grade. However, the clinically important and unanswered question is whether this detrimental effect was the cause of the venous reflux or the end result of it. If the former is the answer, a new era will be open for the etiology of the varicocele under a title of congenital structural smooth muscle deficiency of the varicose veins. I think an analogous experimental study, conducted in a rat model [1] before and after varicocele, which is divided into different follow-up groups, may solve this paradox and determine whether this deficiency is a cause or an end result and the possible detrimental duration effect to the spermatic vein wall under varicocele. Moreover, it was shown that varicocele may have a progressive impact on adolescence testis and appear as atrophy [2].

The age of the study and control groups (no data available about the mean ages) of this study were not correlated because of possible ethical concerns and can be regarded as one of its limitations. It is surprising for me that any structural differences of the normal spermatic vein walls of the young study group and high age control subjects were found in this study. However, it is well known that aging as an independent factor has a detrimental effect on the structure of the vein wall by decreasing compliance, dysfunction of smooth muscle, increasing fibrous activity, and alterations of some molecules against the elasticity of the vein [3–5]. Moreover, it should also be considered that the morphologic alterations in varicose veins become more pronounced with advancing age [5,6]. Despite these facts, depending on the results of the present study, the vein wall of the young study group with varicocele was worse than the older controls without varicocele and this gave rise to the idea that the damage (either cause or end result) related with the varicocele surpasses the effect of aging.

The pathogenesis of varicose veins is still receiving attention in the medical literature and more multidisciplinary clinical/experimental well-designed investigations are needed.

References


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We appreciate the comments by Professor Ayhan Verit and agree with his general request for well-designed multidisciplinary investigations regarding varicocele development.

In our study, there is an age difference between the studied normal population and varicocele patients as discussed in the article. This issue can hardly be overcome for ethical reasons. However, we did not see any histologic changes between normal spermatic veins of the younger population in comparison with normal veins of the older patients. Furthermore, we did not see essential structural differences among varicocele veins of same grade from patients of different ages. Thus, we believe that age does not influence the described structural composition of spermatic veins substantially,
although general age-related alterations in leg veins, particularly regarding vein compliance, have been shown [1]. Apart from this, the age distribution of varicocele in comparison to chronic venous insufficiency also argues for an age-independent primary pathology of varicocele development in comparison to the age-related etiology of varicosis. Even though the structure of leg veins can be compared to that of spermatic veins to a certain extent [2], the cause of varicosis is thought to arise from venous wall dilatation and subsequent valve insufficiency, whereas varicocele origin does not seem to be associated with valve incompetence and still remains a matter of debate [3,4].

Professor Verit further comments on the open question whether the muscular degeneration in varicocele veins is the cause of venous reflux or its end result. In this context he suggests using an established rat model to answer this point of principle [5]. Although we agree that an appropriate in vivo model for the study of varicocele testis would improve our understanding of this venous disease, we are not convinced that the rat would serve as good model because of essential differences in testicular vascular organisation between rats and humans. First of all, we have to evaluate which species offers a venous wall structure in the spermatic cord similar to that in humans.

Finally, our published study indeed provides a new perspective regarding the development of varicocele testis and further studies are needed to clarify whether the demonstrated structural alterations of the wall structure of the spermatic veins are a cause or a result of the varicocele testis.

References


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Re: Alan M. Nieder, Mark S. Soloway and Harry W. Herr. Should We Abandon the FISH Test? Eur Urol 2007;51:1469–71

We read with interest your editorial on “Should We Abandon the FISH Test.” It has always bothered us, as to why a deal of fundamental research done has not translated into any useful genetics-based detection methods for transitional cell carcinoma (TCC). We fully agree that a genetics-based test is still a good while away from finding widespread acceptance. We wish to highlight some points.

Unlike other cancers, multiple lesions of different genetic lineage can coexist in one bladder. Although many genetic alterations are responsible for the genesis, recurrence, and progression of TCC, two main pathways exist viz the p53 and the Rb pathways [1]. Most high-grade lesions have varying degrees of alterations in both. Although the fluorescence in situ hybridization (FISH) test can detect the abnormalities on the p53 pathway, it is incapable of detecting Rb pathway defects. Therefore, lesions caused predominantly due to the latter can go undetected. Moreover, genetic defects can be caused by mutations, deletions, and complete aneuploidy. FISH is known to pick up mainly those defects caused by aneuploidy [2]. Although cytology detects the end result of all genetic alterations (the TCC lesion), FISH detects a set of causative abnormalities. Hence, current genetics-based tests are still nowhere near replacing cytology and cystoscopy. They may, at best, be complementary with other procedures.