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ORIGINAL RESEARCH

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Comparison of the effect of heparin, reteplase, and taurolock in the prevention of thrombosis in hemodialysis catheters

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Abstract

Background and Aim: One of the complications of using catheters is the occurrence of thrombosis, which can be dangerous for patients. The main objective of this study is to compare the effect of heparin, reteplase, and taurolock in the prevention of thrombosis in hemodialysis catheters.

Methods: The present study is a clinical trial, in which the effect of three drugs, heparin, reteplase, and taurolock, in the prevention of thrombosis in hemodialysis catheters, has been investigated. The research units were studied in two intervention and control groups. The stratified random allocation method was used to assign patients to five groups (control, Heparin 50, Heparin 1000, reteplase, and taurolock), with strata based on the patient's age (20–70 years), gender, and duration of dialysis. Within each stratum, patients were also assigned to groups using the randomized block permutation method and a random number table tool. To prevent bias, this study is triple-blinded. This means that the patient, the thrombosis assessor, and the statistical analyst are unaware of the type of intervention received by the patient.

Results: Gender ($p < 0.999$), age distribution ($p = 0.774$), and duration of dialysis ($p = 0.875$) showed no statistically significant relationship with thrombosis. However, significant differences were observed among the five groups regarding thrombosis incidence. The relative risk of thrombosis in the Heparin 50, Heparin 1000, reteplase, and taurolock groups compared to the control group was 92.5%, 92.2%, 98.2%, and 89% lower, respectively.

Conclusion: Our study underscores the efficacy of heparin, reteplase, and taurolock in preventing thrombosis in hemodialysis catheters. While all three drugs demonstrated efficacy, the Heparin 50 group exhibited the highest relative risk reduction. These findings suggest that heparin, particularly at a low dose, should be considered a standard prophylactic treatment in hemodialysis patients.

KEYWORDS

catheter, hemodialysis, heparin, reteplase, thrombosis, trolac

1 | INTRODUCTION

Patients undergoing maintenance hemodialysis for kidney failure face elevated risks of bleeding and thrombosis compared to the general population. In addition, they are prone to inflammation, common comorbidities like hypertension and diabetes, and mineral metabolism disorders, heightening their susceptibility to cardiovascular events.[1] Balancing these risks, particularly the delicate equilibrium between bleeding and thrombosis poses a significant clinical challenge in their care. For instance, the prothrombotic nature of hemodialysis can increase thrombosis risk due to platelet activation and coagulation.[2] Conversely, heparin anticoagulant therapy, often used to prevent clotting in the extracorporeal circuit, may transiently heighten bleeding risk. Moreover, prolonged platelet activation by the dialyzer and tubing can paradoxically elevate bleeding risk.

In addition, drugs can mitigate these risks: erythropoiesis-stimulating agents, which are widely used to treat anemia in patients receiving maintenance hemodialysis, prevent thrombosis and stroke at the cost of increasing the risk of bleeding, while oral anticoagulant drugs, which sometimes prescribed in patients receiving maintenance hemodialysis, reduce the risk of thrombosis and stroke at the cost of increasing the risk of bleeding.[3]

Adverse vascular and thrombotic events are rare but important considerations for patients undergoing maintenance hemodialysis.[4] Permanent central venous catheters are preferred due to significantly lower rates of complications, particularly infection and thrombosis.[5]

Hemodialysis, a primary method of kidney replacement therapy for end-stage renal disease, requires reliable vascular access. Currently, three methods are used: temporary jugular catheters, permanent catheters, and arteriovenous fistula (AVF) creation.[6]

While AVF is preferred for its long-term use and low complication rates,[7] it has limitations, including a lengthy adaptation period and poor suitability for certain patients.[8]

For patients requiring acute hemodialysis or those unsuitable for AVF, temporary or permanent tunnel catheters are recommended.[9] Compared to temporary catheters, permanent catheters offer lower rates of malfunction, infection, and thrombosis, making them preferable for accesses needed beyond a month.[10]

However, permanent catheters carry risks such as central vein stenosis, thrombosis, and infection, with urgent complications like arterial puncture, pneumothorax, and hematoma.[11] To mitigate these risks, strict aseptic conditions and guidance tools like fluoroscopy and ultrasound are essential.

Until now, due to the lack of available data in the literature to answer the question about the benefits of heparin, reteplase, and taurolock, no precise recommendation has been made for performing clinical tasks. Therefore, on the one hand, since more than one-third of the population suffering from end-stage renal disease use permanent catheters, which are associated with complications such as thrombosis, and on the other hand, the possibility of the effectiveness of heparin, reteplase, and taurolock in preventing these complications, the main goal of this study is to compare the effect of heparin, reteplase, and taurolock in preventing thrombosis in hemodialysis catheters.

2 | METHODS

This study is a clinical trial in which the effects of three drugs, heparin, reteplase, and taurolock, in preventing thrombosis in hemodialysis catheters are investigated. Thrombosis refers to the formation of blood clots within blood vessels, which can be highly dangerous, particularly when occurring in arteries responsible for oxygen delivery, as they are considered the main cause of heart attacks and strokes.

This study utilizes observational and measurement methods to gather data. Patients meeting the study's criteria receive the designated drug upon admission, and their information is recorded. Follow-up occurs for up to 1 year postinjection.

Participants are hospitalized dialysis patients with permcath catheters at Shahid Rahimi Hospital in Khorramabad, admitted based on inclusion criteria and parental/guardian consent.

Patients are divided into intervention and control groups through randomization, despite non-probability sampling. Stratified random allocation places patients into five groups based on age, gender, and dialysis duration, resulting in 8 strata. Within each stratum, patients are randomly assigned to groups using a random permutation block method and a random number table.

This study is triple-blind, ensuring impartiality. Neither the patient, thrombosis evaluator, nor statistical analyst knows the patient's intervention. The thrombosis evaluator and codebreaker are independent of the research team. Eligible patients are monitored from admission until symptom stabilization. Groups include control, low-dose heparin, high-dose heparin, reteplase, and taurolock.

Eligible patients were monitored from hospitalization until symptom stabilization. Intervention groups included control, low-dose heparin (50 units/mL), high-dose heparin (1000 units/mL), reteplase (1 mg/mL), and taurolock. Heparin was administered prophylactically, with subcutaneous doses given 2 h before hemodialysis and every 12 h until discharge. The control group received standard clinical care. Blood cells, inflammatory factors, catheter type, and ventilation methods were examined in both control and experimental groups.

Inclusion criteria: Dialysis patients aged 20–70 with a permcath and consent.

Exclusion criteria: Patients with permcath removal, medication sensitivity, death during the study, or dissatisfaction.

Sampling: Sequential non-probability sampling selects eligible patients from the dialysis unit to meet sample size. Upon admission, patient characteristics are recorded, and drugs are administered based on grouping. Follow-up lasts 3–6 months or up to 1 year. Thrombosis treatment is administered if needed during follow-up.

The total sample size aimed for 175 participants, following a similar study by Arti and Ruzbehani,[12] was calculated using PASS software version 15. Each group targeted 35 participants, with a total

enrollment of 185 to account for potential dropouts, resulting in 37 participants per group.

The study utilizes a questionnaire, a common tool in survey research, to gather data. This questionnaire consists of two parts:

1. Patient information form: Collects details such as age, gender, height, weight, marital status, and education level, along with past medical history obtained through interviews with family members.
2. Clinical status assessment form: Records information on reasons for hospitalization, surgical status, number of dialysis sessions, ventilation method, and medications taken, gathered through observation and patient files.

2.1 | Data analysis

Following the collection of data from the research questionnaire and subsequent scoring of study tools, data analysis was conducted using SPSS software version 26. A suite of statistical tests was employed to elucidate various aspects of the dataset. The independent-samples chi-square test was utilized to compare the frequency distribution of demographic and background variables among the study groups, while the Kruskal–Wallis test was applied to assess the frequency distribution of clinical and laboratory features among patients. Fisher's exact test and additional independent-samples chi-square tests were employed to explore the relationship between demographic and background variables and the occurrence of thrombosis, with the Mann–Whitney *U* test utilized for assessing the relationship between clinical and laboratory features and thrombosis. Furthermore, the occurrence of thrombosis between groups was compared using the independent-sample chi-square test. To control for confounding variables, a logistic regression model was employed. A significance level of $p < 0.05$ was considered indicative of statistical significance.

Moreover, to ensure adherence to research ethics, all necessary introduction letters were obtained from the ethics committee of Lorestan University of Medical Sciences (Ethics Code: IR.LUMS.REC.1400.206). In addition, this study was registered in the International Iranian Clinical Trials Registration Center under the IRCT number IRCT20220103053614N1. These measures underscore the commitment to ethical research conduct and transparency in reporting clinical trial data.

3 | RESULTS

3.1 | Comparison of a frequency distribution of demographic and background variables of studied patients by experimental group

Table 1 presents the frequency distribution of demographic and contextual variables across the experimental groups. Statistical analysis using the chi-square test of independence revealed several significant findings. First, the gender distribution did not exhibit a statistically significant difference among the experimental groups ($p = 0.820$).

TABLE 1 Frequency distribution of demographic and background variables of patients.

Variables	Order	Taurolock		Reteplase		Heparin 1000		Heparin 50		Control		*p* Value
		%	Frequency	%	Frequency	%	Frequency	%	Frequency	%	Frequency	
Gender	Female	37.8	14	35.1	13	29.7	11	43.2	16	37.8	14	**0.820**
	Male	62.2	23	64.9	24	70.3	26	56.8	21	62.2	23	
Marital status	Married	100	37	94.6	35	83.8	31	100	37	94.6	35	**0.010**
	Single	0	0	5.4	2	16.2	6	0	0	5.4	2	
Occupation	Self-employment	59.5	22	59.5	22	54.1	20	59.5	22	59.5	22	**0.020**
	Housekeeper	40.5	15	32.4	12	24.3	9	37.8	14	37.8	14	
	Other	0	0	8.1	3	21.6	8	2.7	1	2.7	1	
Blood group	A	5.4	2	21.6	8	21.6	8	45.9	17	37.8	14	**<0.001**
	B	27	10	24.3	9	45.9	17	10.8	4	5.4	2	
	AB	16.2	6	27	10	16.2	6	16.2	6	21.6	8	
	O	51.4	19	27	10	16.2	6	27	10	35.1	13	
Dialysis frequency	2	5.4	2	0	0	24.3	9	0	0	0	0	**<0.001**
	3	94.6	35	100	37	75.7	28	100	37	100	37	
Cause of failure	Diabetes	48.6	18	18.9	7	24.3	9	10.8	4	43.2	16	**<0.001**
	Hypertension	48.6	18	78.4	29	45.9	17	51.4	19	48.6	18	
	Other	2.7	1	2.7	1	29.7	11	37.8	14	8.1	3	

However, a significant difference was observed in the marital status distribution ($p = 0.010$). Notably, in the Heparin 1000 group, 83.8% (31 individuals) were married, while 16.2% (6 individuals) were single, differing notably from other groups. Similarly, occupational distribution also revealed a significant difference ($p = 0.020$). In the Heparin 1000 group, 54.1% (20 individuals) were self-employed, 24.3% (9 individuals) were housewives, and 21.6% (8 individuals) had other occupations.

In addition, blood group distribution showed a significant difference ($p < 0.001$). For instance, in the Tauroloc group, 5.4% (2 individuals) had Blood Group A, 27% (10 individuals) had Blood Group B, 16.2% (6 individuals) had Blood Group AB, and 51.4% (19 individuals) had Blood Group O. Furthermore, the distribution of the number of dialysis sessions demonstrated a significant difference ($p < 0.001$). In the Heparin 1000 group, 24.3% (9 individuals) underwent dialysis twice, while 75.7% (28 individuals) underwent it thrice.

Moreover, a significant difference was observed in the distribution of causes of patient failure ($p < 0.001$). For instance, in the reteplase group, 18.9% (7 individuals) experienced insufficiency due to diabetes, 78.4% (29 individuals) due to blood pressure, and 2.7% (1 individual) due to other reasons, markedly differing from other groups.

Table 2 depicts the frequency distribution of clinical and laboratory characteristics across the experimental groups. Statistical analysis using the Kruskal–Wallis test revealed several significant differences. First, there was a significant difference in the age distribution of patients among the experimental groups ($p = 0.013$). For instance, the lowest average age was observed in the control group at 50.12 ± 12.87 years, while the highest average age was noted in the Heparin 50 group at 60.78 ± 11.36 years.

Similarly, a significant difference was found in the BMI distribution of patients ($p < 0.013$). The Heparin 1000 group had the lowest average BMI (23.48 ± 3.66), whereas the Tauroloc group had the highest (26.53 ± 1.62). Moreover, significant differences were observed in the duration of dialysis ($p < 0.001$), with the Heparin 1000 group having the lowest average duration (2.62 ± 0.27) and the Heparin 50 group having the highest (3.24 ± 0.25).

Furthermore, statistically significant differences were found in body temperature ($p < 0.001$), pulse rate ($p = 0.001$), mean arterial pressure (MAP) ($p < 0.013$), white blood cell count (WBC) ($p < 0.001$), hemoglobin (HB) ($p < 0.001$), hematocrit (HCT) ($p < 0.013$), creatinine (CR) ($p < 0.013$), and potassium (K) levels ($p < 0.013$) among the experimental groups.

However, no statistically significant differences were observed in terms of patients' breathing ($p = 0.135$), platelet count (PLT) ($p = 0.366$), and erythrocyte sedimentation rate (ESR) ($p = 0.093$). Nonetheless, variations in these parameters provide valuable insights into the diverse clinical and laboratory profiles among the different treatment groups.

3.2 | Investigating the relationship between demographic and background variables with thrombosis

Table 3 examines the correlation between demographic and background variables with thrombosis. Fisher's exact test revealed no

TABLE 2 Frequency distribution of clinical and laboratory characteristics of patients.

Variables	Taurolock		Reteplase		Heparin 1000		Heparin 50		Control		*p* Value
	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	
Age	05.11	59.55	07.14	76.56	24.17	30.55	36/11	78.60	87.12	11.50	**0.013**
BMI	62.1	53.26	75.1	95.25	66.3	48.23	16/3	78.24	35.2	40.25	**<0.001**
Duration	51.0	99.2	23.0	14.3	27.0	62.2	25/0	24.3	25.0	20.3	**<0.001**
Body temperature	36.0	75.36	21.0	99.36	35.0	03.37	39/0	59.36	32.0	69.36	**<0.001**
breathing	11.1	38.16	01.1	62.16	28.1	97.15	98/0	38.16	1	19.16	**0.135**
pulse	15.6	32.77	26.4	41.80	58.8	97.74	91/4	95.80	95.1	49.79	**0.001**
MAP	55.4	59.116	87.8	27.119	08.7	14.106	80/5	118.84	38.5	30.116	**<0.001**
WBC	944	5021	1354	6075	1754	6172	1197	5821	1127	4613	**<0.001**
PLT	26,750	175,432	19,092	173,621	70,640	175,837	28,588	171,459	32,131	163,108	**0.366**
ESR	65.2	73.10	56.2	92.11	50.2	95.11	88/3	12.38	4	59.12	**0.093**
HB	25.1	28.11	85.0	47.12	47.1	29.11	96/0	81.10	66.0	57.10	**<0.001**
HCT	32.2	63.24	82.1	94.27	13.3	49.25	20/4	93.29	21.2	94.24	**<0.001**
CR	66.0	25.7	41.0	85.7	55.0	67.7	03/1	94.6	74.0	44.6	**<0.001**
K	45.0	25.4	38.0	11.4	56.0	61.4	46/0	15.4	25.0	95.3	**<0.001**

TABLE 3 Investigating the relationship between demographic and background variables with thrombosis.

Variables	Order	Thrombosis status		*p* Value
		No	Yes	
Gender	Female	52 (% 76.47)	16 (% 23.53)	0.999
	Male	88 (% 75.21)	29 (% 24.79)	
Marital status	married	135 (% 77.14)	40 (% 22.86)	0.065
	Single	5 (% 50)	5 (% 50)	
Occupation	Self-employment	85 (% 78.70)	23 (% 21.30)	0.035
	housekeeper	49 (% 76.56)	15 (% 23.44)	
	Other	6 (% 46.15)	7 (% 53.85)	
Blood group	A	35 (% 71.43)	14 (% 28.57)	0.223
	B	28 (% 66.67)	14 (% 33.33)	
	AB	30 (% 83.33)	6 (% 16.67)	
	O	47 (% 81.03)	11 (% 18.97)	
Dialysis frequency	2	8 (% 72.73)	3 (% 27.27)	0.730
	3	132 (% 75.86)	42 (% 24.14)	
Cause of failure	Diabetes	43 (% 79.63)	11 (% 20.37)	0.673
	Hypertension	74 (% 73.27)	27 (% 26.73)	
	Other	23 (% 76.67)	7 (% 23.33)	

significant link between patient gender and thrombosis ($p < 0.999$). Similarly, marital status showed no significant association with thrombosis ($p = 0.065$), although thrombosis incidence was higher among single patients (50%) compared to married patients (22.86%).

Occupational status displayed a significant relationship with thrombosis ($p = 0.035$). Thrombosis rates were 21.30% for self-employed patients, 23.44% for homemakers, and 53.85% for those with other occupations.

Blood group and number of dialysis sessions did not exhibit significant associations with thrombosis ($p = 0.223$ and $p = 0.730$, respectively). Likewise, the cause of renal failure showed no significant relationship with thrombosis ($p = 0.673$).

In Table 4, the relationship between clinical and laboratory variables of patients with thrombosis was analyzed. The Mann–Whitney *U* test revealed no statistically significant difference in the age distribution between patients with and without thrombosis ($p = 0.774$). Similarly, no significant difference was found in BMI distribution ($p = 0.551$) or the duration of dialysis ($p = 0.875$) between the two groups. However, a statistically significant difference was observed in body temperature distribution ($p = 0.067$), with patients having thrombosis showing an average body temperature of 36 ± 0.47 compared to 36 ± 0.78 in those without thrombosis. In addition, there was a significant difference in breathing distribution ($p = 0.033$), where the average breathing rate was 16.1 ± 60.05 for patients with thrombosis and 16.21 ± 1.09 for those without thrombosis. No significant differences were found in pulse distribution ($p = 0.366$) or MAP distribution ($p = 0.743$) between the two groups. While no significant difference was observed in WBC distribution ($p = 0.119$), the average WBC count was notably lower in patients with thrombosis (1359 ± 5673) compared to those without (5498 ± 1454). Similarly, no significant difference was found

TABLE 4 Investigating the relationship between clinical and laboratory variables of patients with thrombosis.

Variables	Thrombosis status		*p* Value
	No	Yes	
Age	55.66 ± 13.96	55.84 ± 13.39	**0.774**
BMI	25.18 ± 2.64	25.36 ± 3.29	**0.551**
Duration	3.03 ± 0.39	3.05 ± 0.35	**0.875**
Body temperature	36.78 ± 0.32	36.86 ± 0.47	**0.067**
Breathing	16.21 ± 1.09	16.60 ± 1.05	**0.033**
Pulse	78.31 ± 6.28	79.60 ± 6.34	**0.366**
MAP	115.43 ± 8.17	115.40 ± 7.68	**0.743**
WBC	5498 ± 1454	5673 ± 1359	**0.119**
PLT	175157 ± 41210	161733 ± 32658	**0.063**
ESR	12.16 ± 2.97	11.13 ± 3.83	**0.060**
HB	11.27 ± 1.26	11.30 ± 1.23	**0.944**
HCT	25.84 ± 2.93	28.88 ± 4.09	**<0.001**
CR	7.23 ± 0.80	7.22 ± 1.04	**0.854**
K	4.23 ± 0.50	4.15 ± 0.39	**0.491**

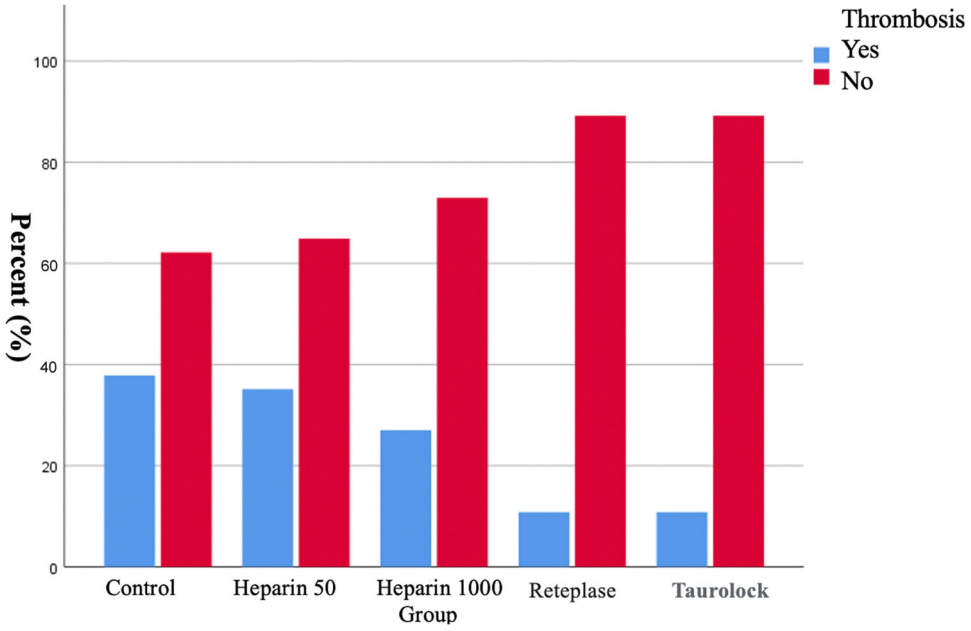

FIGURE 1 Comparison of groups in terms of the incidence of thrombosis.

TABLE 5 Logistic regression model.

	Confidence level							
	Upper bound	Lower bound	Odd ratio	df	Wald Test	SEM	Linear regression	*p* Value
Experimental group	–	–	–	4	21.173		–	**<0.001**
Heparin 50 compared to the control group	0.396	0.014	0.075	1	9.295	0.851	−2.594	**0.002**
Heparin 1000 compared to the control group	0.530	0.011	0.078	1	6.807	0.978	−2.552	**0.009**
reteplase compared to the control group	0.108	0.003	0.018	1	19.451	0.907	−3.999	**<0.001**
taurolock compared to the control group	0.549	0.022	0.110	1	7.231	0.822	−2.211	**0.007**

in PLT distribution ($p = 0.063$), although the average PLT count was lower in patients with thrombosis (161,733 ± 32,658) compared to those without (175,157 ± 41,210). There was no significant difference in ESR distribution ($p = 0.060$), with patients with thrombosis having an average ESR of 11.13 ± 3.83 and those without thrombosis having 12.16 ± 2.97. No significant difference was observed in HB distribution ($p = 0.944$). However, a significant difference was found in HCT distribution ($p < 0.001$), with patients with thrombosis having an average HCT of 28.88 ± 4.09 compared to 25.84 ± 2.93 in those without thrombosis. Finally, no significant difference was observed in CR distribution ($p = 0.854$) or *K* distribution ($p = 0.491$) between the two groups.

3.3 | Comparison of groups in terms of the incidence of thrombosis

Figure 1 illustrates the thrombosis frequency distribution across experimental groups. The chi-square test of independence revealed a significant difference among the groups regarding thrombosis percentage ($p = 0.009$).

Table 5 displays the logistic regression model findings, indicating a statistical difference in thrombosis percentage among experimental groups after adjusting for variables such as blood type, occupation, marital status, body temperature, respiration, WBC, PLT, ESR, and HCT ($p < 0.009$). Relative chances of thrombosis were notably lower in the heparin 50 group (92.5% less), heparin 1000 group (92.2% less), reteplase group (98.2% less), and taurolock group (89% less) compared to the control group.

4 | DISCUSSION

This study evaluates the efficacy of heparin, reteplase, and taurolock in preventing thrombosis in hemodialysis catheters. Previous quantitative research has primarily examined outcomes related to vascular access types in hemodialysis patients, with

limited focus on major bleeding rates, often among users of oral anticoagulants.

In an international study, patients who required maintenance hemodialysis and were not using oral anticoagulants, aspirin, or antiplatelet drugs, had a major bleeding rate of 4.9 per 100 person-years.

In a Canadian study, patients who started maintenance dialysis (80% receiving hemodialysis, 20% receiving peritoneal dialysis, and 12% receiving warfarin) had a major bleeding rate of 5.3 per 100 persons per year.[13]

In a Canadian study, hemodialysis patients using arteriovenous access experienced venous thromboembolism at a rate of 2.8 events per 100 individuals per year.[14] However, it is unclear how many patients in this recent study were using oral anticoagulants, which can lower thrombosis incidence.

For end-stage kidney disease patients, hemodialysis remains the top kidney replacement therapy option. An AVF is recognized as the preferred method. Alternatively, a permanent catheter is considered among the best options for patients unable to use AVF for hemodialysis.

In the study by Vidya et al.,[15] 31 catheters (96.87%) were successfully placed during 1 year, but one patient failed to have the catheter placed using a central vein. The mean age of patients who had catheter placement was 18.10 ± 50.25 years. In a study conducted in end-stage renal disease in Nepal, the mean age was 15.5 ± 49.6 years, but in a similar study conducted at another center in Nepal, the mean age group placed under tunnel catheter was 12.77 ± 67.57 years.[16]

In the study by Vidya et al., the use of AVG compared to AVF in hemodialysis is associated with an increased risk of venous thromboembolism. According to Vidya et al.,[15] a permanent tunnel catheter can be a substitute for AVF. A permanent catheter is a suitable option for accessing dialysis in selected patients due to its openness and longer safety.

In a study conducted by Sepas et al. in Iran in 2019, the patency of permanent catheters was reported to be 57.4 ± 65.5 months.[17] Similarly, in another study conducted by Tsao et al. on 108 patients in 1994, the proposed 1-year patency was between 91% and 93%.[18] As with Vaidya et al.,[15] among 32 patients, patency ranged from 78.12% to 100% after manipulation in 7 patients. Changes in patency may be due to improper catheter management, lack of proper aseptic environment, and sometimes failure in the treatment of infections.

According to Chouhani et al.,[19] AVF is the first vascular access in hemodialysis that provides the best performance, the longest survival, and the least complications. In a study conducted by Abu Sharq et al.[20] among 59 patients, central venous thrombosis was observed in 20.9%.[21]

According to Deniz et al., heparin can be used safely in some selected patients at risk of thrombosis if needed.[22]

The results of the study by Winicki et al. show that the use of trolamine reduces the incidence of catheter-related infections and catheter dysfunction in hemodialysis patients.[23] This is also consistent with the findings of other researchers, although they used heparin as the control group.[24–28]

It also seems that fibrinolytics, such as urokinase and alteplase, influence reducing catheter-related infections. This hypothesis is based on the findings of Hamillgaran et al.[29]

In Bueloni et al.,[30] the use of prophylactic treatment only in tunneled catheters for hemodialysis patients was investigated, with a follow-up of at least 6 months, compared to antibiotic-containing solutions (gentamicin + cephalosporin) versus antimicrobial solutions (taurothymidine + citrate) were studied. These solutions provided similar results in reducing catheter-related bloodstream infections and exit-site infections.

According to the study by Filippoulos et al.,[31] in non-tunneled hemodialysis catheters, the use of gentamicin–heparin, taurolidine–citrate, or only heparin (historical control group) was compared with a 3-month follow-up. They found similar rates of catheter-related bloodstream infections among the groups that used gentamicin and taurolidine, and the rates were higher in the heparin-only group. There was no difference in the incidence of thrombosis.[32]

5 | CONCLUSION

The primary hypothesis of this study is that there is a notable difference in thrombosis rates among hemodialysis catheters across the five experimental groups. The study suggests employing all three drugs—particularly heparin 50 and reteplase—in the treatment regimen for hemodialysis patients with permcath catheters, based on their effectiveness in preventing thrombosis, as indicated by the study's results. It is crucial to address certain methodological limitations. One notable aspect is the lack of balance in group randomization, which may have influenced the study outcomes. The authors acknowledge the need to delve into the background of the randomization process and its potential shortcomings.

AUTHOR CONTRIBUTIONS

Morteza Azadbakht: Resources; software; supervision; validation; visualization; writing—original draft; writing—review and editing. **Azadeh Razian**: Investigation; methodology; project administration; visualization; writing—original draft; writing—review and editing. **Ali Pooria**: Conceptualization; methodology; project administration; resources; supervision; validation; visualization. **Babak Hadian**: Conceptualization; data curation; formal analysis; funding acquisition; investigation; writing—original draft; writing—review and editing.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

TRANSPARENCY STATEMENT

The lead author Morteza Azadbakht affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted;

and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA AVAILABILITY STATEMENT

All relevant data and materials are provided within manuscript.

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