Antithrombotic management during percutaneous mechanical circulatory support –

defining the status quo, before agreeing quo vadis

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The incidence of cardiogenic shock (CS) is increasing,\(^1\)-\(^3\) and continues to carry a very high in-hospital mortality rate of 40-50%.\(^4\),\(^5\) Patients often present late, and manifest already a downward haemodynamic spiral of progressive myocardial depression. Percutaneous temporary mechanical circulatory support (pMCS) devices, comprising mainly veno-arterial extracorporeal membrane oxygenation (V-A ECMO) and micro-axial pumps, when available, are increasingly used in an attempt to improve haemodynamic indices and survival in this high-risk group.

However, the effectiveness of pMCS is encumbered by the double-edged sword of device-associated thrombotic complications, due mainly to platelet and contact pathway activation by the artificial circuit on the one hand, and the risk of major bleeding complications due to anticoagulation and shear-induced von Willebrand syndrome, on the other.

In the real world, complications of pMCS tend to be higher than in carefully conducted clinical trials. However, even in the ECLS-SHOCK trial in patients with acute myocardial infarction (AMI) complicated by CS, nearly 1 in 4 patients receiving VA-ECMO experienced moderate-to-severe bleeding complications, compared to only 9.6% of those treated without MCS (relative risk [RR] 2.44; 95% confidence interval [CI], 1.50 to 3.95), with pMCS increasing the rate of vascular complications necessitating intervention (11.0%
vs 3.8%, RR 2.86; 95% CI, 1.31 to 6.25), as well as the rate of stroke or systemic embolization (3.8% vs. 2.9%, RR 1.33; 95% CI, 0.47 to 3.76).\(^6\)

The recently published DanGer Shock trial, comparing the use of a microaxial flow pump (Impella CP) against no pMCS in patients with AMI-related CS, showed that use of a microaxial flow pump led to a lower risk of all-cause death at 180 days.\(^7\) Whilst this will undoubtedly lead to an increase in the use of Impella support in these patients, the reported device-related complication rate is sobering, with the number needed to harm with microaxial-flow-pump being only 6 patients. The composite safety end-point occurred in 24% of patients in the microaxial-flow-pump group and only 6.2% in the standard-care group (RR 4.74; 95% CI, 2.36 to 9.55). The relative risk of the microaxial-flow-pump support compared to standard-care for the exploratory endpoints of moderate or severe bleeding was 2.06 (95% CI, 1.15 to 3.66), for limb ischemia 5.15 (95% CI, 1.11 to 23.84), for renal-replacement therapy 1.98 (95% CI, 1.27 to 3.09) and for stroke 3.9 vs. 2.3% (RR 1.75, 0.5-6.01).

It is apparent that the delicate balance between bleeding and thrombosis in patients with CS treated with pMCS leads to a number of complications, which in part relate to the choice, intensity and monitoring of antithrombotic therapy. Therefore, there is an important unmet need to optimise care to minimise these relatively frequent complications and improve outcomes in these patients.

To do so, the first step is to actually understand the status quo: how are these patients currently managed in terms of (i) choice, intensity and number of antithrombotic
medications, (ii) monitoring the effectiveness of anticoagulation, (iii) monitoring for bleeding and (iv) transfusion requirements.

In this issue of the EHJ-ACVC, Vandenbriele, Van Edom and colleagues publish the results of an international survey to address these important questions, under the auspices of the European Society of Cardiology. The online survey of antithrombotic practices and transfusion thresholds received feedback from 99 centres based across 26 European countries. The survey reveals very significant variation in antithrombotic practices, with only 40% of respondents having both an anticoagulation and transfusion protocol in their centre. This contrasts with ELSO surveys on ECMO in 2013 and 2021, in predominantly paediatric and neonatal ICUs, where 72% and 79% centres had both protocols. Notably, 72.4% of respondents adhered to locally established anticoagulation protocols, with unfractionated heparin (UFH) being the predominant anticoagulant (Impella 97.0% and V-A ECMO: 96.1%). Only a minority, 10.8% and 14.5%, respectively, utilized anti-factor-Xa assay with activated partial thromboplastin time in parallel for UFH monitoring during Impella and V-A ECMO support. Anticoagulant targets varied across institutions, as did the response to UFH target overshooting. Following an ACS presentation, even in patients who had not undergone percutaneous coronary intervention (PCI), 54.0% and 42.7% of respondents administered dual antiplatelet therapy (DAPT) during Impella and V-A ECMO support, increasing to 93.7% and 84.0% after PCI. The threshold for blood and platelet transfusion were also varied, and some 40% of respondents, despite the known high bleeding risk and the prevalence of DAPT use (in addition to UFH), would only give platelet transfusion if the platelet count fell below $40 \times 10^9/l$. 
The paper highlights three important areas for improvement. Firstly, the lack of standardised protocols and targets when monitoring anticoagulant effect in patients on pMCS, in terms of the tests used (or available) and the frequency of monitoring, including the use of tests to detect bleeding. Secondly, the lack of standardised protocols for antithrombotic medication, including lack of protocols for anticoagulant and antiplatelet therapy (including the use of single or dual antiplatelet therapy and its intensity). It would appear that many centres are directly translating “routine” guidelines for antiplatelet medication in patients with ACS to this high-risk cohort, in which evidence for “triple therapy” (combination of DAPT and anticoagulation) is lacking. Furthermore, since by definition, all patients on pMCS should be considered high bleeding risk, in all but the very highest ischaemic risk patients, the guidelines for “de-escalation” to minimise the duration and intensity of antiplatelet therapy should be followed. We would advocate individual assessment of ischaemic risk in ACS patients that should take into account the nature and complexity of the coronary disease and the technical details of any recent revascularisation, as well as concomitant ischaemic risk factors. Although not formally evaluated exclusively in the setting of CS, there is a growing body of data that de-escalation of DAPT intensity or duration can significantly reduce bleeding without increasing ischaemic risk. Finally, the wide variability in the approach to the management of blood and platelet transfusions is concerning and there is no reason why this should not be standardised.

Whilst some recommendations have previously been proposed to mitigate against bleeding and ischaemic risks in this cohort, it is clear that these are not informing...
routine care. Furthermore, the management of such patients by a combination of specialists that include intensivists, interventional cardiologists, and the heart failure team, with or without expert haematology input, can result in differing expertise with possibly conflicting approaches to the management of antithrombotic therapy and transfusion thresholds.

Since there is an absence of evidence base for treatment and monitoring of these patients, the first step is to agree to risk assess individual patients for the magnitude of bleeding and ischaemic risks, to agree standardised pathways for monitoring and treatment, and then to work towards developing pathways to provide personalised care.

Doctors Vandenbriele, Van Edom and colleagues should be congratulated for this important work, which highlights the significant variation in clinical practice and is hopefully, the first step in translating this into recommendations to standardise antithrombotic monitoring and treatment, and minimise complications in this very high-risk group.

References


