Re: Testis Sparing Surgery of Small Testicular Masses: Retrospective Analysis of a Multicenter Cohort

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To the Editor: This retrospective study analyzes a large series of 147 patients who underwent testis sparing surgery (TSS) for a small testicular mass. Overall, the authors reported 108 benign tumors, and 21 patients with testicular cancer underwent radical orchiectomy (RO).

There are 2 aspects of this study that we would like to address. In the group of benign tumors the authors included 54 Leydig cell tumors (LCTs) and 6 Sertoli cell tumors. It is noteworthy, especially when counseling our patients, that these tumors are not invariably benign. Around 10% of all LCTs are reportedly malignant, although this rate has been significantly lower in more recent studies.[1,2] In addition, the authors did not report any potential malignant features of LCTs beyond tumor size on pathological examination, such as nuclear atypia, more than 3 mitoses per 10 high power fields, infiltrative borders, necrosis and vascular invasion. Since the median followup in this series was 24 months, malignant forms of LCTs cannot be excluded with certainty.

Furthermore, when testicular cancer was present on frozen section examination, the authors converted the operation to radical orchiectomy. RO is currently the standard of care in these patients since there is a potentially high local recurrence rate. The 2 main factors influencing local recurrence are tumor multifocality and presence of germ cell neoplasia in situ (GCNIS).[3] With GCNIS the risk of germ cell tumor development is around 50% within 5 years.[4] However, in the present study 2 patients were diagnosed with GCNIS associated with benign tumors but did not undergo conversion to RO. In our view the risk of local recurrence is not related mainly to the nature of the primary tumor since the rate of positive margins in TSS is minimal, but rather to the presence of GCNIS. The risk of GCNIS progression if diagnosed during testis sparing surgery should be included in information for patients, even if it is associated with benign disease.

Respectfully,

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Reply by Authors: Recent studies have contributed to improved knowledge regarding LCTs.[5–7] In a retrospective analysis of a large multicenter study of 204 LCT cases in Germany only 5 tumors (2.5%) were malignant.[6] Four of the patients with malignant LCTs presented with systemic disease at diagnosis and metastasis developed during followup in only 1. In another study the risk of malignancy in LCT was correlated with size of the primary tumor, with metastasizing vs nonmetastasizing lesions having a mean diameter

of 4.7 cm vs 2.6 cm ($p=0.008$).[8] Mean diameter of the LCTs in our series was 0.69 cm (range 0.2 to 1.7). In our view such small lesions further reduce the risk of metastasis after tumorectomy.

More importantly, as Bumbasirevic and Bojanic correctly indicate, to define a benign LCT, you need to exclude 1 or more pathological features that may increase the risk of malignancy, ie nuclear atypia, high proliferative index, infiltrative borders, necrosis and vascular invasion.[3] LCTs in our series had none of these features or they would have been considered and classified as malignant neoplasms. The same applies to Sertoli cell tumors, which also had no features of malignancy and had a mean nodule diameter of 0.56 cm (range 0.3 to 0.8). Therefore, according to the recently reported incidences of malignant LCT of less than 5%, performing RO for a LCT might mean an unnecessary sacrifice of testis in more than 95% of the cases, with consequent possible malpractice issues. Given the small size of the LCTs in our study, this rate would have been even higher. For this reason we consider TSS the optimal choice of treatment and strongly recommend it when a diagnosis of LCT is made based on frozen section analysis. The same conclusion was actually reached by Bumbasirevic and Bojanic in their study on this issue.[3]

Regarding GCNIS, we agree with Bumbasirevic and Bojanic that patients who have undergone TSS for a benign or malignant mass should receive further treatment consisting of RO or testicular radiotherapy (RT).[9] As stated in the results section of our article, the 2 patients with GCNIS who underwent TSS and had benign lesions actually decided to postpone adjuvant treatment to preserve fertility and elected active surveillance with close ultrasound followup while being informed of the associated risks. After 24 and 60 months, respectively, no tumor recurrences were noted. We believe that when the other testis is present and healthy, adjuvant RO appears to be a better choice than RT, due to the possible adverse effects of RT on spermatogenesis and hormonal production of the contralateral healthy testis.[9] In patients with monorchidism or bilateral tumors adjuvant RT may alternatively be considered an optimal choice to prevent germ cell tumors while preserving androgen production.

In conclusion, considering the low risk of malignant LCT recurring after TSS and the possible presence of GCNIS (which should be appropriately managed), we strongly support routine adoption of the described approach for small testicular masses, including tumorectomy, frozen section examination and radical orchiectomy or testis sparing surgery based on frozen section results. Preoperative ultrasound determination of nodule size still represents the most accurate way to predict malignancies. Further studies are needed to elucidate this issue and confirm this strategy.

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