Impact of Colloid Infusion on Outcomes in Patients with Septic Shock

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Research

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Abstract

Background: Although colloid solution has been widely used in practice, its impact on mortality in patients with septic shock remains unknown. We evaluated the association of colloid infusion with outcomes in septic shock patients.

Methods: Medical Information Mart for Intensive Care (MIMIC)-III was used to identify patients with septic shock. Propensity score matching (PSM) was employed to balance the baseline differences. Cox proportional hazards model, Wilcoxon rank-sum test, and logistic regression were utilized to determine the associations of colloid infusion with mortality, length of stay, and recovery of kidney function, respectively.

Results: A total of 4,553 septic shock patients were studied, including 1,158 with colloid infusion, and 3,395 without colloid infusion. After PSM, 1,012 pairs of patients were matched. Significant benefits in the mortality rate were observed in the colloid group compared with the non-colloid group, with the 28-day mortality [hazard ratio (HR) 0.62; 95% confidence interval [CI], 0.52-0.73; P < 0.001], and the 90-day mortality [HR 0.76; 95% CI 0.65-0.88; P < 0.001]. Colloid infusion was not associated with the renal function recovery [HR 1.06; 95% CI 0.87–1.29; P = 0.547] in either population. Nevertheless, subgroup analysis revealed that colloid infusion did not affect the 28-day mortality in people with sepsis of AKI stage 1. In addition, the use of dextran did not decrease the 28-day mortality (HR 1.41; 95% CI 0.19-10.59; P = 0.736).

Conclusion: In septic shock patients, colloid infusion (albumin or hydroxyethyl starch) improved short-term survival, but had no clear effect on the recovery of renal function.

Introduction

Septic shock syndrome resulting from systemic inflammation and excessive host immune responses to infection is a top cause of death in patients in the hospitals, with 40–50% mortality [1, 2]. For decades, natural or synthetic colloids have been given to patients with shock to maintain sufficient colloid-osmotic pressure (COP) and the volume of vessels [3–5]. However, a recent large meta-analysis indicated that the administration of colloid made no difference to mortality in critically ill patients, as compared with crystalloid solutions [6]. Meanwhile, some studies reported contradicting results [7–10].

The colloid family includes natural [e.g. albumin or fresh frozen plasma (FFP)] or artificial [e.g. hydroxyethyl starch (HES) or dextran] solution [11]. Colloids have larger molecules, cost more, and may promote faster expansion in the vessel volume, but it may result in coagulation dysfunction, allergic reactions, or renal failure [6]. Whether colloid infusion can impact the clinical outcomes in the early resuscitation of septic shock is not clear [9, 12, 13]. Currently, no clear colloid infusion strategies for patients with sepsis and septic shock are recommended in the national guidelines [14]. Therefore, we carried out a retrospective observational study to determine the impact of colloids (albumin, HES, or dextran) on outcomes in septic shock patients.

Material And Methods

Data Source

The data utilized in this retrospective study was from MIMIC-III, which is an openly accessible US-based critical care repository [15]. The MIMIC III database includes clinical information on patients hospitalized from 2001 to 2012 in the adult ICUs of Beth Israel Deaconess Medical Center. It is also approved by the Massachusetts Institute of Technology Institutional Review Boards. Patients were selected using the PostgreSQL 9.6 software from the latest version (MIMIC-III v1.4), which was released on the 2nd of September 2016. After successfully completing the course of the Collaborative Institutional Training Initiative Program (Record ID 35897056), we were allowed to utilize the stored clinical data from the MIMIC-III repository.

Participants and definition

PgAdmin (version 4.1, Bedford, USA) was used to mine data from the MIMIC III data bank. The study inclusion criteria included: (1) Patients that were diagnosed with sepsis. According to the Sepsis-3 definition[16], sepsis was defined as patients with suspected or verified infection, plus the *SOFA* scores ≥2 during the first day after ICU admission [16]. Infection was diagnosed according to the method established by Angus in the MIMIC-III database; (2) All sepsis patients who were supported with vasopressor within 24 hours after ICU admission were defined as patients with septic shock. For a patient with more than one ICU admissions, only the first admission was included. According to the colloid infusion status within 48 hours after ICU admission, the participants were separated into two groups: A Colloid group (intervention) and a Non-colloid group (control).

Baseline data were obtained from the MIMICIII. The first laboratory data since ICU admission was recorded. Sequential organ failure assessment (SOFA) score, Simplified Acute Physiology Score II (SAPSII), and Glasgow coma score (GCS) were calculated as described in previous studies[17, 18]. AKI was defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria [19]. The use of crystalloid and colloid solution during the first 48 h of ICU admission was included in this analysis.

No more than 25% missing values were recorded in all variables (Supplementary Table S1).
Missing values were filled by single imputation or linear regression as appropriate.

Endpoints

The primary end point was 28-day mortality. The secondary end points are 90-day mortality, recovery of renal function, length of stay (LOS) in hospital, and LOS in ICU. Recovery of renal function was defined if the urine output on discharge is normal (> 0.5 ml/kg/h for 24 h) and a return to a creatinine level of 150% as of the baseline on ICU discharge.

Statistics analysis

Continuous variables are expressed as median [interquartile range (IQR)] due to their non-normal distribution. The differences between groups were determined by the Mann-Whitney U test. Categorical variables are shown as frequencies and percentages. The comparisons were performed by the χ^2 test or Fisher's exact test as appropriate.

To balance the baseline differences, propensity-score matching (PSM) was conducted with a caliper width of 0.2 logits of the standard difference. Patients were divided using 1:1 nearest neighbor matching, so that each person in the Colloid group was matched with those in the Non-colloid group. The standardized mean difference (SMD) was used to assess the effectiveness of PSM to decrease the baseline differences [20](Supplementary Figure S1).

The Cox regression model was performed to assess the relationship between colloid infusion and mortality after adjustment for confounding variables with $p < 0.05$ in univariate analysis (Supplementary Table S2). The logistic regression model was used to assess the impact of colloid infusion on the recovery of renal function after adjusting for age, SOFA score, SAPSII score, and RRT use. LOS in hospital and LOS in ICU were compared by Wilcoxon rank-sum test between two groups. Survival analyses were censored at day 28 and day 90 after PSM.

Various subgroups were classified by different age, lactate, AKI stage, and cardiovascular disease. The association between the daily dose or type of colloid and 28-day mortality was also assessed. Multivariate analysis by Cox regression was used in subgroup analyses after adjusting for potential confounders, which were performed after PSM.

Statistical analysis was carried out using software Stata 15.1 and R 4.0.0 in the Windows operative system. Statistical significance was determined when the *p* value is less than 0.05.

Results

Basic characteristics

A total of 46,520 patients with the first ICU admission were extracted from the MIMIC-III database. A total of 12,884 patients fitted the definition of sepsis-3.0 within 48 h after ICU admission. A total of 4,553 patients were examined in the analysis based on the exclusion criteria. Of the study cohort, 1,158 patients were administrated with colloid infusion in the first 48 h in the ICU, while the remaining 3,395 patients did not receive colloid infusion (Fig. 1).

The baseline characteristics of the two groups before PSM are presented in Table 1. The mean age was slightly lower (68 *vs.* 70), and the weight, SOFA score, SAPSII score was higher in the Colloid group at admission, in comparison with the Non-colloid group. Patients with AKI, hypertension, coagulopathy, or obesity were more likely to be given a colloid solution. The levels of bilirubin, PT, and PH were lower, while the levels of platelet, glucose, hemoglobin, and lactate were statistically higher in the Non-colloid set compared to the Colloid set. The uses of RRT and mechanical ventilation were much more common in

the colloid group. The volume of daily crystalloid infusion was more and the urine output was less in the Colloid group.

Table 1
Baseline characteristics between groups before propensity score matching

Variables	Overall	Non-colloid group	Colloid group	P value	SMD
	4553	3395	1158		
Gender, male (%)	2476 (54.4)	1860 (54.8)	616 (53.2)	0.366	0.032
Age (median [IQR])	69 [57,80]	70 [57,80]	68 [57,78]	0.004	0.04
Weight (median [IQR])	78 [65,93]	77 [64,92]	80 [67,96]	< 0.001	0.128
Ethnicity (%)				0.001	0.166
Asian	112 (2.5)	98 (2.9)	14 (1.2)		
Black	290 (6.4)	233 (6.9)	57 (4.9)		
Hispanic	116 (2.5)	77 (2.3)	39 (3.4)		
Other	113 (2.5)	81 (2.4)	32 (2.8)		
Unknown	703 (15.4)	532 (15.7)	171 (14.8)		
White	3217 (70.7)	2373 (69.9)	844 (72.9)		
SOFA (median [IQR]) [b]	7 [5, 10]	7 [5, 10]	8 [5, 11]	< 0.001	0.298
GCS (median [IQR]) [b]	9 [6, 14]	9 [6, 14]	9 [3, 13]	< 0.001	0.288
SAPSII (median [IQR]) [b]	46 [36,57]	45 [35,56]	48 [39,58]	< 0.001	0.185
RRT (%)	277 (6.1)	181 (5.3)	96 (8.3)	< 0.001	0.118
Ventilation (%)	3515 (77.2)	2468 (72.7)	1047 (90.4)	< 0.001	0.469
Co-morbidities (%)					
AKI (%)	3435 (75.4)	2402 (70.8)	1033 (89.2)	< 0.001	0.474

Abbreviations: SOFA sequential organ failure assessment, *SAPSII* simplified acute physiology score II, *GCS* Glasgow Coma Scale, *RRT* renal replacement therapy, *AKI* acute kidney injury, *ARDS* acute respiratory distress syndrome, *MAP* mean arterial pressure, *PT* prothrombin time, *WBC* white blood cell, *IQR* interquartile range, *SMD* standardized mean difference

[a] The initial value during the first 24 h after ICU admission.

[b] The values were calculated during the first 24 h after ICU admission.

Variables	Overall	Non-colloid group	Colloid group	P value	SMD
AKI stage (%)				< 0.001	0.533
1	673 (14.8)	523 (15.4)	150 (13.0)		
2	1601 (35.2)	1151 (33.9)	450 (38.9)		
3	1164 (25.6)	731 (21.5)	433 (37.4)		
Cardiovascular diseases	3035 (66.7)	2270 (66.9)	765 (66.1)	0.643	0.017
Hypertension	2264 (49.7)	1604 (47.2)	660 (57.0)	< 0.001	0.196
Chronic pulmonary diseases	1056 (23.2)	783 (23.1)	273 (23.6)	0.752	0.012
Diabetes	309 (6.8)	228 (6.7)	81 (7.0)	0.796	0.011
ARDS	29 (0.6)	25 (0.7)	4 (0.3)	0.219	0.053
Coagulopathy	943 (20.7)	578 (17.0)	365 (31.5)	< 0.001	0.343
Obesity	281 (6.2)	182 (5.4)	99 (8.5)	< 0.001	0.126
Anemia	206 (4.5)	143 (4.2)	63 (5.4)	0.098	0.057
Mean heartrate (median [IQR]) [b]	88 [78,101]	88 [78,101]	88 [79,101]	0.183	0.041
Mean MAP (median [IQR]) [b]	71 [67,77]	71 [67,77]	71 [66,77]	0.21	0.054
Platelet (median [IQR]) [a]	190 [129,269]	195 [138,273]	162 [110,248]	< 0.001	0.207
Bilirubin (median [IQR]) [a]	0.8 [0.5,1.7]	0.8 [0.4,1.6]	1.1 [0.6,3]	< 0.001	0.418
Creatinine (median [IQR]) [a]	1.2 [0.8,2]	1.2 [0.8,2]	1.2 [0.8,2]	0.777	0.033
Glucose (median [IQR]) [a]	124 [103,157]	125 [103,161.5]	120 [100,147]	< 0.001	0.209

Abbreviations: SOFA sequential organ failure assessment, *SAPSII* simplified acute physiology score II, *GCS* Glasgow Coma Scale, *RRT* renal replacement therapy, *AKI* acute kidney injury, *ARDS* acute respiratory distress syndrome, *MAP* mean arterial pressure, *PT* prothrombin time, *WBC* white blood cell, *IQR* interquartile range, *SMD* standardized mean difference

[a] The initial value during the first 24 h after ICU admission.

[b] The values were calculated during the first 24 h after ICU admission.

Variables	Overall	Non-colloid group	Colloid group	P value	SMD
Hemoglobin (median [IQR]) [a]	10.4 [9.2,11.9]	10.5 [9.3,12.1]	9.95 [9,11.2]	< 0.001	0.286
PT (median [IQR]) [a]	14.7 [13.4,17]	14.6 [13.3,16.6]	15.2 [13.7,18.2]	< 0.001	0.072
WBC (median [IQR]) [a]	11.9 [8.2,17]	11.9 [8.2,17.2]	11.7 [8.2,16.5]	0.307	0.054
Lactate (median [IQR]) [a]	1.9 [1.3,3.1]	2 [1.4,3.2]	1.7 [1.2,2.9]	< 0.001	0.091
PH (median [IQR]) [a]	7.4 [7.3,7.4]	7.3 [7.3,7.4]	7.4 [7.3,7.4]	0.001	0.086
Crystalloid does (median [IQR]) [b]	1500 [0,3250]	1000 [0,3000]	2300 [750,4500]	< 0.001	0.425
Urine output (median [IQR]) [b]	717.5 [299,1809]	800 [463,2298]	559 [291,952.75]	< 0.001	0.415

Abbreviations: SOFA sequential organ failure assessment, *SAPSII* simplified acute physiology score II, *GCS* Glasgow Coma Scale, *RRT* renal replacement therapy, *AKI* acute kidney injury, *ARDS* acute respiratory distress syndrome, *MAP* mean arterial pressure, *PT* prothrombin time, *WBC* white blood cell, *IQR* interquartile range, *SMD* standardized mean difference

[a] The initial value during the first 24 h after ICU admission.

[b] The values were calculated during the first 24 h after ICU admission.

Relationship between colloid infusion and outcomes

After PSM, 1012 patients who did not receive colloid infusion were matched with 1012 patients who received colloid infusion. The imbalance between the two groups was significantly reduced after PSM, and SMDs of all variables were less than 10% (Table 2 and Figure S1).

Table 2
Comparisons between groups after propensity score matching

Variables	Non-colloid	Colloid	P value	SMD
	1012	1012		
Gender, male, n (%)	516 (51)	531(52.5)	0.533	0.03
Age (median [IQR])	70 [58,80]	69 [58,78]	0.066	0.068
Weight (median [IQR])	80 [67,95]	80 [67,96]	0.657	0.028
Ethnicity, n (%)			0.965	0.053
Asian	11 (1.1)	12 (1.2)		
Black	53 (5.2)	51 (5.0)		
Hispanic	31 (3.1)	34 (3.4)		
Native	1 (0.1)	1 (0.1)		
Other	33 (3.3)	28 (2.8)		
Unknown	134 (13.2)	148 (14.6)		
White	749 (74.0)	738 (72.9)		
SOFA (median [IQR]) [b]	8 [5, 11]	8 [5, 11]	0.275	0.039
GCS (median [IQR]) [b]	8 [5, 13]	9 [3, 14]	0.457	0.029
SAPAII (median [IQR]) [b]	48 [38,60]	47 [38,58]	0.241	0.056
RRT, n (%)	74 (7.3)	73 (7.2)	1	0.004
Ventilation, n (%)	894 (88.3)	906 (89.5)	0.436	0.038
AKI, n (%)	903 (89.2)	889 (87.8)	0.364	0.043
AKI stage, n (%)			0.166	0.1
0	109 (10.8)	123 (12.2)		
1	118 (11.7)	138 (13.6)		
2	452 (44.7)	406 (40.1)		
3	333 (32.9)	345 (34.1)		
Cardiovascular diseases, n (%)	673 (66.5)	683 (67.5)	0.671	0.021
Hypertension, n (%)	578 (57.1)	572 (56.5)	0.822	0.012
Chronic lung disease, n (%)	240 (23.7)	241(23.8)	1	0.002

Variables	Non-colloid	Colloid	P value	SMD
Diabetes, n (%)	81 (8)	74 (7.3)	0.616	0.026
ARDS, n (%)	4 (0.4)	4 (0.4)	1	< 0.001
Coagulopathy, n (%)	270 (26.7)	271(26.8)	1	0.002
Obesity, n (%)	92 (9.1)	86 (8.5)	0.695	0.021
Anemia, n (%)	56 (5.5)	49 (4.8)	0.548	0.031
Mean heartrate (median [IQR]) [b]	90 [79,103]	88 [79,101]	0.2	0.052
Mean MAP (median [IQR]) [b]	72 [66.8,76]	71 [66,77]	0.376	0.055
Platelet (median [IQR]) [a]	184 [123,256.5]	172 [116,260.5]	0.16	0.028
Bilirubin (median [IQR]) [a]	0.9 [0.5,2.1]	1 [0.6,2.4]	0.013	0.039
Creatinine (median [IQR]) [a]	1.2 [0.8,2]	1.2 [0.8,2]	0.469	0.041
Glucose (median [IQR]) [a]	123 [101,152]	121 [102,149]	0.997	0.001
Hemoglobin (median [IQR]) [a]	10 [8.9,11.2]	10 [9,11.2]	0.453	0.038
PT (median [IQR]) [a]	14.7 [13.4,17.2]	15.1 [13.6,17.6]	0.033	0.038
WBC (median [IQR]) [a]	11.5 [7.9,17]	11.7 [8.3,16.3]	0.614	0.032
Lactate (median [IQR]) [a]	1.9 [1.3,3]	1.7 [1.2,2.8]	0.004	0.028
PH (median [IQR]) [a]	7.4 [7.3,7.4]	7.4 [7.3,7.4]	0.891	0.014
Crystalloid does (median [IQR])	2000 [500,4000]	2000 [500,4000]	0.812	0.008
Urine output (median [IQR]) [b]	583.5 [293,985.8]	582 [293,992]	0.72	0.051

Abbreviations: SOFA sequential organ failure assessment, SAPSII simplified acute physiology score II, GCS Glasgow coma score, MAP mean arterial pressure, ARDS acute respiratory distress syndrome, RRT renal replacement therapy, PT prothrombin time, WBC white blood cell, SMD standardized mean difference.

[a] The initial value during the first 24h after ICU admission.

[b] The values were calculated during the first 24h after ICU admission.

In the pre-matched cohort, colloid infusion was related to improved mortality at 28 days (HR 0.65; 95% CI 0.57–0.76; P < 0.001), and at 90 days (HR 0.78; 95% CI 0.69–0.88; P < 0.001), following adjustment of the confounders with P < 0.05 in univariate analysis (Table 3 and Supplementary Table S2). The impact of

colloid infusion on the renal function recovery was assessed by the logistic regression model, and the result showed that colloid infusion was associated with delayed recovery of renal function (HR 0.83; 95% CI 0.71–0.96; P = 0.015). In addition, we found that colloid infusion was associated with extended LOS in ICU and hospital (Table 2).

Table 3
Association between colloid infusion and clinical outcomes in patients with septic shock

Outcomes	Non-colloid	Colloid	*P*-value	HR (95%CI)
Pre-matched cohort	**n = 3395**	**n = 1158**		
Primary outcome				
28-day mortality, n (%) [a]	948 (27.9)	296 (25.6)	< 0.001	0.65 (0.57–0.76)
Secondary outcomes				
90-day mortality, n (%) [a]	1166 (34.3)	412 (35.6)	< 0.001	0.78 (0.69–0.88)
Recovery of renal function, n (%) [b]	2339 (68.9)	700 (60.4)	0.015	0.83 (0.71–0.96)
Length of hospital stay (days, median [IQR]) [c]	10.1 [5.9, 17.4]	16.85 [9.8, 27.4]	< 0.001	
Length of ICU stay (days, median [IQR]) [c]	4 [2, 8.7]	7.25 [3.2, 15.2]	< 0.001	
Post-matched cohort	**n = 1012**	**n = 1012**		
Primary outcome				
28-day mortality, n (%) [a]	325 (32.1)	236 (23.3)	< 0.001	0.62 (0.52–0.73)
Secondary outcomes				
90-day mortality, n (%) [a]	388 (38.3)	338 (33.4)	< 0.001	0.76 (0.65–0.88)
Recovery of renal function, n (%) [b]	614 (60.7)	635 (62.7)	0.547	1.06 (0.87–1.29)

Abbreviations: IQR interquartile range, *ICU* intensive care unit, *HR* hazard ratio, *CI* confidence interval

[a] Cox proportional hazard models were used to assess the impact of colloid infusion on mortality outcomes adjusting for confounders with a *P*-value < 0.05 in univariate analysis.

[b] Recovery of renal function was defined as being discharged from ICU with serum creatinine below 1.5 times the baseline value and normal urine output (> 0.5 ml/kg/h). Impact of colloid infusion on the recovery of renal function was assessed using the logistic regression model adjusting for age, SOFA score, SAPSII score, and RRT use.

[c] Wilcoxon rank sum test was used to assess the association between colloid infusion and length of stay.

Outcomes	Non-colloid	Colloid	*P*-value	HR (95%CI)
Length of hospital stay (days, median [IQR]) [c]	11.7 [7, 19.3]	16.7 [9.8, 27.2]	< 0.001	
Length of ICU stay (days, median [IQR]) [c]	5.1 [2.4, 11]	7 [3.2, 15]	< 0.001	
Abbreviations: IQR interquartile range, *ICU* intensive care unit, *HR* hazard ratio, *CI* confidence interval				
[a] Cox proportional hazard models were used to assess the impact of colloid infusion on mortality outcomes adjusting for confounders with a *P*-value < 0.05 in univariate analysis.				
[b] Recovery of renal function was defined as being discharged from ICU with serum creatinine below 1.5 times the baseline value and normal urine output (> 0.5 ml/kg/h). Impact of colloid infusion on the recovery of renal function was assessed using the logistic regression model adjusting for age, SOFA score, SAPSII score, and RRT use.				
[c] Wilcoxon rank sum test was used to assess the association between colloid infusion and length of stay.				

In the post-matched cohort, similar to the results before PSM, colloid infusion was associated with improved 28-day survival (HR 0.62; 95% CI 0.52–0.73; P < 0.001), and with reduced 90-day mortality (HR 0.76; 95% CI 0.65–0.88; P < 0.001) (Table 3). Nevertheless, the recovery of renal function was not statistically different between the Colloid group and the Non-colloid group (HR 1.06; 95% CI 0.87–1.29; P = 0.547) (Table 3). The colloid infusion was also associated with longer LOS in ICU and hospital (Table 2). Kaplan–Meier's survival estimates of patients according to colloid infusion at ICU admission are shown in Fig. 2. The colloid infusion remained associated with improved the 28-day (P < 0.0001) and the 90-day (P = 0.0021) mortality.

Taking the dose and type of colloid into consideration, we found that colloid infusion did reduce the 28-day mortality, independent of dose (Table S3), except that dextran did not reduce the 28-day mortality (HR 1.41; 95% CI 0.19–10.59; P = 0.736). Albumin (HR 0.64; 95% CI 0.54–0.76; P < 0.001) and HES (HR 0.26; 95% CI 0.1–0.71; P = 0.008) were found to be associated with improved 28-day survival (Table S4).

Subgroup analysis

The relationship between colloid infusion and 28-day mortality in subgroups is shown in Fig. 3. Similarly, the study did manifest significant beneficial effects of colloid infusion on mortality at 28 days in patients with septic shock, regardless of age and lactate concentration. The beneficial effect of colloid infusion on mortality was also observed in people with cardiovascular disease or AKI. Colloid infusion may reduce the risk of death in patients with AKI stage 2 (HR 0.42; 95% CI 0.3–0.59; $p < 0.001$) and stage 3 (HR 0.63; 95% CI 0.49–0.81; $p < 0.001$) but not in patients with AKI stage 1 (HR 1.28; 95% CI 0.69–2.37; $p = 0.437$) (Fig. 3).

Discussion

Our results suggested that colloid infusion within 48 h after ICU admission lowered short-term mortality in people with septic shock, but it may lead to longer LOS in ICU and in hospital. The results of our study also showed that no significant correlation was found between colloid infusion and the recovery of renal function. However, subgroup analysis showed that no significant beneficial effect was observed in patients with AKI stage 1 and treated by colloid infusion. The use of albumin or HES was associated with decreased 28-day mortality, but no apparent survival advantage was observed in the dextran group.

Whether using colloid infusion to resuscitate patients with septic shock will improve patient-centered outcomes, and for whom benefits will outweigh the risks remain debated. Other studies have reported the effectiveness of albumin in critically ill or sepsis patients[6, 8, 11, 21, 22], but only a few studies focused on the use of colloid in patients suffering from septic shock [4, 12]. The prospective sequential analysis [4] showed that hydroxyethyl starch and gelatin may impair renal function. But the study did not assess the impact of colloid infusion on mortality. Our findings may appear not to agree with the results of the trial from Pietro Caironi [12], which suggested that the use of albumin within the first 28 days of treatment did not improve the survival rate compared with crystalloids alone, over a 90-day follow-up. However, Caironi's study had confirmed the physiological benefit of albumin administration, such as larger fluid diffusion in the intravascular space. Besides, albumin may mediate peripheral vasodilation during sepsis as a scavenging agent for nitric oxide [23, 24]. A meta-analysis found that albumin infusion contributed to decreased 90-day mortality in people with severe sepsis and septic shock [9]. Unfortunately, its impacts on renal function and stage of AKI were not conclusive in the study. Further studies are needed to evaluate the effects of colloid infusion on renal function and prognosis in different subgroups of AKI.

Our study found that colloid infusion had no effect on renal function recovery in septic shock people. This finding may be different from the previous report by Bayer et al. [4]. However, it should be noted that septic shock itself can affect the recovery of renal function as well. In addition, our subgroup analysis showed that colloid infusion did not improve the 28-day survival in sepsis patients with AKI stage 1. Therefore, it is suggested that colloid infusion is not necessary for the early stage of septic shock as the renal function of less severe patients is likely to be recovered by crystalloid solution infusion, anti-infection, and other related treatments.

However, there are still several limitations to our study. Firstly, the current research is based on a clinical electronic medical record that contains some missing values. To improve statistical power, multiple imputations were used to decrease the risk of deviation due to missing values. Secondly, we did not report the range of albumin concentrations in this study. The effect of the concentrations of albumin on mortality is unclear. Finally, due to the characteristics of a retrospective research, the relationship between the colloid infusion and mortality can only be interpreted indirectly, which may only provide preliminary evidence for further investigation.

Conclusion

In people with septic shock, the infusion of albumin or HES decreased short-term mortality, but dextran had no apparent survival advantage. In addition, colloid infusion had no effect on renal function recovery in patients with septic shock.

Abbreviations

MIMIC Medical Information Mart for Intensive Care, PSM Propensity score matching, IQR interquartile range, ICU intensive care unit, HR hazard ratio, CI confidence interval, COP colloid-osmotic pressure, FFP fresh frozen plasma, HES hydroxyethyl starch, KDIGO Kidney Disease: Improving Global Outcomes, SOFA sequential organ failure assessment, LOS length of stay, SAPSII simplified acute physiology score II, GCS Glasgow coma score, MAP mean arterial pressure, ARDS acute respiratory distress syndrome, RRT renal replacement therapy, PT prothrombin time, WBC white blood cell, SMD standardized mean difference.

Declarations

Ethics approval and consent to participate

MIMIC III database used in this study was approved by MIT's Institutional Review Board (IRB) and does not include protected health information. Thus, requirement for individual patient consent was waived because the study did not impact clinical care, and all protected health information was deidentified.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used in the present study are available from the first author and corresponding authors on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

CG collected and analyzed data, and co-wrote the manuscript. QP and YJ was helpful for statistical analysis and interpretation of results. ZL and WL prepared the figures and tables. LZ and YA designed

and supervised the study, and YA revised the manuscript. All authors have read and reviewed the final manuscript.

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Figures

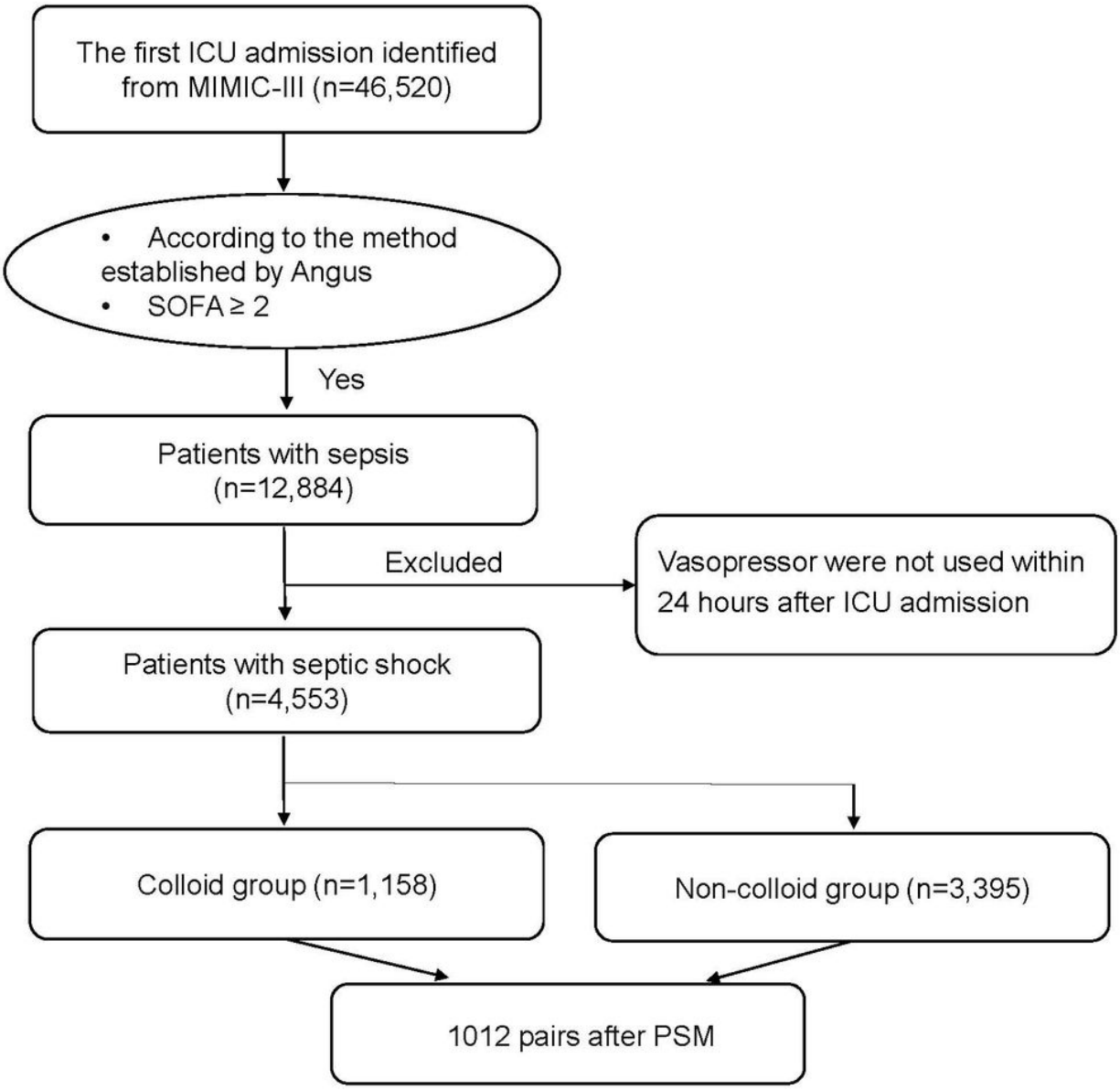
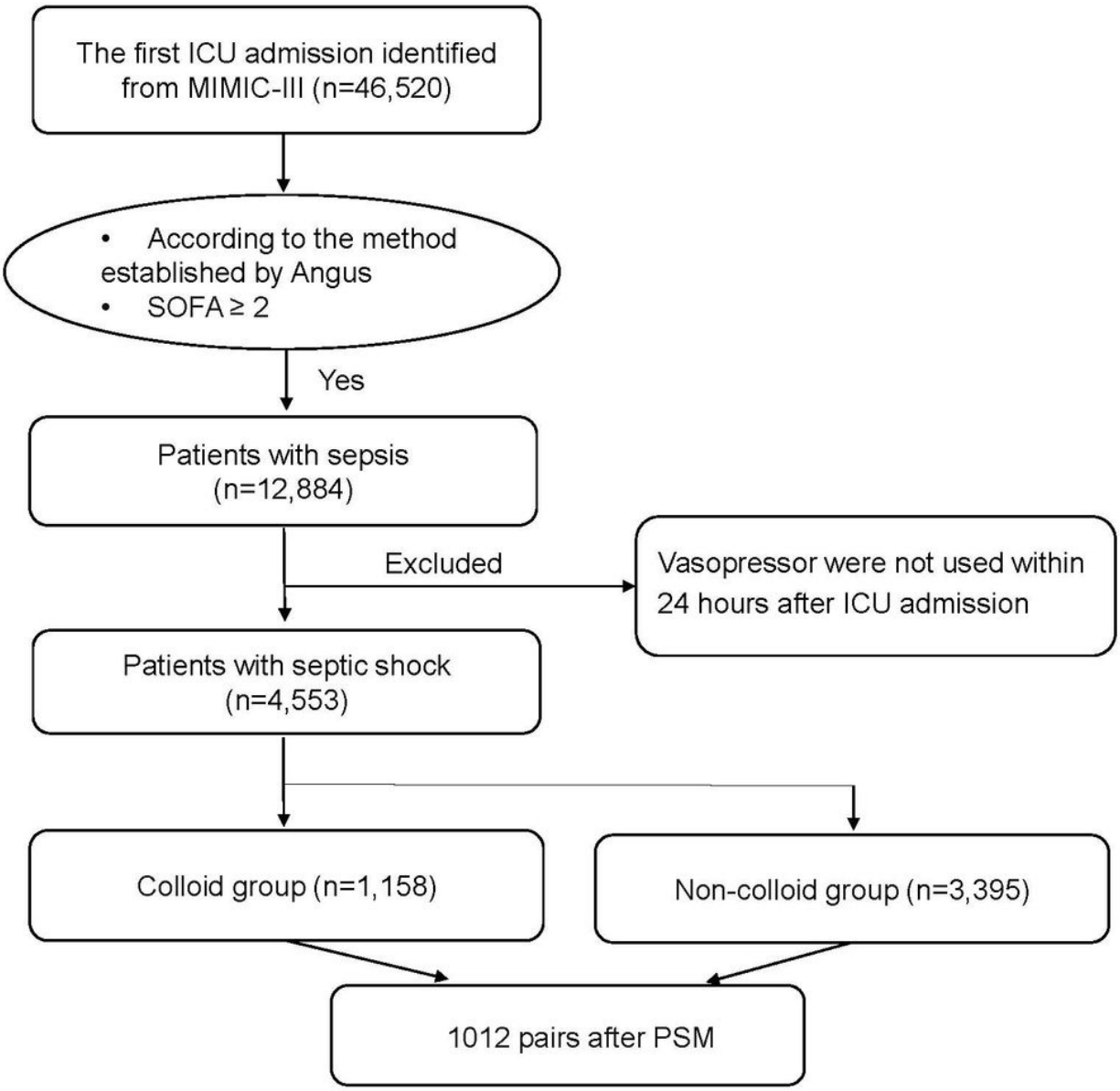


Figure 1

Flowchart of patient selection. ICU: intensive care unit; MIMIC III: Multiparameter Intelligent Monitoring in Intensive Care Database III; SOFA: sequential organ failure assessment; PSM: propensity score matching



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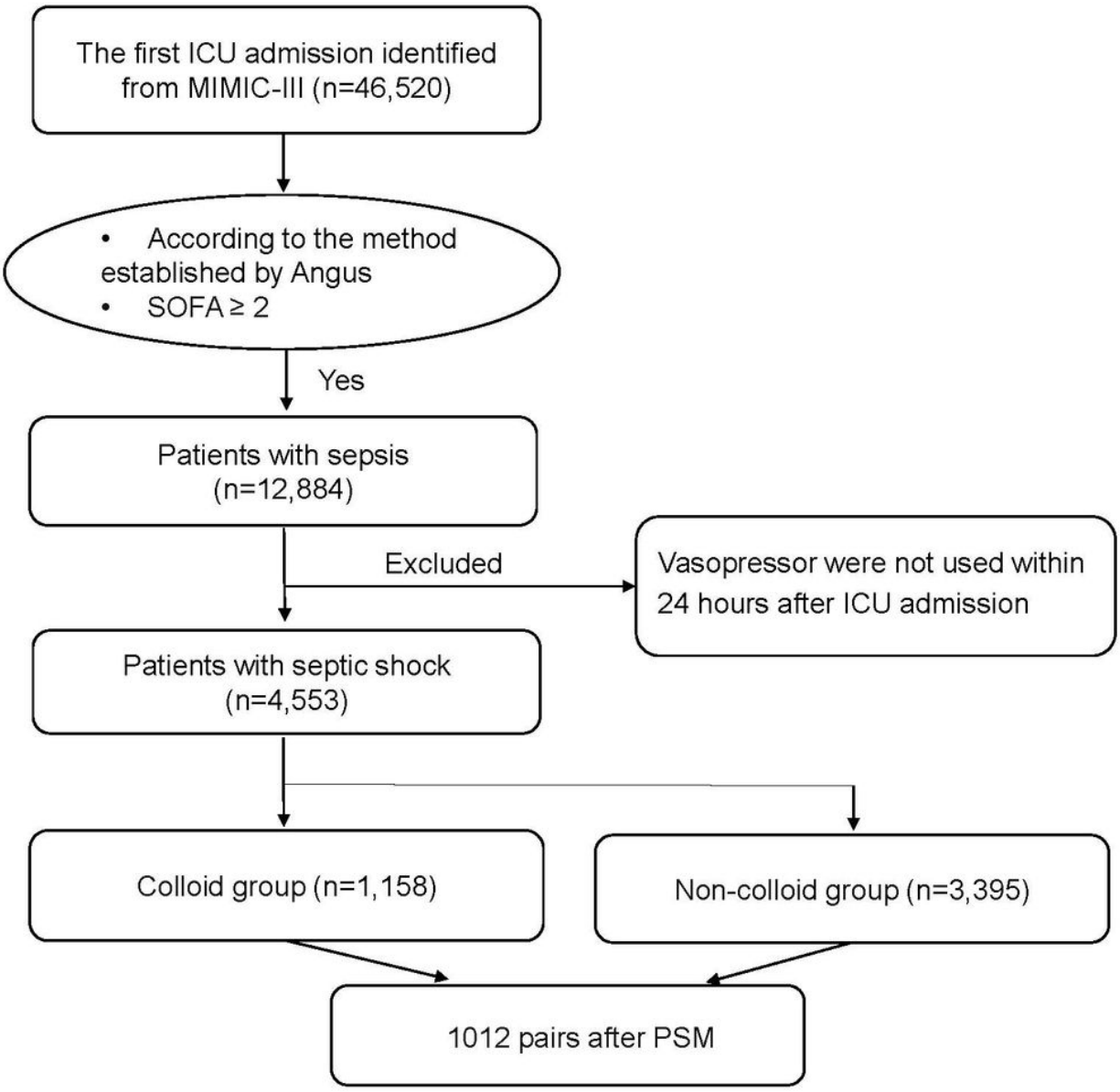

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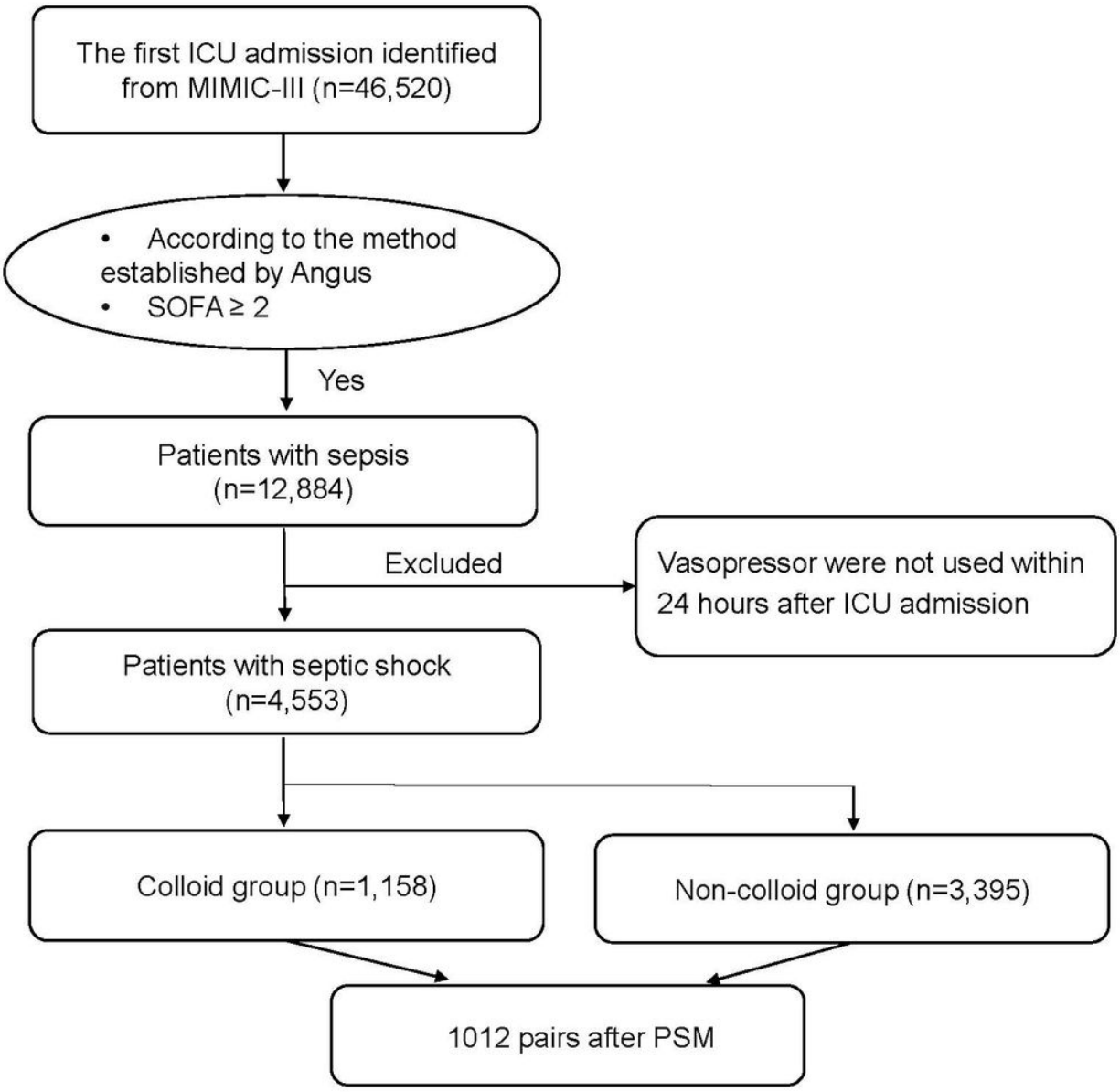

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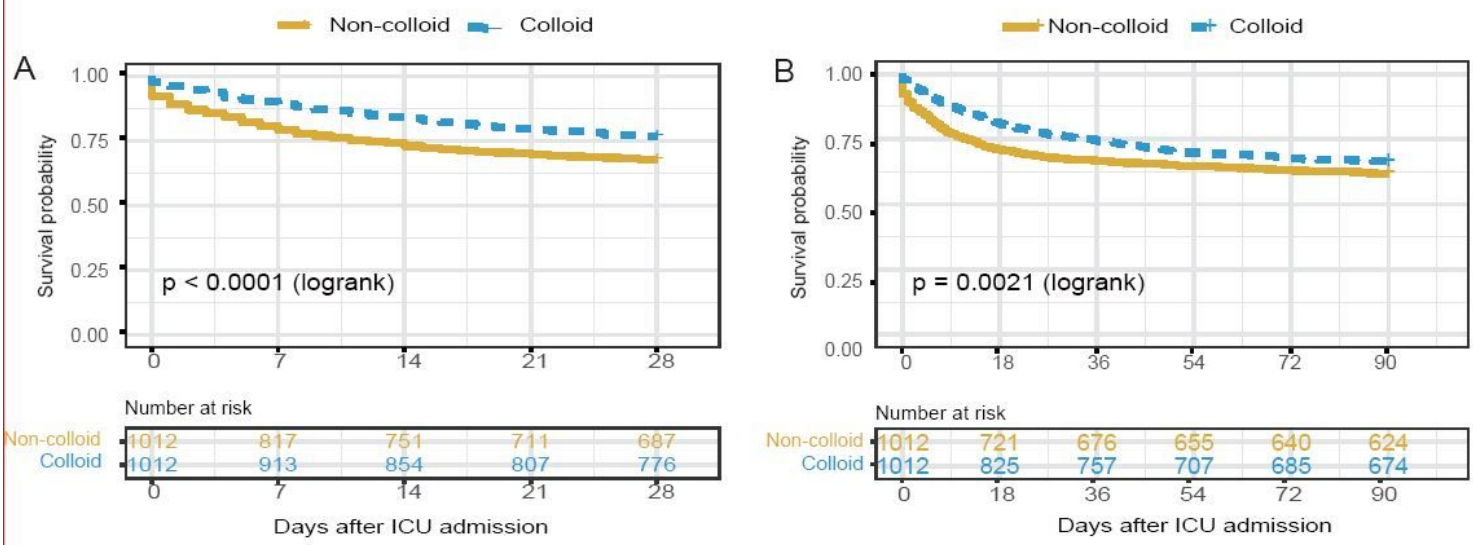
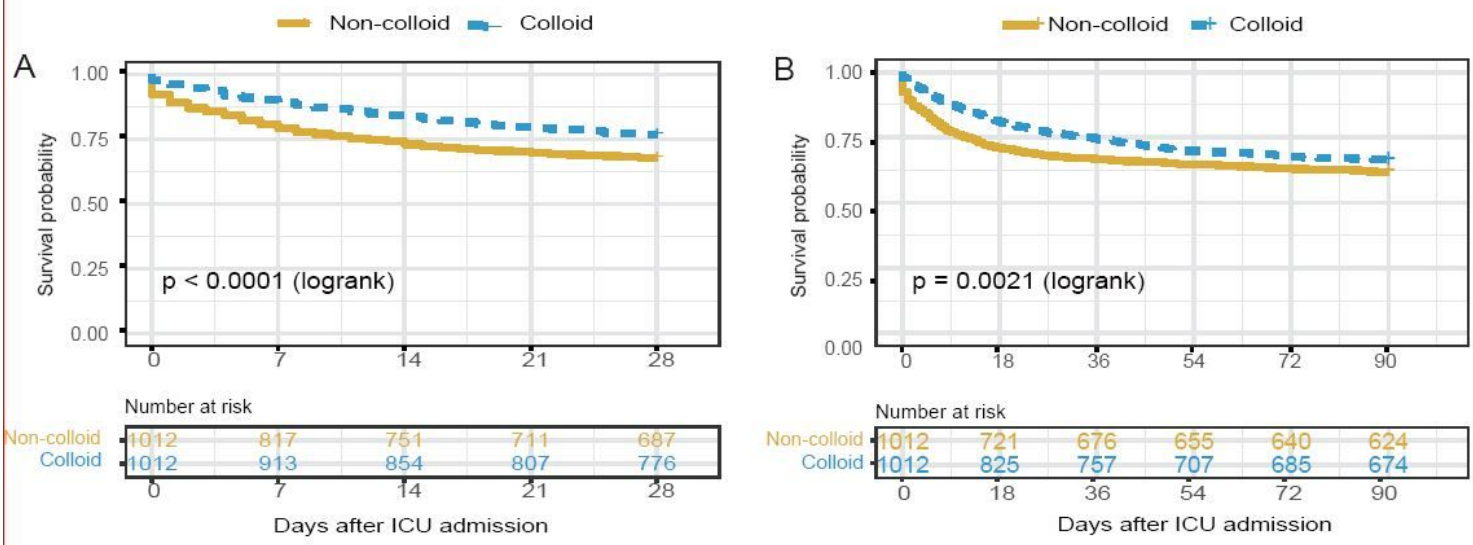


Figure 2

Kaplan–Meier's survival estimates of patients at 28 day (A) and 90 day (B).



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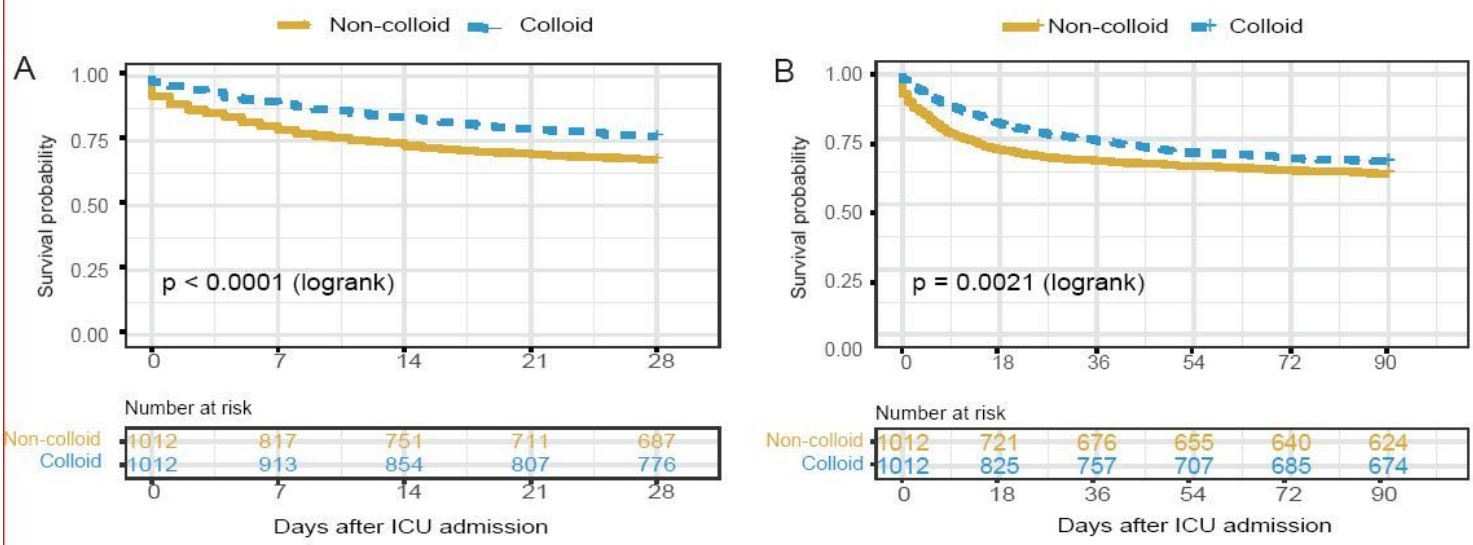

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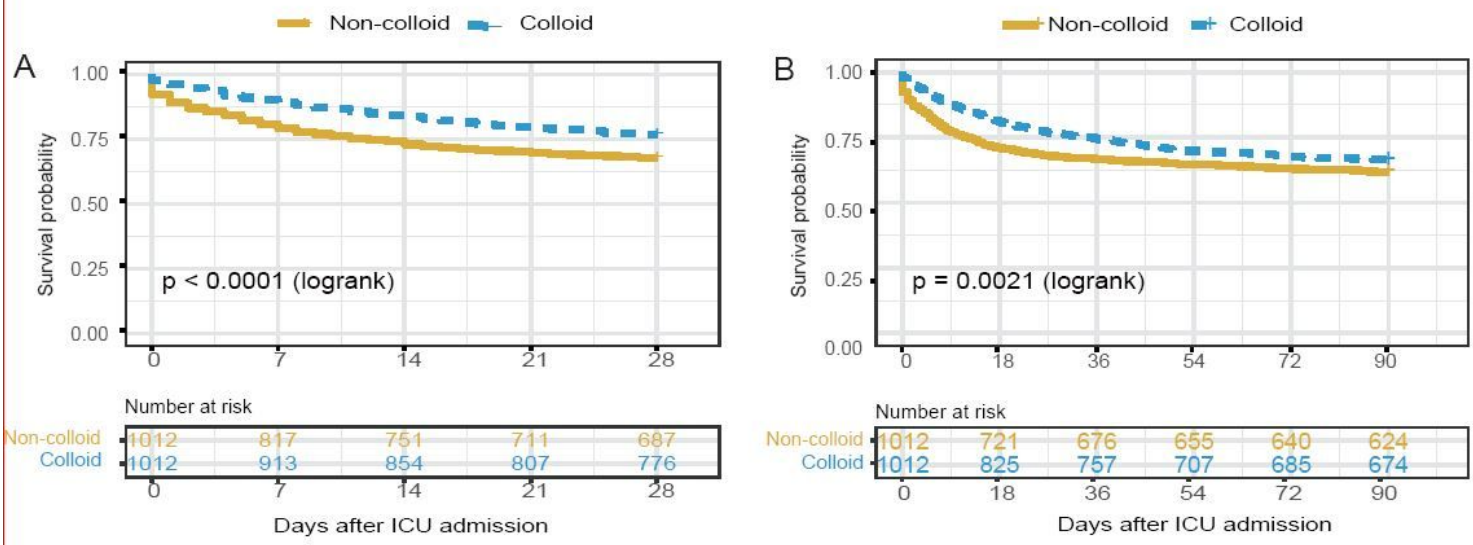

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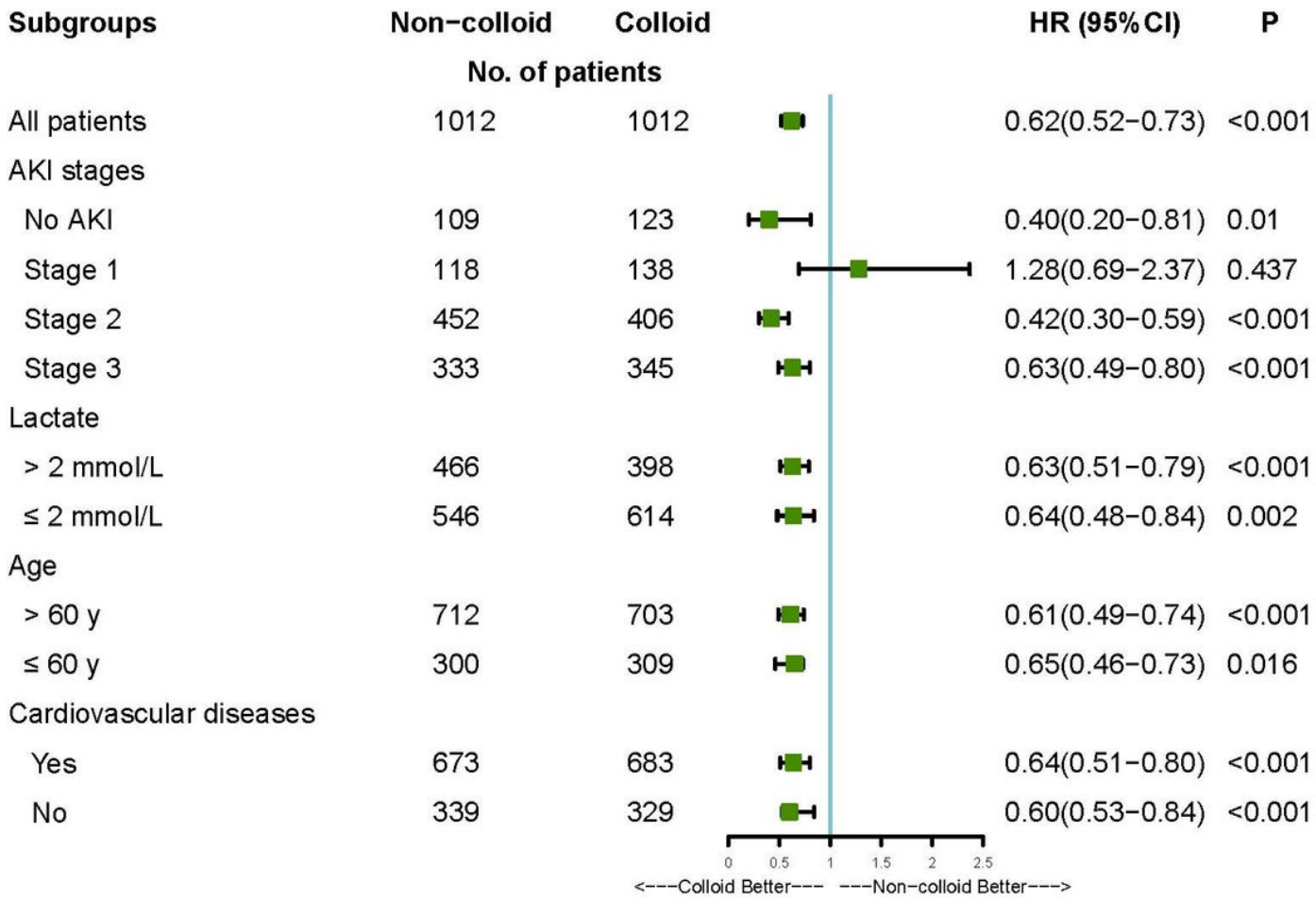
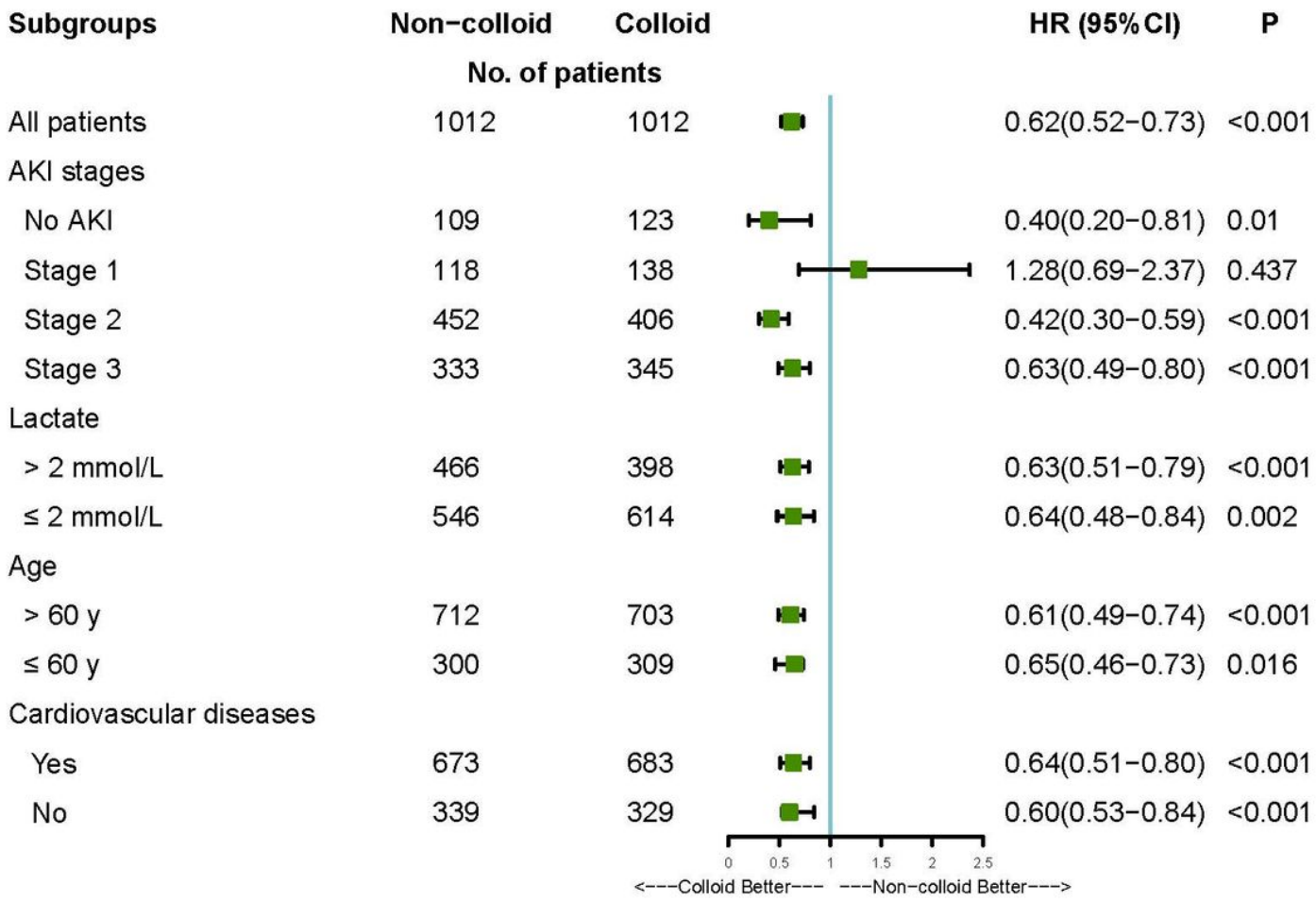


Figure 3

The association between colloid infusion and 28-day mortality in subgroups. AKI: acute kidney injury; HR: hazard ratio; CI: confidence interval



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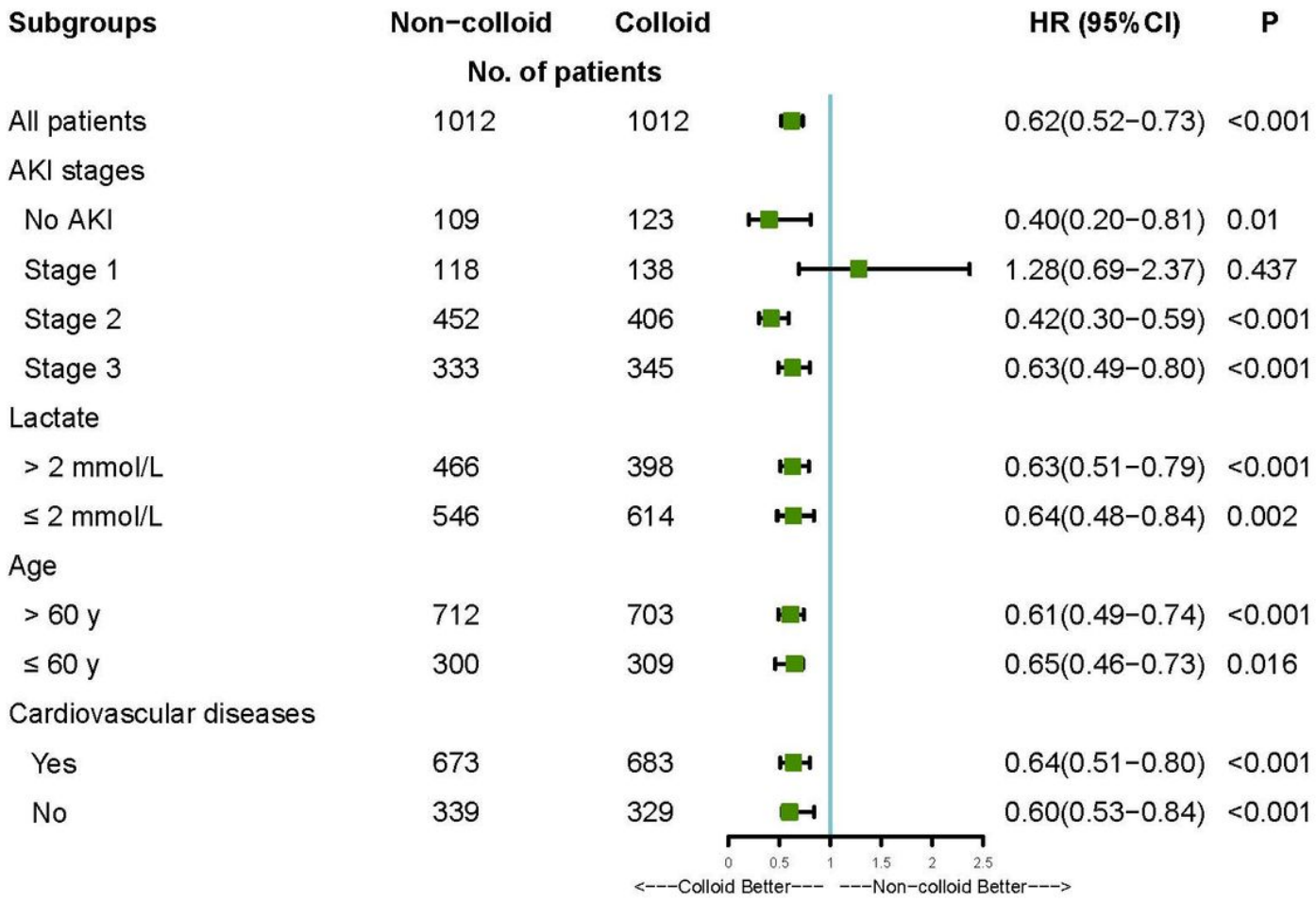

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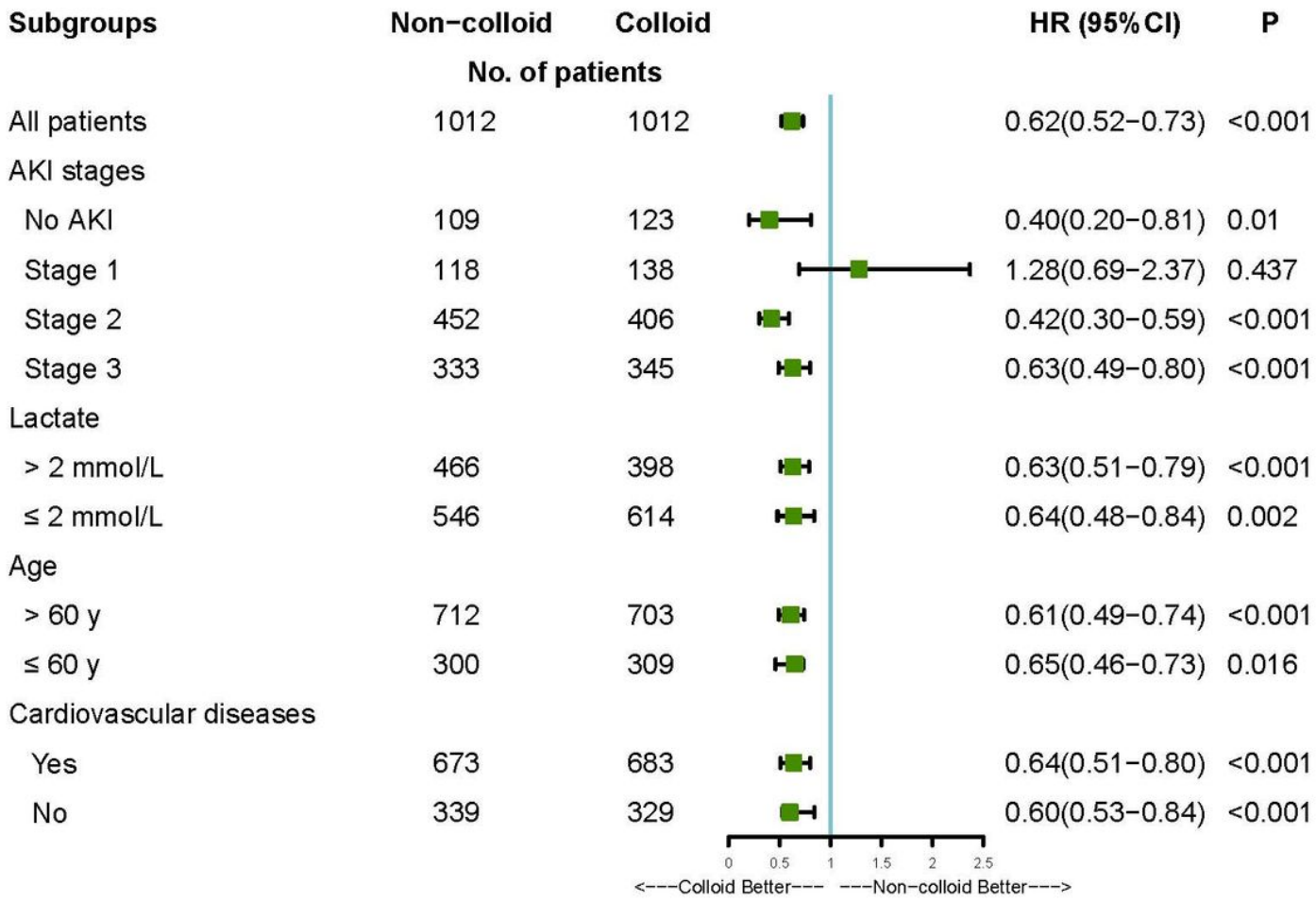

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