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Letters to the Editor

Thrombotic Complications and Cerebrovascular Events in Takotsubo Syndrome: A Systematic Review and Meta-analysis

Despite the reversible nature of left ventricular (LV) dysfunction observed in Takotsubo syndrome (TTS), such condition may be associated with several complications and carries a substantial risk for adverse events. In particular, systemic thromboembolic events are associated with poor outcome and pose specific therapeutic needs.[1] LV thrombus may also interfere with the placement of LV mechanical support devices.

We performed a study-level pooled analysis of published studies reporting the thromboembolic complications of LV thrombosis and cerebrovascular events (CVE) after TTS. Studies with less than 20 patients were excluded. A consort diagram is available in Supplemental Figure S1. Primary endpoints were the occurrence of LV thrombosis and the rate of CVE (stroke or transient ischemic attack), during in-hospital stay or at 30-day follow-up. Pooled estimate rates and 95% confidence intervals (CI) of study outcomes were calculated using a random-effects model. Analyses were conducted with Comprehensive Meta-Analysis v.2 (Biostat Inc, Englewood, NJ).

Twenty-one observational studies (15 retrospective, 6 prospective) were included, for a total of 29,410 patients with TTS. For a summary of studies included in the meta-analysis, see Supplemental Appendix S1. In the pooled analysis, the rate of LV thrombosis among included studies (n = 3823) ranged from 1.3% to 7.7%, with a pooled estimate rate of 1.8% (95% CI: 1.4% to 2.2%); no heterogeneity across studies was found for this endpoint (Q 15.454; I^2 0%; $P_{\text{heterogeneity}} = 0.492$). The rate of CVE ranged from 0.7% to 7.3% among included studies (n = 27,714), with a pooled estimate rate of 2.0% (95% CI: 1.3% to 2.7%); interstudy heterogeneity was high for this endpoint (Q 41.571; I^2 63.92%; $P_{\text{heterogeneity}} < 0.001$). Pooled analyses for the primary endpoints are summarized in Figure 1.

Several factors may favour a hypercoagulability state during TTS, including regional myocardial wall motion abnormalities, systemic inflammation, and endothelial alterations. Although thromboembolic events are well-known complications of TTS, randomized studies on prophylactic anticoagulation in TTS are lacking and only general recommendations or pragmatic therapeutic algorithms have been proposed.[2] Pooling the evidence derived from available observational studies (with a total of 29,410 patients), the rate of LV thrombosis and CVE was approximately 2%. For comparison, an LV thrombosis rate of 5% is reported in anterior acute myocardial infarction[3] and such rate may actually be 25%.[4] Our study has some limitations: first, antithrombotic regimens, patient-level baseline characteristics, and time from TTS onset to the thrombotic complication were not available. Second, heterogeneity across the studies could be partly attributed to different imaging protocols and different diagnostic criteria for LV thrombosis and stroke.

In conclusion, the pooled estimate rate of LV thrombosis in TTS seems relatively low and lower when compared with that of patients with anterior acute myocardial infarction.

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Disclosures

The authors have no relevant conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2018.12.031.

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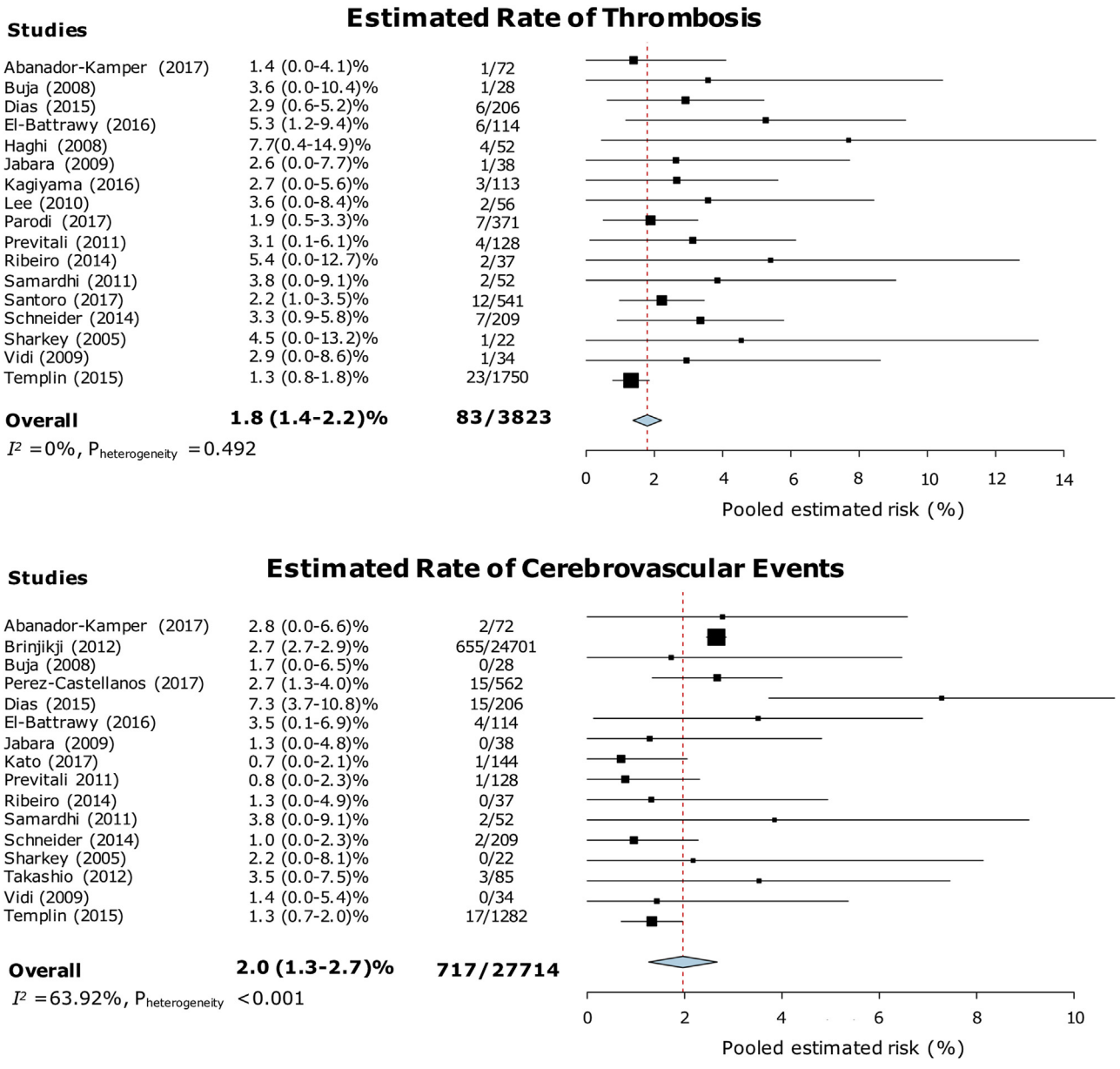

Figure 1. Pooled analyses for the primary endpoints.