Letter by Kurnik et al Regarding Article, “Antithrombotic Therapy and Bleeding Risk in a Prospective Cohort Study of Patients With Cerebral Cavernous Malformations”

To the Editor:

In their prospective cohort study of 87 patients with cerebral cavernous malformations (CCMs), Schneble et al1 observed 11 CCM-related bleeds in 9 patients without antithrombotic treatments, whereas there was no bleeding event in 16 patients on antithrombotic treatment. For their analyses, the authors grouped together patients using antiplatelet drugs (n=11) and warfarin (n=5), although these drugs are associated with substantially different risks of intracranial bleeding in the general population, and although the 5 patients on warfarin (31% of the subgroup receiving antithrombotic therapy) contributed disproportionally to patient-years (68%) and lesion-years (99%) during follow-up in this subgroup. The authors conclude that antithrombotic treatment in patients with CCMs does not increase bleeding risk and speculate about a potential protective effect of antithrombotic treatment against bleeding from CCM. We believe that these conclusions are not fully supported by their findings.

Although the bleeding rate of 0% among patients with CCMs on antithrombotic treatment seems reassuring at first, it is impossible to infer that there is no risk of bleeding in this subgroup. The authors do not provide confidence intervals for the observed bleeding rate of 0% among 16 patients (arguably, a more relevant outcome than bleeding rates per CCM). Using Hanley’s simple Rule of 32 as approximation, the 95% confidence interval for the true bleeding rate can be estimated to be 0.0% to 18.8%, and a more precise estimate using the Wilson method3 yields an upper limit of the 95% confidence interval of 19.4%. Thus, the study results do not rule out a much higher and clinically significant true bleeding rate in patients with CCMs on antithrombotic treatment. Similarly, these findings do not provide evidence that the true bleeding rate in patients on antithrombotic treatment is lower than that observed in the subgroup without antithrombotic treatment (9 of 71 patients; 12.7%), especially after adjustment for the confounder previous CCM hemorrhage at presentation.

We, therefore, believe that because of the small sample size, caution is advised when drawing inferences about the safety of antithrombotic treatment in patients with CCMs from the observed findings. Studies with much larger sample sizes are required for a more precise assessment of the true bleeding risk in this population.

Disclosures

None.

Yvonne Schwammenthal, MD
David Tanne, MD
Department of Neurology
Stroke Unit
Sheba Medical Center
Tel Aviv University, Israel

Daniel Kurnik, MD
Institute of Clinical Pharmacology and Toxicology
Sheba Medical Center
Tel Aviv University, Israel


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Yvonne Schwammenthal, David Tanne and Daniel Kurnik

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