excision of the mass, frozen section analysis

(FSE) was performed in all cases associated with multiple biopsies of the surrounding tissue.

# Results

The diagnosis was incidental in asymptomatic patients. Neoplastic markers were negative in all pts.

Table 1 shows global data of the clinical and pathologic characteristics of the whole patient population.

Pre-operative sonographic patterns for the individual patients are presented in Table 2.

Sonographic appearance of testicular lesions was heterogeneous with a prevalence of hypoecoic pattern. Color Doppler signals of the STMs resulted absent except three cases.

CEUS showed lesional absence of contrast enhancement in 2 lesions (Fig. 1), progressive and weak contrast enhancement in 4 cases (Fig. 2), early hyperenhancement followed by iso-enhancement in 5 cases (Fig. 3, 4) and marked hyperenhancement followed by wash out in 5 pts (fig. 5, 6). At final pathologic analysis the lesions above corresponded respectively to: epidermoid cyst, inflammation, seminoma, leydigioma. 11 pts underwent TSS while all 5 cases of seminoma had radical orchiectomy.

At 12 months US follow-up all patients underwent TSS were free of disease.

**Images for this section:**

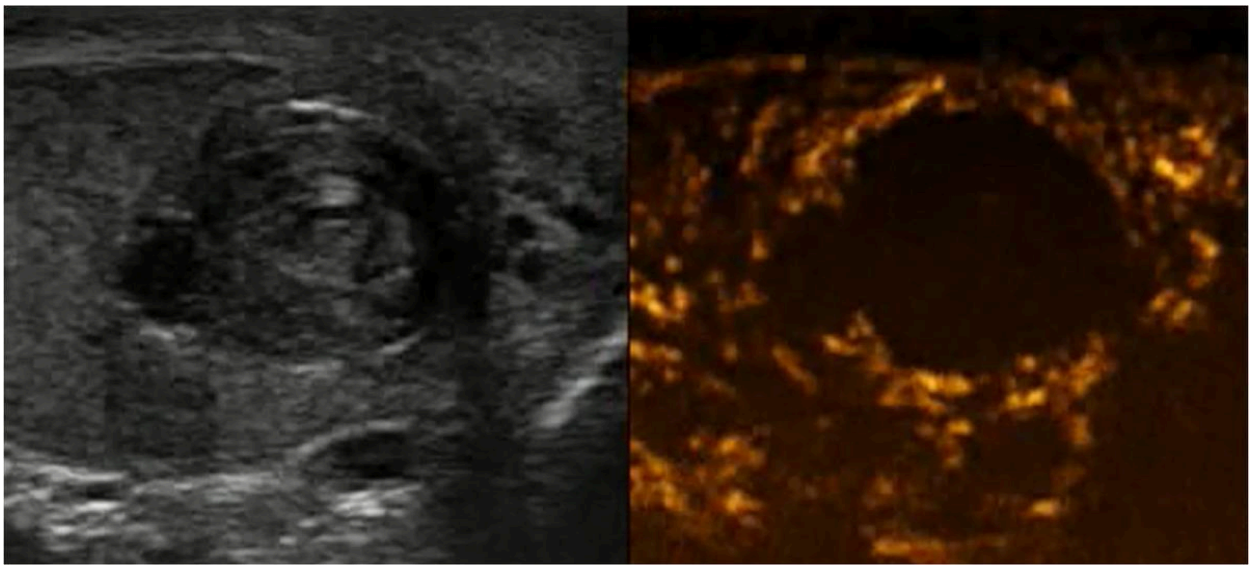

**Fig. 1:** Testicular Epidermoid Cyst, histologically proven. Contrast enhanced ultrasound shows lack of contrast enhancement centrally and at the edge of the lesion.



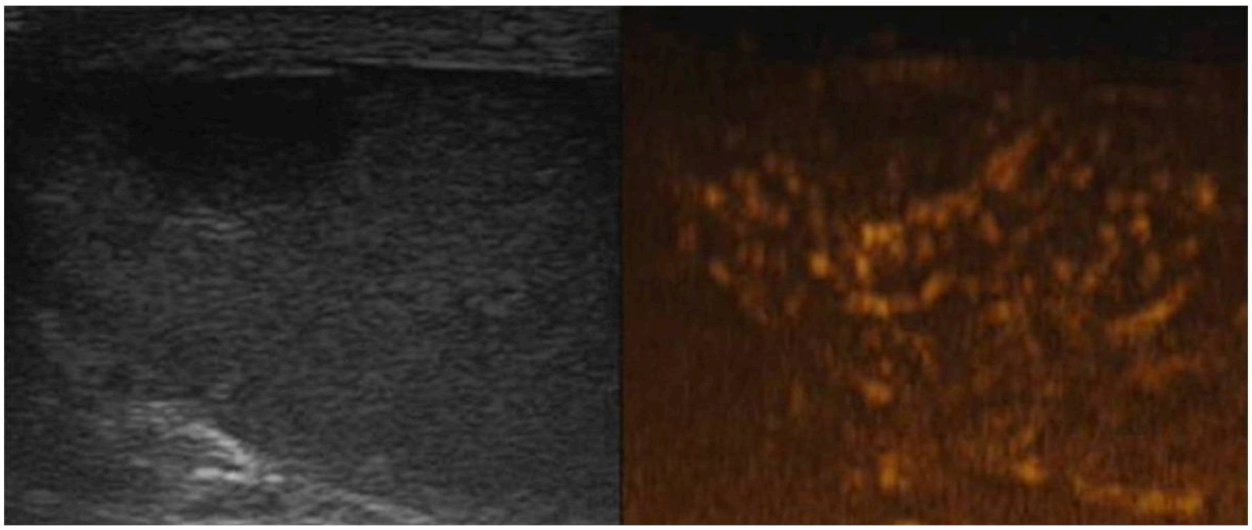

**Fig. 2:** Flogosis, histologically proven. Contrast enhanced ultrasound shows progressive and weak contrast enhancement.

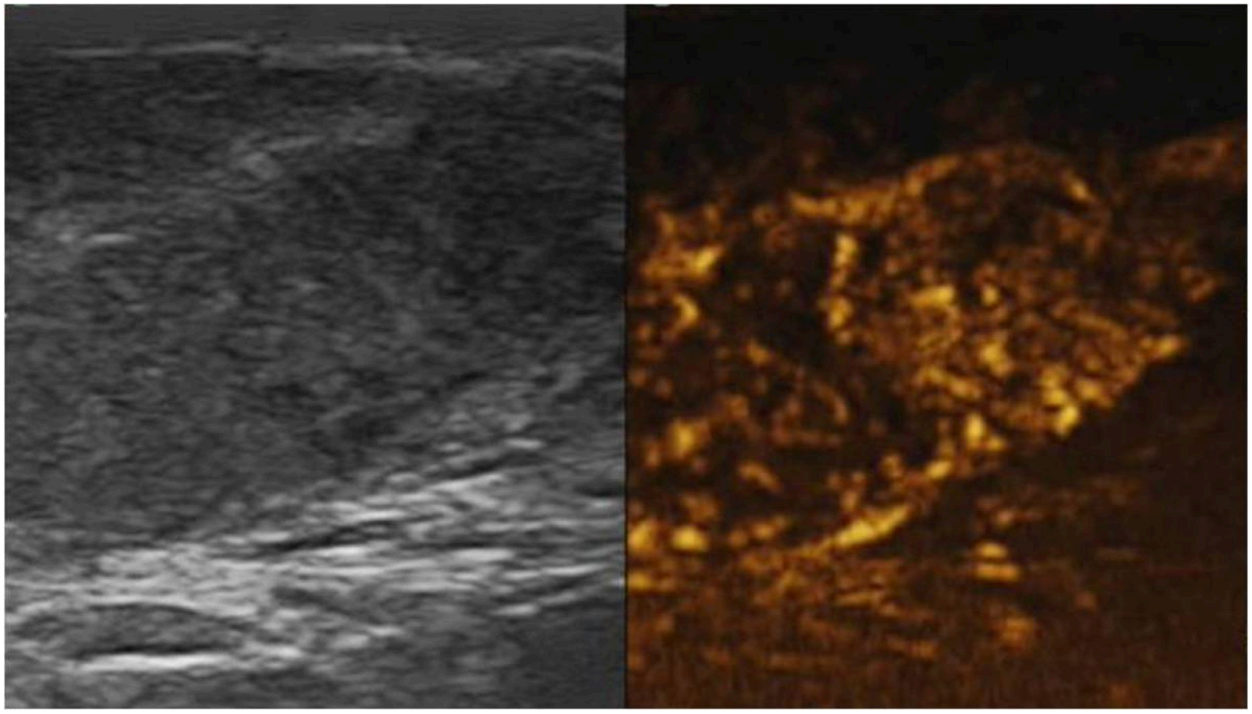

**Fig. 3:** Seminoma, histologically proven. Contrast enhanced ultrasound shows early hyperenhancement.



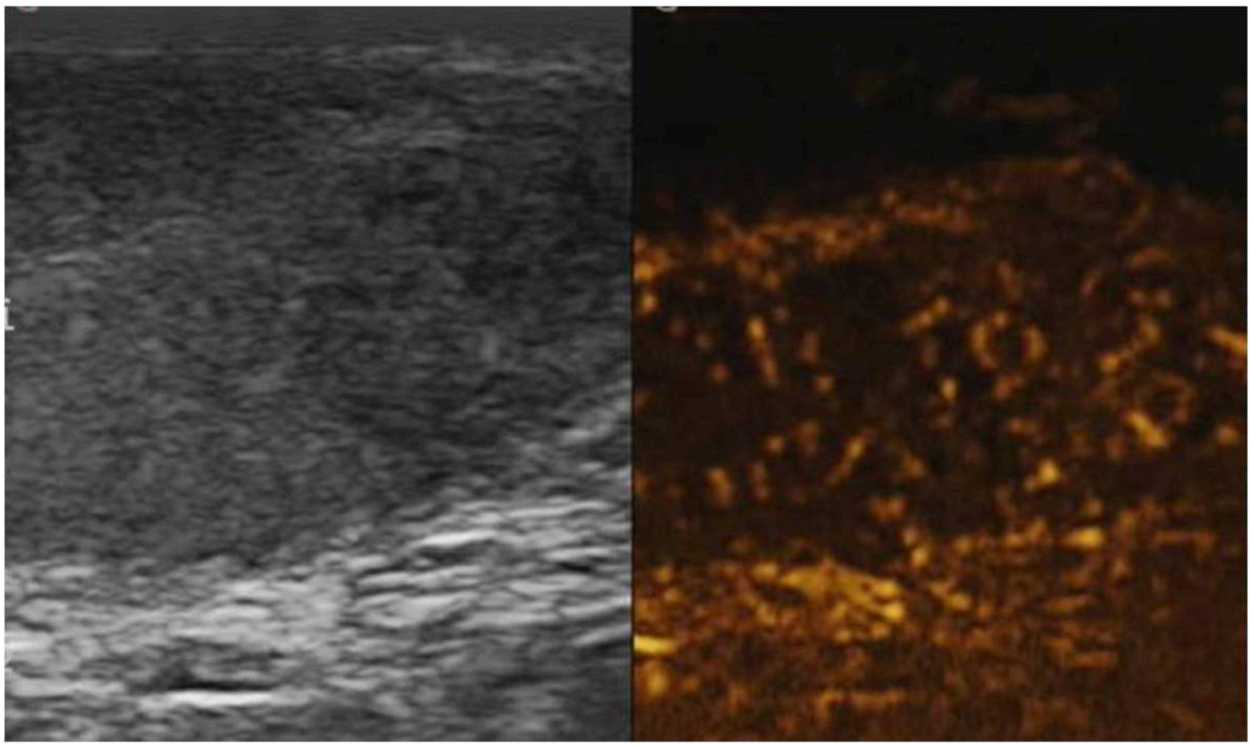

**Fig. 4:** Seminoma, histologically proven. Contrast enhanced ultrasound shows iso-enhancement during the late phase.



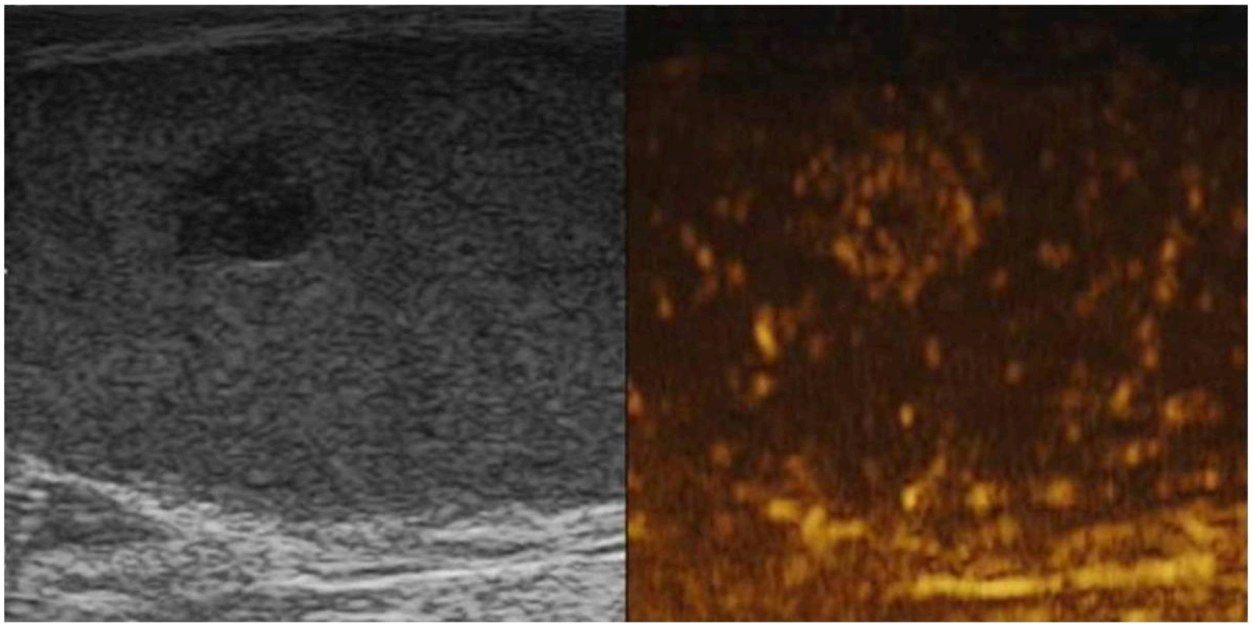

**Fig. 5:** Leydigioma, histologically proven. Contrast enhanced ultrasound shows homogeneous early hyperenhancement



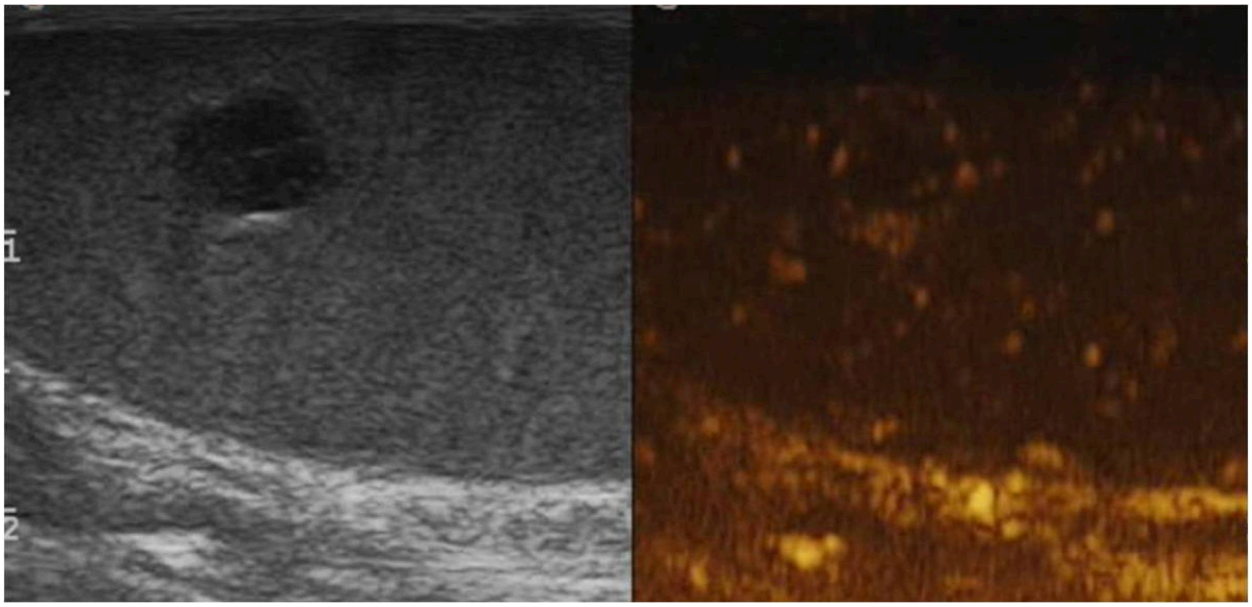

**Fig. 6:** Leydigioma, histologically proven. Contrast enhanced ultrasound shows rapid wash out during the late phase.



| | Number (%) |
|---|---|
| Number of patients | 16 |
| Age (years)<br>mean±SD<br>median (range) | <br>44.3±18.7<br>38.0 (15-84) |
| Clinical presentation (no. of pts)<br>asymptomatic<br>symptomatic | <br>16 (100)<br>0 |
| Preoperative size (mm)<br>mean±SD<br>median (range) | <br>9.5±4.4<br>7.1 (4-21) |
| Pathological size (mm)<br>mean±SD<br>median (range) | <br>10.5±3.1<br>8 (5-16) |
| Intraoperative Ultrasound investigation (no. of patients) | 16 (100) |
| Intraoperative frozen section (no. of patients) | 16 (100) |
| Histologic type at final pathology<br>Leydig cell tumor<br>Flogosis<br>Seminoma<br>Epidermoid Cyst | <br>5 (31.2)<br>4 (25)<br>5 (31.2)<br>2 (12.5) |
| Pathological staging<br>4 Seminoma | <br>pT1NxMxR0Sx |

**Table 1:** Clinical and pathological characteristics of the whole patient population.

| patient (age) | Clinical presentation | B-mode | CDUS | CEUS | Preoperative size (mm) | Pathological size (mm) | IUS | Frozen section | Histologic type at final pathology | TSS | Follow-Up (Mo) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1-15 | asymptomatic (varicocele) | Heterogeneous, with calcifications and concentric rings | absent | No enhancement | 9 | 11 | no | cystic lesion with keratinic inclusion suspicious for teratoma | Epidermoid cyst | Yes | 12 |
| 2-33 | asymptomatic (infertility) | Hypoechoic | absent | hyperenhancement | 4 | 7 | yes | leydig cells proliferation | Leydig cell tumor | Yes | 12 |
| 3-38 | asymptomatic | Heterogeneous | absent | No enhancement | 11 | 13 | no | Epidermoid cyst | Epidermoid cyst | Yes | 12 |
| 4-36 | asymptomatic (varicocele) | Hypoechoic | absent | hyperenhancement | 6 | 7 | yes | gonadic stromal tumor | Leydig cell tumor | Yes | 12 |
| 5-32 | asymptomatic | Hypoechoic | absent | hyperenhancement | 7 | 12 | yes | leydig cells proliferation | Leydig cell tumor | Yes | 12 |
| 6-62 | symptomatic (testicular pain) | Hypoechoic | absent | isoenhancement | 8 | 10 | no | flogosis/testicular atrophy | flogosis | Yes | 12 |
| 7-35 | symptomatic (testicular pain) | Heterogeneous | absent | isoenhancement | 10 | 12 | no | flogosis/testicular atrophy | flogosis | Yes | 12 |
| 8-73 | asymptomatic (urologic visit for BPO) | Hypoechoic | present | hyperenhancement | 12 | 7 | yes | Leydig cells proliferation | Leydig cell tumor | Yes | 12 |
| 9-84 | symptomatic (testicular pain) | Hypoechoic | absent | hyperenhancement | 6 | 8 | yes | seminoma | seminoma | No (orchiectomy) | - |
| 10-45 | asymptomatic (hydrocele) | Hypoechoic | absent | hyperenhancement | 4 | 6 | yes | seminoma | seminoma | No (orchiectomy) | - |
| 11-38 | asymptomatic (infertility) | Hypoechoic | absent | isoenhancement | 5 | 5 | yes | flogosis | flogosis | Yes | 12 |
| 12-32 | asymptomatic (infertility) | Hypoechoic | present | hyperenhancement | 7 | 8 | yes | Leydig cell proliferation | Leydig cell tumor | Yes | 12 |
| 13-42 | symptomatic (testicular pain) | Hypoechoic | absent | isoenhancement | 5 | 5 | yes | normal seminiferous tubules, absence of neoplastic cells | flogosis | Yes | 12 |
| 14-34 | asymptomatic (follow up for epididymal cyst) | Hypoechoic | present | hyperenhancement | 12 | 10 | yes | seminoma | seminoma | No (orchiectomy) | - |
| 15-68 | asymptomatic (testicular trauma) | Hypoechoic | absent | hyperenhancement | 10 | 10 | no | seminoma | seminoma | No (orchiectomy) | - |
| 16-44 | asymptomatic (testicular trauma) | Hypoechoic | absent | hyperenhancement | 10 | 10 | no | seminoma | seminoma | No (orchiectomy) | - |

**Table 2:** Analytical evaluation of patient's population.

# Conclusion

The widespread use of US for the diagnostic evaluation of scrotal disorders and current advances in US technology have allowed a more frequent detection of incidental testicular lesions.

Recent studies show that, approximately 80% of non palpable masses are benign [9]. A proper management in differential diagnosis of these benign entities may preclude the need of radical orchiectomy.

In our experience TSS with detailed pre-operative and intra-operative US can be considered a safe procedure, with an optimal concordance between FS and final pathology.

Although sonographic appearance of testicular masses is various and not specific, CEUS increases the confidence of the interpretation of lesion vascularity, especially identifying avascular lesions without malignant potential [8, 10].

Epidermoid cyst of the testis is a rare benign tumor; however, it should be taken in account when considering testicular masses [11-13]. In this setting CEUS represents a useful adjuct to Color Doppler US to recommend suitability for TSS.

In our study CEUS demonstrate a lack of enhancement in two cases of epidermoid cyst. In case of STMs < 15 mm Color Doppler sonography has a low sensitivity in detection of vascular signals and CEUS represent a useful tool to differentiate Epidermoid Cysts from other solid intratesticular lesions. Intraoperative extemporaneous examination showed no evidence of malignancy, enucleation of the mass was performed and FSE confirmed the diagnosis.

CEUS enhancement pattern might be helpful to differential diagnosis of STMs. In our series all cases with absence of hyperenhancing were inflammatory at final pathological examination.

About CEUS hypervascular lesions, we suspect preoperatively all cases of Leydig cell tumor based on the presence of a homogeneous strong enhancement followed by washout. All these lesions were treated with TSS [14, 15]. However, these findings need confirmation on a larger number of patients.

The principal study limitations were represented by the small number of cases and the the heterogeneity of testicular lesions..

In conclusion our findings suggest that, when MR is not available, CEUS may be a valid alternative for the preoperative assessment of STMs; Preoperative diagnosis combining imaging features with normal biochemical tumour markers will allow for testis-sparing surgery and prevent unnecessary orchiectomy.

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