A milder clinical course for severe hemophilia B: a true or biased effect?

With great interest we read the article in a recent issue of this journal, in which Melchiorre, Linari et al.[1] compared the number of joint hemorrhages and the severity of arthropathy in patients with severe hemophilia A (HA) and B (HB). We would like to congratulate the authors for their contribution to this ongoing debate, and their effort to expand the discussion with serological and histological properties . We agree with the authors' conclusion that in their sample severe hemophilia B has a milder clinical course than severe hemophilia A. We are however concerned that their patient selection strategy may have been biased towards inclusion of more severely affected hemophilia A patients.

Hemophilia A is five to six times more prevalent than hemophilia B.[2] In this study the A:B ratio differs markedly (2:1). This suggests the inclusion period for HA patients was much shorter than that for HB patients, which could lead to an overrepresentation in the HA group of patients who visit the hospital more regularly. Patients using prophylaxis, with frequent bleedings, or with impaired joint health would therefore be more likely to be included in this study. This selection bias favors the inclusion of the most severe cases, and is more prominent in HA than in HB. More data on selection and inclusion of patients would allow assessment of this potential bias. This would increase compliance to the STROBE guidelines[3] as well.

Our second point is regarding the analysis that leads to the conclusion that, even with similar numbers of hemarthroses, HB patients have less severe joint disease. We agree that the number of bleedings should be taken into account when comparing clinical, serological and imaging findings. We were however surprised by the chosen cutoff values for stratification (<10, 10-50, >50): were these pre-specified? This broad middle category allows heterogeneity of the different patients: was the number of hemarthroses in the two groups comparable? Is the difference between HA and HB still observed when the number of joint bleeds is included as a continuous variable?

To summarize: The research from Melchiorre, Linari et al.[1] is an interesting addition to the debate about the clinical course of HA and HB. More data about their study population could help us to fully estimate the additional value of their findings.

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