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ORIGINAL SCIENTIFIC PAPER
Thromboembolic Diseases

European practices on antithrombotic management during percutaneous mechanical circulatory support in adults: a survey of the Association for Acute CardioVascular Care of the ESC and the European branch of the Extracorporeal Life Support Organization

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Aims

Bleeding and thrombotic complications compromise outcomes in patients undergoing percutaneous mechanical circulatory support (pMCS) with veno-arterial extracorporeal membrane oxygenation (V-A ECMO) and/or microaxial flow pumps like Impella™. Antithrombotic practices are an important determinant of the coagulopathic risk, but standardization in the antithrombotic management during pMCS is lacking. This survey outlines European practices in antithrombotic management in adults on pMCS, making an initial effort to standardize practices, inform future trials, and enhance outcomes.

Methods and results

This online cross-sectional survey was distributed through digital newsletters and social media platforms by the Association of Acute Cardiovascular Care and the European branch of the Extracorporeal Life Support Organization. The survey was available from 17 April 2023 to 23 May 2023. The target population were European clinicians involved in care for adults on pMCS. We included 105 responses from 26 European countries. Notably, 72.4% of the respondents adhered to locally established anticoagulation protocols, with unfractionated heparin (UFH) being the predominant anticoagulant (Impella™:

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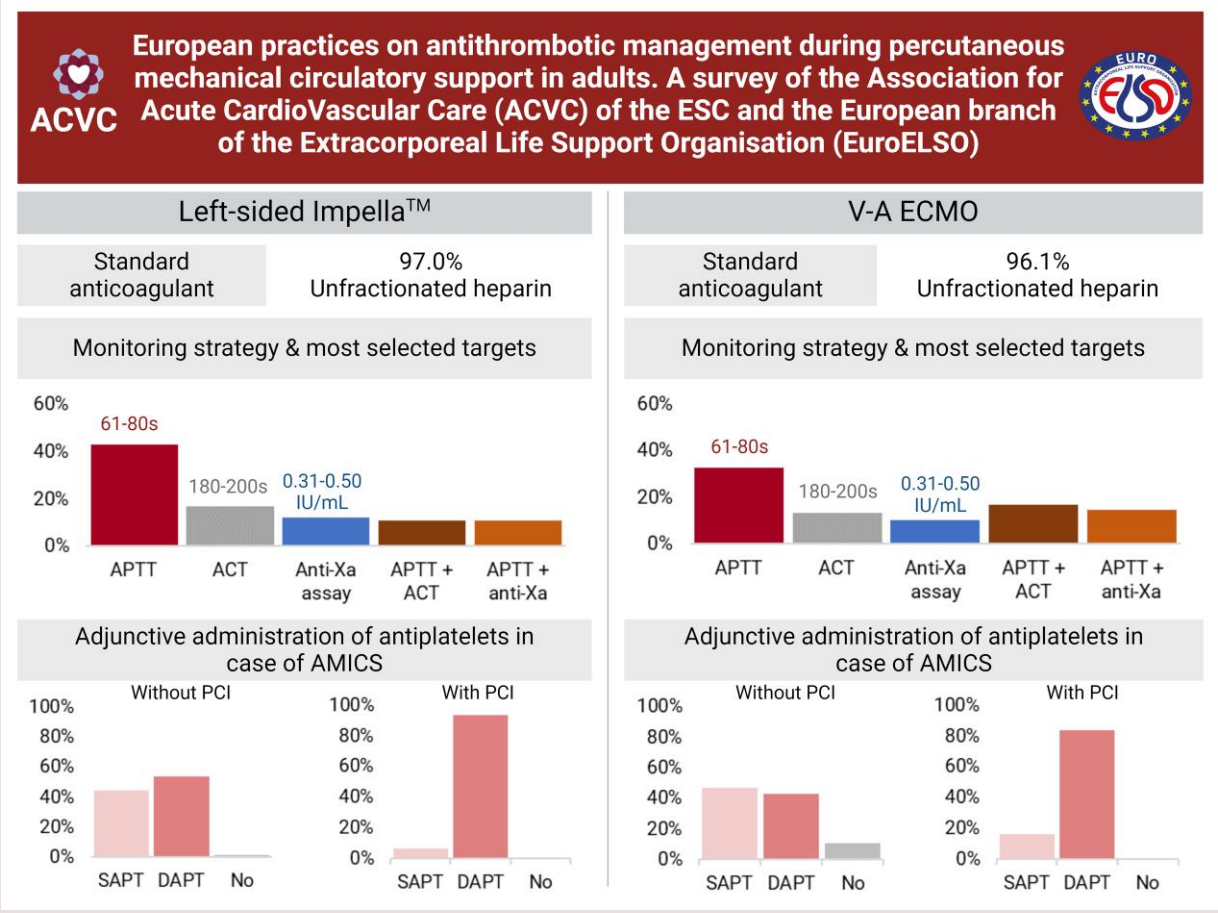
97.0% and V-A ECMO: 96.1%). A minority of the respondents, 10.8 and 14.5%, respectively, utilized the anti-factor-Xa assay in parallel with activated partial thromboplastin time for UFH monitoring during Impella™ and V-A ECMO support. Anticoagulant targets varied across institutions. Following acute coronary syndrome without percutaneous coronary intervention (PCI), 54.0 and 42.7% were administered dual antiplatelet therapy during Impella™ and V-A ECMO support, increasing to 93.7 and 84.0% after PCI.

Conclusion Substantial heterogeneity in antithrombotic practices emerged from participants' responses, potentially contributing to variable device–associated bleeding and thrombotic complications.

Graphical Abstract



AMICS, acute myocardial infarction–induced cardiogenic shock; PCI, percutaneous coronary intervention; SAPT, single antiplatelet therapy; DAPT, dual antiplatelet therapy; APTT, activated partial thromboplastin time; ACT, activated clotting time; anti-Xa assay, heparin anti-factor-Xa assay; V-A ECMO, veno-arterial extracorporeal membrane oxygenation.

Keywords Anticoagulation • Antiplatelets • Mechanical circulatory support • ECMO • Bleeding

Introduction

The use of percutaneous mechanical circulatory support (pMCS) including veno-arterial extracorporeal membrane oxygenation (V-A ECMO) and/or microaxial flow pumps, such as the Impella™ device (Abiomed, Danvers, MA, USA), is seeing an increase during cardiogenic shock (CS).[1] Despite enhanced device design, intensive care unit (ICU)-related complications drive a high mortality rate (50%), significantly driven by coagulopathic events.[2–6] Analyses, including the recent ECLS-SHOCK trial, show elevated bleeding events.[7–10] The precarious haemostatic balance during pMCS for CS is the consequence of a complex multi-directional interplay of several factors influencing haemostasis. This includes the underlying disease and the need for anticoagulation to counteract the activation of the contact pathway by artificial device surfaces and additional pro-thrombotic platelet and neutrophil activation.[11,12] Furthermore, patients on

pMCS in the setting of acute myocardial infarction may receive adjunctive (dual) antiplatelets, possibly increasing the existing bleeding risk. Antithrombotic practices are an important determinant of the coagulopathic risk but rely mostly on experience rather than evidence, since validated guidelines for patients on pMCS during CS do not exist. Indeed, none of the mentioned retrospective trials reported the anticoagulant agents used, the monitoring strategies, nor the anticoagulation target.

Previously, several surveys were performed in the USA. In 2013, the Extracorporeal Life Support Organization (ELSO) performed an international survey to determine practices of anticoagulation in patients supported on ECMO (both V-A and veno-venous) for various indications.[13] A similar survey was performed in 2021 for paediatric physicians in the USA.[14] Additionally, in 2019, a survey on anticoagulation management during Impella™ support was performed in the USA.[15] All previous surveys revealed highly variable anticoagulation practices across centres. The present survey aims to map the different practices and variations in antithrombotic treatment between European pMCS centres for both V-A ECMO and Impella™ in order to serve as a basis to standardize practices, for the development of future trials and ultimately for the improvement of outcomes in this precarious patient population.

Methods

This survey was disseminated through an online newsletter to the European Society of Cardiology members, particularly to those associated with Acute CardioVascular Care (ACVC; non-cardiologists in intensive care and cardiologists in acute cardiac care), and through the European branch of the ELSO (EuroELSO) newsletter. The survey was also promoted on social media channels (Twitter, Facebook, LinkedIn, Med-Mastodon, and Instagram) in organizations as well as on-site during the 11th EuroELSO Congress in Lisbon (26 April 2023 to 29 April 2023). It was accessible online via SurveyMonkey (Version 4.1.1 San Mateo, CA, USA) between 17 April 2023 and 23 May 2023. Ethical approval was obtained from the host institution (Ethics Committee Research UZ/KU Leuven, S66716). Scientific committees from both ACVC and EuroELSO approved the content of the questionnaire, which was composed by all co-authors (see Supplementary material online, *Supplement S1*). No individual patient data or outcomes were collected. Participation in the survey was voluntary; respondents were free to complete their affiliation and/or contact details if they wished to be included as contributors. Redundant responses coming from the same centre and same department were compared, and the most complete response was retained. When multiple responses were received from different departments at the same centre (e.g. cardiology and anaesthesiology), all responses were retained.

Our primary goal was to analyse European practices. Since we also received 81 completed surveys from non-European countries, we compared European with worldwide practices as well. All presented data in the 'Results' section concerns data from European practices, except if specifically stated otherwise. The number of respondents per question is represented in the analysis as the varying denominator for each question. Findings are presented as descriptive statistics, which are in the form of histograms and pie charts. Graphs were crafted using Microsoft Excel and BioRender.

Survey design

The survey included 15 multiple-choice questions on general antithrombotic and transfusion management, 19 questions on antithrombotic practices during Impella™ support, and 16 on V-A ECMO support. In both the Impella™ and the V-A ECMO sections, these questions included four hypothetical cases in which we asked participants about their actions concerning the anticoagulant and the antiplatelet therapies during pMCS. The four scenarios encompassed mild bleeding or severe bleeding in patients admitted for acute myocardial infarction–induced CS (AMICS) with or without recent PCI. More information on the composition of the survey can be found in the Supplementary material online, *Supplement S2*.

Results

Anticoagulation management

We received 111 responses from 26 European countries. No anonymous responses were noted. Six duplicates were removed as coming from the same department at the same centre; thus, 105 responses from 99 different centres were included in the European results (*Figure 1A*). In 72.4% (76/105) of the European respondents' institutions, a standardized local anticoagulation protocol is present, and in 40.0% (42/105), both anticoagulation and blood transfusion protocols are established (*Figure 1B*). Left-sided Impella™ support is available in 73.3% (77/105) of the respondents' institutions. Left-sided Impella™ support is also used by 71.2% (47/66) for elective procedures. Veno-arterial extracorporeal membrane oxygenation support with peripheral cannulation is available in 88.0% (81/92) of the respondents' institutions (*Figure 1C*). Information on the origin of surveys, the presence of protocols, and the average numbers of annual pMCS runs per device in non-European countries can be found in the Supplementary material online, *Supplement S3*.

Unfractionated heparin (UFH) is the most used anticoagulant during Impella™ (97.0%; 64/66) and V-A ECMO (96.1%; 74/77) support in Europe. The direct thrombin inhibitor argatroban is the preferred alternative in case of confirmed heparin-induced thrombocytopenia (HIT) for Impella™ (52.3%; 34/65) and V-A ECMO (50.7%; 39/77; *Figure 2*). Similarly, for the non-European group, UFH is the most frequently used anticoagulant agent. However, in case of HIT, bivalirudin is preferred over argatroban in non-European centres (see Supplementary material online, *Supplement S4*). In Europe, the purge solution during Impella™ support is most frequently based on UFH, with a concentration of 25 IU (42.9%; 27/63) or 50 IU (41.3%; 26/63) UFH per millilitre glucose 5% solution. A bicarbonate-based purge solution (BBPS) as a standard purge is reported by 1.6% (1/63) of the European respondents. In the event of overshooting the UFH target, the preferred next step by the respondents is lowering the UFH concentration in the purge (85.3%; 52/61) rather than switching to BBPS (13.1%; 8/61). In the non-European group, a UFH-based purge solution is used in 82.1% (23/28), and BBPS is the standard for 7.1% (2/28) of the respondents. The majority of respondents does not alter their anticoagulation management in the case of a combined Impella™ plus V-A ECMO approach (ECMELLA; 83.8%; 62/74). In the non-European group, 29/44 (65.9%) respondents indicate that they do not change the anticoagulation strategies for ECMELLA.

An anticoagulation protocol for UFH titration based on activated partial thromboplastin time (APTT) alone is the most common practice in Europe either for Impella™ (43.1%; 28/65) or for V-A ECMO (32.9%; 25/76), although a considerable heterogeneity for UFH monitoring exists between centres. The most frequent APTT target that participants aim for during UFH anticoagulation is 61–80 s for both devices (Impella™: 50.8%; 32/63 and V-A ECMO: 48.0%; 36/75). Notably, 16.9% (11/65) and 13.2% (10/76) indicate measuring only activated clotting time (ACT) during UFH anticoagulation on Impella™ and V-A ECMO support, respectively, and the most selected target is 180–200 s (29.0%; 18/62 and 33.3%; 25/75). There is no specific ACT target for 50% (31/62) and 45.3% (34/75) of the respondents for Impella™ and V-A ECMO, respectively. In Europe, 12.3% (8/65) and 10.5% (8/76) of the respondents rely on anti-Xa alone for UFH titration during Impella™ and V-A ECMO. Activated partial thromboplastin time with anti-Xa in parallel is the preferred UFH titration option for 10.8% (7/65) and 14.5% (11/76) of the respondents for Impella™ and V-A ECMO, respectively. The preferred anti-Xa target during Impella™ support is 0.31–0.50 U/mL (Impella™: 34.9%; 22/63 and V-A ECMO: 42.1%; 32/7). An overview of the most frequently used assays for UFH anticoagulation monitoring and the most frequently indicated UFH anticoagulation targets in the European centres are

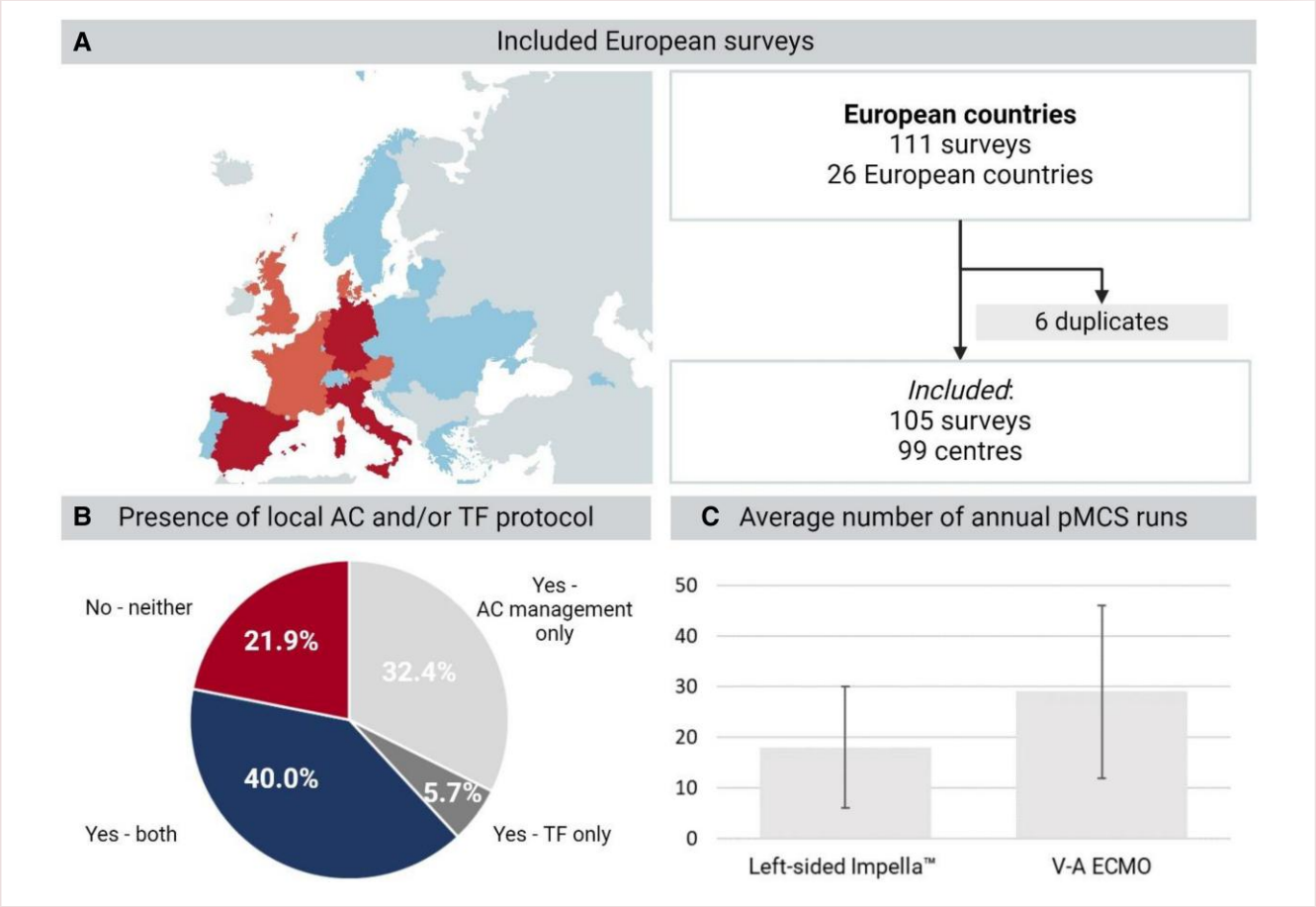


Figure 1 (*A*) The origin of European responses included in the analysis. Responses coming from the same department at the same centre were excluded. The dark red colour indicates >8 responses, light red colour indicates 4–8 responses, and blue colour indicates 1–3 responses per country. (*B*) The local presence/availability of a standardized anticoagulation and/or blood transfusion protocol. In 72.4% (76/105) of the European centres, a standardized anticoagulation protocol is available. A total of 27.9% (29/105) of the European centres indicate that they do not have a local anticoagulation protocol available. (*C*) The average number (and standard deviation) of percutaneous mechanical circulatory support runs per year in Europe is 18 (±12) for Impella™ (66 respondents) and 29 (±17) for veno-arterial extracorporeal membrane oxygenation (77 respondents). AC, anticoagulation; TF, transfusion.

shown in *Figure 3* (Impella™) and *Figure 4* (V-A ECMO). In the Supplementary material online, *Supplement S5* (Impella™) and the Supplementary material online, *Supplement S6* (V-A ECMO), a summary of the non-European data can be found. Unfractionated heparin anticoagulant targets are altered depending on the P-level of Impella™ support by 23.4% (15/64) of the European respondents. However, 59.2% (45/76) of the respondents alter targets based on the V-A ECMO flow level. Similarly, in the non-European group, 34.5% (10/29) and 63.8% (30/47) of the respondents indicate changing the UFH anticoagulant target based on P-levels (Impella™) and flow levels (V-A ECMO), respectively. A 6 h interval for anticoagulation monitoring is the most selected European option for both Impella™ (45.3%; 29/64) and V-A ECMO (38.2%; 29/76). This is comparable in the non-European group (Impella™: 12/29; 41.4% and V-A ECMO: 23/47; 48.9%).

Antiplatelet management for concomitant ischaemic conditions

In AMICS, 54.0% (34/63) and 93.7% (59/63) of the respondents add dual antiplatelet therapy (DAPT) to UFH without or with prior PCI during Impella™ support, respectively. During V-A ECMO support for AMICS, 42.7% (32/75) of the respondents use DAPT in the absence of PCI and 84.0% (63/75) in the case of PCI treatment. Additionally, 1.6% (1/63, Impella™) and 10.7% (8/75, V-A ECMO) of the respondents indicate not adding antiplatelet therapy in case of AMICS without PCI. There are no respondents who do not add antiplatelets in case of PCI-associated AMICS supported by Impella™ or V-A ECMO (*Figure 5*). Non-European antiplatelet therapy practices were comparable with European practices; a slightly reduced tendency to use DAPT in case of Impella™ support after PCI (93.7% in Europe vs. 79.3% in other countries) was noted (see Supplementary material online, *Supplement S7*).

Haematological monitoring and bleeding/transfusion management

Thresholds for transfusion or administration of blood products [packed red blood cells (pRBCs), platelets, fresh frozen plasma (FFP), cryoprecipitate, and antithrombin (AT)] in the absence of acute bleeding vary substantially across centres (*Figure 6*). The most frequently used products for bleeding control in the European group are FFP (86.7%; 91/105), platelets (67.6%; 71/105), fibrinogen (62.9%; 66/105),

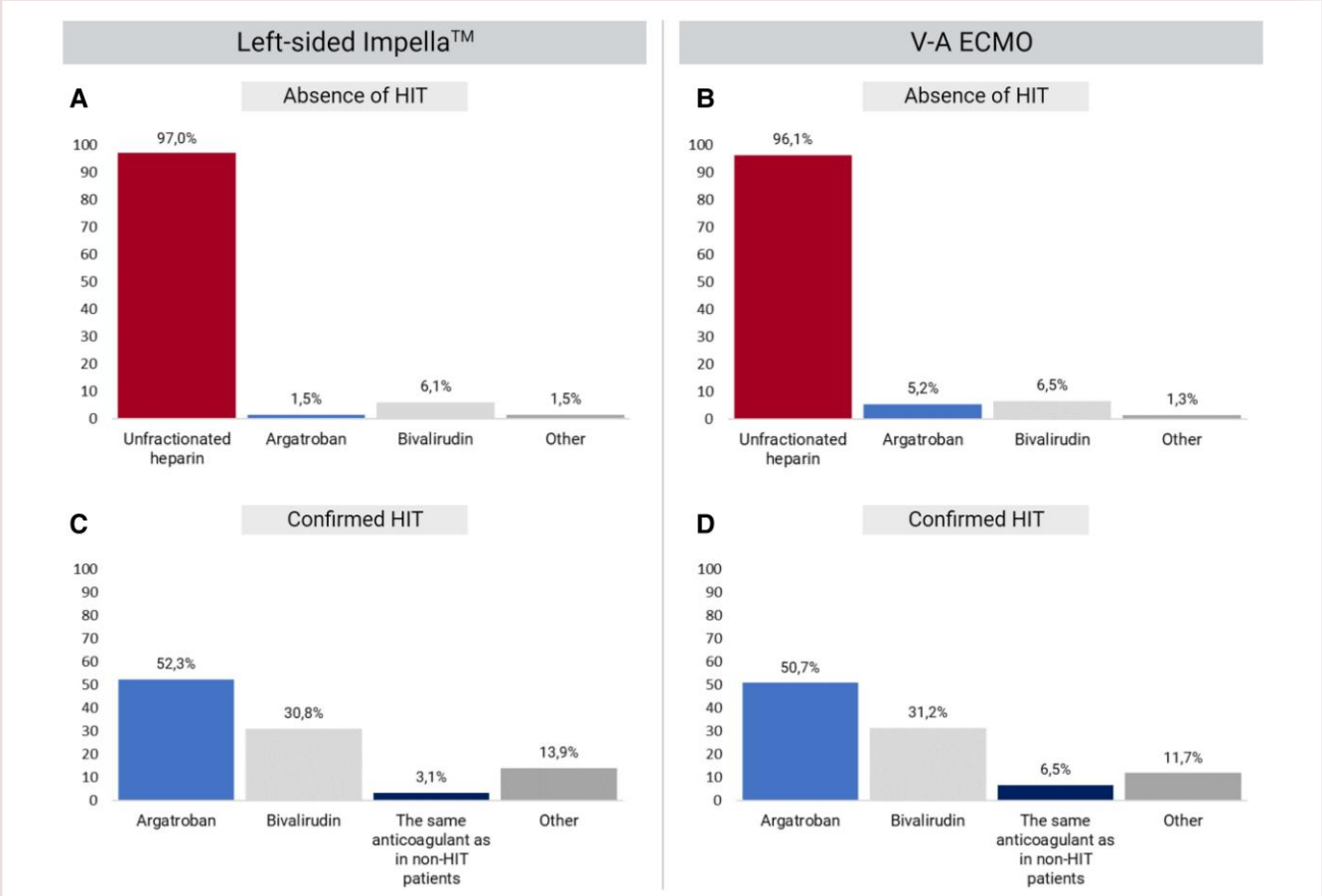


Figure 2 Standard anticoagulant therapy during Impella™ or veno-arterial extracorporeal membrane oxygenation support in the European centres in the presence or absence of confirmed heparin-induced thrombocytopenia. (*A* and *B*) For Impella™ and veno-arterial extracorporeal membrane oxygenation, unfractionated heparin is the most frequently used anticoagulant in the absence of heparin-induced thrombocytopenia. (*C* and *D*) In case of confirmed heparin-induced thrombocytopenia, argatroban is preferred over bivalirudin in most European centres, during Impella™ and veno-arterial extracorporeal membrane oxygenation support.

intravenous tranexamic acid (61.0% 64/105), and prothrombin complex concentrates (54.3%; 57/105). Topical usage of tranexamic acid (22.9%; 24/105) or adrenalin (21.9%; 23/105), activated factor VII (17.1%; 18/105), or recombinant von Willebrand factor (13.3%; 14/105) is less frequent. In the non-European group, FFP is the most frequently used blood product (78.2%; 61/78).

All of the European (105/105) and 98.7% (75/76) of the non-European respondents (*Figure 7A*) measure platelet counts in pMCS patients on a daily basis. Fibrinogen is monitored routinely by 92.2% (95/103) of the European respondents; this is 75.3% (58/77) in the non-European group. Haemolysis is monitored routinely by 82.5% (85/103) of the European respondents, most frequently by lactate dehydrogenase (LDH) and bilirubin, rather than haptoglobin or plasma-free haemoglobin (pfHb) (*Figure 7B*). In the non-European group, haemolysis is routinely measured by 78.7% (59/75); the used markers are, in order of preference, as follows: LDH, bilirubin, pfHb, and haptoglobin. D-dimers are routinely monitored by 71.8% (74/103) of the European respondents, whereas this is only routine practice for 44.6% (33/74) of the non-European respondents.

Next, we presented some hypothetical cases concerning patients on left-sided Impella™ or V-A ECMO support inside or outside the setting of acute percutaneous coronary intervention (PCI) and suffering from mild or severe bleeding [Bleeding Academic Research Consortium (BARC) score below 3 vs. 3 or higher, respectively]. We asked survey participants what action concerning the antithrombotic therapy they would take. Regarding the anticoagulation and antiplatelet therapy in case of severe bleeding with or without PCI, most European respondents prefer total cessation of therapy, both for Impella™ and for V-A ECMO support (*Figure 8*). In case of mild bleeding (BARC <3), anticoagulation is mostly continued, whether or not with a reduced target. Concerning the antiplatelet therapy during Impella™ and V-A ECMO support in case of mild bleeding, a continuation of antiplatelet therapy is preferred. In all scenarios, 20.0–39.0% indicate that the decisions regarding antithrombotic therapy are made on a case-by-case basis without standardized protocols (*Figure 8*). Importantly, none of the case answer options was selected by more than 50% of the respondents—except for the continuation of antiplatelet therapy in case of mild bleeding and recent PCI in case of Impella™ (58.6%; 41/70) or V-A ECMO (55.7%; 49/88) support—further stressing the large heterogeneity in responses (*Figure 8*).

Discussion

Short-term mortality in the setting of CS remains as high as 50%. Despite the increased availability of pMCS devices, mortality improvement is

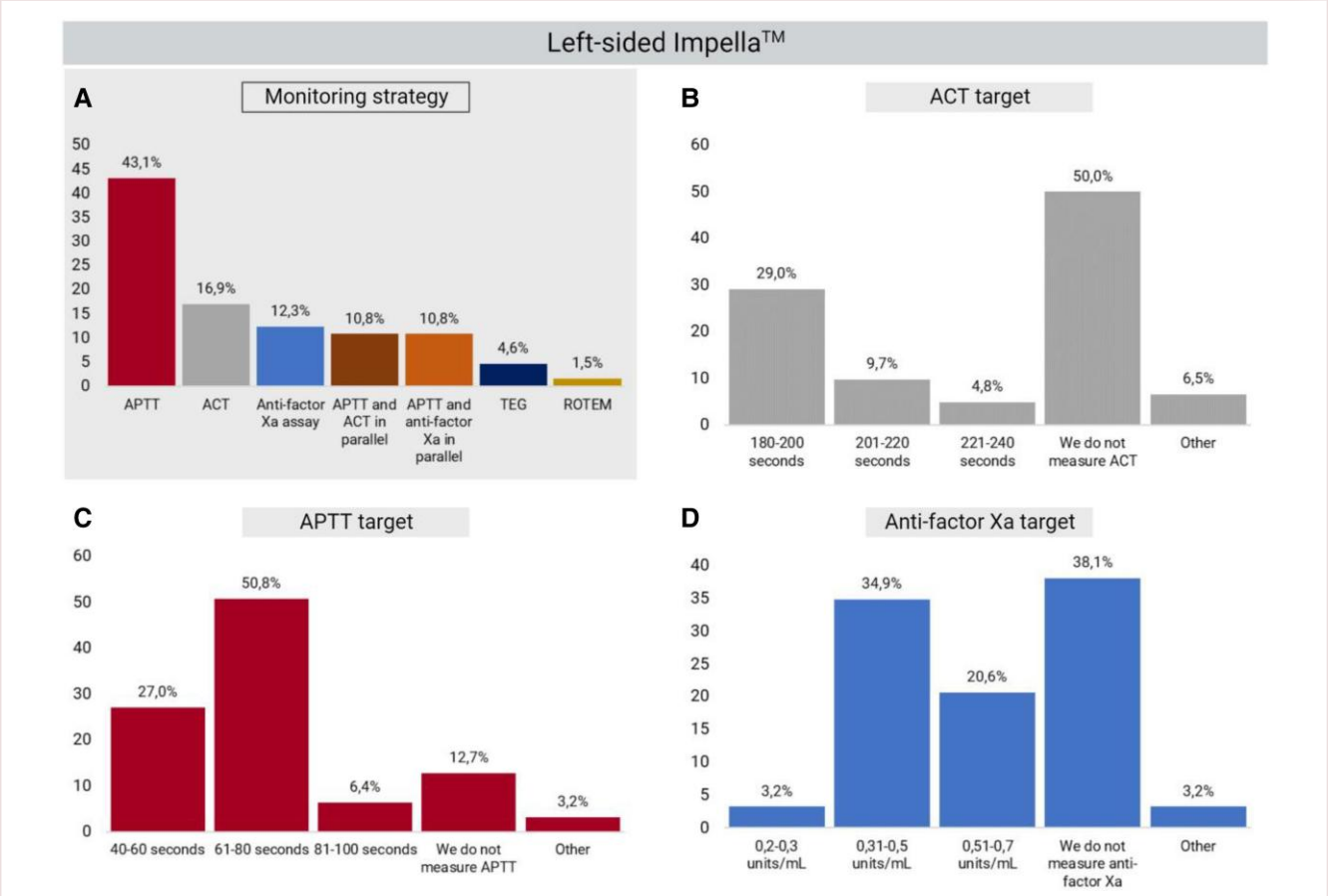


Figure 3 European unfractionated heparin anticoagulation monitoring practices and their targets during left-sided Impella™ support. (*A*) An assay based on which unfractionated heparin dosing is guided. (*B*) Activated clotting time targets for unfractionated heparin therapy. (*C*) Activated partial thromboplastin time target for unfractionated heparin therapy. (*D*) Anti-factor-Xa target for unfractionated heparin therapy. Single testing by activated partial thromboplastin time is the most frequently used assay to guide the unfractionated heparin anticoagulation management (43.1%; 28/65), with preferred target 61–80 s (50.8%; 32/63). ROTEM, rotational thromboelastometry; TEG, thromboelastography.

elusive due to a significant burden of pMCS-related complications. The ECLS-SHOCK trial recently confirmed this, highlighting 23.4% moderate-to-severe bleeding complications, strongly impacting outcomes in AMICS.[5,6,10] Therefore, the antithrombotic management is considered the Achilles' heel of pMCS management and outcome.

This survey reveals significant variation in antithrombotic practices among European centres and globally. Importantly, the survey shows a lack of standardized protocols, as only 40% of the respondents have both an anticoagulation and transfusion protocols. This contrasts with ELSO surveys on ECMO in 2013 and 2021, where 72 and 79% had both protocols.[13,14] However, these responses included very few adult-only ICUs (0 and 3%, respectively), suggesting that protocols might be more prevalent in neonatal/paediatric ICUs.[13,14]

Unfractionated heparin remains the primary anticoagulation choice (Impella™: 97.0%, V-A ECMO: 96.1%), akin to ELSO findings in 2013 (100%) and 2021 (94%).[13,14] Despite the advantages of UFH such as low cost, widespread availability, short half-life, reversibility, and ample experience, its usage can be very challenging due to an unpredictable dose–response effect (depending on AT and long vs. short heparin chain variation). Therefore, direct thrombin inhibitors (DTIs) like bivalirudin and argatroban are introduced as alternative anticoagulants, especially in the setting of ECMO.[16] Nevertheless, the use of DTIs is rarely a standard practice (Impella™: 7.6% and V-A ECMO: 11.7%) and is mainly restricted to HIT patients. Limitations of DTIs are their renal (bivalirudin) and hepatic (argatroban) clearance, the limited availability of specific monitoring strategies, the lack of an antidote, and higher cost. Importantly, there are no comparative trials of DTIs vs. UFH in pMCS patients, as highlighted by the ELSO in their 2021 anticoagulation guidelines.[17] During Impella™ CP support, most (84.1%) respondents report on the use of a UFH-based purge, similar to the Impella™ survey from 2019 (93.7%; 59/63). Recently, BBPS as an alternative purge fluid received a CE-label for the Impella™ CP in Europe. Bicarbonate works through chelation of calcium and neutralization of the acidic pH of dextrose solution, thereby suppressing fibrin formation.[18] Additionally, sodium bicarbonate has a local effect limiting platelet activation and adhesion.[19] The advantage of BBPS is supposed to be three-fold; first, it has no systemic effects as it is rapidly diluted and buffered in the circulation; secondly, it simplifies the anticoagulant management since it eliminates the variable dosages of UFH delivered by the purge system, and thirdly, it can be used in patients with a contraindication for heparin (e.g. HIT). Recently, in a single-centre retrospective study of CS patients on Impella™ support, a lower bleeding rate and a lower rate of supratherapeutic UFH anticoagulation levels were shown in patients receiving BBPS compared with controls receiving UFH-based purge solution with a similar incidence of purge thrombosis.[20] All these findings endorse the usage of BBPS as a growing alternative to a UFH-based

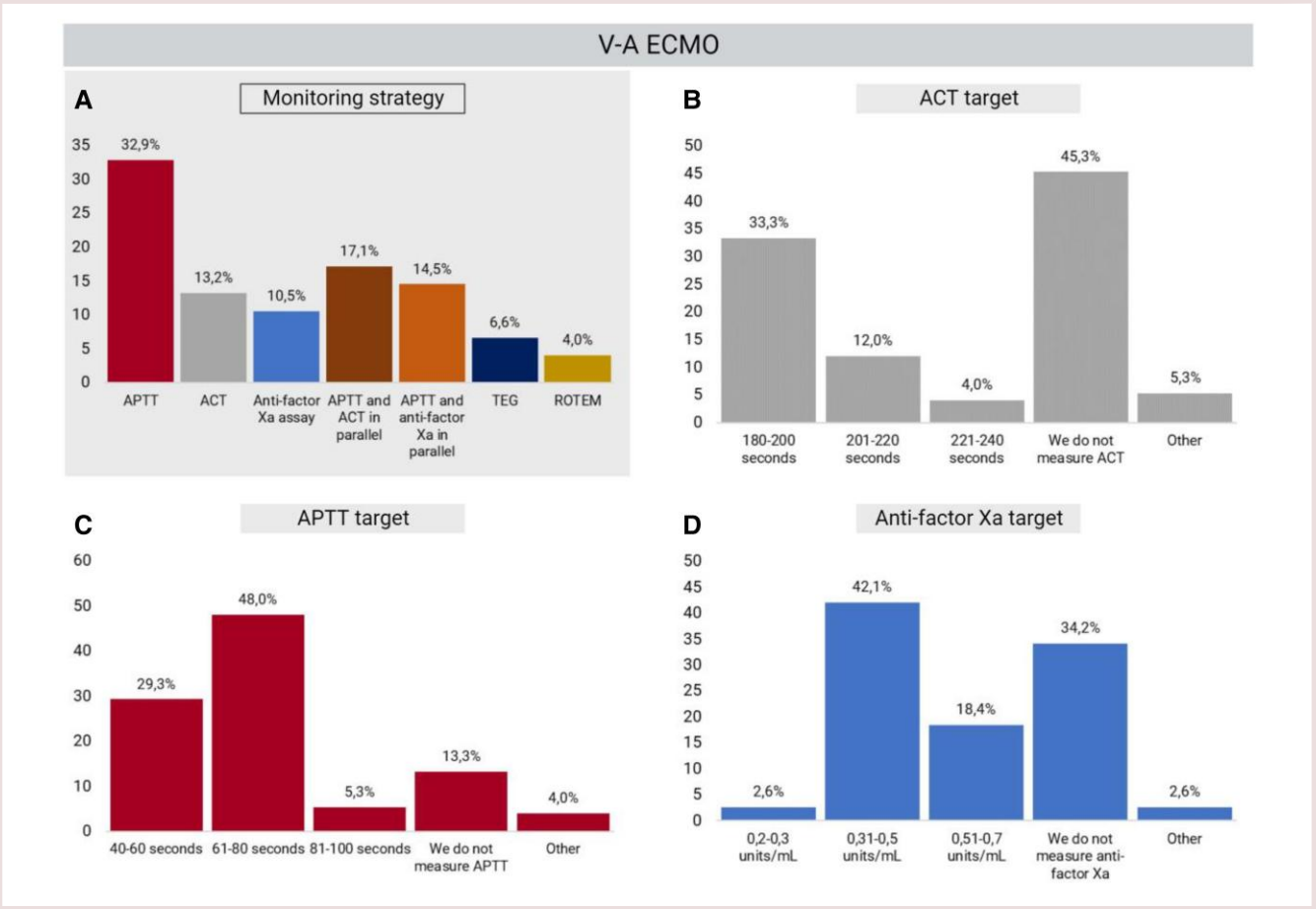


Figure 4 European unfractionated heparin anticoagulation monitoring practices and their targets during veno-arterial extracorporeal membrane oxygenation support. (*A*) An assay based on which unfractionated heparin dosing is guided. (*B*) Activated clotting time targets for unfractionated heparin therapy. (*C*) Activated partial thromboplastin time target for unfractionated heparin therapy. (*D*) Anti-factor Xa target for unfractionated heparin therapy. Isolated activated partial thromboplastin time is the most frequently used assay to guide the unfractionated heparin anticoagulation management (32.9%; 25/76), with preferred target 61–80 s (48.0%; 36/75). ROTEM, rotational thromboelastometry; TEG, thromboelastography.

purge solution, even though this appears to be not yet standard practice in Europe (1.6%).

Monitoring strategies for UFH vary, with 74.5% (Impella™) and 75.9% (V-A ECMO) of the respondents relying on a single test (APTT, anti-Xa, or ACT), despite the established confounding factors in critically ill.[21,22] Historically, ACT was the most frequently used test for UFH monitoring during ECMO, but it is deemed too insensitive since it is influenced by various factors (e.g. platelet count and fibrinogen level).[22,23] Consequently, a shift in monitoring strategy was seen from ACT towards APTT and, more recently, anti-Xa. This is reflected in our survey results as 50.0% (Impella™) and 45.3% (V-A ECMO) of the respondents indicate that they do not measure ACT, whereas 97 and 75% did use ACT for ECMO in the 2013 and the 2021 ELSO surveys, respectively. Activated partial thromboplastin time, on the other hand, can also be affected by various confounding factors as often seen in critically ill such as the up-regulation (e.g. FVIII as acute phase reagents) or down-regulation (e.g. consumption of FXII and FXI, liver failure) of different factors, unrelated to the anticoagulant effect of UFH. Nevertheless, a significant part of the respondents (Impella™: 43.1% and V-A ECMO: 32.9%) rely on a monitoring strategy with APTT alone, similar to the Impella™ survey from 2019 (56.7%).[15] In the surveys from 2013 and 2021 concerning ECMO in a paediatric setting, monitoring by APTT alone was not included in the answer options, as APTT is less likely to be used in this setting due to age-related differences that are more pronounced in young infants, with higher APTT for a given anti-Xa activity of UFH.[13,24] The anti-Xa assay is a chromogenic assay that measures the direct effect of UFH in the blood sample, but the test is more expensive and not available 24/7 in all centres, illustrated by 38.1 and 34.2% of the respondents indicating that they do not measure anti-Xa during Impella™ and V-A ECMO. This increases up to 44.8 and 51.1% in the non-European group for Impella™ and V-A ECMO, respectively. It is suggested that high APTT levels are superior to anti-Xa for assessing the bleeding risk as APTT covers the whole intrinsic pathway, whereas low anti-Xa levels are more predictive of thrombosis.[25,26] Therefore, a combination of monitoring strategies including APTT and anti-Xa might be more informative rather than relying on one single test.[21,22] However, this dual anti-Xa and APTT strategy is only implemented by a limited number of respondents (Impella™: 10.8% and V-A ECMO: 14.5%). Targets for APTT and anti-Xa vary across centres for both Impella™ and V-A ECMO. In the 2013 and the 2021 ELSO surveys, the most commonly reported target for anti-Xa during ECMO was 0.3–0.7 IU/mL.[13,14] For APTT, the target in the 2021 ELSO survey was dependent on the patients' age.[14]

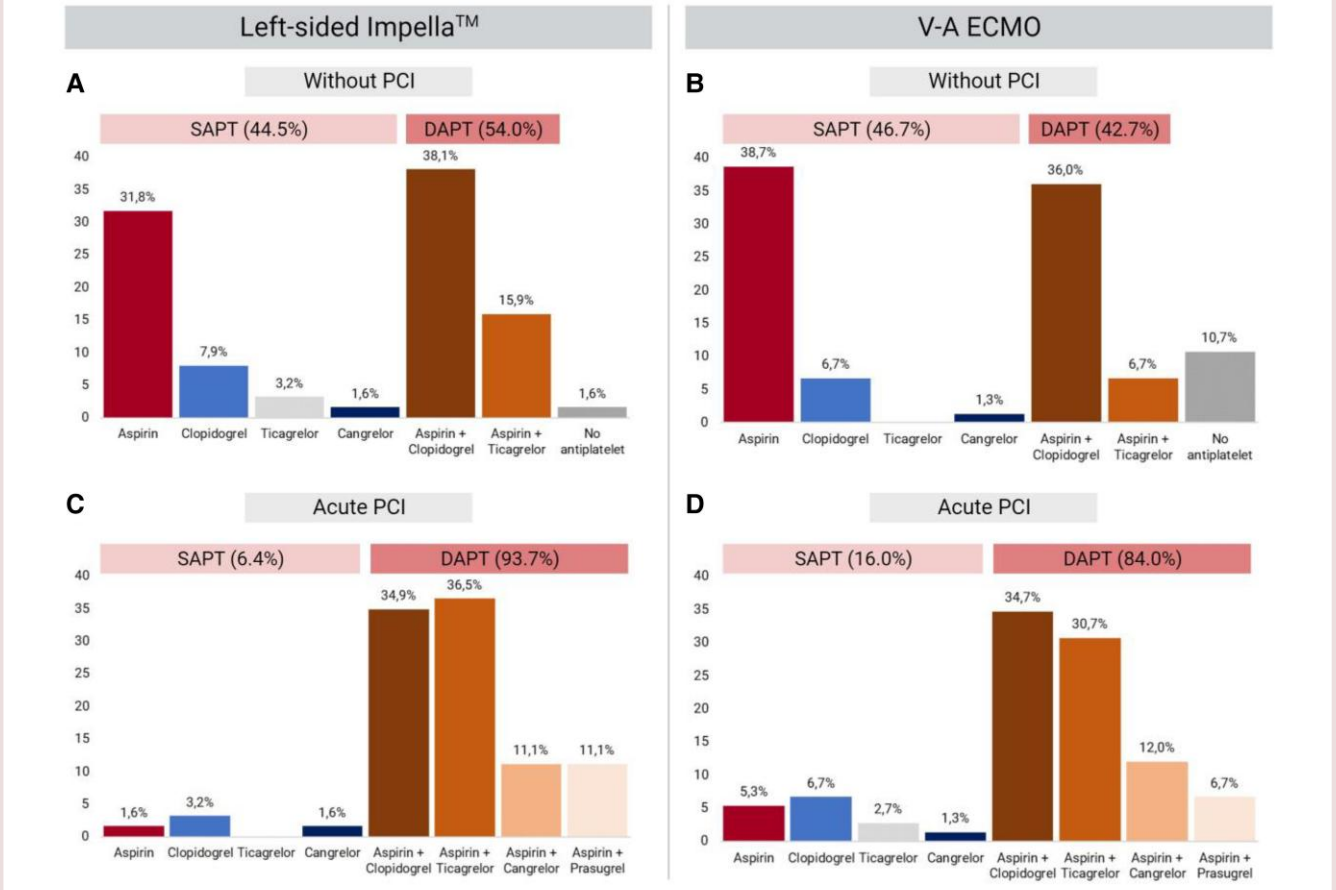


Figure 5 The association of (dual) antiplatelet therapy on top of anticoagulation during acute myocardial infarction induced cardiogenic shock in need for Impella™ or veno-arterial extracorporeal membrane oxygenation support in European centres, with and without recent percutaneous coronary intervention. Left side: (Dual) antiplatelet therapy during left-sided Impella™ support without percutaneous coronary intervention (*A*) and with recent percutaneous coronary intervention (*C*). Right side: (Dual) antiplatelet therapy during veno-arterial extracorporeal membrane oxygenation support without percutaneous coronary intervention (*B*) and with recent percutaneous coronary intervention (*D*). Most European centres combine dual antiplatelet therapy (mostly aspirin plus clopidogrel) with unfractionated heparin after AMI with recent percutaneous coronary intervention on percutaneous mechanical circulatory support. In case of AMI without prior percutaneous coronary intervention, 28/63 (44.5%) and 35/75 (46.7%) of the respondents rely on single antiplatelet therapy for Impella™ and veno-arterial extracorporeal membrane oxygenation support, respectively. DAPT, dual antiplatelet therapy; SAPT, single antiplatelet therapy.

In 2021, an ESC-ACVC-EAPCI Consensus Document regarding antithrombotic therapy in patients with out-of-hospital cardiac arrest or CS was published.[27] Although the authors do not specifically focus on pMCS, they make recommendations, such as the avoidance of potent P2Y12 inhibitors as part of 'triple therapy' (ASA, P2Y12 inhibitor, and UFH) in patients on pMCS. Our survey shows a high variety in antiplatelet therapy, highlighting that these expert recommendations are not uniformly being followed, and again, management is heterogeneous. Alternatively, in a retrospective study including patients on V-A ECMO, mainly for CS or cardiac arrest with indication for PCI in 93.8% of cases, there was no difference in bleeding incidence nor in pRBC transfusion rate in the patients receiving DAPT in addition to UFH compared with those without any antiplatelet therapy.[28] Similarly, in patients receiving DAPT in addition to UFH during V-A ECMO compared with controls receiving only UFH, there was no increased incidence of bleeding events, whereas a significantly lower number of arterial and venous thromboses was found, suggesting that DAPT-induced platelet inhibition (in addition to ECMO-induced platelet count decrease) might be protective against thrombotic events and possibly consumptive coagulopathy without increasing bleeding risk.[29,30] In summary, it appears that the majority of physicians is inclined to adhere to the ESC Guidelines on DAPT after PCI as in patients without pMCS, rather than taking into account the aforementioned consensus document.[31]

Bleeding management in patients receiving (D)APT after AMICS with or without PCI is often individualized, despite the majority of respondents (72.4%) having an anticoagulation protocol, suggesting that this protocol gives general guidance but does not cover bleeding management. The lack of a designated bleeding score for bleeds during pMCS in the ICU contributes to the difficulty in scoring and standardizing the management of these bleeds.[3]

Haemolysis is an important possible complication during Impella™ and V-A ECMO support, with reported rates up to 62.5%.[32] Nevertheless, 17.4% of the institutions do not routinely monitor for haemolysis, showing improvement compared with the Impella™ survey from 2019 (56.7%).[15] Failure to routinely monitor for haemolysis suggests that its detection occurs only in instances of overt symptoms, such as haemoglobinuria, after initiation of its deleterious effects,

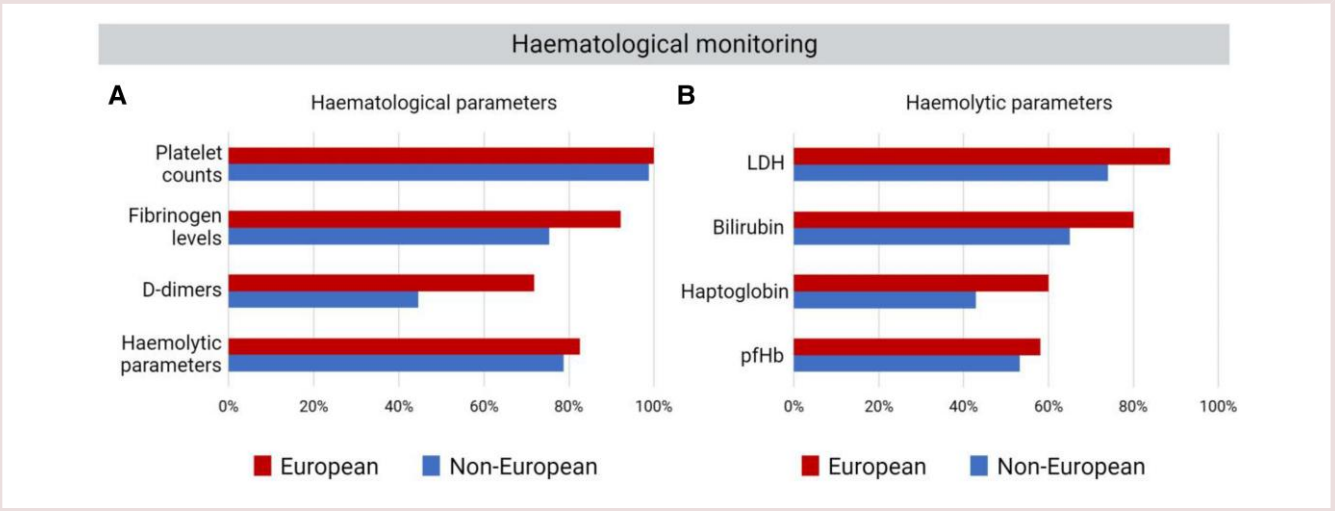


Figure 6 European (red) and non-European (blue) practices on haematological monitoring during percutaneous mechanical circulatory support in adults. (*A*) An overview of various basic haematological parameters (European and non-European countries). Not all basic parameters are routinely monitored. (*B*) Haemolysis is mostly monitored using lactate dehydrogenase (88.6%; 93/105) and bilirubin (80.0%; 84/105), rather than haptoglobin (60.0%; 63/105) or plasma-free haemoglobin (58.1%; 61/105) in Europe. In non-European countries, haemolysis is monitored using lactate dehydrogenase (74.0%; 57/77), bilirubin (65.0%; 50/77), plasma-free haemoglobin (53.2%; 41/77), and haptoglobin (42.9%; 33/77). Lactate dehydrogenase is a non-specific parameter, instead of plasma-free haemoglobin, which is the most sensitive parameter.

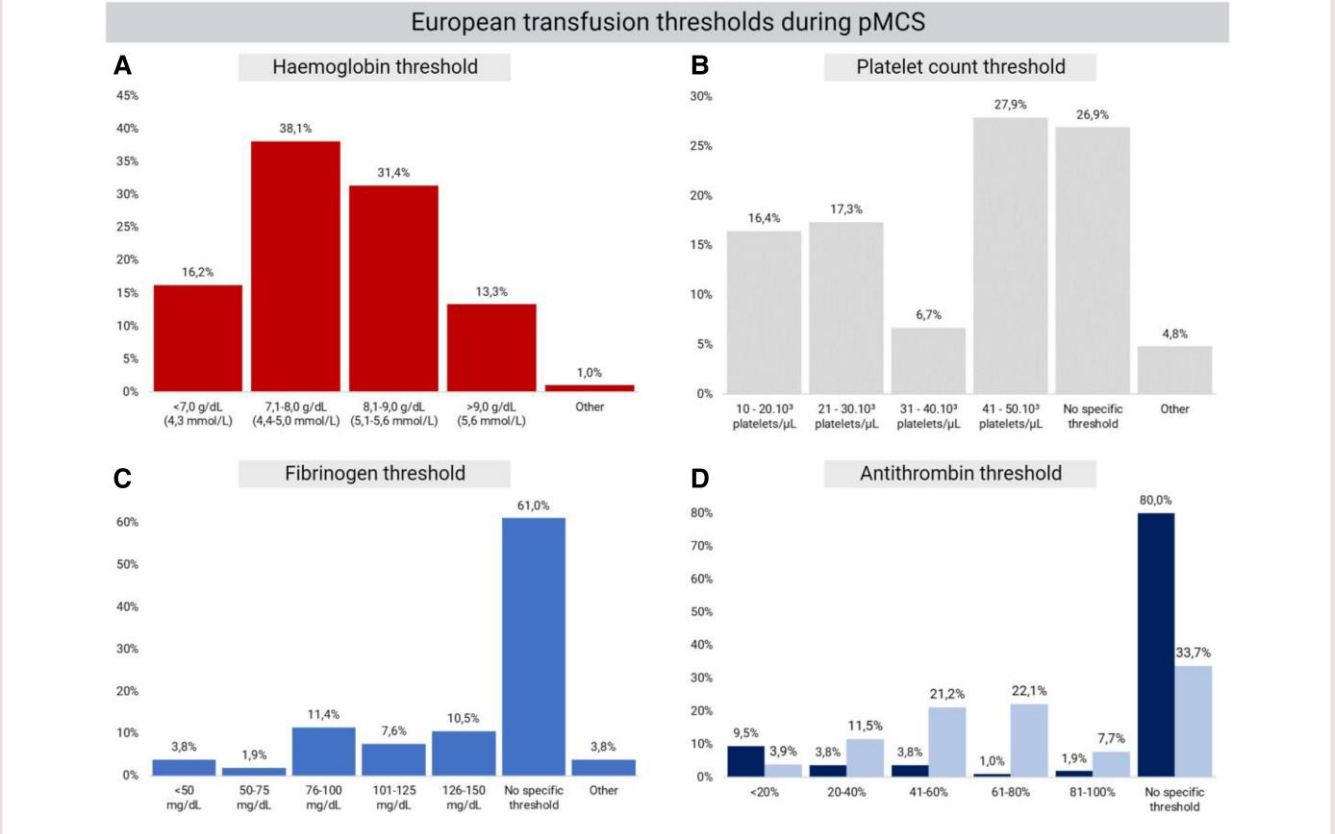


Figure 7 An overview of the heterogeneity of different thresholds for transfusion or administration of blood products in non-bleeding adults in European centres. (*A*) Haemoglobin threshold for red blood cell transfusion. (*B*) Platelet count threshold for platelet transfusion. (*C*) Fibrinogen threshold for fresh frozen plasma transfusion. (*D*) Antithrombin threshold for the administration of fresh frozen plasma (light blue) and antithrombin administration (dark blue).

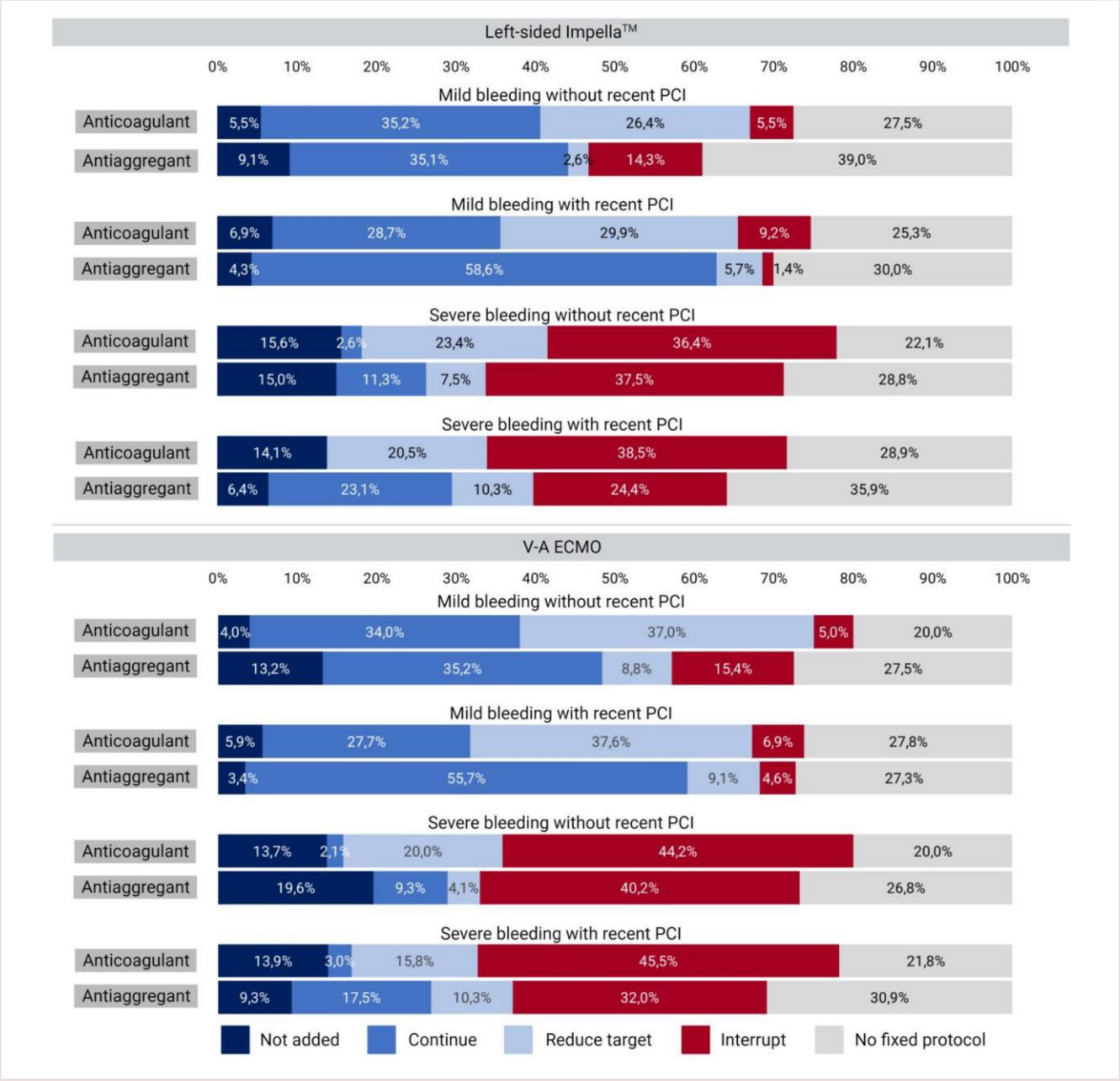


Figure 8 An overview of antithrombotic practices in European centres during percutaneous mechanical circulatory support in case of bleeding. Mild bleeding is defined as a Bleeding Academic Research Consortium score below 3. Severe bleeding is defined as a Bleeding Academic Research Consortium score of 3 or higher. PCI, percutaneous coronary intervention; V-A ECMO, veno-arterial extracorporeal membrane oxygenation.

vasoconstriction, platelet activation and aggregation, kidney failure, and arterial thrombosis, eventually resulting in diffuse ischaemia. Therefore, routine monitoring for haemolysis using the most sensitive parameter (pfHb) is of paramount importance.[3]

Study limitations

Although we present the first data pointing out the current antithrombotic practices during pMCS in Europe, we recognize that it has several limitations. First, survey respondents are random, although our study included over 100 European responses coming from 99 pMCS centres spread over 26 countries, with a considerable average of annual runs (Impella™: 18 and V-A ECMO: 29) and can serve as a first step in optimizing pMCS management in critically ill. Secondly, another limitation resides in the lack of granularity in individual patient's data, which would allow a more precise and measurable data evaluation.[33] Finally, a considerable heterogeneity in the number of responses per country is observed. Indeed, a recent geospatial analysis of ECMO provision in Europe also highlighted significant heterogeneity across the continent.[34] Notably, the European countries having the highest absolute numbers of ECLS centres also exhibit the highest number of responses in our survey. Similarly, the countries with a lower number of ECLS centres tend to have fewer responses in the present survey. Hence, we posit that the observed heterogeneity in response rates across European countries might be a representative reflection of the genuine disparities in ECLS (and pMCS) resources. However, these disparities might be

based on differences in local resources, budgets, reimbursement policies, and local pMCS network organizations among others, which are beyond the scope of this survey.

Conclusions

Our survey validated the considerable variation in antithrombotic management across European centres. There is a pressing demand for a standardized approach to antithrombotic management during pMCS to mitigate the impact of coagulopathic complications and, consequently, enhance outcomes. Prospective trials addressing clinical questions such as anticoagulation targets, monitoring strategies, the addition of DAPT, and other relevant factors could potentially contribute to diminishing inter-centre variability.

Supplementary material

Supplementary material is available at *European Heart Journal: Acute Cardiovascular Care*.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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