Platelet Changes During Extracorporeal Membrane Oxygenation Under Different Support Modes: A Retrospective Cohort Study (Postprint)

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Abstract

Objective To retrospectively analyze the patterns of platelet count changes during adult extracorporeal membrane oxygenation (ECMO) support under different support modes. Methods A total of 40 adult patients who received ECMO support at Gaozhou People' s Hospital between January 2019 and October 2021 were retrospectively enrolled and divided into a post-cardiac surgery ECMO support group (surgical group, n=17) and a non-cardiac surgery ECMO support group (non-surgical group, n=23). A Generalized Estimating Equations (GEE) linear regression model was used to analyze the regression model of each independent variable with platelet changes over time. Results In both groups, platelet count changes exhibited a curvilinear, dual-time pattern, beginning to decline on days 2-3 after ECMO initiation, reaching a nadir on days 3-4, followed by a recovery that displayed different patterns based on prognosis. Specifically, the survival group had relatively higher platelet values and a more stable recovery curve compared to the death group. The average platelet transfusion volume for all patients was (1.60$±$2.00) U, and nearly 60% (59.09%) of patients achieved effective platelet elevation after the first transfusion. Conclusion Platelet changes under ECMO support exhibited a curvilinear, dual-time pattern, typically reaching a nadir on days 3-4, and patient prognosis was correlated with platelet recovery.

Full Text

Preamble

Analysis of Platelet Count Changes and Related Factors During ECMO Support in Adults: A Single-Center Retrospective Cohort

Study

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Abstract

Objective: To retrospectively analyze the patterns of platelet count changes in adults during extracorporeal membrane oxygenation (ECMO) support under different support modes.

Methods: We retrospectively enrolled 40 adult patients who received ECMO support at Gaozhou People' s Hospital between January 2019 and October 2021. Patients were divided into a post-cardiac surgery ECMO support group (surgery group, n=17) and a non-cardiac surgery ECMO support group (non-surgery group, n=23). A generalized estimating equations (GEE) linear regression model was used to analyze the relationship between independent variables and platelet changes over time.

Results: Platelet count changes in both groups exhibited a curved, dual-time pattern, beginning to decline 2–3 days after ECMO initiation, reaching a nadir at 3–4 days, and subsequently rising with different prognostic trajectories. The survival group demonstrated relatively higher platelet values and a more stable recovery curve compared to the death group. The mean platelet transfusion volume was (1.60$±$2.00) units, with nearly 60% (59.09%) of patients achieving effective elevation after the first transfusion.

Conclusion: Platelet changes during ECMO support follow a curved, dual-time pattern, typically reaching their lowest value on days 3–4. Patient prognosis correlates with platelet recovery.

Keywords: ECMO; Platelets; Platelet count; Blood transfusion

Introduction

Thrombocytopenia is a common complication during extracorporeal membrane oxygenation (ECMO) support [1,2]. Studies have reported that the incidence of severe platelet reduction during ECMO can reach as high as 80% [3]. Lower platelet counts increase bleeding risk and consequently affect patient prognosis. Therefore, understanding the trends and patterns of platelet changes during ECMO is crucial for timely clinical intervention and prognostic assessment. To clarify the patterns of platelet changes during ECMO support across different patients, modes, scenarios, and time periods, we designed this retrospective cohort study to provide clinically relevant guidance.

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1. Materials and Methods

We retrospectively analyzed the medical records of adult patients who received venovenous (VV) ECMO or venoarterial (VA) ECMO support at our center between January 2019 and October 2021. Inclusion criteria were: (1) age >18 years; and (2) severe cardiopulmonary failure requiring ECMO support for any reason. Exclusion criteria: ECMO support duration <24 hours. After screening, 40 patients were enrolled and divided into surgery and non-surgery groups for comparative analysis, as well as survival and death groups. This study was approved by the Ethics Committee of Gaozhou People's Hospital (GYLL-2020042). As a retrospective study, informed consent was waived.

ECMO was performed using the Sorin SCP centrifugal pump system with Sorin adult membrane oxygenators. Cannulation was established peripherally or centrally. VV ECMO was established percutaneously via the internal jugular and femoral veins, while VA ECMO was established via surgical cutdown. Anticoagulation strategy: In the absence of contraindications, unfractionated heparin was routinely used for anticoagulation after ECMO initiation. Typically, 0.5–1 mg/kg of unfractionated heparin was administered before cannulation, with cannulation performed after activated clotting time (ACT) exceeded 200 seconds. During ECMO support, ACT was maintained at 160–220 seconds and activated partial thromboplastin time (APTT) at 60–80 seconds. For post-cardiac surgery patients, heparin-free ECMO initiation could be implemented based on specific conditions, with heparin dosage adjusted according to bleeding risk and ACT values during support.

In this study, thrombocytopenia was defined as platelet count <100$\times10^{\{9\}/L.Whenplateletcountfellbelow50\times10}\{9\}/$ 80–100×10^{9}$/L if bleeding complications occurred. The effectiveness of the first platelet transfusion was evaluated using the corrected count increment (CCI), calculated as: (post-transfusion platelet count - pre-transfusion platelet count) × body surface area / total platelets transfused. One therapeutic dose of platelets was calculated as 2.5$\times10^{11}$ platelets. A CCI <5 at 24 hours post-transfusion was considered ineffective.

We collected baseline data including age, sex, body weight, ECMO indication, ECMO mode, continuous renal replacement therapy (CRRT) use, and intra-aortic balloon counterpulsation (IABP) use. Complications including bleeding, thrombosis, and infection were recorded. Platelet counts before ECMO and during ECMO support, as well as platelet transfusion details, were collected. The lowest platelet value for each observation day was recorded. If ECMO was weaned, platelet data collection ceased on the day of decannulation.

Statistical methods: Continuous variables were expressed as mean±standard deviation ($\bar{x}\pm s$) and categorical variables as counts and percentages (n and %). Between-group comparisons were performed using Student' s independent samples t-test or Mann-Whitney U test for non-normally distributed variables. For platelet results measured at multiple time points from admission to 7 days after ECMO initiation, a generalized estimating equations (GEE) linear regression model was used to analyze the relationship between independent variables and platelet changes over time. Kaplan-Meier survival analysis was performed for different platelet change groups. All analyses were conducted using SPSS version 20.0.

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2. Results

The mean patient age was $(48.98\$\pm17.82)years(range18–77years), with25males and15females.Themeanbody$ kg. Patients were divided into non-surgery (n=23) and surgery (n=17) groups. Except for diagnostic distribution ($P<0.001$), no significant differences in baseline characteristics were observed between groups .

The overall incidence of thrombocytopenia before ECMO was 18% (7/40 patients). On ECMO day 1 (D1), the comprehensive incidence of thrombocytopenia was 56% (18/32 patients). In the VV ECMO subgroup, pre-ECMO thrombocytopenia occurred in 3 cases (33.33%, 3/9), all with severe infection. On ECMO D1, thrombocytopenia occurred in 4 cases (66.67%, 4/6). In the VA ECMO subgroup, pre-ECMO thrombocytopenia occurred in 4 cases (13%, 4/31). On ECMO D1, thrombocytopenia occurred in 14 cases (52%, 14/27).

Mean ECMO support duration was (6.00$±$3.22) days (range 2–13 days). Nine patients received VV ECMO and 31 received VA ECMO; 18 received circulatory support, 7 respiratory support, and 14 extracorporeal cardiopulmonary resuscitation (ECPR). Twenty patients received CRRT support and 16 received IABP support. Four patients experienced oxygenator thrombosis, and 5 patients developed bleeding complications (cannulation site bleeding, epistaxis, gastrointestinal bleeding). Nineteen patients developed infections, including 16 bacterial, 2 fungal, and 1 viral infection. The all-cause in-hospital mortality rate was 45% .

Platelet Count Changes During ECMO Support

From a mean value perspective, platelet counts in the non-surgery group were slightly higher than in the surgery group at admission, pre-ECMO, and post-ECMO stages. However, statistical analysis confirmed no significant differences in platelet data changes between the two groups during ECMO support (P>0.05). Platelet counts in both groups gradually decreased, reaching a nadir around days 3-4, then subsequently increased.

Analysis of differences between consecutive days revealed that in the non-surgery group, significant differences were observed from pre-ECMO to day 1 (P<0.001) and day 1 to day 2 (P<0.001), but not from day 2 to day 3 (P=0.827), day 3 to day 4 (P=0.042), day 4 to day 5 (P=0.300), or day 5 to day 6 (P=0.070), indicating the lowest platelet level occurred on day 4. In the surgery group, significant differences were observed from day 1 to day 2 (P=0.007) and day 2 to day 3 (P=0.005), but not from pre-ECMO to day 1 (P=0.053), day 3 to day 4 (P=0.827), day 4 to day 5 (P=0.696), or day 5 to day 6 (P=0.118), indicating the lowest platelet level occurred on day 3.

The mean platelet transfusion volume was 1.60$±$2.00 units, with 60% of patients achieving effective elevation after the first transfusion .

Prognostic Analysis

From a prognostic perspective, the death group had higher age, lower weaning rates, and lower platelet levels on ECMO days 5-7 compared to the survival group. In terms of platelet count trends over time, the survival group showed a recovery trend, with significant differences between groups observed on day 7 (P<0.05) .

Discussion

Research on platelet changes during ECMO is limited, with varying results due to methodological differences and varying definitions (e.g., for thrombocytopenia and its severity). Although previous studies have reported data on thrombocytopenia in ECMO patients, most literature does not clearly specify the time period for statistical results [1,4]. In reality, platelet changes throughout the peri-ECMO period are dynamic and curvilinear, with admission status, pre-ECMO values, different support durations, scenarios, modes, and interventions (such as allogeneic platelet transfusion) all affecting statistical outcomes [5,6]. A distinctive feature of our study is the multidimensional analysis of platelet changes, including time periods, support modes, dynamic trends, application scenarios, and prognostic outcomes.

In our temporal and modal statistical analysis, we primarily presented the incidence of thrombocytopenia before ECMO and on ECMO day 1 under two

support modes (VV and VA). Overall, the incidence of pre-ECMO thrombocytopenia was 18% (7/40), while on ECMO D1 it was 56% (18/32). In the VV ECMO subgroup, pre-ECMO thrombocytopenia occurred in 33.33% (3/9) of patients, with 66.67% (4/6) developing thrombocytopenia on ECMO D1. In the VA ECMO subgroup, pre-ECMO thrombocytopenia occurred in 13% (4/31), with 52% (14/27) developing thrombocytopenia on ECMO D1. Notably, the proportion of pre-ECMO thrombocytopenia was higher in VV mode than in VA mode. We found that all three VV ECMO patients with pre-ECMO thrombocytopenia had severe pneumonia, indicating that severe infection affects platelet values—a conclusion consistent with Jin et al.' s findings [7].

Jiritano et al.' s meta-analysis confirmed a pooled mean prevalence of thrombocytopenia of 21% in ECMO patients, with 23.2% in VA ECMO and 25.4% in VV ECMO [6]. However, these results represent statistically calculated averages. Although our results are higher than these mean values, they fall within the ranges reported in that study. Furthermore, the literature cited regarding thrombocytopenia [8-10] does not clearly define the time points for statistical data, making direct comparison with our study difficult.

Due to our small VV ECMO sample size (n=9), we could not perform cross-temporal dynamic analysis stratified by VV/VA mode. Therefore, we adopted an application scenario grouping strategy, comparing surgery versus non-surgery groups. Considering potential baseline imbalances that might affect results, we first analyzed baseline data (at admission and pre-ECMO), which showed no statistical differences between groups ($P>0.05$). This indicates that although the surgery group might have lower platelet counts due to cardiopulmonary bypass effects, the statistical similarity of baseline values ensures comparability between groups.

To identify the day of lowest platelet count in each group, we used consecutive day-to-day difference testing. The results showed the non-surgery group reached its nadir on day 4, while the surgery group reached it on day 3. This finding is largely consistent with meta-analysis results showing the time to lowest platelet count ranging from 2 to 7 days after ECMO initiation [6]. More importantly, we discovered that the surgery group reached its nadir one day earlier than the non-surgery group. This may be attributed to multiple factors accelerating platelet consumption and destruction in post-cardiac surgery ECMO patients, including persistent heparinization-related bleeding, concurrent infection, and CRRT.

Despite allogeneic platelet supplementation during ECMO support, mean platelet values did not recover to day 1 levels within the observation window, similar to findings reported by Thachil et al. [11]. This may be due to inadequate timeliness and effectiveness of platelet supplementation, as well as patients' comprehensive conditions (disease status, infection, CRRT) making it difficult to achieve dynamic balance between platelet consumption and replacement.

Additionally, we found that approximately half of patients in both groups had platelet counts decreasing to <100$\times10^{9}/Lwithin24hours(60.00\times10^{9}$/L within 48 hours (66.67% vs. 68.75%). In our center, ECMO patients generally have poor baseline status. Due to economic constraints and clinical practice patterns, many patients receive ECMO support relatively late, with platelet supplementation often being neither timely nor sufficient (e.g., due to economic factors or blood product shortages). These factors may contribute to rapid platelet decline and partially explain differences between our results and other literature. Nevertheless, our findings are largely consistent with Jiritano et al.' s meta-analysis [6], suggesting that clinicians should prepare platelets in advance based on this time window and implement appropriate preventive measures.

We also compared platelet changes between survival and death groups. The survival group had higher platelet values, consistent with Opfermann et al.' s findings [12]. Their study demonstrated that survivors showed sustained platelet recovery after ECMO day 5, with a biphasic "U-shaped"curve, while non-survivors showed no significant recovery. Our univariate analysis identified ECMO days 5–7 as prognostically relevant, but in multivariate modeling, only day 7 showed significant statistical difference (P<0.05). Since we did not collect platelet data after ECMO weaning, we could not observe the distinct "U-shaped" recovery trend in survivors.

The mean platelet transfusion volume in this study was 1.60$\pm$2.00 units, with 60% of patients showing effective elevation after the first transfusion. This demonstrates that allogeneic platelet transfusion is meaningful for increasing platelet counts. However, due to various limitations, we could not achieve a balanced platelet supply-demand ratio, which contributed to decreased platelet values.

This study has several limitations. As a retrospective study, confounding factors could not be completely eliminated. Platelet data after ECMO weaning were not included, preventing comprehensive understanding of platelet changes in our center' s ECMO patients. Additionally, transfusion thresholds lacked strict unified management, particularly due to blood product supply shortages. To clarify the relationship between platelets and ECMO, our center plans to conduct a prospective controlled study with standardized platelet transfusion protocols to explore optimal transfusion thresholds and develop predictive models for platelet-related bleeding.

In conclusion, platelet changes during ECMO support follow a curved, dual-time pattern, typically reaching their lowest value on days 3–4. Patient prognosis correlates with platelet recovery. The majority of patients show improved platelet values after the first transfusion. These findings suggest that clinicians can prepare appropriate interventions based on platelet change patterns to reduce complications from critically low platelet counts.

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Note: Figure translations are in progress. See original paper for figures.