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Extracorporeal circuit clotting in hemodialysis: Incidence and associated factors in real-world practice

Coagulación del circuito extracorpóreo en hemodiálisis: incidencia y factores asociados en la práctica clínica real

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ABSTRACT

Background and hypothesis: Extracorporeal circuit (ECC) clotting during hemodialysis (HD) compromises dialysis efficacy, increases workload, and jeopardizes patient safety. However, in routine clinical practice, ECC performance is influenced by the interaction of patient-related, technical, and pharmacological factors that are rarely evaluated simultaneously in large multicentre cohorts.

Methods: We conducted a multicentre retrospective observational study including all consecutive HD sessions performed across 15 hemodialysis units of Fundación Renal Española between January 1, 2023 and February 15, 2024. Recorded variables included anticoagulation type and dose, dialysis modality (high-flux HD or online HDF), vascular access, dialyzer surface area, session duration, and dialysis adequacy (KT). ECC clotting was assessed at the end of each session using a standardized visual grading scale. Associations were explored using unadjusted analyses, multivariable logistic regression adjusted for dialysis centre, and a patient-level generalized linear mixed model.

Results: A total of 186,637 HD sessions were analysed. ECC clotting was infrequent: 96.3% of sessions showed no or minimal clotting, 1.8% partial clotting, and 2.0% complete clotting. Sessions complicated by ECC clotting delivered a lower dialysis dose (mean KT 49.5 ± 11.1 vs 52.2 ± 10.1; $p < 0.001$). In unadjusted analyses, higher clotting rates were observed in sessions without anticoagulation, with low-molecular-weight heparin (LMWH), during predilution HDF, with central venous catheters, larger dialyzer surface area, and short session duration (< 60 min). In adjusted analyses and in the patient-level mixed-effects model, absence of anticoagulation, central venous catheter use, and dialyzers with surface area > 2.0 m^2 were independently associated with increased clotting risk. LMWH was associated with lower clotting risk in both models, whereas postdilution HDF showed a lower risk only in the patient-level mixed-effects model.

Conclusion: Although ECC clotting during HD was infrequent, it had a clear negative impact on dialysis delivery and was consistently associated with identifiable and potentially modifiable factors. Catheter-based access, lack of anticoagulation, and larger dialyzer surface area were the strongest determinants of clotting risk. The marked patient-level variability underscores the need for individualized anticoagulation and dialysis prescriptions to optimize circuit patency, dialysis adequacy, and patient safety in routine clinical practice.

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Palabras clave:
Anticoagulación
Dosis de heparina
Adecuación dialítica
Permeabilidad del circuito
Acceso vascula

RESUMEN

Antecedentes e hipótesis: La coagulación del circuito extracorpóreo (CCE) durante la hemodiálisis (HD) compromete la eficacia de la diálisis, aumenta la carga de trabajo y puede afectar a la seguridad del paciente. Sin embargo, en la práctica clínica habitual, el funcionamiento del circuito extracorpóreo está influido por la interacción de factores relacionados con el paciente, aspectos técnicos y factores farmacológicos que rara vez se evalúan de forma simultánea en grandes cohortes multicéntricas.

Métodos: Realizamos un estudio observacional retrospectivo multicéntrico que incluyó todas las sesiones consecutivas de HD realizadas en 15 unidades de hemodiálisis de la fundación Renal Española entre el 1 de enereo de 2023 y el 15 de febrero de 2024. Se registraron variables como el tipo y la dosis de anticoagulación, la modalidad de diálisis (HD de alto flujo o HDF en línea), el acceso vascular, la superficie del dializador, la duración de la sesión mediante una escala visual estandarizada. Las asociaciones se exploraron mediante análisis no ajustados, regresión logística multivariable ajustada por centro de diálisis y un modelo lineal generalizado mixto a nivel del paciente.

Resultados: Se analizaron 186.637 sesiones de HD. La CCE fue infrecuente: el 96,3% de las sesiones no mostró coagulación o presentó coagulación mínima, el 1,8% presentó afectación parcial i el 2,0% coagulación completa. Las sesiones complicadas por CCE alcanzaron una menor dosis de diálisis (KT medio 49,5 ± 11,1 frente a 52,2 ± 10,1; $p < 0{,}001$). En los análisis no ajustados, se observaron mayores tasas de coagulación en las sesiones sin anticoagulación, con heparina de bajo peso molecular (HBPM), durante la HDF en predilución, con catéter venoso central, con dializadores, de mayor superficie y en sesiones de corta duración (<60 min). En los análisis ajustados y en el modelo mixto a nivel de paciente, la ausencia de anticoagulación, el uso de catéter venosos central y los dializadores con superficie >2.0 m^2 se asociaron de forma independiente con un mayor riesgo de coagulación. La HBPM se asoció con menor riesgo de coagulación en ambos modelos, mientras que la HDF posdilución mostró menor riesgo únicamente en el modelo mixto a nivel de paciente. Se observo una marcada variabilidad interindividual en el riesgo de coagulación.

Conclusión: Aunque la CCE durante la HD fue infrecuente, tuvo un impacto negativo claro sobre la diálisis administrada y se asoció de forma consistente con factores identificables y potencialmente modificables. El acceso mediante catéter, la ausencia de anticoagulación y el uso de dializadores de mayor superficie fueron los principales determinantes del riesgo de coagulación. La marcada variabilidad a nivel de paciente subraya la necesidad de individualizar la anticoagulación y la prescripción dialítica para optimizar la permeabilidad del circuito, la adecuación dialítica y la seguridad del paciente en la práctica clínica habitual.

Introduction

Hemodialysis (HD) is an essential renal replacement therapy for patients with advanced chronic kidney disease. Its effectiveness largely depends on maintaining the patency of the extracorporeal circuit (ECC). Extracorporeal circuit clotting is a clinically relevant complication, as it may interrupts the dialysis session, require equipment replacement, causes blood loss, and increases both workload and costs. Moreover, it reduces the effective delivered dialysis dose, which may lead to fluid overload, toxin accumulation, higher hospitalization rates, and impaired quality of life.[1]

Anticoagulation of the ECC relies primarily on unfractionated heparin (UFH) and low-molecular-weight heparins (LMWH). However, the efficacy of these strategies is influenced by multiple factors, including vascular access type, dialysis modality (HD/HDF), administered heparin dose, and dialyzer characteristics. Several studies have evaluated extracorporeal circuit clotting and anticoagulation strategies in hemodialysis; however, most have been conducted in small cohorts, single-centre experiences, or highly standardized protocol-driven settings, with limited assessment of the combined clinical and technical determinants of ECC performance under routine clinical practice.[2,3]

In addition, even in the absence of overt circuit clotting, HD patients exhibit a degree of subclinical thrombosis, reflected by persistent elevations in biomarkers such as D-dimer, indicating that a procoagulant state is continuously present.[4] This observation underscores the need to optimize anticoagulation strategies and to better understand the factors associated with visible circuit clotting.

Despite these contributions, important gaps remain. The existing literature tends to address anticoagulant therapy in isolation, whereas large, multicentre studies that comprehensively evaluate the combined clinical, technical, and pharmacological factors associated with ECC clotting, and their impact on dialysis efficacy, are scarce.[5–7]

The aim of this study was to analyse the incidence of extracorporeal circuit clotting during hemodialysis sessions under real-world clinical practice conditions and to evaluate associated factors, including heparin type and dose, HD/HDF modality, vascular access, dialyzer characteristics, session duration, and achieved dialysis adequacy.

Materials and methods

Study design and setting

We conducted a multicentre retrospective observational study across 15 hemodialysis units of the Spanish Renal Foundation between January 1, 2023, and February 15, 2024, capturing 409 consecutive days of routine clinical practice.

Population and included sessions

All HD sessions performed in prevalent HD patients during the study period were included, without restrictions based on age, sex, or treatment modality. Only sessions with incomplete data for the variables of interest were excluded. Data were extracted from the Nefrosoft® electronic health record system, which is routinely used for clinical documentation in all participating units.

Assessment of extracorporeal circuit clotting

Extracorporeal circuit (ECC) clotting was assessed by nursing staff at the end of each HD session and recorded in the electronic health record following a standardized local protocol. A visual grading scale developed for routine clinical use was applied to evaluate clotting of the dialyzer and the arterial and venous lines. The degree of clotting was classified into four categories (Fig. 1):

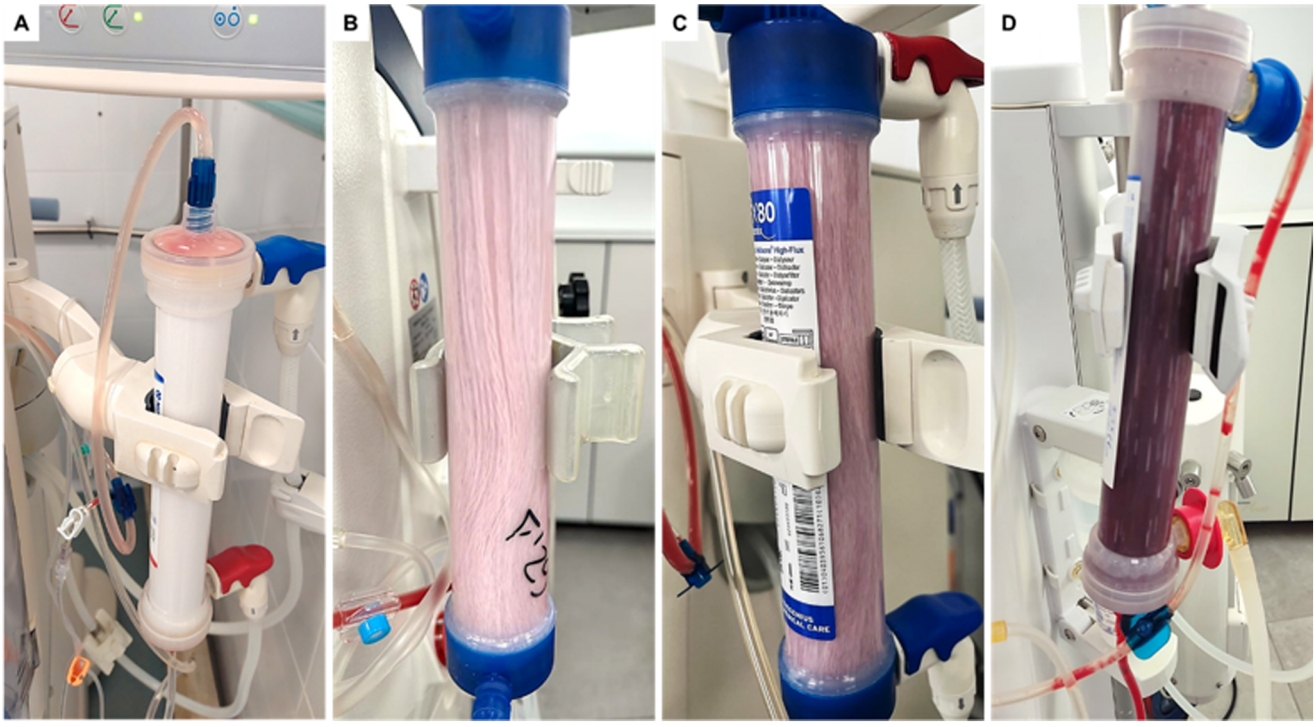

Fig. 1. Visual grading scale for extracorporeal circuit (ECC) clotting at the end of hemodialysis sessions. Representative examples of the four clotting categories used in routine clinical assessment: (A) clean capillaries or minimal fibrin deposits; (B) mild to moderate clotting with fibrin present in multiple capillaries; (C) severe clotting with clots present in chambers or blood lines; (D) complete clotting of the dialyzer or extracorporeal circuit.

- Clean capillaries or minimal fibrin deposits.
- Mild to moderate clotting (fibrin present in multiple capillaries).
- Severe clotting (clots present in chambers or lines).
- Complete clotting of the dialyzer or circuit.

Variables collected

The primary outcome variable was the presence of ECC clotting, assessed using a four-level visual scale (from no/minimal clotting to complete clotting) and subsequently grouped for analysis according to severity. The following independent variables were recorded:

- *Anticoagulation*: type (unfractionated heparin, UFH; low-molecular-weight heparins, LMWH; or heparin-free sessions) and administered dose. For UFH and LMWH, dose was analysed both as a continuous variable (mean ± SD) and as predefined dose categories. Anticoagulation was systematically administered through the venous line of the extracorporeal circuit according to a standardized protocol across all participating centres.
- *Vascular access*: arteriovenous fistula, graft, or central venous catheter.
- *Treatment modality*: high-flux conventional HD, or hemodiafiltration (HDF) in pre-dilution or post-dilution mode.
- *Dialyzer*: manufacturer and effective surface area (m^2). Dialyzers were grouped according to membrane material into asymmetric triacetate membranes, conventional high-flux synthetic membranes, and other synthetic dialyzer types.
- *Dialysis adequacy*: dialysis dose (KT) calculated using a standardized formula.
- *Session duration*: in minutes.

Statistical analysis

Quantitative variables were expressed as mean ± standard deviation (SD). Categorical variables were summarized as absolute frequencies and percentages. The incidence of extracorporeal circuit (ECC) clotting was calculated per hemodialysis session. Group comparisons for categorical variables were performed using the χ^2 test or Fisher's exact test, as appropriate. Differences in continuous variables were assessed using Student's *t*-test or one-way ANOVA for normally distributed variables, and the Mann–Whitney *U* or Kruskal–Wallis tests for non-normally distributed variables. Associations were first explored using unadjusted bivariate analyses, followed by multivariable logistic regression adjusted for dialysis centre. A generalized linear mixed model including a random intercept for patient was additionally fitted to account for within-patient correlation. All analyses were performed using SPSS software, version 29.0.2.0 (Armonk, NY: IBM Corp.) and R (R Foundation for Statistical Computing, Vienna, Austria), using the R Commander graphical user interface (version 4.4.2). A p-value ≤ 0.05 was considered statistically significant.

Results

A total of 186,637 haemodialysis sessions from 1757 patients were analysed during the study period. Most sessions (179,709 sessions; 96.3%) showed clean circuit or involvement of few capillaries; while extensive capillary involvement occurred in 3278 sessions (1.8%) and complete clotting in 3650 sessions (2.0%). Regarding anticoagulation strategy, unfractionated heparin (UFH) was used in 147,591 sessions (79.1%), low-molecular-weight heparin (LMWH) in 4964 sessions (2.7%), and no systemic anticoagulation in 34,082 sessions (18.3%).

Factors associated with extracorporeal circuit clotting

To further identify determinants of extracorporeal circuit (ECC) clotting, clinical and procedural factors showing variation across sessions were analysed (Table 1 and Fig. 2).

Table 1
Factors associated with extracorporeal circuit clotting during hemodialysis.

Variable	Category	Clean/few capillaries *n* (%)	Extensive capillary involvement *n* (%)	Complete clotting *n* (%)	*p*-Value
Total sessions		179,709 (96.3)	3,278 (1.8)	3,650 (2.0)	–
Type of heparin, n = 186,637	No heparin	32,733 (96.0)	674 (2.0)	675 (2.0)	<0.001
	Unfractionated heparin	142,449 (96.5)	2,358 (1.6)	2,784 (1.9)	
	LMWH	4,527 (91.2)	246 (5.0)	191 (3.8)	
Dialysis modality, n = 186,598	Standard high-flux HD	52,635 (96.2)	879 (1.6)	1,179 (2.2)	<0.001
	Predilution HDF	922 (93.7)	39 (4.0)	23 (2.3)	
	Post-dilution HDF	126,113 (96.3)	2,360 (1.8)	2,448 (1.9)	
Dialyzer surface area, n = 186,327	1.6–1.7 m^2	14,916 (97.1)	173 (1.1)	277 (1.8)	<0.001
	1.8–1.9 m^2	81,810 (96.2)	1,636 (1.9)	1,601 (1.9)	
	>2.0 m^2	82,675 (96.2)	1,467 (1.7)	1,772 (2.1)	
Vascular access, n = 186,414	AV fistula	100,351 (96.6)	1,780 (1.7)	1,739 (1.7)	<0.001
	Graft	9,495 (96.8)	163 (1.7)	155 (1.6)	
	Catheter	69,655 (95.8)	1,328 (1.8)	1,748 (2.4)	
Session duration (min)		219.0 ± 26.4	217.3 ± 26.5	217.5 ± 31.7	<0.001
KT >45, n = 181,190	No	34,467 (95.4)	759 (2.1)	921 (2.5)	<0.001
	Yes	140,110 (96.6)	2,419 (1.7)	2,514 (1.7)	
KT (mean ± SD)		52.2 ± 10.1	50.6 ± 9.7	49.5 ± 11.1	<0.001

AV, arteriovenous; HD, hemodialysis; HDF, hemodiafiltration; KT, dialysis dose; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin.

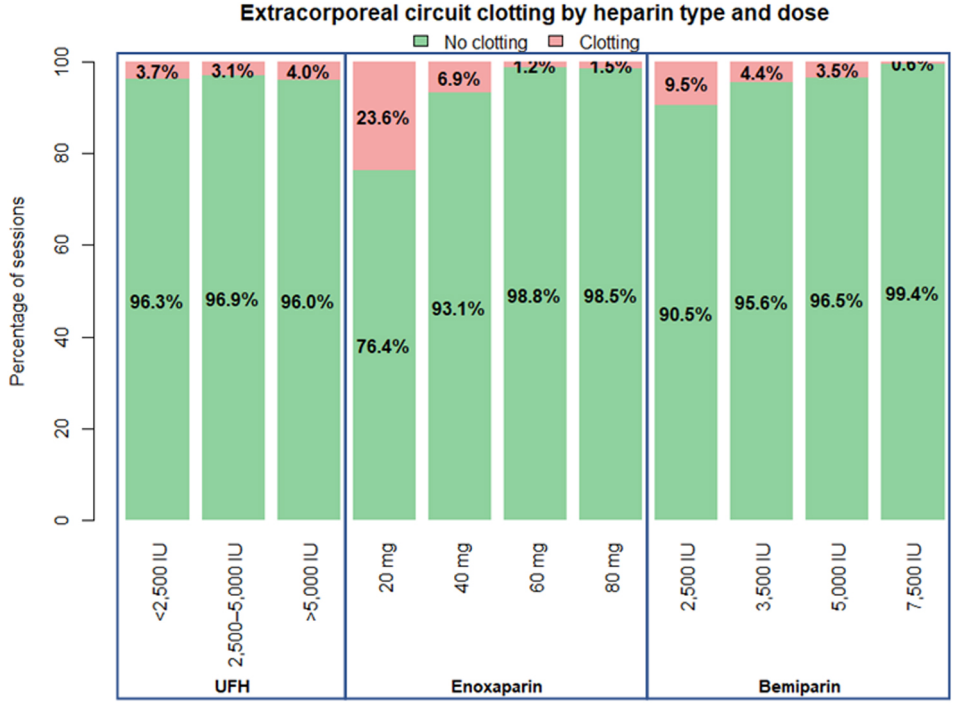

Fig. 2. Percentage of hemodialysis sessions with and without extracorporeal circuit clotting according to heparin type and dose category (UFH, enoxaparin, and bemiparin).

Table 2
Multivariable logistic regression analysis of factors independently associated with extracorporeal circuit clotting, adjusted for dialysis centre.

Variable	Category	OR (95% CI)	*p*-Value
Type of heparin (reference: UFH)	No heparin	1.09 (1.02–1.16)	0.012
	LMWH	0.82 (0.72–0.93)	0.002
Dialysis modality (reference: standard high-flux HD)	Predilution HDF	1.57 (1.20–2.05)	<0.001
	Post-dilution HDF	0.96 (0.91–1.02)	0.235
Vascular access (reference: AV fistula)	Graft	1.05 (0.93–1.18)	0.408
	Catheter	1.46 (1.38–1.55)	<0.001
Dialyzer surface area (reference: 1.6–1.7 m^2)	1.8–1.9 m^2	1.12 (1.00–1.25)	0.047
	>2.0 m^2	1.22 (1.09–1.37)	<0.001

AV, arteriovenous; CI, confidence interval; HD, hemodialysis; HDF, hemodiafiltration; LMWH, low-molecular-weight heparin; OR, odds ratio; UFH, unfractionated heparin.

Type of anticoagulation

In the unadjusted analysis (Table 1), sessions performed without heparin and those using unfractionated heparin (UFH) showed similarly high proportions of clean or minimally affected circuits (approximately 96%), with low rates of extensive involvement and complete clotting. In contrast, sessions treated with low–molecular-weight heparin (LMWH) showed a lower proportion of clean circuits (approximately 91%) and higher frequencies of both extensive involvement (approximately 5%) and complete clotting (approximately 4%) ($p < 0.001$). However, in the multivariable model adjusted for dialysis centre (Table 2), using UFH as the reference, heparin-free sessions were associated with a higher risk of extracorporeal circuit clotting (OR 1.09, 95% CI 1.02–1.16; $p = 0.012$), whereas LMWH was associated with a lower risk (OR 0.82, 95% CI 0.72–0.93; $p = 0.002$).

Dialysis modality

Standard high-flux hemodialysis and post-dilution hemodiafiltration (HDF) showed comparable and low rates of ECC clotting. Predilution HDF was associated with a lower proportion of clean circuits and higher rates of extensive involvement and complete clotting ($p < 0.001$). In the multivariable model adjusted for dialysis centre (Table 2), and using standard high-flux hemodialysis as the reference category, predilution HDF was independently associated with an increased risk of extracorporeal circuit clotting (OR 1.57, 95% CI 1.20–2.05; $p < 0.001$), whereas post-dilution HDF showed no significant association.

Dialyzer surface area

Smaller dialyzers (1.6–1.7 m^2) showed the lowest incidence of ECC clotting. Increasing membrane surface area was associated with progressively higher clotting rates, with dialyzers >2.0 m^2 showing the highest frequency of complete clotting ($p < 0.001$). In the multivariable model adjusted for dialysis centre (Table 2), and using dialyzers with a surface area of 1.6–1.7 m^2 as the reference category, larger dialyzer surface area was independently associated with an increased risk of clotting, including 1.8–1.9 m^2 (OR 1.12, 95% CI 1.00–1.25; $p = 0.047$) and >2.0 m^2 (OR 1.22, 95% CI 1.09–1.37; $p < 0.001$).

Vascular access

The use of central venous catheters was associated with a higher frequency of complete ECC clotting compared with arteriovenous fistulas and grafts (2.4% vs approximately 1.6–1.7%; $p < 0.001$). In the multivariable model (Table 2), and using arteriovenous fistula as the reference category, central venous catheter use was independently associated with an increased risk of clotting (OR 1.46, 95% CI 1.38–1.55; $p < 0.001$), whereas grafts showed no significant association.

Session duration

Short dialysis sessions (<60 min) showed the highest proportion of complete ECC clotting (approximately 6.5%), whereas longer sessions (>180 min) were associated with substantially lower clotting rates (approximately 1.9%; $p < 0.001$).

Dialysis adequacy (KT)

Sessions complicated by ECC clotting achieved lower mean KT values than sessions without clotting, and failure to reach the target KT >45 was associated with a higher frequency of complete clotting ($p < 0.001$).

Heparin dose

For UFH, intermediate doses (2500–5000 IU) were associated with the lowest rates of complete ECC clotting, whereas both lower and higher doses showed higher clotting frequencies, suggesting a limited dose–response effect. In contrast, LMWH (both enoxaparin and bemiparin) showed a clear dose–response relationship, with underdosing associated with higher rates of ECC clotting ($p < 0.001$).

In the combined analysis of dialyzer type and anticoagulation strategy (Fig. 3), marked differences in the percentage of hemodialysis sessions complicated by extensive or complete extracorporeal circuit clotting were observed across dialyzers, closely reflecting the anticoagulation strategies with which they were used. Across all dialyzer types, sessions performed without anticoagulation or with low-molecular-weight heparin (LMWH) consistently showed higher clotting rates than those using unfractionated heparin (UFH). FX® and VitaPES® membranes displayed the highest clotting rates, particularly in LMWH-treated sessions (11.5% and 12.5%, respectively), resulting in higher overall mean clotting rates (6.5% and 6.8%). In contrast, Solacea™ membranes showed uniformly low clotting rates across all anticoagulation strategies (no heparin 2.7%, UFH 1.8%, LMWH 3.4%), with an overall rate of 2.6%.

Sensitivity analysis: patient-level generalized linear mixed model

In a sensitivity analysis using a generalized linear mixed model with a random intercept for patient, a substantial proportion of extracorporeal circuit clotting risk was attributable to patient-level variability (random intercept variance 1.21) (Table 3). Heparin-free sessions were associated with a higher risk of extracorporeal circuit clotting compared with unfractionated heparin (adjusted OR 1.69, 95% CI 1.51–1.89; $p < 0.001$), whereas low-molecular-weight heparin was associated with a lower risk (adjusted OR 0.58, 95% CI 0.45–0.75; $p < 0.001$). Post-dilution hemodiafiltration was associated with reduced clotting risk compared with standard high-

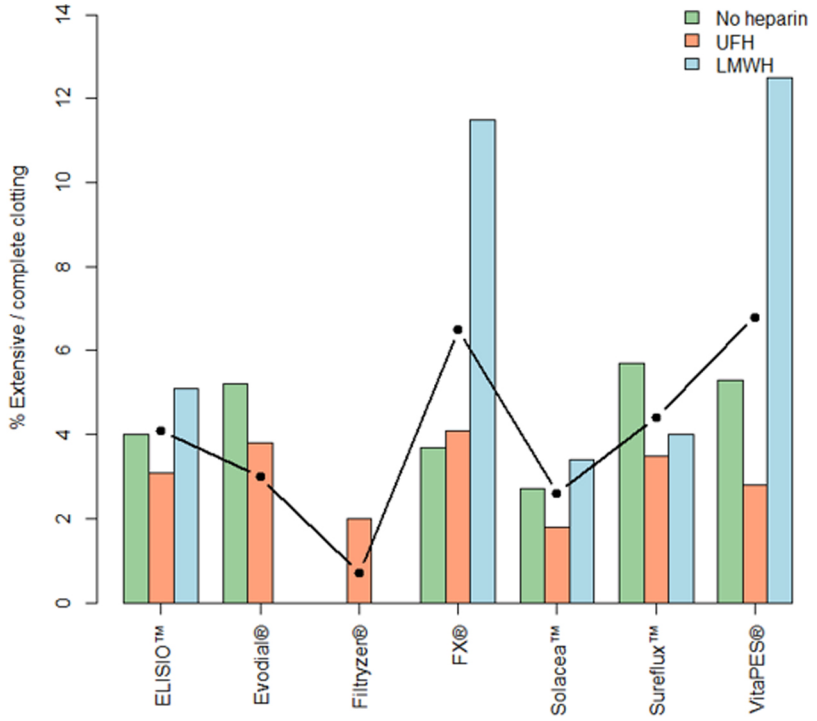

Fig. 3. Percentage of hemodialysis sessions with extracorporeal circuit clotting by dialyzer type and anticoagulation regimen. The black line indicates the overall clotting rate per dialyzer. *Abbreviations*: LMWH: low-molecular-weight heparin; UFH: unfractionated heparin.

Table 3
Patient-level generalized linear mixed-effects model of factors independently associated with extracorporeal circuit clotting, including a random intercept for patient.

Variable	Category	Adjusted OR (95% CI)	*p*-Value
Type of heparin (ref: UFH)	No heparin	1.69 (1.51–1.89)	<0.001
	LMWH	0.58 (0.45–0.75)	<0.001
Dialysis modality (ref: standard high-flux HD)	Predilution HDF	1.00 (0.66–1.50)	0.98
	Post-dilution HDF	0.89 (0.81–0.98)	0.018
Vascular access (ref: AV fistula)	Graft	0.93 (0.74–1.18)	0.57
	Catheter	1.45 (1.30–1.63)	<0.001
Dialyzer surface area (ref: 1.6–1.7 m^2)	1.8–1.9 m^2	0.99 (0.81–1.21)	0.94
	>2.0 m^2	1.29 (1.04–1.60)	0.018

AV, arteriovenous; CI, confidence interval; HD, hemodialysis; HDF, hemodiafiltration; LMWH, low-molecular-weight heparin; OR, odds ratio; UFH, unfractionated heparin.

flux hemodialysis (adjusted OR 0.89, 95% CI 0.81–0.98; $p = 0.018$), while predilution hemodiafiltration showed no association.

Central venous catheter use remained independently associated with an increased risk of clotting (adjusted OR 1.45, 95% CI 1.30–1.63; $p < 0.001$). Dialyzers with a surface area >2.0 m^2 were associated with higher clotting risk (adjusted OR 1.29, 95% CI 1.04–1.60; $p = 0.018$), with no significant effect for intermediate surface areas ($p = 0.94$).

Discussion

In this large multicentre real-world cohort, extracorporeal circuit clotting (ECC) was an infrequent event (<4% of sessions) but was associated with clinically relevant consequences. Sessions complicated by clotting were shorter and were consistently associated with lower KT values, highlighting a direct impact on dialysis adequacy and treatment safety. These findings confirm that ECC is not merely a technical issue but a relevant determinant of quality of care, even when it occurs in a small proportion of sessions, in line with previous studies showing that even partial circuit clotting can compromise effective dialysis time and overall treatment quality.[1,2,8,9]

Adjusted analyses, including multivariable models and a patient-level mixed-effects model, allowed the identification of factors associated with ECC risk that are clinically plausible and largely potentially modifiable. The absence of anticoagulation and the use of central venous catheters were consistently associated with a higher risk of clotting, whereas low–molecular-weight heparin (LMWH) was associated with a lower risk in both adjusted models. Post-dilution hemodiafiltration was associated with a lower risk only in the patient-level mixed-effects model.

With regard to anticoagulation, unadjusted analyses showed a higher frequency of ECC in sessions performed with LMWH, particularly at low doses. However, this association was reversed after adjustment for dialysis centre and, more robustly, in the patient-level mixed-effects model, in which LMWH was associated with a lower risk of circuit clotting compared with unfractionated heparin (UFH). This finding indicates that the excess risk observed in crude analyses primarily reflects clinical practice patterns, patient selection, and conservative dosing strategies rather than reduced intrinsic efficacy of LMWH.

Dose emerged as a key determinant of anticoagulation performance. For UFH, intermediate doses (2500–5000 IU) were associated with the lowest clotting rates, whereas both lower and higher doses

showed poorer performance, suggesting the existence of an optimal therapeutic window and a potential ceiling effect, in line with previous reports.[7]

Similarly, for LMWH – particularly enoxaparin – a clear dose–response relationship was observed, with an increased risk of circuit clotting associated with underdosing.[10] These findings reinforce the notion that, in routine clinical practice, the main limitation of LMWH is not its intrinsic efficacy but the difficulty in achieving appropriate dosing that adequately balances thrombotic and bleeding risks.[3] Achieving optimal anticoagulation remains a clinical challenge, as insufficient dosing increases the risk of clotting, whereas excessive dosing is associated with bleeding complications and reduced quality of life.[2,7,10] Although the lower molecular weight of LMWH compared with UFH has been proposed as a potential mechanism for reduced persistence of anticoagulant effect during prolonged or convective dialysis modalities,[11] our results suggest that, when appropriately dosed, LMWH provides effective circuit protection in real-world hemodialysis settings.

Dialysis modality also influenced the risk of ECC. In unadjusted analyses, pre-dilution hemodiafiltration showed the highest rates of extracorporeal circuit clotting, whereas no relevant differences were observed between conventional high-flux hemodialysis and post-dilution hemodiafiltration. The increased risk observed with pre-dilution may be explained by dilution of both blood and anticoagulant before entering the dialyzer, thereby reducing the effective heparin concentration within the fibres. This phenomenon may interfere with the formation of a stable protein layer on the membrane, alter blood rheology, and promote platelet activation and triggering of the coagulation cascade.[12,13] However, the heterogeneity of published results suggests that this effect depends on the technical context and on fine-tuning of the dialysis prescription.[14,15]

As expected, the use of central venous catheters was consistently associated with a higher risk of ECC, in line with the literature describing increased flow turbulence, blood stasis, and catheter-related thrombosis, including fibrin sheath formation and access dysfunction.[7,16] Unmeasured factors, such as lower effective blood flow (QB), which could not be analysed in this study, may partly contribute to the increased risk observed. Previous studies have shown that, despite advances in catheter design, effective QB and delivered dialysis dose remain lower than those achieved with arteriovenous access, often requiring longer treatment sessions to reach comparable KT values.[17]

Short-duration sessions (<60 min) showed the highest rates of ECC, largely due to premature interruption of treatment caused by clotting events. This reflects not only a technical complication but also a state of underdialysis, as patients fail to receive the prescribed treatment time. In contrast, longer sessions (>180 min) were associated with a lower risk of clotting, underscoring the importance of circuit stability for achieving effective dialysis. Accordingly, sessions complicated by clotting achieved significantly lower KT values, confirming the direct impact of ECC on delivered dialysis dose. Previous studies have shown that circuit clotting reduces the effective dialyzer surface area and impairs solute clearance,[9] and that recurrent circuit thrombosis in continuous therapies markedly reduces delivered dose and Kt/V.[18,19]

Regarding dialyzer characteristics, larger membrane surface areas were associated with a higher risk of ECC. After adjustment for confounding factors, only dialyzers with surface areas greater than 2.0 m^2 remained independently associated with increased clotting risk. Experimental and clinical studies have shown that membrane surface characteristics influence platelet activation and procoagulant responses in hemodialysis circuits, supporting the concept that larger surfaces may be more sensitive to suboptimal anticoagulation.[20,21] These findings suggest that dialyzer size affects not only depurative efficacy but also coagulation risk, an aspect that remains insufficiently explored and warrants further investigation.

Recent advances in membrane biocompatibility, including asymmetric triacetate (ATA™) membranes, have reduced extracorporeal circuit clotting and enabled hemodialysis sessions to be performed with minimal or no systemic anticoagulation. Clinical trials such as SAFE and SOLFA have shown that up to 60% of sessions using Solacea® can be performed without anticoagulation, compared with 24% when using other synthetic membranes.[22,23] These studies confirm that membrane design and material are key determinants of extracorporeal circuit performance.[24] Improved biocompatibility attenuates inflammatory activation, oxidative stress, and procoagulant responses, allowing reduced exposure to anticoagulants in patients at high bleeding risk.[21,25,26]

A key finding of this study was the identification of substantial inter-individual variability in ECC risk. The mixed-effects model showed that a relevant proportion of clotting risk is attributable to patient-specific factors beyond technical prescription. This finding supports the clinical perception that certain patient profiles are more prone to circuit clotting and reinforces the need for truly individualized strategies.

Our findings support personalized anticoagulation strategies, appropriate selection of dialysis modality, and the use of highly biocompatible dialyzers to minimize circuit clotting without compromising treatment efficacy. Systematic anticoagulation monitoring may facilitate more precise dose adjustment and help prevent both thrombotic and bleeding complications.[27] Recent reviews emphasize that the current challenge is not merely maintaining circuit patency, but doing so in a safe, efficient, and sustainable manner for both patients and dialysis units.[28] However, the available evidence remains limited, as most studies were not designed to assess clinically relevant outcomes related to anticoagulation strategies.[29,30] This highlights the need for further research in this field.

This study has limitations that should be considered when interpreting the results. First, its retrospective design and the reliance on visual assessment of extracorporeal circuit clotting may introduce some degree of subjectivity. In addition, relevant clinical factors such as blood flow (QB), hemoconcentration parameters, inflammatory status, and intrinsic thrombotic risk were not included in the present analysis and may contribute to inter-individual variability in clotting risk. These factors represent an important area for future research.

The inclusion of multiple sessions per patient entails a degree of pseudoreplication, a limitation inherent to many observational studies based on real-world clinical practice. To address this latter issue, a sensitivity analysis using a patient-level mixed-effects model with a random intercept was performed, which confirmed the robustness of the main associations and allowed inter-individual variability in clotting risk to be taken into account. In this regard, an important strength of the study is the identification of a substantial contribution of patient-related factors to circuit clotting risk beyond technical prescription. Among the main strengths of this study are its very large sample size, multicentre design, and the combined use of conventional multivariable models and patient-level mixed-effects models, which allowed a robust and complementary assessment of both technical and clinical determinants of extracorporeal circuit clotting under real-world clinical practice conditions.

Extracorporeal circuit clotting during hemodialysis was infrequent but clinically relevant, as it was associated with shorter sessions and lower delivered KT. Absence of anticoagulation, central venous catheter use, and larger dialyzer surface area independently increased clotting risk, whereas appropriately dosed low–molecular-weight heparin and post-dilution hemodiafiltration were associated with greater circuit stability. Marked inter-individual variability further underscored patient-specific susceptibility.

Taken together, these findings support a personalized approach to anticoagulation and dialysis prescription, integrating patient characteristics with careful selection of dialysis modality, vascular access, and dialyzer type to optimize circuit patency, dialysis adequacy, and patient safety in routine clinical practice.

Authors' contributions

DH and MDAJ conceived the study. DH, AA, MP, EG, CP, MLST, JG, MSJM, MB, AMS, AG, AI, CL, DC, CP, CO, AH, TC, DP, and MDAJ collected the data. JAG and MDAJ performed the statistical analysis. DH, JAG, and MDAJ drafted the manuscript. All authors critically revised the manuscript and approved the final version.

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Conflict of interest

The authors declare no conflicts of interest.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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