Original Study

Reliability of Frozen Section Examination in a Large Cohort of Testicular Masses: What Did We Learn?

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Abstract

In this report, we assessed the reliability of frozen section examination of testicular masses in determining whether patients could receive surgery that would save their testicle or have surgery to remove the testicle and the mass. The results showed that the frozen section examination could greatly aid in making this decision.

Background: Frozen section examination (FSE) for testicular masses is gaining popularity because of the possibility of performing testis-sparing surgery (TSS) on the basis of the FSE results. The aim of our study was to investigate the reliability of FSE in the diagnosis of testicular masses. **Patients and Methods:** From 1999 to 2016, 144 of 692 patients who underwent surgery in our tertiary center for testicular masses had FSE. The indications for FSE were: masses < 1 cm, nonpalpable, multiple, or with unusual presentation. Mean follow-up for patients was 25.5 months. The algorithm of surgery determined by FSE was: orchiectomy if malignant or nonconclusive pathology; TSS if benign or nontumor pathology. FSE data were analyzed retrospectively. Specificity and sensitivity of the method was calculated for benign, malignant, seminoma, and nonseminoma tumors. **Results:** Intraoperative FSE was conducted on 21% of candidates for surgery on testicular masses. The sensitivity and specificity of FSE were 93% and 98%, respectively, for malignant tumors, and 90% and 99%, respectively, for benign tumors. The κ agreement coefficient between FSE and final histopathology was statistically significant (0.76). TSS was performed in 57 (40%) patients, including 6 of 23 monorchid patients. **Conclusion:** FSE correlates well with final histopathological diagnosis of testicular masses. Thus, it reliably identifies patients who might benefit from TSS. FSE should be considered always in small, nonpalpable, multiple, or uncommonly presenting masses in solitary testis or both testes.

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Introduction

In recent decades, the management of testicular masses has changed because of the refinement of diagnostic ultrasound techniques and increased public awareness of testicular tumors. Masses of small diameter (< 1 cm), often nonpalpable, are more and more found during ultrasound examination.[1]

According to the most recent reports, the incidence of nontumor and benign testicular masses is increasing, which is confirmed in the largest orchiectomy series.[2] Improved knowledge of treating testicular tumors has led to a testicle-sparing approach in selected cases of benign tumors (such as Leydig tumors) or other nontumoral masses.[3,4] As a result, the management of testicular masses, especially those associated with low serum markers and suggestive

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clinical findings, such as pain, small size,[5] nonpalpable mass,[6] or masses in a single testicle, should be reconsidered.

Although ultrasound has a high sensitivity for detecting testicular masses (96.6%), its specificity in distinguishing malignant from benign lesions is rather low (44.4%).[7,8] As a result, a critical evaluation of tumor masses before and at the time of surgery is required.

The final discrimination between malignant, benign, or nontumor masses depends on the histopathological diagnosis. The reported specificity and sensitivity of frozen section examination (FSE) of testicular tumors improved from lower values[9,10] up to 100%.[11,12] As a consequence, FSE might play a paramount role in the management of patients with testicular masses, although the supporting data come only from retrospective studies.[5,6,9-17]

Despite the high sensitivity of FSE, the routine use of FSE and its role in testis masses management is still debatable,[16] because some authors advocate postponing radical orchiectomy until malignancy is documented at final histopathological examination.[18] However, in all published series FSE resulted as useful in intraoperative decision-making.[5,6,9-17]

The aim of the present study was to test FSE specificity and sensitivity in a large, single-center cohort, and to evaluate its role in the management of testicular masses.

Patients and Methods

Patients

Between January 1999 and January 2016, 144 of 692 patients scheduled to undergo surgery for suspected testicular cancer had FSE in our tertiary center. The indications for FSE were: testicular pain (thus suspicious for orchitis); bilateral, multiple, small (< 1 cm), or nonpalpable masses; postchemotherapy lesions; or persistent masses suspected to be cancerous harvested in solitary testicle (Table 1). All patients had normal α-fetoprotein, β-human chorionic gonadotropin, and lactate dehydrogenase serum concentrations.

Frozen Section Analysis

All samples were cut in half, if too small they were examined in full. Were carefully oriented in Crymod (Tissue-tek Cryomol; Sakura [Japan]) making sure to evaluate also a testicular pulp, embedded in Killik (Cryostat embedding medium; BioOptica [Italy]) and frozen in isopentane, chilled using liquid nitrogen or, since 2010 using Clini RF Low Temperature Freezer (Bright Instrument Co Ltd [United Kingdom]). For each embedded sample, 3 sections were cut at least at 10-μm intervals and stained with hematoxylin and eosin for microscopic examination. A general senior pathologist (with at least 5 years of experience, after board certification, in surgical pathology and FSE) performed the FSE. Almost all of the lesions were classified as malignant, benign, nontumoral, and nonconclusive. Only a few cases were defined as "suggestive of" or "suspected to be." The remaining frozen section tissues were formalin-fixed, paraffin-embedded and sectioned at 1 level. Two experienced uropathologists reviewed slides of the frozen as well as the permanent sections and confirmed histologic diagnosis and tumor classification according to the World Health Organization classification of tumors of the urinary system and male genital organs.

Table 1 Indications for Frozen Section Examination in Our Cohort of 692 Patients

Number	Indication	Patients, n (%)
1	Non palpable lesions	55 (38.2)
2	Small lesions <1 cm	29 (20.1)
3	Solitary testis	23 (16)
4	Testicular pain	15 (10.4)
5	Multiple	11 (6.9)
6	Post chemotherapy lesion	4 (2.8)
7	Persistent suspicious lesion	3 (2.1)
8	Paratesticular	3 (2.1)
9	Bilateral lesions	2 (1.4)

Total 144 of 692 patients (20.8%).

Surgical Technique

The testicle was exteriorized through a groin incision, and the spermatic cord was clamped with a silicon loop, never exceeding 20 (mean, 15; range 12-20) minutes. A small albugineal incision was carried out to access the lesion, whether palpable, or echographically identified if nonpalpable. The pathologist was aware of the incoming material for FSE to minimize the testicular ischemia time. Meanwhile, the albuginea incision was sutured with a running absorbable suture. The algorithm of the therapeutic approach determined using FSE was orchiectomy in cases with malignant or nonconclusive pathologic features of the mass or testis-sparing surgery (TSS) in all cases with benign or nontumor masses. TSS was performed with additional vaginal resection, before the repositioning of the testis into the scrotum. In the 4 false negative cases a delayed orchiectomy was carried out.

Statistical Analysis

Age, clinical, and pathologic data of 144 patients were retrospectively reviewed after ethical approval of the study by the local committee. Statistical association of FSE data with categorical variables was assessed using the χ^2 test. Agreement between FSE and final pathology findings was assessed using the κ method of interrater agreement; a κ level > 0.7 was considered clinically significant. All P values were 2-sided, and statistical significance was defined as $P < .05$. Statistical analyses were performed with R statistical software (3.2.5. version; www.r-project.org).

Results

In the past 17 years, 144 of 692 candidates (20.8%) for orchiectomy for testicular masses received intraoperative FSE. The average age of the patients was 34 (interquartile range [IQR], 29-42) years. The indications for FSE are reported in Table 1. Approximately two-thirds of patients had small masses (< 2 cm). Four (2.8%) had received chemotherapy (bleomycin, etoposide, cisplatin [BEP] schedule for 4 cycles) for bulky retroperitoneal disease, and testicular exploration was required because of a an intratesticular ultrasound image suspected to indicate cancer. The average diameter of the testicular lesions was 1.5 (IQR, 1-2) cm, including 43 lesions (29.9%) ≤ 1 cm, 66 (45.8%) > 1 cm and ≤ 2 cm, and 35 (24.3%) > 2 cm. Thirteen patients (9%) had more than 2 lesions, including 2 patients (1.4%) with synchronous bilateral lesions.