

META-ANALYSIS

What influences interruption of continuous renal replacement therapy in intensive care unit patients: A review with meta-analysis on outcome variables

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Abstract

Background: Evidence suggests that 8%–10% of ICU patients receive renal replacement therapy. However, there is a high rate of unplanned CRRT interruption, ranging between 17% and 74%. Studies on unplanned interruption of CRRT mainly focused on the retrospective investigation of related risk factors and conclusions have been diverse.

Aims: This article aims to clarify the main influencing factors related to unplanned interruption of continuous renal replacement therapy (CRRT) in adult patients in intensive care units (ICUs).

Study Design: A literature review and meta-analysis were undertaken. Following the application of the Newcastle–Ottawa Scale (NOS), a total of 15 articles were included in a total of 2132 patients who underwent 3690 CRRT procedures and 2181 unplanned interruption times. The methodological guideline of a scoping review was applied for the evidence synthesis while applying the meta-analysis quantitative methodological guideline to identify and clarify main influencing factors related to unplanned interruption of CRRT. The reporting Prisma Protocol was followed.

Results: Longer filter life and prothrombin activation time, higher red blood cell count, greater transmembrane pressure, faster blood flow rate, intermittent saline irrigation, lower creatinine level, low prothrombin activity and pre-dilution are factors identified to potentially affect unplanned CRRT in ICU patients.

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Xia Xiaomei and Chong Yuliang have contributed equally to the article.

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Conclusions: Available evidence suggests four clinical challenges associated with unplanned CRRT interruption, namely: (a) effects of red blood cell count, filter life, cross-mode pressure, blood flow velocity, prothrombin activity and activated partial thrombin time on unplanned interruption; (b) influence of dilution mode on unplanned interruption; (c) influence of intermittent saline irrigation on unplanned interruption; (d) influence of Scr level on unplanned interruption.

Relevance to Clinical Practice: The potential to increase the ability to better manage unplanned CRRT in ICUs has been identified in this article and constitutes a relevant potential health care management contribution that can be implemented by nurses.

KEYWORDS

continuous renal replacement therapy, critical care, health care management, ICU patients, meta-analysis

1 | INTRODUCTION

Continuous renal replacement therapy (CRRT) is adopted to help remove toxins from the blood and promote the recovery of renal function. Continuous extracorporeal circulation blood purification is the general term for all treatment methods that continuously and slowly eliminate water and solutes.¹ CRRT technology has been widely used in clinical practice as an important tool to save the lives of critically ill patients. Recent research has suggested² that 8%–10% of ICU patients receive renal replacement therapy, but due to the particularity of CRRT technology, the complexity of operation and the influence of various factors, many problems have been identified, forcing a high rate of unplanned treatment interruption, ranging from 17.14% to 74.51%.³ This not only delays the treatment time and affects the treatment effect but also increases the economic burden of patients and the workload of clinical staff.

2 | BACKGROUND/JUSTIFICATION FOR STUDY

Recent studies on unplanned interruption of CRRT have increased, but mainly focus on the retrospective investigation of related risk factors, and the conclusions are diverse. Thus, this article applies the meta-analysis method to identify and clarify main influencing factors related to unplanned interruption of CRRT, in order to provide scientific basis for practice in critical care.

3 | AIMS AND OBJECTIVES OF STUDY

CRRT is adopted to help remove toxins from the blood and promote the recovery of renal function. Recent research has suggested that 8%–10% of ICU patients receive renal replacement therapy. However, due to the particularity of CRRT technology, the complexity of operation and the influence of various other factors, many problems have been identified forcing a high rate of unplanned CRRT interruption, ranging between 17% to 74%. Studies on unplanned interruption of CRRT have

What is known about the topic

- Evidence suggests that 8%–10% of ICU patients receive renal replacement therapy. However, there is a high rate of unplanned CRRT interruption, ranging between 17% and 74%. Studies on unplanned interruption of CRRT mainly focused on the retrospective investigation of related risk factors and conclusions have been diverse.

What this paper adds

- The potential to increase the ability to better manage unplanned CRRT in ICUs has been identified in this article and constitutes a relevant potential health care management contribution that can be implemented by nurses.

increased but have mainly focused on the retrospective investigation of related risk factors and conclusions have been diverse. This article aims to clarify the main influencing factors related to unplanned interruption of CRRT in adult patients in intensive care units (ICU).

4 | DESIGN AND METHODOLOGICAL GUIDELINES: SETTING AND SAMPLE, DATA COLLECTION TOOLS AND METHODS, DATA ANALYSIS

4.1 | Data and methods

The methodological guideline of a scoping review was applied for the evidence synthesis with the objective of identifying and mapping relevant evidence that met predetermined inclusion criteria regarding the topic while applying the meta-analysis quantitative methodological guideline to identify and clarify main influencing factors related to unplanned interruption of CRRT, in order to provide scientific basis for practice in critical care. The reporting Prisma Protocol was followed.

4.2 | Registration research

This study was reported in accordance with the PRISMA Statement and registered at INPLASY.Com (registration number: INPLASY2023100091).

4.3 | Literature search strategy

The databases including CNKI, Wanfang Database, VIP, Web of Science, Pubmed and Embase were searched. The keywords used were continuous renal replacement therapy/continuous blood purification/blood purification/haemodialysis, unplanned interruption/filter life, etc. The keywords applied in English were: continuous renal replacement therapy/CRRT/CVVH/CVVHDF CVVHD, unplanned/unscheduled interruptions, etc. Subject words and replacement words are freely combined, and flexibly adjusted according to each database. The search period was from the establishment of the database to September 2022, including all published literature in both Chinese and English. At the same time, in order to prevent omissions, this study also collected the references attached to the included literature, supplemented by manual search, and included relevant studies that met the criteria.

4.3.1 | Inclusion criteria

The inclusion criteria were: (1) Study type: all observational studies in Chinese and English, including prospective observational study and retrospective observational studies. (2) Study subjects: patients ≥ 18 years old and admitted to ICU for CRRT. (3) The literature data is accurate and complete or the required data can be calculated according to the information provided. (4) The quality of the literature was high, and the Newcastle–Ottawa Scale (NOS) score was >6 points.

4.3.2 | Exclusion criteria

The exclusion criteria were: (1) Randomized controlled trial. (2) Literature review, conference report, case report, dissertation, etc. (3) Repeated publication or failure to obtain the full text.

4.4 | Literature screening and quality evaluation

We conducted literature screening and quality evaluation which was cross-checked independently by two researchers according to the inclusion and exclusion criteria. If there was any disagreement, a third researcher was consulted and a decision was taken. The Newcastle–Ottawa Scale⁴ was used to evaluate the quality of the included documents. The total score of the scale is 9 points, including the selection of research objects (0–4 points), comparability (0–2 points) and result determination (0–3 points). The higher the score, the higher the

quality of the literature. Only high-quality literature with NOS score >6 was included in this study.

4.5 | Data extraction

The basic data collected included the first author/publication year, study region, disease type, age, sex, sample size (number of unplanned interruption times) and 29 major influencing factors. These include sex, age, treatment mode, whether anticoagulants are used, catheter placement, whether ventilators are used, whether blood products and fat milk are transfused, filter life, activated prothrombin time, prothrombin activity, red blood cell count, transmembrane pressure, blood flow velocity, intermittent saline irrigation, creatinine level, dilution mode, haemoglobin level, platelet count, blood calcium level, albumin level, replacement fluid velocity, prothrombin time, haematocrit, International Normalized Ratio, white blood cell count, organ failure score, blood potassium level, ICU admission time, replacement fluid velocity.

4.6 | Statistical processing

Meta-analysis was performed using RevMan5.3 software. Standardized mean difference (OR) values (odds ratio), MD values (mean difference) and/or SMD values (95% CI) were used for binary and continuous data, respectively. The chi-squared test was used for heterogeneity analysis. If $p > .10$ and $I^2 < 50\%$, the fixed effects model was used for meta-analysis; otherwise, the random effects model was used, and sensitivity analysis was performed to determine the stability of the results. The funnel plot was used to analyse publication bias for the relevant factors with the number of included articles ≥ 10 . We confirmed whether the basic symmetry on both sides indicated that there was no publication bias; If not, there was the possibility of publication bias.

5 | RESULTS

5.1 | Literature search results

According to the proposed search strategy, 748 articles were initially obtained, and were screened strictly according to the inclusion and exclusion criteria. Finally, 15 articles were included, including eight in Chinese and seven in English (see Figure 1).

5.2 | Basic features of included literature and methodological quality assessment results

A total of 15^{5–19} papers were included in this study, involving seven provinces in China, Australia, South Korea and Spain, with extensive sample coverage and strong representativeness. A total of 2132 patients had 3690 CRRT episodes, of which 2181 were unplanned

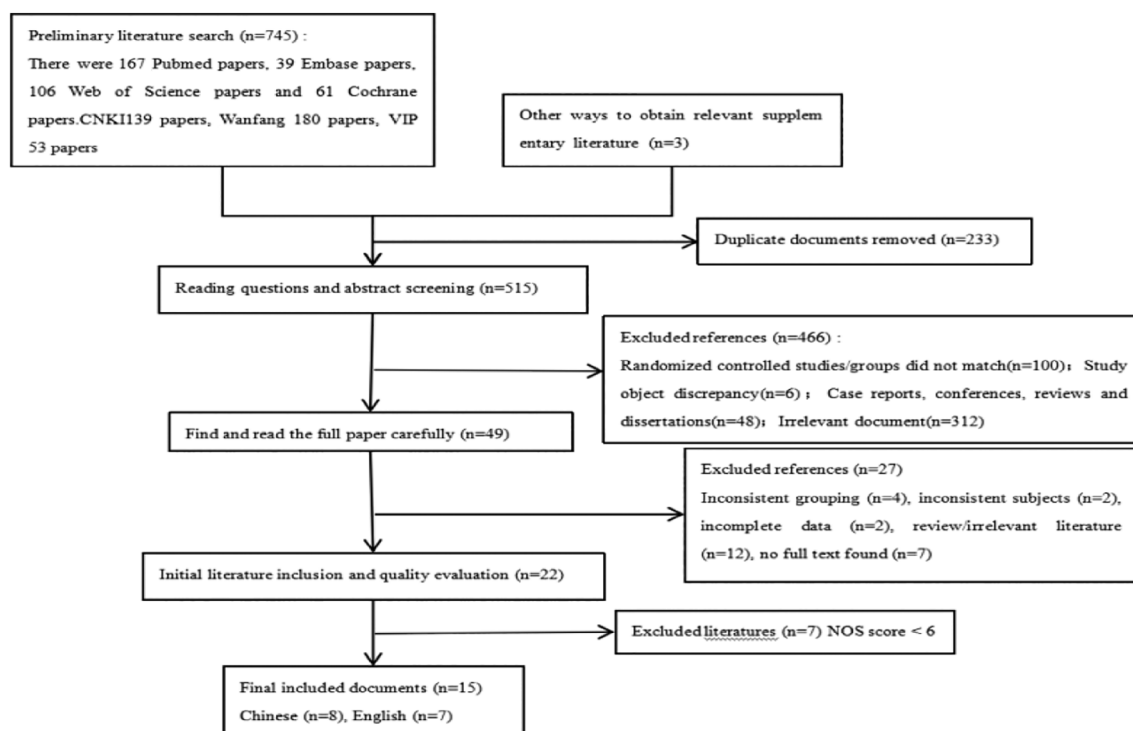


FIGURE 1 Flow chart of literature screening.

interruptions. In strict accordance with the inclusion and exclusion criteria, the final included documents were of high quality (NOS >6 points, see Table 1).

5.3 | Meta-analysis results

The results suggest that filter life, presented in Table 2, activated prothrombin time, prothrombin activity, red blood cell count, transmembrane pressure, blood flow velocity, intermittent saline irrigation, creatinine level; dilution mode was significantly correlated with unplanned interruption ($p < .05$). Gender, age, treatment mode, whether anticoagulants were used, catheter placement, whether ventilators were used, whether blood products and fat milk were transfused, haemoglobin level, platelet count, blood calcium level, albumin level, replacement fluid velocity, prothrombin time, hematocellular volume, International Normalized Ratio, white blood cell count, organ failure score, blood potassium level, ICU admission time and the displacement fluid velocity were not correlated with the change ($p > .05$). The combined effect size of the random effects model and the fixed effects model is basically the same, so this result is stable and the possibility of publication bias is less. The forest map of the results of meta-analysis is depicted in Figure 2.

5.4 | Sensitivity analysis

The sensitivity analysis was carried out by means of one-by-one elimination and subgroup analysis. Sensitivity and subgroup analyses of filter life

factors did not find the source of heterogeneity, which may be due to regional differences and different filter models. Factors such as activated prothrombin time, red blood cell count, blood flow velocity and creatinine level were eliminated one by one with heterogeneity $I^2 < 50\%$ and the $p > .05$. After the combined effect, [MD = -5.28, 95% CI (-6.43 to -4.13), $p < .05$], red blood cell count [MD = 0.48, 95% CI (0.41-0.56), $p < .05$], blood flow velocity [MD = -12.38, 95% CI (-14.65 to -10.10), $p < .05$] and creatinine level were [MD = 1.34, 95% CI (1.19-1.49), $p < .05$], were statistically significant. The results are shown in Table 3.

6 | DISCUSSION

Recent evidence^{27,28} on unplanned interruption of CRRT suggests that more evidence should be produced to support the development of risk assessment methods on risk prediction models, formulating relevant prevention strategies as well as on further identifying influencing factors on the incidence of unplanned interruptions in critical patients undergoing CRRT. Our results contribute to the needs on further research identified in these recent studies, as presented in the next sections of the article.

6.1 | Effects of red blood cell count, filter life, cross-mode pressure, blood flow velocity, prothrombin activity and activated partial thrombin time on unplanned interruption

Studies have suggested²⁰ that the increase of red blood cell density, blood viscosity and plasma protein level after haemodialysis may

TABLE 1 Basic characteristics and quality evaluation results of included literature.

Literature (first author)	Document type	Area of study	Major disease types	Age	Gender (male/female)	Number of unplanned disembarks occurred/none occurred	Related factors	NOS score
Wang Yuan Yuan et al. ⁵ 2020	①	China Anhui	—	67.54 ± 10.29	31/29	117/58	①②③⑥⑧⑨⑩⑪⑫⑬⑭⑮⑯⑰⑱⑲⑳㉑㉒㉓㉔㉕㉖㉗㉘㉙㉚㉛㉜㉝㉞㉟㊱㊲㊳㊴㊵㊶㊷㊸㊹㊺㊻㊼㊽㊾㊿	8
Chen Jincan et al. ⁶ 2021	②	China Anhui	—	52.93 ± 6.00	45/35	35/45	①②⑥⑧⑨⑫⑬⑭⑮⑯⑰⑱⑲⑳㉑㉒㉓㉔㉕㉖㉗㉘㉙㉚㉛㉜㉝㉞㉟㊱㊲㊳㊴㊵㊶㊷㊸㊹㊺㊻㊼㊽㊾㊿	9
Cha Liling et al. ⁷ 2018	②	China Jiangxi	②③④⑥⑧⑨⑩⑪	58.70 ± 18.60	102/85	349/168	①②③⑥⑧⑨⑫⑬⑭⑮⑯⑰⑱⑲⑳㉑㉒㉓㉔㉕㉖㉗㉘㉙㉚㉛㉜㉝㉞㉟㊱㊲㊳㊴㊵㊶㊷㊸㊹㊺㊻㊼㊽㊾㊿	9
Zhang Zhonghua et al. ⁸ 2019	②	China Hubei	①③⑩⑪	47.70 ± 15.32	180/77	125/132	①⑤⑨⑫⑬⑭⑮⑯⑰⑱⑲⑳㉑㉒㉓㉔㉕㉖㉗㉘㉙㉚㉛㉜㉝㉞㉟㊱㊲㊳㊴㊵㊶㊷㊸㊹㊺㊻㊼㊽㊾㊿	9
Xie Halbiao et al. ⁹ 2020	①	China Guangdong	②⑦⑧	65.80 ± 13.40	35/30	14/51	①②④⑤⑦⑲	9
Chang Liu et al. ¹⁰ 2021	②	China Hubei	②⑧	63.00 ± 5.25	534/375	718/191	①②⑤⑦⑬⑲	9
Joan M et al. ¹¹ 2018	②	Spain	②	62.44 ± 15.52	57/29	19/67	②⑤⑦⑬⑲	8
Nigel Fealy et al. ¹² 2013	①	Australia	①④⑤⑥⑧	54.75 ± 17.98	18/28	121/133	①②③④⑥⑨⑪⑫⑬⑭⑮⑯⑰⑱⑲⑳㉑㉒㉓㉔㉕㉖㉗㉘㉙㉚㉛㉜㉝㉞㉟㊱㊲㊳㊴㊵㊶㊷㊸㊹㊺㊻㊼㊽㊾㊿	8
Baek SD et al. ¹³ 2019	②	Korea	②③⑩	64.85 ± 13.86	81/43	65/59	①②⑤⑦⑨⑪⑬⑭⑮⑯⑰⑱⑲⑳㉑㉒㉓㉔㉕㉖㉗㉘㉙㉚㉛㉜㉝㉞㉟㊱㊲㊳㊴㊵㊶㊷㊸㊹㊺㊻㊼㊽㊾㊿	9
Kim IB et al. ¹⁴ 2010	②	Australia	③⑥⑨⑫	57.00 ± 19.00	11/19	19/121	②③④⑤⑥⑨⑪⑫⑬⑭⑮⑯⑰⑱⑲⑳㉑㉒㉓㉔㉕㉖㉗㉘㉙㉚㉛㉜㉝㉞㉟㊱㊲㊳㊴㊵㊶㊷㊸㊹㊺㊻㊼㊽㊾㊿	7
Li Kejia et al. ¹⁵ 2020	①	China Beijing	①②③④⑤⑥⑨	72.59 ± 16.32	66/93	50/296	③④⑥⑧⑩⑪⑬⑭⑮⑯⑰⑱⑲⑳㉑㉒㉓㉔㉕㉖㉗㉘㉙㉚㉛㉜㉝㉞㉟㊱㊲㊳㊴㊵㊶㊷㊸㊹㊺㊻㊼㊽㊾㊿	7
Wan Na et al. ¹⁶ 2022	②	China Beijing	⑤⑥	53.00 ± 12.25	33/12	218/92	④⑧⑨⑩⑪⑫⑬⑭⑮⑯⑰⑱⑲⑳㉑㉒㉓㉔㉕㉖㉗㉘㉙㉚㉛㉜㉝㉞㉟㊱㊲㊳㊴㊵㊶㊷㊸㊹㊺㊻㊼㊽㊾㊿	9
Tan CS et al. ¹⁷ 2011	②	Singapore	②③⑥	64.25 ± 9.62	7/6	44/19	⑤⑩⑪⑬⑲	7
Zhang ZH et al. ¹⁸ 2012	①	China Zhejiang	③⑩⑫	64.61 ± 14.06	39/15	205/50	⑤⑩⑪⑬⑭⑮⑯⑰⑱⑲⑳㉑㉒㉓㉔㉕㉖㉗㉘㉙㉚㉛㉜㉝㉞㉟㊱㊲㊳㊴㊵㊶㊷㊸㊹㊺㊻㊼㊽㊾㊿	8
Wang Xiuzhe et al. ¹⁹ 2018	②	China Shanxi	—	59.04 ± 4.25	25/20	82/27	⑩⑪⑬⑭⑮⑯⑰⑱⑲⑳㉑㉒㉓㉔㉕㉖㉗㉘㉙㉚㉛㉜㉝㉞㉟㊱㊲㊳㊴㊵㊶㊷㊸㊹㊺㊻㊼㊽㊾㊿	8

Note: Literature type: ① prospective observational study ② retrospective observational study. Disease types: ① liver failure/transplant ② kidney failure/transplant ③ heart disease ④ shock ⑤ heart failure ⑥ respiratory/lung failure ⑦ multiple organ failure ⑧ infection/drug poisoning ⑨ digestive system diseases ⑩ thrombocytopenia/bleeding ⑪ following other surgical procedures ⑫ blood disease. Relevant factors: ① Gender ② Age ③ Treatment mode ④ Whether to use anticoagulants ⑤ filter life ⑥ Pipe position ⑦ Whether to use a ventilator ⑧ Whether blood products/fat milk are transfused ⑨ Haemoglobin level ⑩ Activation of prothrombin time ⑪ Platelet count ⑫ red blood cell count ⑬ nationalization standardized values ⑭ white blood cell count ⑮ blood cell volume ⑯ creatinine ⑰ prothrombin time ⑱ albumin levels ⑲ blood calcium level ⑳ original ㉑ blood enzyme activity ㉒ transmembrane pressure ㉓ organ failure ㉔ blood flow velocity ㉕ intermittent brine rinse ㉖ potassium levels ㉗ ICU admission time ㉘ whether merger slow disease ㉙ displacement fluid velocity ㉚ dilution method.

TABLE 2 Results of meta-analysis of influencing factors for unplanned disembarkation of continuous renal replacement therapy in intensive care unit patients.

Influencing factors	Number of articles included (articles)	Sample size (example)	Heterogeneity		Model selection	Combined effect size		Z	p
			I ² (%)	p		OR/MD	95% CI		
Gender	9 ⁵⁻¹³	2173	37	.12	Fixed	0.96	0.79 to 1.17	0.39	.69
Age	8 ^{5-7,10-14}	2009	80	<.01	Random	-1.45	-4.56 to 1.66	0.91	.36
Treatment mode	5 ^{6-7,12,14-15}	1423	79	<.01	Random	1.11	0.58 to 2.12	0.32	.75
Whether anticoagulants are used	5 ^{9,12,14-16}	1087	82	<.01	Random	1.18	0.47 to 2.93	0.35	.72
Life of filter	6 ^{8,10,13,14,17,19}	1748	99	<.01	Random	-1.83	-3.27 to -0.40	2.50	.01
Catheter position	4 ^{5-7,15}	1228	0	.57	Fixed	1.02	0.67 to 1.54	0.10	.92
Whether to use breathing machine	4 ^{9-11,13}	1183	92	<.01	Random	0.59	0.13 to 2.64	0.68	.49
Whether to import blood products and fat emulsions	5 ^{5-7,15-16}	1527	69	.01	Random	1.20	0.74 to 1.96	0.75	.46
Haemoglobin level	8 ^{5,7-8,12-14,16,18}	1495	71	<.01	Random	2.40	-0.14 to 4.94	1.85	.06
APTT	9 ^{5,7,12,14-19}	1887	95	<.01	Random	-4.31	-7.63 to -0.99	2.55	.01
Platelet count	11 ^{5-7,12-19}	2091	96	<.01	Random	13.26	-2.50 to 29.02	1.65	.10
Blood calcium level	5 ^{7,13,16,18-19}	1241	100	<.01	Random	0.22	-0.10 to 0.53	1.35	.18
Albumin level	2 ^{13,19}	379	92	<.01	Random	1.13	-2.78 to 5.04	0.57	.57
Displacement fluid velocity	3 ⁵⁻⁷	704	53	.05	Random	-3.97	-75.31 to 67.36	0.11	.91
Prothrombin time	8 ^{5,7-8,15-19}	1958	93	<.01	Random	-0.93	-2.12 to 0.25	1.54	.12
Specific blood cell volume	5 ^{6,8,16,18}	1005	98	<.01	Random	3.25	-0.95 to 7.45	1.52	.13
Prothrombin activity	2 ^{6,8}	337	8	.30	Fixed	9.35	7.73 to 10.98	11.27	<.01
Internationalized normalized value	6 ^{8,12,14-16,18}	789	65	.04	Random	-0.20	-0.41 to 0.01	1.88	.06
Red cell count	5 ^{5,7,8,14,16}	1774	82	<.01	Random	0.38	0.26 to 0.51	5.87	<.01
White cell count	3 ^{6,8,13}	461	86	<.01	Random	-0.12	-2.04 to 1.81	0.12	.91
Transmembrane pressure	2 ^{15,19}	601	0	.68	Fixed	43.06	23.00 to 63.13	4.21	<.01
Organ failure score	2 ^{10,13}	1033	94	<.01	Random	-0.08	-2.33 to 2.17	0.07	.94
Blood flow velocity	3 ⁵⁻⁷	704	73	.02	Random	-10.55	-13.78 to -7.32	6.40	<.01
Intermittent saline irrigation	2 ^{6,8}	302	0	.91	Fixed	2.97	1.44 to 6.15	2.94	<.01
Potassium levels	2 ^{8,13}	381	65	.09	Random	0.20	-0.07 to 0.48	1.46	.14
Length of ICU stay	2 ^{6,13}	204	100	<.01	Random	-14.62	-42.78 to 13.55	1.02	.31
Creatinine level	4 ^{8,10,13,17}	1353	94	<.01	Random	0.98	0.35 to 1.61	3.07	<.01
Displacement fluid velocity	3 ⁵⁻⁷	255	73	.05	Random	-74.63	-290.51 to 141.25	0.68	.50
Mode of dilution	2 ^{5,7}	797	0	.67	Fixed	0.26	0.18 to 0.37	7.34	<.01

cause red blood cell aggregation. These cell changes not only affect microcirculation haemodynamics, but also make patients prone to abnormal coagulation during CRRT. At the same time, it can also cause the increase of transmembrane pressure, slow down the blood flow rate, lead to the blockage of the filter membrane hole and greatly shorten the life of the filter. Prothrombin activity is a commonly used index to monitor coagulation function in clinical practice. When prothrombin activity decreases significantly, the synthesis of coagulation factors decreases, which may increase the risk of bleeding or haemostasis. On the contrary, it will lead to hypercoagulability of patients, increasing the risk of unplanned disconnection of patients. Hongyan

Xu et al.²¹ believed that if the blood flow velocity is low, high filtration fraction and high blood concentration may lead to coagulation in the extracorporeal circulation system, which is consistent with the results of this study. Studies²² have shown that for every 10% increase in prothrombin activity, the risk of CRRT unplanned interruption increases by 19%. Karkar et al.²⁰ pointed out that the safety and effectiveness of heparin anticoagulant therapy during CRRT is based on monitoring activated partial thromboplastin time (APTT), which is also an indicator for predicting coagulation and bleeding risk of patients, and suggested that the systemic APTT should be adjusted between 35 and 45 s. It can significantly prolong the treatment time

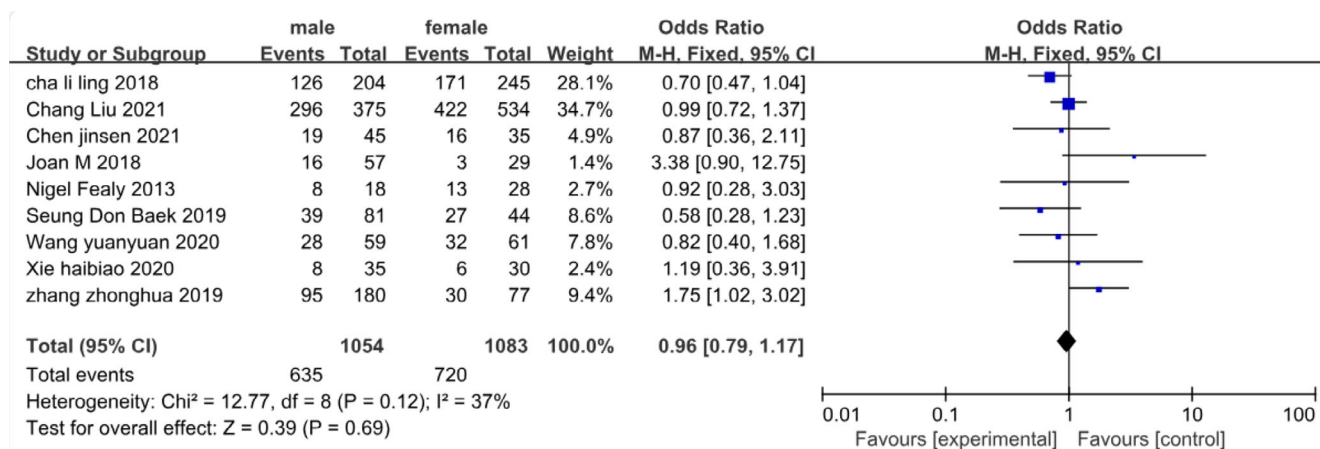


FIGURE 2 Gender factor forest map.

TABLE 3 Sensitivity analysis results of factors influencing continuous renal replacement therapy unplanned disembarkment in intensive care unit patients.

Influencing factor	Number of excluded literature (articles)	Number of articles included after elimination (articles)	Sample size (example)	Heterogeneity		Model selection	After excluding		
				I² (%)	p		Combined effect of the amount	OR/ MD	95% CI
APTT	1 ¹⁵	5	679	4	.39	Fix	−5.28	−6.43 to −4.13	<.01
Creatinine level	1 ⁸	3	1096	23	.27	Fix	1.34	1.19 to 1.49	<.01
Red cell count	1 ¹⁴	4	1330	0	.46	Fix	0.48	0.41 to 0.56	<.01
Blood flow velocity	1 ⁷	2	255	0	.96	Fix	−12.38	−14.65 to −10.10	<.01

of CRRT. Therefore, activated partial thromboplastin time is closely related to the unplanned deactivation of CRRT.

6.2 | Influence of dilution mode on unplanned interruption

Dilution mode is also one of the main influencing factors for unplanned interruption in CRRT patients, and dilution before fluid replacement is a protective factor for unplanned interruption in CRRT patients. The reason may be that in pre-dilution mode, the pre-filtration mixture of blood and replacement solution can reduce the blood concentration and coagulation factor concentration in the filter, promote blood flow, achieve a relatively high membrane shear rate and reduce the solute membrane interaction. At the same time, pre-dilution can also promote the transfer of some compounds by creating a concentration gradient, thereby inducing solute migration out of red blood cells, which can reduce the risk of thrombosis. Post-diluted blood filtration is inherently limited by the maximum flow rate and filtration fraction. At this time, the operation of the filter not only increases the chance of condensation of the filter, but also leads to pore blockage due to the high concentration of protein in the

secondary film on the membrane surface, thus affecting the filter life.²³ Other studies have shown²⁴ that the combination of front and back dilution scheme can significantly reduce the risk of filter agglutination compared with the simple post-dilution scheme.

6.3 | Influence of intermittent saline irrigation on unplanned interruption

A previous study²⁰ suggested that saline irrigation is one of the strategies to prevent clotting. Strategies to prevent coagulation include general measures such as saline irrigation and pre-dilution, as well as different anticoagulants such as low-molecular-weight heparin and topical citric acid anticoagulants. Citrate anticoagulation is based on citrate freely ionizing calcium by binding and chelating to prevent cardiopulmonary coagulation, and part of the complex is lost in the CRRT effluent. The other part is transported to the systemic circulation through venous blood and metabolized in the liver, but in the case of severe liver failure, citrate accumulation may occur. Intermittent saline irrigation, on the one hand, can increase solute clearance and maintain internal environment stability; on the other hand, it has lower bleeding risk than heparin anticoagulant flushing solution, so it can reduce the

risk of unplanned withdrawal.²⁰ Other studies have pointed out⁸ that intermittent saline irrigation has the following advantages: (1) it is conducive to the visual observation of the condensation of filters and pipelines, and provides guidance for the replacement of filters after predictive treatment interruption; (2) blood dilution is conducive to reducing blood concentration and preventing thrombosis; (3) flush the sediment on the inner wall of the pipeline to prevent the adhesion of blood tangible components to form thrombus.

6.4 | Influence of Scr level on unplanned interruption

Studies have suggested²⁵ that Scr level is not only a reliable indicator of renal function, but also a reflection of solute clearance by CRRT, and adequate solute clearance can temporarily reduce the risk of unplanned CRRT withdrawal. Studies²⁶ indicated that 6-h timed urine collection was performed in patients with acute tubular necrosis when urine volume exceeded 750 mL/day. If the measured creatinine clearance is <12 mL/min, RRT should be continued, if >20 mL/min, RRT should be stopped, and if the measured creatinine clearance is between 2 and 20 mL/min, it should be left to the clinician to determine. Therefore, the level of Scr can provide an important reference value for clinical decision-making.

7 | CONCLUSION

The relevant literature and available evidence suggest four clinical challenges associated with unplanned CRRT interruption, namely: (a) effects of red blood cell count, filter life, cross-mode pressure, blood flow velocity, prothrombin activity and activated partial thrombin time on unplanned interruption; (b) influence of dilution mode on unplanned interruption; (c) influence of intermittent saline irrigation on unplanned interruption; (d) influence of Scr level on unplanned interruption.

The review assumes recent perspective on healthcare management research needs^{29–32} and updates the knowledge on main influencing factors of the interruption of unplanned continuous renal replacement therapy (CRRT) in adult ICU patients and the need to improve skills of clinical nursing staff to adjust relevant parameters according to patients' conditions. The potential to increase the ability to better manage unplanned CRRT in ICUs has been identified and constitutes a relevant potential health care management contribution that can be implemented by nurses.

8 | LIMITATIONS

Due to the strict inclusion and exclusion criteria of this study, the final number of included literature is relatively small, and the age, haemoglobin level, replacement fluid speed, prothrombin time and other aspects are different from other relevant studies. Meta-analysis and meta-regression were not performed in this study, which may be different

from other research results. Therefore, the results of this study only represent the main influencing factors of unplanned interruption of CRRT in some types of ICU patients. Thus, larger samples and higher quality studies are needed in the future to verify and update the above conclusions, in order to add other representative results, and provide a broader set of evidence and contribution to a theoretical basis for further clarifying the main risk factors and options to reducing the risk of unplanned CRRT discontinuation in ICU patients.

9 | IMPLICATIONS FOR PRACTICE

The review updates knowledge on main factors affecting the interruption of unplanned CRRT in adult ICU patients and contributes to improve skills of clinical nursing staff to adjust relevant parameters according to patients' conditions.

The potential to increase the ability to better manage unplanned CRRT in ICUs has been identified in this article and constitutes a relevant potential health care management contribution that can be implemented by nurses.

AUTHOR CONTRIBUTIONS

Study design: Xi.X. and CY; Data collection: Xi.X. and CY; Data analysis: QJ; Study supervision: Xu.X.; Manuscript writing: Xi.X. and CY; Critical revisions for important intellectual content: PM.

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DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

ETHICS STATEMENT

Non-applicable to literature reviews; no patient data were generated.

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