RESEARCH LETTER

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Thromboembolic events in peripartum cardiomyopathy: Results from the ESC EORP PPCM registry

Peripartum cardiomyopathy (PPCM) is a form of heart failure (HF) that develops towards the end of pregnancy or within the first months after delivery.[1] Rates of thromboembolism in PPCM are reportedly higher than in many other cardiomyopathies.[2] In the United States, thromboembolism was the most common serious complication in PPCM, occurring in 6.6% of affected women.[3] In the multinational European Society of Cardiology (ESC) EURObservational Research Programme (EORP) PPCM registry, 5% of patients had a thromboembolic event (TE) during the index hospitalization.[4] The peripartum period is a hypercoagulative phase, an evolutionary remnant to minimize postpartum haemorrhage.[5] The combination of left ventricular (LV) dilatation, endothelial injury, immobility, and postpartum hypercoagulable state, may explain the high prevalence of TE in women with PPCM. However, the thromboembolic risk after discharge remains poorly understood. Therefore, we investigated the clinical characteristics and post-discharge outcomes of women hospitalized with PPCM and TE in the prospective observational ESC EORP PPCM registry.[4]

Briefly, between 2012 and 2018, 752 women with PPCM were enrolled prospectively into this ongoing study performed in 51 countries. Eligible women developed HF in the peripartum period with signs and/or symptoms of HF, an LV ejection fraction (LVEF) ≤45%, with no other identifiable cause. The first visit where a specialist diagnosed PPCM was considered baseline. Data on demographics, medical and obstetric history, symptoms and signs of HF, blood tests, and echocardiography were captured at enrolment. The investigators participated on a voluntary basis, with no remuneration. Participating centres managed the approvals of national or regional ethics committees or Institutional Review Boards, according to local regulations. Data on TEs were captured at baseline, and at 6-month and 1-year follow-ups. TEs were defined as any arterial (including ischaemic stroke) or venous thrombosis during the pregnancy or postpartum. LV function was assessed at 6 months and categorized as recovered (LVEF ≥50%), persistent moderate LV dysfunction (LVEF 36–49%), or persistent severe LV dysfunction (LVEF ≤35%). We report characteristics and outcomes according to TE status at baseline. Continuous variables are reported as means and standard deviations or medians and interquartile ranges (IQR), where appropriate. The Kruskal–Wallis test was used to test for differences between non-normal continuous variables. The chi-squared test was used to test for differences between categorical variables. A two-sided *p*-value <0.05 was considered statistically significant. All analyses were performed using STATA 15.0.

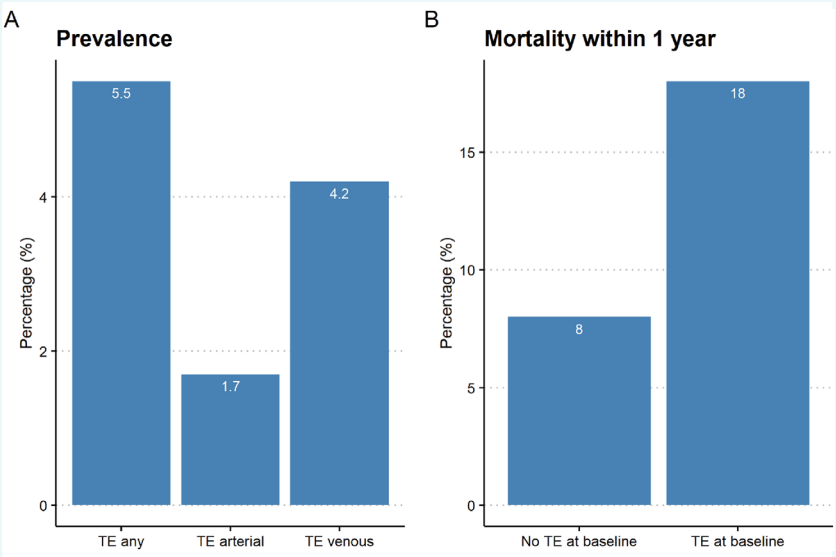

Figure 1 (*A*) Prevalence of thromboembolic events (TE) at baseline and (*B*) mortality within 1 year stratified according to TE at baseline.

Of 749 women with baseline data on TE, 41 (5.5%) had a TE at the time of PPCM diagnosis (*Figure 1A*), 1.1% had a stroke, 1.7% an arterial TE and 4.2% a venous TE. The mean age was 31 ± 6 years, which did not differ between women with and without a TE at baseline ($p = 0.70$). Women with TE were more frequently current or former smokers (21% vs. 13% in women without TEs, $p = 0.19$). None had atrial fibrillation/flutter on the electrocardiogram (vs. 2.4% in women without TEs, $p = 0.33$), and 2.4% (vs. 3.2% in women without TEs, $p = 0.80$) had diabetes. However, these differences were not statistically significant. Stratified to region, 3% of patients from the Asia-Pacific and Africa, 6% from the Middle East and 8% from the European region had a TE event at baseline ($p = 0.074$). In women with TE, the median LVEF was 30% (IQR 20–36%) versus 32% (IQR 25–39%) in those without TE ($p = 0.28$). One-year mortality data were available for 535 (71%) women, both baseline and 1-year TE data for 519 (69%) women and 6-month echocardiographic data for 475 (63%). Five (1%) women had a new (first) TE, and none had a recurrent TE after baseline, up to 1 year. In total, 45 (8%) women died within 1 year. Women with a TE event at baseline had a trend towards higher mortality within 1 year than women without a TE event (18% vs. 8%, $p = 0.064$; *Figure 1B*). In Cox regression analyses, TE events at baseline were not significantly associated with all-cause mortality (hazard ratio [HR] 2.45, 95% confidence interval [CI] 0.97–6.20, $p = 0.051$). The most

common causes of death were HF and stroke (each accounting for 40% of deaths) in women with TE compared with HF in women without TE (41% due to HF, 33% sudden). Rates of LV recovery at 6 months did not differ between the two groups ($p = 0.309$). Data on both baseline treatment and TE events up to 1 year were available in 137 women. Overall, 7 (5.1%) of these women had a TE event at baseline. Among the 137 women, at baseline 15 (10.9%) women were on anticoagulation (2/7 [28.6%] in the TE group, 13/130 [10%] in the no TE group, $p = 0.125$).

In the EORP PPCM registry, women developing TE during the index hospitalization had similar clinical characteristics, echocardiographic parameters and disease severity compared to women not developing TE. This suggests that disease severity is not a strong marker of TE risk in patients with PPCM and highlights the unmet need to identify better risk markers to guide anticoagulation.[6] TEs within 1-year follow-up were uncommon and affected 1% of women. However, there was a statistical trend that women with TE were more likely to die within 1 year than women without TE at baseline. Anticoagulation therapy was not associated with TE during follow-up. However, due to the small sample size and confounding by indication, these results alone should not inform coagulation treatment decisions. However, the low incidence of TE within 1 year in women who did not have TE during the index hospitalization does not support routine long-term treatment with anticoagulants in women with PPCM. Unfortunately, we were unable to investigate the association between bromocriptine treatment and new onset TE due to our limited sample size. Furthermore, almost one third of patients was lost to follow-up or did not have data on TE during follow-up.

In summary, 5% of women with PPCM present with a TE, but the risk of a first TE after initial hospitalization is low (1% in the first year). Having a TE during the initial diagnosis was a marker of poor prognosis.

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Appendix: PPCM

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