Upper Gastrointestinal Bleeding in Adults Under Veno-Arterial Extracorporeal Membrane Oxygenation: A Single-Center Retrospective Study

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Research

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Abstract

**Objective.** Upper gastrointestinal bleeding is a common complication in adults treated with veno-arterial Extracorporeal Membrane Oxygenation (VA-ECMO) for refractory cardiogenic shock or cardiac arrest. We aimed to determine risk factors, prevalence and outcomes associated with upper gastrointestinal bleeding (UGIB) in adult patients under VA-ECMO.

**Design.** We conducted a retrospective cohort study (2014-2017) on consecutive VA-ECMO patients.

**Setting.** Medical and Infectious Disease intensive care unit of university hospital Bichat-Claude Bernard in Paris, France.

**Patients.** UGIB was defined as 1) an overt bleeding (hematemesis, melena, hematochezia), or 2) acute anemia associated with a lesion diagnosed on upper gastrointestinal endoscopy. Cause-specific models were used to identify factors associated with UGIB and death, respectively.

**Measurements and Main Results.** 257 patients were included, of whom 48 (19%) were diagnosed with UGIB after a median of 18 [7; 43] days following cannulation; median SAPS II was 59 [43; 76]. 100 (39%) patients were implanted after cardiac surgery. Mortality occurred in 31 (65%) patients with UGIB and 121 (58%) patients without. UGIB patients had longer ICU stays (41 [19; 82] vs. 15 [6; 26]; p<.01), longer ECMO (10.5 [7; 15] vs 6 [3; 10]; p <.01) and mechanical ventilation durations (31 [18; 45] vs. 9 [5; 18]; p <.01) in days, as compared to non-UGIB patients. Ninety-nine upper gastrointestinal endoscopies (UGE) were performed and the most frequent lesions detected were gastro-duodenal ulcers (n=28, 28%), leading to 12/99 therapeutic procedures. Neither antiplatelet therapy prior to ICU admission nor a history of peptic ulcer were associated with UGIB in univariate analysis. By multivariate analysis (table), a BMI (body mass index) > 30 kg/m$^2$ (Cause-specific hazard ratio (CSHR) [95% CI]): 3.06 [1.56; 5.98]), and extracorporeal cardiopulmonary resuscitation (ECPR) (CSHR 2.34 [1.03; 5.35]) were independently associated with an increased risk of UGIB.

**Conclusions.** In adult patients under VA-ECMO, obesity and ECPR were independently associated with UGIB. This study highlights the potential role of obesity and acute ischemia reperfusion injury in the pathophysiology of VA-ECMO-associated UGIB.

Introduction

Veno-arterial Extra Corporeal Membrane Oxygenation (VA-ECMO) is an emergency technique used in adult patients to treat refractory cardiogenic shock or refractory cardiac arrest [1]. There has been a massive increase in its use over the last decade [2, 3].

Upper gastrointestinal bleeding (UGIB) is a frequent complication of critical illness, occurring in 0.6–7% of cases. [4–6]. It is associated with adverse outcome, including increased ICU length of stay and increased mortality [7].
In a multicenter study in 1994 on 2252 critically ill patients, Cook et al. identified two independent risk factors for gastrointestinal bleeding, namely respiratory failure and coagulopathy [8]. In the recent SUP-ICU trial conducted on 1034 patients in 2016, variables independently associated with clinically important “stress ulcers” were: three or more coexisting diseases, coexisting coagulopathy, coexisting liver disease, use of renal replacement therapy, acute coagulopathy, and a high organ failure score [6].

The main pathophysiological mechanism of UGIB in critically ill patients is splanchnic hypoperfusion, resulting from both hypotension and release of proinflammatory cytokines at the acute phase. This can notably be increased by an ischemia-reperfusion phenomenon, leading paradoxically to an increase in mucosal ischemia [9]. The clinical presentation of UGIB is non-specific in the absence of overt bleeding and is usually suspected in the presence of unexplained acute anemia, hemodynamic instability and/or hyperuremia. A definitive diagnosis is made with upper gastrointestinal endoscopy, which can sometimes lead to a therapeutic action (hemostatic injection, vasoconstrictor injection, clipping...).

Hemorrhagic complications, including UGIB, are frequent during ECMO support and are associated with a poor outcome [10]. Hemorrhagic complications may be observed in VA-ECMO patients for multiple reasons: First, anticoagulation is often used to avoid thrombosis of the oxygenation membrane. Second, ECMO circuits induce a short term loss of high molecular weight von Willebrand factor multimer, which is necessary for primary hemostasis [11]. Last, thrombopenia and low fibrinogen concentrations are frequent under ECMO [12–14].

Pathophysiological mechanisms involved in the development of UGIB under ECMO may include patient-related factors (i.e. previous ulcer, chronic use of antiplatelet therapy ...), illness-related factors (i.e. mechanical ventilation, illness severity anticoagulation, thrombopenia ...) [9] and potential ECMO-related factors (i.e. decreased gastric mucosal perfusion [15, 16], ischemia-reperfusion injury [17]...).

Mazzeffi et al. [18] described a prevalence of 13,6% of gastrointestinal bleeding in a mixed cohort of 132 patients placed on ECMO, including 64 patients on veno-venous ECMO.

In the present study, we aimed to identify risk factors, prevalence and outcomes associated with upper gastrointestinal bleeding (UGIB) in adult patients supported with VA-ECMO.

**Methods**

**Design.** We performed a single-center retrospective cohort study in the 26-bed medical Intensive Care Unit (ICU) of the Bichat-Claude Bernard University Hospital, APHP, Paris, France.

**Ethics.** This study was approved by the ethical committee of the French Society of Intensive Care (SRLF). The database was declared to the French National Commission of data processing (CNIL).

**Patients.** We included consecutive adult patients who received VA-ECMO support for refractory cardiogenic shock or refractory cardiac arrest, between January 1st 2014 and December 31st 2017. Exclusion criteria were 1) age < 18 years; 2) missing data on UGIB, UGE and/or outcome in the ICU.
**Data collection.** Clinical parameters were extracted from the medical charts. These included baseline characteristics at admission (weight, height, comorbidities: chronic use of antiplatelet therapy, history of stroke (ischemic or hemorrhagic cerebral stroke reported in the medical report), history of cancer (cured or ongoing cancer reported in the medical report), peptic ulcer, simplified acute physiology score (SAPS II) [19], Charlson score [20], sepsis related organ failure assessment (SOFA) score [21], characteristics at the time of cannulation (i.e., SAVE score [22]), use of antiplatelet therapy during ICU stay, site of implantation, place of implantation, etiology of cardiogenic shock or refractory cardiac arrest, occurrence of pre-ECMO cardiopulmonary resuscitation (CPR), cannulation under chest compression (i.e., extracorporeal CPR (ECPR)) and outcome characteristics (duration of mechanical ventilation (MV), ICU length of stay (LOS), use of renal replacement therapy (RRT), duration and outcome of VA-ECMO, date and cause of death in non-survivors).

Biological parameters were collected at the time of cannulation (hemoglobin, platelets, prothrombin time, creatinine and lactate) and 24 hours before bleeding events (hemoglobin, platelets, prothrombin time, activated partial thromboplastin time) in patients who developed bleeding events.

Transfusion data were extracted retrospectively from the blood bank database of our hospital EFS (Etablissement Français du Sang). For each patient, all red blood cell (RBC) units, fresh frozen plasma (FFP) and platelet units transfused were identified and the date of transfusion was noted.

**UGIB definitions and UGE procedures.** UGIB was described as an overt bleeding (hematemesis, melena, hematochezia) or acute anemia associated with a lesion found on the UGE. All upper gastrointestinal endoscopy (UGE) procedures performed in the ICU during VA-ECMO support were analyzed. UGE was prescribed by the physician in charge in cases of overt bleeding or acute anemia with a suspicion of GI bleeding. UGE was performed by endoscopy specialists. The results of UGE procedures were classified in a pre-defined list of etiologies. If two or more lesions were found on the same UGE, only the most clinically significant one was described in our study.

**Stress ulcer prophylaxis, thromboprophylaxis, feeding and transfusion policies.** All patients placed on VA-ECMO received a stress ulcer prophylaxis with a proton pump inhibitor (intravenous omeprazole, 40 mg per day) from the day of ICU admission, until ICU discharge. To prevent thrombotic events and membrane clotting during VA-ECMO support, every patient received a continuous infusion of unfractionated heparin, with an anti-Xa target of 0.2 to 0.3 UI/ml that was continued for at least 1 month after ECMO explantation. The decision to stop heparin because of thrombopenia or hemorrhagic events was left to the discretion of the treating physician. Enteral feeding via an oral gastric tube was started within the first 24 hours of admission, if feasible, in order to achieve appropriate energy needs (25–35 kCal/kg/day) within the first 7 days. The hemoglobin threshold for transfusion was 8.0 g/dL in the absence of bleeding. In the case of bleeding events, transfusions were determined by the physician in charge.

**Statistical analysis.** Data are described as numbers (%) for categorical variables and medians (interquartile range, IQR) for continuous variables. Comparisons relied on Fisher’s exact test for categorical data, and the Wilcoxon test for continuous data. Using cause-specific models, we determined
risk factors for the occurrence of UGIB in adult patients on VA-ECMO during their ICU stay, considering death as a competing risk. For this purpose, risk factors were explored by univariate analyses. Then, variables yielding a p-value < 0.1 were entered into a multivariate model using a backward selection procedure. Results were expressed as cause-specific hazard ratios (CSHR) with their 95% confidence intervals (95% CI). Missing data were imputed to the median or to the highest frequency. All analyses were performed using SAS software, version 9.4 (SAS Institute Inc, Cary, North Carolina). A p-value of less than 0.05 was considered statistically significant.

Results

Study population. Between January 2014 and December 2017, 259 patients received VA-ECMO support in our ICU. Two patients were excluded because of missing files and 257 patients were finally studied. A study flow chart is provided in additional file 1.

Patient characteristics at ICU admission are shown in Table 1. Median age was 59 [50; 67] years, patients were mainly men (n = 193, 75%), median Charlson score was 4 [2; 6], median SAPS II was 59 [43; 76] and median SOFA was 10 [7; 12]. Compared to non-UGIB patients, patients with UGIB had more frequent diabetes (44% vs. 25%; p = 0.01), chronic renal disease (29% vs. 17%; p = 0.06), a higher BMI (27.2 [24.3; 32.4] vs. 26.2 [22.8; 29.4] kg/m²; p = 0.08) and a lower SAPS II (51 [41; 68] vs. 60 [44; 80]; p = 0.05). Other characteristics were comparable between UGIB and non-UGIB patients.

Patient characteristics at time of cannulation are presented in Table 2. Medical indication was the main reason for VA-ECMO implantation (n = 157, 61%): myocardial infarction was the main diagnosis (n = 53, 21%) followed by dilated cardiomyopathy (n = 43, 17%). 100 patients (39%) received VA-ECMO support because of cardiac surgery, of which 45 patients (18%) had primary graft dysfunction (PGD) after heart transplant. Overall, 79 (31%) patients received pre-ECMO CPR, including 41 (16%) ECPR patients. Patients were mainly cannulated in the operating room (n = 172, 68%). Principal sites of implantation were femoral-axillary (n = 126, 49%) and femoral-femoral (n = 122, 48%). The median SOFA at the time of cannulation was 10 [7; 12] and the median SAVE score was − 6 [-10; -2].

Outcomes are presented in Table 3. 152 patients (59%) died in the ICU. Mechanical ventilation duration and ICU length of stay were 12 [5; 23] and 18 [8; 34] days, respectively. Median numbers of units transfused were 16 [8; 30] for red blood cells (RBC), 4 [1; 10] for platelets and 7 [3; 14] for fresh frozen plasma (FFP). Seventy-two (28%) patients received intermittent renal replacement therapy (RRT) and 66 (26%) patients received continuous RRT during their ICU stay. ECMO duration was 7 [4; 12] days. Overall, 113 (44%) patients were successfully weaned, 111 (43%) patients were never weaned, 19 cases (7%) were bridged to a heart transplant and 14 cases (5%) were bridged to a left ventricular assist device (LVAD). 165 (64%) patients died during their hospital stay: the main causes of death were refractory multiple organ failure (MOF) (n = 96, 58%), withdrawal of life sustaining therapies (WLST) (n = 25, 15%), and septic shock (n = 20, 12%). Compared to non-UGIB patients, UGIB patients had longer mechanical ventilation duration (31 [18; 45] vs. 9 [5; 18] days; p < 0.01), longer ICU length of stay (41 [19; 82] vs. 15 [6; 26] days; p
Variables associated with UGIB. Figure 1 presents the multivariate analysis (univariate analysis is presented in additional file 2) for UGIB in a cause-specific manner with death as a competitive risk: characteristics associated with UGIB were: BMI > 30 kg/m^2 (CSHR 3.06 [1.56; 5.98]; p < 0.01), 8.05] and an extracorporeal cardiopulmonary resuscitation (ECPR) (CSHR 2.34 [1.03; 5.35]; p = 0.04). Characteristics associated with ICU mortality were: a history of stroke (CSHR 1.97 [1.19; 3.26]; p = 0.01), a history of peptic ulcer (CSHR 2.95 [1.47; 5.9]; p < 0.01), a history of cancer (CSHR 3.38 [1.59; 7.18]; p < 0.01), ECPR (CSHR 3.15 [2.0; 4.96]; p < 0.01), and a medical indication for ECMO implantation (CSHR 1.96 [1.25; 3.03]; p < 0.01).

UGE characteristics. Upper gastrointestinal endoscopy (UGE) findings are presented in Fig. 2. Seventy-four (29%) patients underwent at least one UGE, 18 [7; 43] days after cannulation. Among UGEs, 30/74 (41%) were reported as normal, 19/74 (26%) revealed at least one gastro-duodenal ulcer, and 10 (14%) revealed gastritis. Nine out of 74 (12%) patients were submitted to an endoscopic therapeutic procedure during the first UGE (n = 5, epinephrine injection therapy; n = 3, endoclip application and n = 1, thermal coagulation). Among the 74 patients who underwent UGE, 25/74 (34%) patients were submitted to a second endoscopy. Among these patients 9/25 (36%) were found to have gastro-duodenal ulcers, 7/25 (28%) were reported as normal and 3/25 (12%) had signs of gastric erosion. Four out of 25 (16%) patients underwent an endoscopic procedure during the second UGE (n = 3 endoclip application and n = 1 epinephrine injection therapy). 20% (n = 5) of patients with lesions on the second endoscopy, had a first endoscopy described as normal.

Transfusion characteristics on the day of the UGE procedure are presented in the additional file 2.

Measures of diagnostic accuracy of main clinical and biological characteristics present in the last 24 hours before UGE are presented in the additional file 2. The existence of melena, the transfusion of a least 3 units of red blood cells before UGE, and hematemesis had the highest specificities (96%, 93%, and 89%, respectively). However, all these three parameters had low sensitivities (31%, 8%, 27%, respectively).

Discussion

In this single center retrospective study that evaluated incidence, risk factors and outcomes associated with UGIB in adult VA-ECMO patients, we found that UGIB occurred in 19% of patients, after a median of 18 [7; 43] days following cannulation. The main findings during UGE were gastro-duodenal ulcers and a few UGE led to endoscopic therapeutic procedures. A history of obesity and ECPR were the main risk factors. UGIB patients had longer ICU stays, and longer ECMO and mechanical ventilation durations, as compared to non-UGIB patients.

In large studies conducted in the general ICU population, UGIB occurred in 2–5% of cases [6, 8, 23]. The high proportion of UGIB in VA-ECMO patients observed in our cohort could be simply explained by the
severe condition of patients on ECMO. These patients often present several risk factors, including high organ failure score, use of renal replacement therapy, coagulopathy, and respiratory failure [6, 8]. These variables were not associated with UGIB in our study, as almost every patient received mechanical ventilation, and more than half of the patients received renal replacement therapy.

The population which presented UGIB appeared to be less severely ill at admission (lower SAPS II) which could explain their difference in length of stay, ECMO duration and mechanical ventilation duration. It is noteworthy that UGIB was rarely diagnosed within the first days following ICU admission. It is thus possible that UGIB was undetected in the most severe patients who died early and in whom diagnostic endoscopic procedures were not performed. This likely explains why UGIB was not associated with death in our analyses.

In our study, we used a competing risk regression model with death as a competing risk to identify risk factors for UGIB. This model allowed us to evaluate the relationship of covariates to cause-specific events [24], in this case, UGIB and death. In this manner we could identify two independent risk factors for UGIB: BMI > 30 kg/m$^2$ (CSHR 2.48 [1.47; 5.52]; p < 0.01) and a cannulation under chest compression (CSHR 7.83 [1.59; 38.47]; p = 0.01). These different risk factors could reflect the potential role of obesity, and the importance of ischemia-reperfusion phenomena [25] in the splanchnic hypoperfusion which occurs during shock and VA-ECMO. Obesity is commonly associated with other comorbidities, such as antiplatelet therapy and diabetes. Nevertheless, in our multivariate analysis taking into account these potential cofounders, obesity remained independently associated with UGIB. Obesity is a known risk factor for gastrointestinal complications such as gastroesophageal reflux, erosive esophagitis and gastritis, which is explained by a higher intraabdominal pressure leading to an increase in esophageal acid exposure [26]. Moreover, a decrease in adiponectin has been found in obese patients which is associated with a higher risk of erosive gastritis [27]. To our knowledge, this is the first study to evaluate obesity as a risk factor for UGIB in ICU patients. Second, the digestive tissue might be very sensitive to ischemia-reperfusion-related damage: intestinal villosities contain the highest concentration in the body of xanthine dehydrogenase which is responsible for the production of superoxide anions, radical oxygen species, in the case of ischemia-reperfusion [28]. Mechanisms involving radical oxygen species that increase the damage caused by ischemia-reperfusion are well-known, including endothelial dysfunction, and platelet and leucocyte activation [29–31].

In our study, among the 99 UGE performed, the main findings were lesions of the digestive mucosa and gastroduodenal ulcer. In a previous study [18], stress gastritis was the most frequent diagnosis among ECMO patients but UGE was only performed in 7 patients. In another study [32], carried out in a medico-surgical intensive care unit without patients on ECMO, 84 UGE were performed: erosion (21%) was the most frequent diagnosis, followed by gastritis (17%) and peptic ulcer (15%) and 25 endoscopies (30%) were described as normal. This cohort seems to present the lesions found in our population in approximately in the same proportion as in our study group. This may suggest that the lesions found in our population may not be specific to the presence of VA-ECMO. In our cohort, 37 UGE (37%) were described as normal. This high proportion of normal endoscopy may reflect the difficulty in diagnosing
acute anemia in patients with VA-ECMO. Overt bleeding appeared to be more frequently associated with lesions. Information about increases in norepinephrine and urea – creatinine dissociation was missing and could perhaps be of interest to determine a priori patients with lesions. Although some of these lesions may not result in therapeutic changes, they remain a reflection of splanchnic hypoperfusion and may be responsible for progressive anemia. 9 UGE led to hemostatic endoscopic procedures, a prevalence which, although low, remains high compared to other studies on ICU patients [32].

Our study has several limitations: 1) this is a single-center study, and our results may not be extrapolable to other ECMO centers: it should be noted that we had a relatively high proportion of both post-cardiac surgery VA-ECMO patients and patients with primary graft dysfunction following heart transplantation. However, cardiac infarction and dilated cardiopathy remained the main reasons for ECMO implantation; 2) Our study is based on a retrospective analysis of data. However, all upper gastrointestinal endoscopy reports were computer-based and we can therefore safely assume that no important information about endoscopic procedures was missing; 3) Because the decision to perform UGE was based on clinical suspicion, some asymptomatic gastrointestinal lesions may have been missed; 4) We lacked quantitative information on enteral feeding, which is associated with a decrease in the prevalence of UGIB; we also lacked information concerning anticoagulant therapy and antiplatelet agent management (the occurrence of UGIB could lead to the discontinuation of the anticoagulants); 5) We did not include lesions found in lower gastrointestinal endoscopy, which is more often prescribed to look for mesenteric ischemia; we aim to investigate the clinical impact of such lesions in a future study.

Conclusion

UGIB is a frequent complication among adult patients under VA-ECMO. Obesity and a cannulation under chest compression are independently associated with UGIB in this population. This study highlights the potential role of obesity and ischemia-reperfusion in the pathophysiology of ECMO-associated UGIB.

Declarations

Ethical approval:

This study was approved by the ethical committee of the French Society of Intensive Care (SRLF). The database was declared to the French National Commission of data processing (CNIL).

Consent for publication:

Not applicable

Availability for supporting data:

The datasets analyzed during the current study are available from the corresponding author on reasonable request.
Competing interest:
The authors declare that they have no competing interests.

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Author's contribution:
JS, JR, CV and LB collected the data. JS, CD and RS analyzed the data. All authors read and approved the final manuscript.

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Tables

Table 1. Baseline characteristics
| Characteristic                          | Total (n = 257) | Without UGIB (n = 209) | With UGIB (n = 48) | P value |
|----------------------------------------|-----------------|------------------------|--------------------|---------|
| Age, years                             | 59 [50; 67]     | 59 [50; 67]            | 60 [49; 67]        | 0.78    |
| Males                                  | 193 (75)        | 157 (75)               | 36 (75)            | 0.99    |
| BMI, kg/m²                              | 26.2 [22.9; 29.5] | 26.2 [22.8; 29.4]     | 27.2 [24.3; 32.4]  | 0.08    |
| **Comorbidities**                      |                 |                        |                    |         |
| Charlson score                         | 4 [2; 6]        | 4 [2; 5]               | 4 [2; 6.5]         | 0.19    |
| Myocardial infarction                  | 76 (30)         | 60 (29)                | 16 (33)            | 0.53    |
| Congestive heart failure               | 128 (50)        | 102 (49)               | 26 (54)            | 0.50    |
| Peripheral vascular disease            | 31 (12)         | 24 (12)                | 7 (15)             | 0.55    |
| Peptic ulcer                           | 15 (6)          | 12 (6)                 | 3 (6)              | 0.89    |
| Chronic liver disease                  | 8 (3)           | 5 (2)                  | 3 (6)              | 0.17    |
| Diabetes                               | 74 (29)         | 53 (25)                | 21 (44)            | 0.01    |
| Chronic renal disease                  | 50 (20)         | 36 (17)                | 14 (29)            | 0.06    |
| Chronic hemodialysis                   | 29 (11)         | 24 (11)                | 5 (10)             | 1.00    |
| Hypertension                           | 108 (42)        | 89 (43)                | 19 (40)            | 0.70    |
| Smoking                                | 44 (17)         | 34 (16)                | 10 (21)            | 0.45    |
| Dyslipidemia                           | 81 (32)         | 62 (30)                | 19 (40)            | 0.18    |
| Alcoholism                             | 19 (7)          | 15 (7)                 | 4 (8)              | 0.78    |
| Antiplatelet therapy                   | 87 (34)         | 69 (33)                | 18 (37,5)          | 0.55    |
| **Severity on admission**              |                 |                        |                    |         |
| SAPS II                                | 59 [43; 76]     | 60 [44; 80]            | 51 [41; 68]        | 0.05    |
| SOFA                                   | 10 [7; 12]      | 10 [7; 12]             | 9 [7; 13]          | 0.64    |

Results are expressed as n (%) or median [interquartile range]

UGIB: Upper Gastrointestinal Bleeding; BMI: Body Mass Index; ECMO: Extra Corporeal Membrane Oxygenation; RRT: Renal replacement therapy; SAPS: Simplified Acute Physiology Score; SOFA: Sepsis
Organ Failure Assessment

**Table 2.** Characteristics at time of cannulation
| Characteristic                      | Total | Without UGIB | With UGIB | p value |
|------------------------------------|-------|--------------|----------|---------|
|                                    | (n = 257) | (n = 209) | (n = 48) |         |
| **Reason for ECMO implantation**   |       |              |          |         |
| Cardiac surgery                    | 100 (39) | 77 (37) | 23 (48) | 0.19    |
| Bypass or valve surgery            | 55 (21)  | 40 (19) | 15 (31) | 0.08    |
| PGD                                | 45 (18)  | 37 (18) | 8 (17)  | 1.00    |
| Myocardial infarction              | 53 (21)  | 41 (20) | 12 (25) | 0.43    |
| Dilated cardiomyopathy             | 43 (17)  | 36 (17) | 7 (15)  | 0.83    |
| Myocarditis                        | 14 (5)   | 13 (6)  | 1 (2)   | 0.58    |
| Pulmonary embolism                 | 7 (3)    | 6 (3)   | 1 (2)   | 1.00    |
| Endocarditis                       | 5 (2)    | 5 (3)   | 0 (0)   | 0.58    |
| Septic shock                       | 2 (1)    | 1 (1)   | 1 (2)   | 0.34    |
| Other                              | 33 (12)  | 30 (14) | 3 (6)   | 0.16    |
| **pre-ECMO CPR**                   | 79 (31)  | 69 (33) | 10 (21) | 0.10    |
| Post cardiac arrest shock          | 38 (15)  | 36 (17) | 2 (4)   | 0.02    |
| ECPR                               | 41 (16)  | 33 (16) | 8 (17)  | 0.88    |
| **Place of implantation**         |       |              |          |         |
| ICU                                | 56 (22)  | 44 (21) | 12 (25) | 1.00    |
| Operating room                     | 172 (68)| 140 (68)| 32 (67) | 1.00    |
| Other                              | 26 (10)  | 22 (11) | 4 (8)   | 0.79    |
| **Site of implantation**          |       |              |          |         |
| centralized                        | 9 (3)   | 9 (4)   | 0 (0)   | 0.21    |
| femoral-axillary                   | 126 (49)| 100 (48)| 26 (54) | 0.63    |
| femoral-femoral                    | 122 (48)| 100 (48)| 22 (46) | 1.00    |
| **Severity**                       |       |              |          |         |
| SOFA                               | 10 [7; 12] | 10 [7; 13] | 9 [8; 12] | 0.52    |
| Platelets (G/L)                    | 156 [108; 230] | 156 [107; 235] | 152 [115; 205] | 0.77    |
|                         | 10.4 [9; 12.6] | 10.6 [9.1; 12.8] | 9.6 [8.5; 11.5] | 0.06 |
|-------------------------|----------------|------------------|----------------|------|
| Hemoglobin (g/dL)       | 59 [42; 75]    | 58 [40; 74]      | 62 [44; 81]     | 0.25 |
| QT (%)                  | 138 [99; 202]  | 138 [103; 194]   | 140 [85; 251]   | 0.56 |
| Creatinine (µmol/L)     | 5.4 [2.6; 9.6] | 5.6 [2.9; 9.7]   | 4 [2.4; 8.2]    | 0.09 |
| Lactate (mmol/L)        | -6 [-10; -2]   | -6 [-10; -2]     | -7 [-11; -2]    | 0.50 |

Results are expressed as n (%) or median [interquartile range]

UGIB: Upper Gastrointestinal Bleeding; ECMO: Extra Corporeal Membrane Oxygenation; PGD: Primary Graft Dysfunction; CPR: Cardio Pulmonary Resuscitation; ECPR: Extracorporeal CPR; ICU: Intensive Care Unit; SOFA: Sepsis Organ Failure Assessment; QT: Quick Time; LVAD: Left Ventricular Assist Device

Table 3 Outcome characteristics and comparison between patients with and without UGIB
| Characteristic          | Total | Without UGIB | With UGIB | p value |
|------------------------|-------|--------------|-----------|---------|
|                        | (n = 257) | (n = 209) | (n = 48) |         |
| **ICU Outcomes**       |       |              |           |         |
| ICU Death              | 152   | 121          | 31        | 0.40    |
| MV duration, days      | 12 [5; 23] | 9 [5; 18]  | 31 [18; 45] | <.01  |
| ICU LOS, days          | 18 [8; 34] | 15 [6; 26]  | 41 [19; 82] | <.01  |
| No RRT                 | 119   | 103          | 16        | 0.07    |
| Intermittent RRT       | 72    | 58           | 14        | 0.86    |
| Continuous RRT         | 66    | 48           | 18        | 0.13    |
| RBC transfusion        | 16 [6; 31] | 13 [5; 24]  | 32 [20; 47] | <.01  |
| Platelet transfusion   | 3 [1; 7] | 3 [1; 6]    | 6 [2; 11] | <.01    |
| FFP transfusion        | 7 [2; 14] | 6 [2; 14]   | 9 [4; 21] | 0.13    |
| **ECMO outcomes**      |       |              |           |         |
| successfully weaned    | 113   | 89           | 24        | 0.33    |
| never weaned           | 111   | 96           | 15        | 0.06    |
| bridge to transplant   | 19    | 16           | 3         | 0.77    |
| bridge to LVAD         | 14    | 8            | 6         | 0.03    |
| ECMO duration, days    | 7 [4; 12] | 6 [3; 10]   | 10.5 [7; 15] | <.01  |
| Re cannulation         | 42    | 31           | 11        | 0.19    |
| **Cause specific hospital** |     |              |           | 0.44    |
| mortality *            |       |              |           |         |
| Refractory MOF         | 96    | 79           | 17        |         |
| WLST                   | 25    | 19           | 6         |         |
| Septic shock           | 20    | 13           | 7         |         |
| Brain death            | 10    | 9            | 1         |         |
| Cardiac arrest         | 13    | 9            | 4         |         |
| Hemorrhagic shock      | 1     | 1            | 0         |         |
Results are expressed as n(%) or median [interquartile range]

*: 165 patients (64%) died during their hospital stay

UGIB: Upper Gastrointestinal Bleeding; ICU: Intensive Care Unit; MV: Mechanical Ventilation; LOS: Length of Stay;

MOF: Multiple Organ Failure; WLST: Withdrawal of life support treatment; RBC: Red blood cell; FFP: Fresh Frozen Plasma; RRT: Renal Replacement Therapy

Figures

Cause specific Hazards Ratio

Results are presented as Hazard ratio [95% confidence interval]
Acute renal failure was defined as a renal SOFA score > 2
UGIB: Upper Gastrointestinal Bleeding; BMI: Body Mass Index, ECMO: Extracorporeal membrane oxygenation, SOFA: Sequential Organ Failure Assessment, ECPR: Extracorporeal cardiopulmonary resuscitation

Figure 1

Risk factors for UGIB, cause-specific multivariate analysis Results are presented as Hazard ratio [95% confidence interval] Acute renal failure was defined as a renal SOFA score > 2 UGIB: Upper Gastrointestinal Bleeding; BMI: Body Mass Index, ECMO: Extracorporeal membrane oxygenation, SOFA: Sequential Organ Failure Assessment, ECPR: Extracorporeal cardiopulmonary resuscitation
Figure 2

Characteristics of upper gastrointestinal endoscopy (UGE)

Supplementary Files

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- figure1.tiff
- Supplementaldata09042021correx.docx