Sir,

In the article "Varicocele in Brothers of Patients With Varicocele,\(^1\)" the authors have addressed an interesting clinical question: does having a brother with varicocele expose a person to a higher risk of having the same disease? Nevertheless, this study cannot answer the above question due to the following reasons: First, according to the methods section, this study is case-control. In case-control studies, controls should be disease-free when they are included. The outcome in this study is having varicocele and we see that 10% of controls suffer from this condition. Apparently, the authors have excluded infertile persons from control group, while varicocele is the outcome of interest in this research, but not infertility.

Second, in the exclusion criteria for brothers, it was indicated that those with a positive family history of varicocele were excluded. This is while all of them are brothers of patients with varicocele.

Third, this study cannot be considered a case-control. In a case-control, subjects are grouped according to having/not having the disease, eg having/not having varicocele (Figure). The design seems to be a duplication of the study by Raman and colleagues which appears in reference 13 of the above paper and is a retrospective cohort.\(^2\)

Fourth, the rationale for sample size used is not explained. This can affect the power and interpretation of results.

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REFERENCES

REPLY
Barbarian and Karbakhsh made comments on a paper by Mohammadali Beigi and colleagues (Urol J. 2007;4:33-5) which reflects a common confusion about the study design. Mohammadali Beigi and colleagues compared varicocele frequency and its grading in 3 groups: 56 patients with varicocele, 131 brothers of the first group, and 150 control group without a family history of varicocele. In comparison between the patients with and without a family history of varicocele (as defined by varicocele in brothers), grouping was based on the exposure to the risk factor. Accordingly, it resembled cohort studies. However there was not a real follow-up or longitudinal evaluation from the exposure time to the outcome. More importantly, in cohort studies, all participants must be disease free in the beginning of the course, whereas this assumption is not met in this study. On the other hand, the study could not be a case-control one, as mentioned by Barbarian. Therefore, it was a cross-sectional study, comparing 3 groups of the population with respect to the disease frequency. Despite this fallacy, the results are still valid and not influenced by the design error.
Let me clarify the issue by this example that I usually use for my students. A grocery owner complained from cracked eggs. He believed that a kind of egg-holder shells (shell A) used by one of the factories was mainly responsible for this problem. He had 3 options to evaluate the subject. Firstly, he could count the number of cracked eggs in each box from different factories (a cross-sectional study). Secondly, he could alternatively separate damaged eggs from intact ones and assess the frequency of the shell A in each group (case-control). Thirdly, he had this option to take identical intact eggs and separate them to the shell A and non-A. Then, he had to transport them from the factory to the shop and count the number of damaged eggs in the A and non-A groups (cohort study). Now, think again and tell which approach is more compatible to the published study (Figure)!

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