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Proton pump inhibitors versus histamine-2 receptor antagonists for stress ulcer prophylaxis during extracorporeal membrane oxygenation: a propensity score-matched analysis

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ABSTRACT

Purpose Patients receiving extracorporeal membrane oxygenation (ECMO) generally receive proton pump inhibitors (PPIs) or histamine-2 receptor antagonists (H_2RAs) to avoid major gastrointestinal bleeding. Our aim was to compare outcomes between patients receiving PPIs and H_2RAs for stress ulcer prophylaxis during ECMO.

Materials and methods We performed a retrospective cohort study using the Japanese Diagnosis Procedure Combination Database, using data recorded from 1 July 2010 to 31 March 2017. We defined patients who received PPIs within 2 days after starting ECMO as the PPIs group and those who received H_2RAs within 2 days after starting ECMO as the H_2RAs group. We performed propensity score matching to compare outcomes. The primary outcomes were gastrointestinal bleeding requiring endoscopic haemostasis and in-hospital mortality. The secondary outcomes were red blood cell transfusion, hospital-acquired pneumonia and *Clostridium difficile* infection during hospitalisation.

Results Of 11 328 eligible patients, 9738 received PPIs and 1590 received H_2RAs. Propensity score matching created 1556 pairs. No significant differences were seen regarding endoscopic haemostasis (1.2% vs 0.8%; p=0.37), in-hospital mortality (53.0% vs 53.1%; p=0.94), red blood cell transfusion rates (91.4% vs 89.7%; p=0.11), hospital-acquired pneumonia (13.0% vs 12.4%; p=0.59) or *C. difficile* infection (0.1% vs 0.2%; p=0.32) between the PPIs and H_2RAs groups, respectively.

Conclusion We found no differences in the evaluated outcomes between the PPIs and H_2RAs groups. Both PPIs and H_2RAs are treatment options for stress ulcer prophylaxis in patients undergoing ECMO.

Strengths and limitations of this study

- Both proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H_2RAs) are treatment options for stress ulcer prophylaxis in patients undergoing extracorporeal membrane oxygenation (ECMO).
- To the best of our knowledge, this study is the first report comparing PPIs and H_2RAs for stress ulcer prophylaxis during ECMO.
- The proportion of patients with gastrointestinal bleeding may have been underestimated because the current study included only patients with severe bleeding requiring endoscopic haemostasis.

PURPOSE

Extracorporeal membrane oxygenation (ECMO) therapy is widely used for circulatory and respiratory support for critically ill patients. Although the use of ECMO is increasing, in-hospital mortality and bleeding complications among critically ill patients receiving ECMO remain high.[1 2] Clinically important gastrointestinal bleeding (CIGIB) often results in death because ECMO requires anticoagulants. To avoid CIGIB, patients receiving ECMO generally also receive stress ulcer prophylaxis drugs. The use of ECMO equipment in critically ill patients may result in gastrointestinal ischaemia because ECMO can change the blood flow. Proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H_2RAs) are the main stress ulcer prophylactic drugs. The American Society of Health-System Pharmacists' guidelines recommend using PPIs as the first-line drugs for critically ill patients.[3 4] A systematic review of randomised controlled trials also showed that PPIs were superior to H_2RAs in preventing CIGIB without increasing the risk of adverse effects.[5]

Recently, some studies have thrown doubt on the efficacy of PPIs.[6 7] In 2014, an observational study reported that PPIs were associated with a higher risk of CIGIB (OR, 2.24 (95% CI 1.81 to 2.76)) compared with H_2RAs, in critically ill patients.[6] In 2018, a larger observational study showed that PPIs were associated with a higher risk of CIGIB compared

with H_2RAs in critically ill patients.[7] A recent randomised controlled trial showed no difference in CIGIB between PPIs and H_2RAs[8]; however, to our knowledge, no previous study has assessed the superiority of PPIs over H_2RAs in patients receiving ECMO.

The aim of the present study was to compare outcomes between PPIs and H_2RAs to prevent stress ulcers in patients receiving ECMO using a Japanese National Inpatient Database.

MATERIALS AND METHODS

The requirement to obtain patients' informed consent was waived because of the anonymous nature of the datasets. Patients and the public were not involved in the design or planning of the study.

Study design and data collection

This retrospective cohort study was performed using the Japanese Diagnosis Procedure Combination Database, which comprises administrative claims and discharge abstract data from more than 1200 acute-care hospitals in Japan.[9] The database covers approximately 90% of all tertiary-care emergency hospitals and includes the following patient variables: age, sex, weight, height, consciousness level, primary diagnosis, comorbidities at admission, postadmission complications, procedures, prescriptions and discharge status. The main diagnosis, primary diagnosis on admission, comorbidities present on admission and comorbidities diagnosed during each episode of hospitalisation are recorded using the International Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) codes, with text data in Japanese. A previous validation study for the database showed a high specificity for the recorded diagnoses and a high sensitivity and specificity for the recorded procedures.[10]

Study participants

Data recorded from 1 July 2010 to 31 March 2017 in the database were used in the present study. We studied critically ill patients receiving ECMO and excluded patients (1) who were younger than 18 years of age, (2) who died or were discharged within 2 days of receiving ECMO, (3) who had a history of gastric ulcer or gastritis before stress ulcer prophylaxis, (4) who received sucralfate within 2 days of ECMO, (5) who underwent endoscopic haemostasis before ECMO, (6) who received neither PPIs nor H_2RAs, (7) who received both PPIs and H_2RAs within 2 days of ECMO (because gastrointestinal bleeding within 2 days of ECMO suggests existence of gastritis before ECMO) and (8) whose reason for receiving ECMO was unspecified. Eligible patients were divided into those who received PPIs within 2 days after starting ECMO (PPIs group) and those who received H_2RAs within 2 days after starting ECMO (H_2RAs group). We included patients receiving both PPIs and H_2RAs after 2 days of ECMO. Patients who used PPIs first and then used H_2RAs were categorised to the PPIs group, and vice versa.

Variables and outcomes

For this study, we examined the following patient characteristics: age, sex, Japan Coma Scale (JCS) score, body mass index (kg/m^2), Charlson Comorbidity Index score, fiscal year, aetiology (online supplemental table 1), ambulance use, academic hospital, cardiac surgery before ECMO, interventions (mechanical ventilation, continuous renal replacement therapy, chest tube drainage, intra-aortic balloon pumping, defibrillation, chest compression, tracheostomy, arterial pressure monitoring and hypothermia treatment) within 2 days of ECMO, drugs (dopamine, dobutamine, norepinephrine, epinephrine and vasopressin) within 2 days of ECMO and transfusion (red blood cells, fresh-frozen plasma, platelets and albumin) within 2 days of ECMO. The JCS score was categorised into four groups: 0 (alert), 1–3 (dizziness), 10–30 (somnolence) and 100–300 points (coma). JCS scores are well correlated with Glasgow Coma Scale scores, and a JCS score of 100 is equivalent to a Glasgow Coma Scale score of 6–9.[11] Charlson Comorbidity Index scores predict the risk of death by weighting or classifying comorbidities.[12] Several validation studies for the Charlson Comorbidity Index have been reported.[13 14]

We identified diagnoses of hospital-acquired pneumonia with the ICD-10 codes J152, J159, J180, J181, J189, J209, J690 and J958. We also identified diagnoses of *Clostridium difficile* infection with the ICD-10 code A047.

The primary outcomes were gastrointestinal bleeding requiring endoscopic haemostasis and in-hospital mortality. The secondary outcomes were red blood cell transfusion, hospital-acquired pneumonia and *C. difficile* infection during hospitalisation.

Statistical analysis

We used propensity score matching to compare the outcomes between the PPIs and H_2RAs groups and a multivariable logistic regression model to predict propensity scores for receiving PPIs. Predictor variables included age, sex, fiscal year, admission to a teaching hospital, ambulance use, body mass index at admission, JCS at admission, Charlson Comorbidity Index, reason for ECMO, cardiac surgery before ECMO, interventions (mechanical ventilation, continuous renal replacement therapy, chest tube drainage, intra-aortic balloon pumping, defibrillation, chest compression, tracheostomy, arterial line and hypothermia treatment) within 2 days of ECMO, drugs (dopamine, dobutamine, norepinephrine, epinephrine and vasopressin) within 2 days of ECMO and transfusion (red blood cells, fresh-frozen plasma, platelets and albumin) within 2 days of ECMO. One-to-one nearest-neighbour matching without replacement was performed for patients' estimated propensity scores using a calliper width set at 20% of the SD of the propensity scores.[15 16]

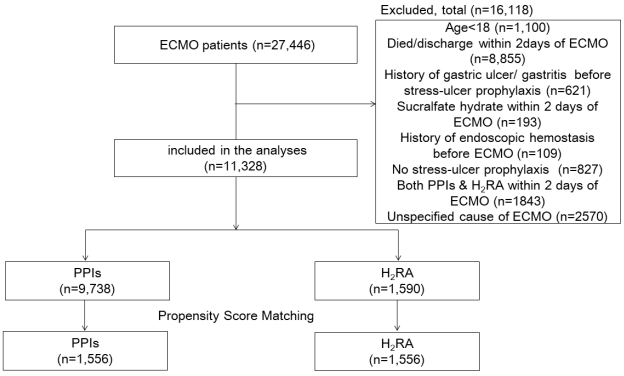

Figure 1 Flow diagram of patients receiving extracorporeal membrane oxygenation (ECMO). H_2RA, histamine-2 receptor antagonist; PPIs, proton pump inhibitors.

A standardised difference of −10% to ≤10% was considered to denote negligible imbalances in the variables between the propensity score-matched PPIs and H_2RAs groups.[17] We performed propensity score matching using the Stata (StataCorp) module PSMATCH2.[18]

We used a generalised estimating equation approach for comparisons of the primary and secondary outcomes, accompanied by cluster-robust standard errors that treated both propensity score-matched pairs and individual hospitals as clusters.[19] ORs and 95% CIs were calculated for the primary and secondary outcomes. These estimates were obtained by generalised estimating equation models with logit link functions, irrespective of outcome types.[20] We performed sensitivity analyses using the variables within 1 day of ECMO instead of the variables within 2 days of ECMO.

We performed sensitivity analyses by the stabilised inverse probability of treatment weighting (IPTW) method to account for differences in baseline covariates between the groups. Stabilised IPTW is a propensity score-based method to adjust for measured potential confounding factors and creates a pseudodataset by preserving the sample size.[21] Stabilised IPTW estimates the average treatment effects over a marginal distribution of measured covariates in the matched cohort.[22]

Continuous variables are presented as medians and IQRs. Categorical variables are presented as numbers and percentages. Baseline characteristics and crude outcomes were compared using the Mann-Whitney test for continuous variables with a skewed distribution and the χ^2 test or Fisher's exact test for categorical variables between the groups.

The two-sided significance level for all tests was $p<0.05$. All analyses were performed using Stata/MP V.15 (StataCorp).

Patient and public involvement

Patients or members of the public were not involved in the design or implementation. Patients and the general public will be informed of the results via publication.

RESULTS

A total of 11 328 patients met the inclusion criteria during the study period. Of these, 9738 (86.0%) patients received PPIs and 1590 (14.0%) patients received H_2RAs (figure 1). Patients' characteristics before and after propensity score matching are shown in table 1. Before propensity score matching, the PPIs group had higher proportions of patients with ischaemic heart disease (40.4% in the PPIs group and 34.7% in the H_2RAs group) and congestive heart failure (15.8% in the PPIs group and 12.2% in the H_2RAs group), whereas the H_2RAs group had higher proportions of patients with aortic dissection/aneurysm (5.4% in the PPIs group and 11.4% in the H_2RAs group) and trauma/intoxication (3.4% in the PPIs group and 7.0% in the H_2RAs group). The PPIs group was more likely to receive continuous renal replacement therapy (32.2% in the PPIs group and 25.4% in the H_2RAs group), intra-aortic balloon pumping (65.6% in the PPIs group and 49.1% in the H_2RAs group), norepinephrine (77.1% in the PPIs group and 69.9% in the H_2RAs group), and epinephrine (61.6% in the PPIs group and 55.6% in the H_2RAs group). The H_2RAs group was more likely to receive arterial blood pressure lines (84.7% in the PPIs group and 89.2% in the H_2RAs group), cardiac surgery (13.1% in the PPIs group and 28.5% in the H_2RAs group) and dopamine (56.4% in the PPIs group and 65.7% in the H_2RAs group). The proportions of patients receiving PPIs increased annually during the study period compared with the proportions of patients receiving H_2RAs. After propensity score matching, patients' characteristics were well balanced between the two groups.

Crude in-hospital mortality and the proportion of patients receiving red blood cell transfusions were significantly higher in the PPIs group (57.2%) than H_2RAs group (52.6%) (table 2). The proportions of patients undergoing endoscopic haemostasis, developing hospital-acquired pneumonia and acquiring *C. difficile* infection did not differ significantly between the two groups. In the propensity score-matching analysis, no outcomes were significantly different between the groups (table 2).

A generalised estimating equation analysis after propensity score matching showed no significant differences in any outcomes between the PPIs and H_2RAs groups (table 3). The results of the sensitivity analyses using the variables within 1 day of ECMO were similar to those using the variables within 2 days (online supplemental table 2). The stabilised IPTW analysis also showed no significant differences in any of the outcomes (table 4).

DISCUSSION

The use of PPIs increased annually during our study period; however, our results showed no obvious benefits of PPIs regarding reducing the need for endoscopic haemostasis or in-hospital mortality. In addition, we found no significant differences in the number of transfusions, the proportions of patients developing in-hospital acquired pneumonia or the proportions of patients acquiring *C.*

Table 1 Patients' backgrounds in the unmatched and propensity score-matched groups

	Unmatched group			Propensity score-matched group		
	PPIs (n=9738)	H_2RAs (n=1590)	SD, %	PPIs (n=1556)	H_2RAs (n=1556)	SD, %
Age in years	65 (53 to 73)	66 (54 to 74)	−1.8	65 (54 to 73)	65 (54 to 74)	−0.4
Sex						
Male	7314 (75.1)	1151 (72.4)	6.1	1123 (72.2)	1127 (72.4)	−0.6
Consciousness						
Alert (0)	4623 (47.5)	797 (50.1)	−5.7	770 (49.5)	778 (50.0)	−1.0
Dizziness (1–3)	881 (9.0)	122 (7.7)	4.9	133 (8.5)	122 (7.8)	2.6
Somnolence (10–30)	449 (4.6)	60 (3.8)	4.1	63 (4.0)	60 (3.9)	1.0
Coma (100–300)	3785 (38.9)	611 (38.4)	1.4	590 (37.9)	596 (38.3)	−0.8
Body mass index						
<18.5	667 (6.8)	105 (6.6)	1.1	106 (6.8)	104 (6.7)	0.5
18.5–22.9	4982 (51.2)	842 (53.0)	−3.8	838 (53.9)	823 (52.9)	1.9
23.0–24.9	2152 (22.1)	355 (22.3)	−0.9	338 (21.7)	347 (22.3)	−1.4
25.0–29.9	661 (6.8)	88 (5.5)	5.6	88 (5.7)	86 (5.5)	0.6
≥30.0	1276 (13.1)	200 (12.6)	1.9	186 (12.0)	196 (12.6)	−2.0
Charlson Comorbidity Index						
0	3806 (39.1)	665 (41.8)	−5.1	641 (41.2)	644 (41.4)	−0.4
1	3319 (34.1)	536 (33.7)	0.6	524 (33.7)	526 (33.8)	−0.3
2	1524 (15.7)	237 (14.9)	1.9	257 (16.5)	235 (15.1)	3.9
3	694 (7.1)	87 (5.5)	6.6	79 (5.1)	87 (5.6)	−2.3
>4	395 (4.1)	65 (4.1)	−0.2	55 (3.5)	64 (4.1)	−3.0
Fiscal year						
July 2010–Mar 2011	519 (5.3)	200 (12.6)	−25.7	226 (14.5)	188 (12.1)	7.2
April 2011–March 2012	1036 (10.6)	284 (17.9)	−20.9	322 (20.7)	277 (17.8)	7.3
April 2012–March 2013	1230 (12.6)	298 (18.7)	−17.1	289 (18.6)	291 (18.7)	−0.3
April 2013–March 2014	1506 (15.5)	218 (13.7)	4.8	213 (13.7)	218 (14.0)	−0.9
April 2014–March 2015	1708 (17.5)	232 (14.6)	8.9	215 (13.8)	226 (14.5)	−2.0
April 2015–March 2016	1851 (19.0)	196 (12.3)	18.5	163 (10.5)	195 (12.5)	−6.4
April 2016–March 2017	1888 (19.4)	162 (10.2)	26.0	128 (8.2)	161 (10.3)	−7.3
Aetiology						
Postcardiac arrest	1980 (20.3)	325 (20.4)	0.3	310 (19.9)	319 (20.5)	−1.4
Ischaemic heart disease	3937 (40.4)	552 (34.7)	11.5	504 (32.4)	542 (34.8)	−5.2
Arrhythmia	529 (5.4)	78 (4.9)	2.2	75 (4.8)	76 (4.9)	−0.3
Congestive heart failure	1543 (15.8)	194 (12.2)	10.4	186 (12.0)	194 (12.5)	−1.6
Aortic dissection/aneurysm	528 (5.4)	182 (11.4)	−22.0	194 (12.5)	175 (11.2)	3.8
Pulmonary embolism	373 (3.8)	61 (3.8)	−0.1	70 (4.5)	61 (3.9)	2.9
Septic shock	106 (1.1)	20 (1.3)	−1.6	21 (1.3)	20 (1.3)	0.6
ARDS/ARF	207 (2.1)	37 (2.3)	−1.0	39 (2.5)	36 (2.3)	1.3
Pneumonia	201 (2.1)	30 (1.9)	1.2	39 (2.5)	30 (1.9)	3.9
Trauma/intoxication	334 (3.4)	111 (7.0)	−16.0	118 (7.6)	103 (6.6)	3.8
Ambulance use	7032 (72.3)	1063 (67.2)	11.2	1024 (65.8)	1054 (67.7)	−4.1
Academic hospital	8844 (90.8)	1398 (87.9)	9.50	1366 (87.8)	1370 (88.0)	−0.8
Mechanical ventilation started within 2 days of ECMO	8802 (90.4)	1397 (87.9)	8.3	1339 (86.1)	1373 (88.2)	−6.5
CRRT started within 2 days of ECMO	3133 (32.2)	404 (25.4)	15.0	361 (23.2)	399 (25.6)	−5.7

Continued

Table 1 Continued

	Unmatched group			Propensity score-matched group		
	PPIs (n=9738)	H_2RAs (n=1590)	SD, %	PPIs (n=1556)	H_2RAs (n=1556)	SD, %
Arterial blood pressure line started within 2 days of ECMO	8252 (84.7)	1419 (89.2)	−13.3	1395 (89.7)	1386 (89.1)	1.9
Intra-aortic balloon pumping	6385 (65.6)	780 (49.1)	34.0	700 (45.0)	773 (49.7)	−9.4
Cardiac surgery followed by ECMO	1272 (13.1)	453 (28.5)	−39.0	479 (30.8)	432 (27.8)	6.6
Drugs started within 2 days of ECMO						
Dopamine	5488 (56.4)	1045 (65.7)	−20.0	1051 (67.5)	1023 (65.7)	3.8
Dobutamine	5501 (56.5)	932 (58.6)	−3.9	907 (58.5)	908 (58.4)	−0.1
Norepinephrine	7506 (77.1)	1112 (69.9)	16.6	1080 (69.4)	1095 (70.4)	−2.1
Vasopressin	804 (8.3)	110 (6.9)	5.2	88 (5.7)	109 (7.0)	−5.5
Epinephrine	6002 (61.6)	884 (55.6)	12.4	84 (54.0)	871 (56.0)	−3.9
Transfusion started within 2 days of ECMO						
Red blood cells	7854 (80.7)	1255 (78.9)	4.2	1245 (80.0)	1228 (78.9)	2.7
Fresh-frozen plasma	6191 (63.6)	978 (61.5)	4.4	937 (60.2)	959 (61.6)	−2.9
Platelets	3445 (35.4)	610 (38.4)	−6.3	624 (40.1)	597 (38.4)	3.6
Albumin	6535 (67.1)	1047 (65.8)	2.5	1012 (65.0)	1029 (66.1)	−2.3

Data are presented as number (%) except for median (IQR) for age.
ARDS, acute respiratory distress syndrome; ARF, acute respiratory failure; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; H_2RAs, histamine-2 receptor antagonists; PPIs, proton pump inhibitors.

difficile infection between the groups. The stabilised IPTW analysis also showed no differences between the groups; therefore, our results are robust.

To the best of our knowledge, ours is the first report comparing PPIs and H_2RAs for stress ulcer prophylaxis during ECMO. Most previous studies comparing PPIs and H_2RAs focused on critically ill patients with heterogeneous backgrounds.[3] CIGIB is pronounced in ECMO patients because of the required high doses of heparin and the mechanically high blood flow rates. Thus, complications related to haemorrhage in ECMO are frequent and have a significant negative impact on outcomes.[23]

Our results showed no significant differences for in-hospital mortality or the proportions of patients requiring endoscopic haemostasis, similar to results in previous randomised controlled trials.[24–26] Some previous studies have shown conflicting results regarding the efficacy of PPIs and H_2RAs for stress ulcer prophylaxis.[7 27] In the present study, we found no significant difference in *C. difficile* infection rates between patients receiving PPIs versus H_2RAs for stress ulcer prophylaxis. Previous studies showed that stress ulcer medical prophylaxis increased the risk of *C. difficile* infection, but it remains unclear whether the risk of *C. difficile* infection differs between patients receiving PPIs versus H_2RAs.[28 29] *C. difficile* infection and community-acquired pneumonia may occur because of gastric acid suppression. Our results indicate that either PPIs or H_2RAs can be used.

In a previous study, endoscopic therapy was feasible and helped to achieve complete bleeding control,

Table 2 Outcomes in the unmatched and propensity score-matched groups

	Unmatched group			Propensity score-matched group		
	PPIs (n=9738)	H_2RAs (n=1590)	P value	PPIs (n=1556)	H_2RAs (n=1556)	P value
Endoscopic haemostasis	112 (1.2)	14 (0.9)	0.34	18 (1.2)	13 (0.8)	0.37
In-hospital mortality	5573 (57.2)	837 (52.6)	<0.001	824 (53.0)	826 (53.1)	0.94
RBC transfusion	9052 (93.0)	1424 (89.6)	<0.001	1422 (91.4)	1396 (89.7)	0.11
Hospital-acquired pneumonia	1363 (14.0)	197 (12.4)	0.085	203 (13.0)	193 (12.4)	0.59
Clostridium difficile infection	26 (0.3)	3 (0.2)	0.57	1 (0.1)	3 (0.2)	0.32

Data are presented as number (%).
H_2RAs, histamine-2 receptor antagonists; PPIs, proton pump inhibitors; RBC, red blood cells.

Table 3 Logistic regression analyses of the outcomes fitted using with a generalised estimation equations for the outcomes in the propensity-score-matched population

		ORs	P value
Endoscopic haemostasis	H_2RAs	Reference	
	PPIs	1.39 (0.65 to 2.99)	0.40
In-hospital mortality	H_2RAs	Reference	
	PPIs	0.99 (0.79 to 1.25)	0.96
RBC transfusion rate	H_2RAs	Reference	
	PPIs	1.22 (0.89 to 1.66)	0.22
Hospital-acquired pneumonia	H_2RAs	Reference	
	PPIs	1.06 (0.84 to 1.34)	0.63
Clostridium difficile infection	H_2RAs	Reference	
	PPIs	0.38 (0.03 to 3.19)	0.34

Data are presented as ORs (95% CI).
H_2RAs, histamine-2 receptor antagonists; PPIs, proton pump inhibitors; RBC, red blood cells.

and the data showed that it may contribute to reduced mortality.[30] Our study showed no differences in mortality between the groups, which may have occurred because of the similar proportions of patients achieving endoscopic haemostasis.

This study has several limitations. First, information on the type of gastric ulcer and laboratory data such as serum haemoglobin levels were not available in the Diagnosis Procedure Combination Database. Second, the proportion of patients with gastrointestinal bleeding may have been underestimated because we included only patients with severe bleeding requiring endoscopic haemostasis. Third, we could not exclude all patients with previously diagnosed gastric ulcers or gastritis. Finally, this was a retrospective study, and recorded diagnoses were less well validated than those in prospective registries.

Table 4 Logistic regression analyses of fitted with generalised linear model for the outcomes in stabilised inverse probability of treatment weighted population

		ORs	P value
Endoscopic haemostasis	H_2RAs	Reference	0.27
	PPIs	1.48 (0.74 to 2.99)	
In-hospital mortality	H_2RAs	Reference	0.98
	PPIs	1.00 (0.85 to 1.17)	
RBC transfusion	H_2RAs	Reference	0.77
	PPIs	1.04 (0.81 to 1.33)	
Hospital-acquired pneumonia	H_2RAs	Reference	0.92
	PPIs	1.01 (0.82 to 1.25)	
Clostridium difficile infection	H_2RAs	Reference	0.44
	PPIs	1.63 (0.47 to 5.67)	

Data are presented as ORs (95% CI).
H_2RAs, histamine-2 receptor antagonists; PPIs, proton pump inhibitors; RBC, red blood cells.

CONCLUSIONS

No significant differences in endoscopic haemostasis or in-hospital mortality were shown between the PPIs and H_2RAs groups in this study. Both PPIs and H_2RAs are treatment options for stress ulcer prophylaxis in patients receiving ECMO.

Contributors YK conceived this study, analysed the data and drafted the manuscript. HO, HM and KF collected and analysed the data. HY and HT revised the design and manuscript. All authors checked and agreed on the final manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

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Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available.

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