Blood and Anticoagulation Management in Extracorporeal Membrane Oxygenation for Surgical and Nonsurgical Patients: A Single-Center Retrospective Review

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Objective: **To describe blood management and anticoagulation practice for cardiac and respiratory extracorporeal membrane oxygenation (ECMO) with consideration of major surgery at the time of its initiation.**

Design: **A single-center retrospective review over 18 months of blood product usage and anticoagulation in patients treated with veno-venous (VV) ECMO versus veno-arterial (VA) ECMO and after major surgery (Sx) versus no surgery (Nsx).**

Setting: **Tertiary metropolitan hospital and state ECMO referral and heart and lung transplantation center.**

Participants: **The study comprised 42 patients representing 48 consecutive ECMO runs (16 VV, 32 VA, 26 Sx, 22 Nsx).**

Interventions: **None.**

Measurements and Main Results: **Thirty-three percent of the total run time of 362 days was with no continuous infusion of heparin. The mean (standard deviation) daily dose of heparin was lower for Sx versus Nsx patients (11,397 [9,297] *v* 17,324 [10,387] U, p = 0.047). Sx patients also received more fresh frozen plasma (1.1 [1.93] *v* 0.2 [0.59] U per day, p = 0.049) and platelets (0.5 [0.51] *v* 0.1 [0.25] U per day, p = 0.003). VV patients received fewer packed red cells (0.7 [0.45] *v* 2.0 [2.04] U per day, p = 0.016) and platelets (0.1 [0.18] *v* 0.4 [0.49] U per day, p = 0.008) compared with VA patients. Survival to hospital discharge was 69%.**

Conclusions: **Heparin doses were low, with frequent interruption of anticoagulation. This was more pronounced in patients with a high bleeding risk recovering from major surgery. The overall usage of blood products was low in VV and Nsx patients, with an overall excellent survival rate.**

KEY WORDS: ***extracorporeal membrane oxygenation, extracorporeal life support, transfusion, blood management, anticoagulation, hemorrhage***

BECAUSE OF TECHNOLOGIC advances and increasing clinical experience, the use of veno-venous extracorporeal membrane oxygenation (VV ECMO) as a rescue therapy in patients with acute respiratory distress syndrome (ARDS) has become safer and easier to establish.[1-3] The use of veno-arterial ECMO (VA ECMO) for cardiac support in patients with cardiac failure, both from medical and postcardiac surgery pathologies, also has increased dramatically.[1] One randomized controlled trial supported its use in severe ARDS.[4] ECMO is invasive and associated with a number of complications, including severe hemorrhage; therefore, this treatment has been relegated to the role of rescue therapy in patients in whom established treatments have failed.[5,6]

The requirements for systemic anticoagulation and blood transfusions are standard in ECMO to avoid platelet activation and subsequent catastrophic extracorporeal circuit failure or thromboembolic disease. Development of next-generation centrifugal pumps and low-resistance polymethylpentene oxygenators has aimed to reduce circuit-based hemolysis and thrombogenicity of the ECMO circuit.[2,7] Anticoagulation carries the risk of hemorrhagic complications, which are common (15%-25%) and can be fatal[1,3]; less serious complications include increased burden of anemia and the risks associated with increasing transfusion requirements in the critically ill population. Secondary to this, interest in minimizing anticoagulation strategies has increased.

Only a few contemporary single-center studies have reported on the use of blood products in association with anticoagulation practice. Little is known about how ECMO initiation (perioperative *v* medical) and the type of support (VA *v* VV ECMO) influence blood management and anticoagulation.

The aim of this study was to retrospectively compare blood product transfusion rates, hemorrhagic complications, and survival in adult surgical and nonsurgical patients for whom ECMO was required, comparing both VA and VV ECMO runs in a single-center setting over 18 months.

Consequently, the authors described 4 qualitatively distinct patient groups as those with primary respiratory failure and VV ECMO as opposed to those with primary cardiac failure and VA ECMO; these groups subsequently were divided further according to the need for cardiothoracic surgery directly before the initiation of ECMO. The authors made this distinction on the basis of the inherently different bleeding and clotting propensity within the surgical and medical patient groups and the effect that VV versus VA ECMO circuit requirements may have had on this relationship.[1]

METHODS

This research was approved by the local ethics committee and did not receive any specific grant from funding agencies.

Patients and Equipment

Data were extracted retrospectively from consecutive patient files at a single tertiary center intensive care unit in Sydney, Australia, over an 18-month period (January 2009 to June 2010). St. Vincent's Hospital is a tertiary metropolitan hospital,

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which also serves as a heart and lung transplantation center and ECMO referral hospital for the state of New South Wales, Australia (population 7.5 million). Only ECMO runs of 24 hours or fewer were excluded. All ECMO circuits comprised a centrifugal blood pump (Maquet, Rastatt, Germany) and driven circuit flow and polymethylpentene low-resistance oxygenators (Quadrox D; Maquet). Circuits were heparin bonded, and vascular cannulae were inserted through a peripheral approach into either the femoral or jugular or both vessels. Blood flow was maintained at 2.5-to-3.5 L/min for VA ECMO and 3-to-4.5 L/min for VV ECMO. VA ECMO support was reduced temporarily to 1.5 L/min during weaning.

Anticoagulation and Blood Management

All ECMO circuits were run on unfractionated heparin infusions for anticoagulation as per protocol, with the aim of an activated partial thromboplastin time (APTT) between 1.5-to-2 times over the upper reference range, unless contraindicated (50-70 s). This target was reached by a protocol-driven, stepwise increase of a continuous heparin infusion and 4-to-6 hourly APTT tests. In the case of major hemorrhage or in the likelihood of hemorrhage, the target was varied as deemed appropriate by the treating intensive care specialist, which included temporary interruption of anticoagulation. Conventional coagulation tests included platelet count, prothrombin time, international normalized ratio, APTT, and fibrinogen level. Activated clotting time (ACT) was not measured in the center's protocol because of its unreliability at lower heparin doses. Blood products were administered to correct coagulopathy only if the patient was bleeding or deemed to be at a high risk of bleeding. Fresh frozen plasma (FFP) was administered to correct an abnormal international normalized ratio, and cryoprecipitate was used to increase fibrinogen levels when deemed necessary. No a priori trigger for platelet transfusion was mandated. Clotting factor concentrates were not available for use in the treatment of acquired coagulopathies in the authors' jurisdiction. Packed red blood cell (RBC or PRBC) cell transfusions generally were considered at hemoglobin concentrations of less than 8 g/L.

Endpoints

The authors detailed the type of circuit configuration established (VA or VV) and whether ECMO support was or was not established immediately after major cardiothoracic surgery. Within this framework, the following endpoints were examined: (1) the length of time spent on ECMO; (2) the incidence and type of hemorrhagic complications; (3) anticoagulant in terms of anticoagulant dose (units of unfractionated heparin), APTT, and time spent off heparin; (4) blood product replacement in terms of units of packed red blood cells (PRC), pooled platelets, FFP, and cryoprecipitate administered per day of ECMO; and (5) survival to hospital discharge.

Statistical Analysis

Results were analyzed using SPSS statistical software (IBM Corp., Armonk, NY). Significance tests were carried out using 2-sample *t*-test, the Mann-Whitney *U* nonparametric test, or the Pearson chi-square test. The Shapiro-Wilk and Levene tests were used to test normality of distribution or raw data. A p value of <0.05 was considered statistically significant and 95% confidence intervals were calculated where appropriate.

RESULTS

Forty-eight serial ECMO runs in 42 patients were analyzed. Four patients required 2 ECMO runs, and 1 patient required 3 runs. Three runs were excluded because they lasted fewer than 24 hours.

Four subgroups contributed to a total of 362 ECMO days. Runs with and without association with major surgery were almost equal (26 *v* 22 runs). Although 32 (approximately two-thirds) runs were VA, the time spent on either modality was comparable because the durations of VV and nonsurgical runs were longer (200 *v* 162 days and 212 *v* 150 days for VV *v* VA and nonsurgical *v* surgical, respectively).

Baseline characteristics of all ECMO runs are presented in Table 1. VV and nonsurgical patients were younger. Of the 42 patients included, 29 survived to hospital discharge (69%). The survival rate was more than 60% for most indications, except

Table 1. Baseline Characteristics

	All	VA	VV	Sx	NSx	Surv	Nsurv
N	48	32	16	26	22	29	13
Mean age (SD)	44 (17)	48 (16)	35 (13)	50 (16)	37 (13)	44 (16)	44 (18)
Male (%)	28 (58)	19 (59)	9 (56)	13 (50)	15 (68)	15 (52)	11 (85)
Mean ECMO duration in days (SD)	8 (7.0)	5 (2.8)	13 (9.5)	6 (3.6)	10 (9.0)	6 (5.4)	10 (8.7)
RRT (%)	17 (35)	13 (41)	4 (25)	10 (38)	7 (32)	6 (21)	11 (85)
Inotropes (%)	30 (63)	20 (63)	10 (63)	17 (65)	13 (59)	18 (62)	12 (92)
Indications (%)							
ARDS	12 (25)		12 (75)	1 (4)	11 (50)	8 (28)	2 (15)
PGF (lung)	3 (6)		3 (19)	3 (12)		2 (7)	
PGF (heart)	8 (17)	8 (25)		8 (31)		7 (24)	1 (8)
Post-CPB	6 (13)	6 (19)		6 (23)		1 (3)	4 (31)
CS	14 (29)	14 (44)		8 (31)	6 (27)	9 (31)	3 (23)
ECPR	4 (8)	4 (13)			4 (18)	1 (3)	3 (23)
Asthma	1 (2)		1 (6)		1 (5)	1 (3)	

Abbreviations: ARDS, acute respiratory distress syndrome; CS, cardiogenic shock; CPB, cardiopulmonary bypass (excluding transplantation); ECMO, extracorporeal membrane oxygenation; Nsurv, nonsurvivors to hospital discharge; PGF, primary graft failure; RRT, renal replacement therapy; Surv, survivors to hospital discharge.