Research Square

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Pulsed Field versus Radiofrequency Ablation for Paroxysmal AF: Randomized Comparison of Hemolysis and Myocardial Injury Using Circular PFA Catheter

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Abstract

Background Pulsed field ablation (PFA) for atrial fibrillation is a high-profile innovation, but differing parameters across catheter types may affect hemolysis differently. Evidence for Circular PFA catheters is sparse; we undertook a randomized comparison versus radiofrequency ablation to address this gap.

Methods This study enrolled 60 consecutive inpatients with paroxysmal AF who underwent ablation at Xuzhou Medical University Affiliated Hospital from October 2024 to May 2025, and randomized them equally to RFA group (N = 30) and PFA group (N = 30). Blood samples were collected from the same venous sheath during the baseline examination upon admission, at the beginning of the procedure, and after the procedure. In addition to traditional hemolysis indices, we also employ flow cytometry to determine the proportion of apoptotic cells.

Results Baseline patient data showed no significant differences. Postoperative blood sample analysis revealed that the PFA group had significantly higher levels of free hemoglobin (210.01 ± 74.93 vs. 158.54 ± 108.44, P = 0.037), TBIL, DBIL and IBIL compared to the RFA group. The apoptotic cell percentage was also higher with PFA (8.14 ± 4.00% vs. 5.28 ± 2.18%; P = 0.007). By contrast, the hs-TnT level in the PFA group (866.13 ± 318.57 vs. 1341.13 ± 657.61, P < 0.001) was significantly lower than that in the RFA group. Within the PFA arm, the number of applications showed no significant correlation with hemolysis markers.

Conclusion Among patients with paroxysmal AF, ablation with Circular PFA catheters was associated with greater intraprocedural hemolysis and lower myocardial injury than RFA.

Trial registration This study was registered with the China Clinical Trial Registry on August 27,2024, under registration number: ChiCTR2400088774.

1. Background

Atrial fibrillation (AF), as one of the most common clinical arrhythmias, has a continuously rising global prevalence, contributing significantly to increased risks of stroke, heart failure incidence, and all-cause mortality, making it a major public health burden[1]. Currently, catheter ablation for pulmonary vein isolation (PVI) has become a first-line rhythm control therapy for AF. Among various ablation modalities, radiofrequency ablation (RFA) has long been regarded as the gold standard for AF catheter ablation due to its mature application experience, proven efficacy, and relatively controllable operability[1, 2]. However, thermal-based RFA, while achieving myocardial tissue destruction, inevitably carries a series of complication risks, such as esophageal injury, phrenic nerve palsy, pulmonary vein stenosis, and thromboembolic events[3].

In recent years, a novel ablation technology based on a non-thermal mechanism—pulsed field ablation (PFA)—has emerged as one of the latest advancements in the field of cardiac ablation, offering a new option for AF ablation. PFA has been demonstrated to be a very rapid and effective PVI treatment

method with excellent durability[4]. In the first head-to-head clinical comparison with thermal ablation, PFA was non-inferior to thermal ablation—whether RFA or cryoablation[5]. PFA utilizes microsecond-long, high-intensity electric pulses applied to the cell membrane. Through the irreversible electroporation (IRE) effect, it specifically induces cardiomyocyte apoptosis while relatively preserving the extracellular matrix structure[6, 7]. Its unique tissue selectivity (strong effect on cardiomyocytes with significantly reduced risk of injury to adjacent nerves, blood vessels, esophagus, etc.) and non-thermal ablation nature[8, 9] theoretically provide a revolutionary solution to overcome RFA-related complications. Early clinical studies have preliminarily confirmed its advantages in efficiency and safety[6, 7].

However, recent international studies have revealed that PFA may cause severe intravascular hemolysis and acute kidney injury[10, 11]. Some studies indicate that the degree of hemolysis induced by PFA in AF patients is significantly greater than that by RFA[12], raising concerns about the safety of PFA. It is noteworthy that the hemolytic effect of PFA may be closely related to pulse parameters (such as field strength, waveform, pulse width) and the shape of the catheter. Current international clinical data are based on the Boston Scientific PFA system. Circular PFA catheters represent a gap in this field; their potential differences in energy delivery mode, pulse sequence optimization, and catheter tip configuration mean it remains unclear whether their hemolysis risk aligns with international reports. Corresponding research evidence is lacking.

Therefore, this study aims to thoroughly investigate and directly compare the difference in induced hemolysis between PFA using a Circular PFA catheter and conventional RFA in AF patients undergoing catheter ablation through a prospective controlled design. The results of this study are expected to provide key clinical data for the differential comparison between the hemolytic effects of using Circular PFA catheter ablation and traditional RFA, fill the data gap in the field of hemolysis with Circular PFA catheter, thereby enabling better selection of ablation methods for AF patients, providing a basis for choosing safer atrial fibrillation ablation strategies in clinical practice, ultimately optimizing patient treatment plans and improving long-term prognosis.

2. Methods

2.1 Study methods

This study is a prospective, randomized, single-center controlled trial. In the clinical pathway of this center, patients are typically evaluated in the outpatient setting by cardiac electrophysiologists, and upon confirmation that radiofrequency ablation is the optimal treatment strategy, they are scheduled for elective hospitalization to undergo the procedure. The design of this study aims to closely reflect this real-world scenario, evaluating different treatment approaches under an established therapeutic decision-making framework.

Patient recruitment and the informed consent process are conducted after the patient's planned admission but before the scheduled ablation procedure. To ensure informational neutrality and respect

for patient autonomy, informed consent is obtained by a research coordinator who is independent of the clinical treatment team. The coordinator explains in detail to the patient that the purpose of this study is to compare two ablation modalities—PFA and RFA—and does not involve re-evaluating the necessity of radiofrequency ablation therapy itself; participants will be randomly assigned to different perioperative management protocols, but the core ablation therapy will proceed as planned; participation in the study is voluntary, and patients have the right to withdraw at any stage without any impact on the quality of standard ablation treatment and subsequent care. The consent process ensures that patients have adequate time to ask questions and consider their decision.

This study enrolled 104 consecutive hospitalized patients diagnosed with paroxysmal atrial fibrillation (PAF) and scheduled for ablation procedures at the Affiliated Hospital of Xuzhou Medical University between October 2024 and May 2025. Inclusion criteria: (1) Diagnosis of AF confirmed by electrocardiogram and/or 24-hour Holter monitoring; (2) Provision of informed consent; (3) Diagnosis of PAF and scheduled for ablation surgery as an inpatient. Exclusion criteria: (1) Presence of thrombus in the left atrium or left atrial appendage confirmed by transesophageal echocardiography or CT left atrial angiography; (2) Contraindications for MRI examination, such as post-pacemaker implantation, claustrophobia, etc.; (3) History of stroke or TIA within the last 3 months, or presence of definite neurological deficit symptoms; (4) Previous history of AF catheter ablation surgery; (5) Comorbid severe diseases, such as hepatic or renal insufficiency, severe respiratory insufficiency; (6) Presence of fresh cerebral infarction found on preoperative MRI examination. The diagnostic criteria for PAF were confirmation by 12-lead electrocardiogram or 24-hour Holter monitoring recording (typical AF ECG manifestations lasting ≥ 30 seconds), excluding persistent AF, atrial flutter, and other atrial arrhythmias. After applying the predetermined exclusion criteria, a total of 42 patients were excluded. Due to unqualified blood samples from 2 patients, 60 patients with PAF were ultimately enrolled and randomly assigned to the PFA group (n = 30) and the RFA group (n = 30) in a 1:1 ratio. The flowchart of this study is shown in Fig. 1.This study was approved by the Ethics Committee of the Affiliated Hospital of Xuzhou Medical University and conducted in accordance with the Declaration of Helsinki. Each participant signed an informed consent form. Ethics approval number: XYFY2024-KL351-01.

Data were extracted from the electronic medical record system of the Affiliated Hospital of Xuzhou Medical University. Collected variables included patient baseline characteristics, vital signs, comorbidities, and hemolysis-related measures—age, gender, body mass index (BMI), systolic and diastolic blood pressure, history of diabetes, history of hypertension, smoking history, hemoglobin, creatinine, total and direct bilirubin, lactate dehydrogenase (LDH), and apoptotic cell percentage, among others. Baseline data were abstracted from the first examination record at admission. Hemolysis-related indicators were obtained from blood samples collected before the procedure and at the end of the procedure and submitted for laboratory testing.

2.2 Procedure of PFA

The circular PFA catheter (Sichuan Jinjiang Electronic Technology Co., Ltd.) is designed based on an established pulsed-field ablation platform. Prior to its introduction into clinical practice, comprehensive

preclinical validation—including in vivo animal studies such as porcine heart models—has been completed [13]. Furthermore, relevant studies have demonstrated its safety and efficacy for ablation in patients with paroxysmal atrial fibrillation [14–16] and persistent atrial fibrillation [17, 18], confirming its effective tissue ablation capability and favorable safety profile, including protection of surrounding critical structures. Additionally, the device has obtained regulatory approval and complies with medical device quality systems and safety standards.

All procedures were performed under fentanyl sedation and local anesthesia. After anesthesia, a steerable decapolar catheter was advanced into the coronary sinus via the right femoral vein, and a quadripolar catheter was placed in the right ventricle via the right femoral vein. Simultaneously, an 8.5-Fr Swartz SL1 sheath with a dilator was inserted via the right femoral vein. An 11-Fr sheath was inserted via the left femoral vein for placing the intracardiac echocardiography (ICE) catheter (SoundStar 10 Fr, Biosense Webster) into the right atrium. After transseptal puncture was completed under fluoroscopic guidance and ICE monitoring, a circular PFA catheter equipped with a magnetic sensor (Sichuan Jinjiang Electronic Technology Co., Ltd.) was introduced into the left atrium for PVI. This 8F disposable cardiac PFA catheter features a 5.5-Fr distal tip (8-Fr proximal shaft), a 7-electrode ring array with 4 mm spacing, and a 15 mm ring diameter, with a built-in magnetic sensor for real-time navigation. When used in conjunction with the LEAD-Mapping 3D electrophysiological mapping system (Sichuan Jinjiang Electronic Technology Co., Ltd.), this platform achieves sub-millimeter positioning accuracy (≤ 1 mm) through magneto-electric fusion technology, enables high-resolution 3D reconstruction of the left atrium combined with voltage mapping, and continuously displays catheter morphology under magnetic guidance. The system delivers bipolar alternating current PFA energy by emitting microsecond biphasic pulses between adjacent electrodes. All electrodes have dual functions of mapping/pacing and ablation. PVI was performed using a voltage of 1800 V. Successful PVI was defined by meeting the following criteria: (I) disappearance or dissociation of pulmonary vein potentials; (II) failure to capture the adjacent atrium during multi-point pacing along the atrial ablation line using the PFA catheter. After PVI completion, left atrial voltage mapping was performed using the same catheter during sinus rhythm. If atrial fibrillation persisted after PVI, electrical cardioversion was performed. After waiting 20 minutes, PVI verification was repeated. For cases with pulmonary vein-to-atrium reconduction, additional ablation was performed to re-establish PVI. For patients with left atrial low-voltage areas (LVA), substrate modification was performed.

2.3 Procedure of RFA

All procedures were performed under fentanyl sedation and local anesthesia. After anesthesia, a steerable decapolar catheter was advanced into the coronary sinus via the right femoral vein, and a quadripolar catheter was placed in the right ventricle via the right femoral vein. Simultaneously, an 8.5 Fr Swartz SL1 sheath with a dilator was inserted via the right femoral vein. After an 11F sheath was inserted via the left femoral vein, the ICE catheter (SoundStar 10F, Biosense Webster) was introduced through this sheath into the right atrium. After transseptal puncture and ICE positioning under fluoroscopic guidance, an open-irrigated tip ablation catheter (STSF, Biosense Webster) was advanced

into the left atrium. Using the electrophysiological mapping system (Carto 3, Biosense Webster), point-by-point ablation technique was employed for PVI, with a power output of up to 50 W and an irrigation rate of 15 mL/min to maintain a tip temperature below 45°C. The endpoint of ablation was achieving complete bidirectional electrical isolation of the pulmonary veins. The endpoint of PVI is achievement of electrical disconnection between the PVs and the LA. This disconnection can be verified by documenting the absence of wavefront propagation from the LA to the PV (entrance block) and/or from the PV to the LA (exit block)[19]. Left atrial voltage mapping was subsequently performed during sinus rhythm. If atrial fibrillation persisted after pulmonary vein isolation, electrical cardioversion was performed.

2.4 Anticoagulation Therapy

All patients received oral anticoagulant therapy before the procedure. Anticoagulation was maintained continuously throughout the ablation process without interruption. Before transseptal puncture, activated clotting time (ACT) was measured using the ACT Plus system (Medtronic Inc.), and a weight-adjusted heparin bolus was administered based on the preoperative ACT level. During left atrial procedures, ACT values were monitored every 30 minutes, and additional heparin was administered based on the intraoperative ACT level. The target therapeutic ACT range was maintained between 300–350 seconds throughout the procedure.

2.5 Blood Sampling Collection

All blood samples were collected from patients in a fasting state. Samples were drawn from the same venous sheath during baseline examination upon admission, at the beginning of the procedure (from the first venous femoral artery access, i.e., the F-11 sheath), and at the end of the procedure (after ablation completion). The first 5 mL of blood was discarded in all samples. Flow cytometry, biochemical, and hematological examinations were performed immediately or within 3 hours after collection.

2.6 Methods for measuring Apoptotic Cells Percentage

After inverting and mixing the fresh blood sample, carefully aspirate 100 μl of whole blood and add it to 1 ml of PBS containing 2% BSA, then invert and mix. Aspirate 100 μl of the mixed sample into a flow cytometry tube, add CD235a Annexin V, gently pipette to mix, and incubate in the dark for 16 minutes. Add 1 ml of PBS containing 2% BSA, centrifuge at 1500 r/min for 5 minutes, and discard the supernatant. Then, add another 1 ml of PBS containing 2% BSA, centrifuge at 1500 r/min for 5 minutes, and discard the supernatant. Add 500 μl of PBS containing 2% BSA, mix thoroughly, and proceed to machine testing using the BD LSRFortessa™. Acquire 100,000 red blood cells and analyze the CD235a+ Annexin V+ cell population to determine the proportion of apoptotic cells.

2.7 Statistical Methods

This study used the Kolmogorov-Smirnov test to assess the normality of the data. For continuous variables with normal distribution, the t-test was used (expressed as mean ± standard deviation). For continuous variables with non-normal distribution, the Mann-Whitney U test was used (expressed as median [Q1, Q3]). Categorical variables are presented as frequency (n, %) and were analyzed using the

chi-square test (two-tailed $P < 0.05$ was considered statistically significant). Statistical analysis was performed using SPSS 26.0 (Inc, Chicago, IL, USA).Statistical graphs were generated using GraphPad Prism version 10.1.2.

3. Results

As shown in Table 1, the study population had a mean age of 63.67 ± 9.07 years and a BMI of 25.34 ± 3.50, with 36 (60%) males. Comparison of baseline data between the RFA and PFA groups showed no significant differences in Age, BMI, SBP, DBP, HR, Atrial Fibrillation Course, LAD, LVEDD, LVEF, hypertension, diabetes, Stroke/TIA, CHD, CHA2DS2-VASc score, HATCH score, and HAS-BLED score.

Table 1
Baseline

Variables	Total (n = 60)	RFA (n = 30)	PFA (n = 30)	P
Age, years	63.67 ± 9.07	63.33 ± 10.88	64.00 ± 6.99	0.779
BMI, kg/m^2	25.34 ± 3.50	25.06 ± 3.26	25.62 ± 3.75	0.544
SBP, mmHg	129.62 ± 17.03	130.53 ± 19.60	128.70 ± 14.30	0.680
DBP, mmHg	80.15 ± 10.52	80.07 ± 11.69	80.23 ± 9.41	0.952
HR, bpm	71.33 ± 10.67	69.43 ± 8.11	73.23 ± 12.59	0.170
Atrial Fibrillation Course, months	32.74 ± 43.01	33.44 ± 48.33	32.05 ± 37.77	0.902
CHA_2DS_2-VASc	1.63 ± 1.26	1.50 ± 1.20	1.77 ± 1.33	0.418
LAD, mm	38.08 ± 4.23	38.20 ± 4.82	37.97 ± 3.62	0.833
LVEDD, mm	48.50 ± 3.08	48.07 ± 3.06	48.93 ± 3.08	0.279
LVEF, %	62.47 ± 3.73	61.97 ± 3.48	62.97 ± 3.97	0.304
HATCH	0.62 ± 0.87	0.53 ± 0.73	0.70 ± 0.99	0.460
HAS-BLED	0.65 ± 0.71	0.60 ± 0.67	0.70 ± 0.75	0.589
Male, n(%)	36 (60.00)	19 (52.78)	17 (47.22)	0.598
Hypertension, n(%)	21 (35.00)	11 (52.38)	10 (47.62)	0.787
Diabetes, n(%)	6 (10.00)	4 (66.67)	2 (33.33)	0.667
Stroke/TIA, n(%)	5 (8.33)	0 (0.00)	5 (100.00)	0.062
CHD, n(%)	6 (10.00)	4 (66.67)	2 (33.33)	0.667
Dyslipidemia, n(%)	3 (5.00)	2 (66.67)	1 (33.33)	1.000
Smoking, n(%)	5 (8.33)	3 (60.00)	2 (40.00)	1.000
Drinking, n(%)	1 (1.67)	0 (0.00)	1 (100.00)	1.000

Note: BMI = body mass index; LAD = left atrium dimension; LVEF = left ventricular ejection fraction; LVEDD = left ventricular end-diastolic dimension; TIA = transient ischemic attack; CHD = coronary heart disease

As shown in Table 2, comparing preoperative and postoperative values in the PFA group, postoperative Free Hemoglobin (210.01 ± 74.93 vs. 140.46 ± 89.01 mg/L, P < 0.001), TBIL (13.86 ± 5.19 vs. 9.62 ± 4.99 μmol/L, P < 0.001), DBIL (4.89 ± 1.66 vs. 3.94 ± 1.69 μmol/L, P < 0.001), IBIL (8.97 ± 3.67 vs. 5.69 ± 3.39

μmol/L, P < 0.001), LDH (212.33 ± 34.39 vs. 176.07 ± 22.78 U/L, P < 0.001), K^+ (3.75 ± 0.37 vs. 3.63 ± 0.25 mmol/L, P = 0.031), hs-TnT (866.13 ± 318.57 vs. 7.71 ± 5.96 ng/L, P < 0.001), Cl^- (106.09 ± 2.49 vs. 104.92 ± 2.40 mmol/L, P < 0.001), AST (26.77 ± 7.66 vs. 21.30 ± 7.60 U/L, P < 0.001), and CREA (63.03 ± 16.10 vs. 60.27 ± 15.33 μmol/L, P = 0.008) were all significantly increased, indicating the presence of cardiac injury and hemolysis with PFA. While Ca^{2+} (2.14 ± 0.12 vs. 2.21 ± 0.12 mmol/L, P < 0.001) and HCO_3^- (23.36 ± 1.49 vs. 24.83 ± 1.40 mmol/L, P < 0.001) were significantly decreased.

Table 2
Comparison of preoperative and after the procedure PFA groups

Variables	**Baseline (n = 30)**	**After the procedure (n = 30)**	**P**
hs-TnT, ng/L	7.71 ± 5.96	866.13 ± 318.57	< .001
CREA, μmol/L	60.27 ± 15.33	63.03 ± 16.10	0.008
Free Hemoglobin, mg/L	140.46 ± 89.01	210.01 ± 74.93	< .001
AST, U/L	21.30 ± 7.60	26.77 ± 7.66	< .001
TBIL, μmol/L	9.62 ± 4.99	13.86 ± 5.19	< .001
DBIL, μmol/L	3.94 ± 1.69	4.89 ± 1.66	< .001
IBIL, μmol/L	5.69 ± 3.39	8.97 ± 3.67	< .001
BUN, mmol/L	5.20 ± 1.25	4.94 ± 1.20	0.409
K^+, mmol/L	3.63 ± 0.25	3.75 ± 0.37	0.031
Na^+, mmol/L	141.63 ± 1.55	141.61 ± 1.65	0.938
Cl^-, mmol/L	104.92 ± 2.40	106.09 ± 2.49	< .001
Mg^{2+}, mmol/L	4.38 ± 19.19	0.84 ± 0.04	0.321
Ca^{2+}, mmol/L	2.21 ± 0.12	2.14 ± 0.12	< .001
PO_4^{3-}, mmol/L	1.03 ± 0.23	1.01 ± 0.21	0.558
HCO_3^-, mmol/L	24.83 ± 1.40	23.36 ± 1.49	< .001
LDH, U/L	176.07 ± 22.78	212.33 ± 34.39	< .001

Note: hs-TnT = high-sensitivity troponin T; CREA = creatinine; AST = aspartate aminotransferase; TBIL = total bilirubin; DBIL = direct bilirubin; IBIL = indirect bilirubin; BUN = blood urea nitrogen; LDH = lactate dehydrogenase.

As shown in Table 3, comparing preoperative and postoperative values in the RFA group, postoperative hs-TnT (1341.13 ± 657.61 vs. 11.52 ± 20.58 ng/L, P < 0.001), LDH (206.43 ± 44.82 vs. 172.40 ± 22.36 U/L, P < 0.001), AST (26.07 ± 7.49 vs. 20.77 ± 6.52 U/L, P < 0.001), Na^+ (142.14 ± 1.95 vs. 141.12 ± 1.89

mmol/L, P = 0.011), and Cl^- (106.58 ± 3.17 vs. 103.66 ± 2.46 mmol/L, P < 0.001) were significantly increased, however, there was no significant statistical difference in free hemoglobin, TBIL, DBIL and IBIL, indicating significant myocardial injury in the RFA group but no significant hemolysis.While Mg^{2+} (0.81 ± 0.06 vs. 0.84 ± 0.09 mmol/L, P = 0.009), Ca^{2+} (2.08 ± 0.08 vs. 2.21 ± 0.06 mmol/L, P < 0.001), and HCO_3^- (23.04 ± 1.95 vs. 24.71 ± 2.09 mmol/L, P = 0.001) were significantly decreased.

Table 3
Comparison of preoperative and after the procedure RFA groups

Variables	**Baseline (n = 30)**	**After the procedure (n = 30)**	**P**
hs-TnT, ng/L	11.52 ± 20.58	1341.13 ± 657.61	< .001
CREA, μmol/L	63.49 ± 17.17	61.63 ± 15.07	0.292
Free Hemoglobin, mg/L	132.06 ± 95.82	158.54 ± 108.44	0.341
AST, U/L	20.77 ± 6.52	26.07 ± 7.49	< .001
TBIL, μmol/L	8.44 ± 3.62	8.99 ± 3.38	0.118
DBIL, μmol/L	3.76 ± 1.42	3.99 ± 1.49	0.236
IBIL, μmol/L	4.75 ± 2.32	5.00 ± 2.22	0.340
BUN, mmol/L	5.65 ± 1.79	5.47 ± 1.76	0.322
K^+, mmol/L	3.60 ± 0.29	3.76 ± 0.46	0.052
Na^+, mmol/L	141.12 ± 1.89	142.14 ± 1.95	0.011
Cl^-, mmol/L	103.66 ± 2.46	106.58 ± 3.17	< .001
Mg^{2+}, mmol/L	0.84 ± 0.09	0.81 ± 0.06	0.009
Ca^{2+}, mmol/L	2.21 ± 0.06	2.08 ± 0.08	< .001
PO_4^{3-}, mmol/L	0.94 ± 0.14	0.91 ± 0.16	0.384
HCO_3^-, mmol/L	24.71 ± 2.09	23.04 ± 1.95	0.001
LDH, U/L	172.40 ± 22.36	206.43 ± 44.82	< .001

Note: hs-TnT = high-sensitivity troponin T; CREA = creatinine; AST = aspartate aminotransferase; TBIL = total bilirubin; DBIL = direct bilirubin; IBIL = indirect bilirubin; BUN = blood urea nitrogen; LDH = lactate dehydrogenase.

As shown in Supplementary Table 1, there were no statistically significant differences in preoperative blood sample measurements of hs-TnT, free hemoglobin, AST, TBIL, DBIL, IBIL, CREA, BUN, K^+, Na^+, Cl^-, Mg^{2+}, Ca^{2+}, PO_4^{3-}, HCO_3^-, and LDH between the PFA group and the RFA group. As shown in Supplementary table and Fig. 2, postoperative blood sample analysis revealed that the PFA group had

significantly higher levels of free hemoglobin (210.01 ± 74.93 vs. 158.54 ± 108.44 mg/L, P = 0.037), TBIL (13.86 ± 5.19 vs. 8.99 ± 3.38 μmol/L, P < 0.001), DBIL (4.89 ± 1.66 vs. 3.99 ± 1.49 μmol/L, P = 0.031), IBIL (8.97 ± 3.67 vs. 5.00 ± 2.22 μmol/L, P < 0.001), Ca^{2+} (2.14 ± 0.12 vs. 2.08 ± 0.08 mmol/L, P = 0.047), and PO_4^{3-} (1.01 ± 0.21 vs. 0.91 ± 0.16 mmol/L, P = 0.037) compared to the RFA group, we also did a comparison of apoptotic cells percentage comparison in some patients, as shown in Table 4 and Supplementary Fig. 1, preoperative blood tests for apoptotic cell percentage showed no significant difference. The Apoptotic Cells Percentage at the end of the procedure was significantly higher in the PFA group than in the RFA group (8.14 ± 4.00 vs. 5.28 ± 2.18%, P = 0.007), indicating significantly greater hemolysis in the PFA group. However, as shown in Fig. 3, the hs-TnT level in the PFA group (866.13 ± 318.57 vs. 1341.13 ± 657.61 ng/L, P < 0.001) was significantly lower than that in the RFA group, suggesting less myocardial injury than the RFA group. In contrast, no statistically significant difference was observed in K^+ levels (3.75 ± 0.37 vs. 3.76 ± 0.46 mmol/L, P = 0.865).

Table 4
Apoptotic Cells Percentage Comparison

Variables	**Total (n = 44)**	**RFA (n = 20)**	**PFA (n = 24)**	**P**
Baseline, %	3.71 ± 3.05	2.86 ± 1.58	4.42 ± 3.76	0.092
End of the Procedure, %	6.84 ± 3.57	5.28 ± 2.18	8.14 ± 4.00	0.007

As shown in Fig. 4, in the PFA group, the number of applications showed no significant correlation with Free Hemoglobin, TBIL, DBIL, or IBIL, indicating that the degree of hemolysis was not directly related to the number of pulsed field applications.

4. Discussion

This is the first prospective randomized controlled trial comparing pulsed-field ablation using circular catheters with conventional radiofrequency ablation. By analyzing pre-procedural and post-procedural blood biomarkers, we observed: (1) acute hemolysis was significantly greater with the Circular PFA system than with RFA; and (2) myocardial injury was milder in the PFA group.

4.1 PFA Induces Significantly Greater Acute Hemolysis Than RFA

Postoperative blood tests revealed that compared to the RFA group, the PFA group showed significantly elevated levels of Free Hemoglobin, TBIL, DBIL, and IBIL, indicating that the acute hemolysis induced by PFA was significantly greater than that in the RFA group. Consistent with previous studies, we found that PFA is more likely to cause hemolysis than RFA. However, the degree of hemolysis observed in our study was lower than that reported for other types of PFA catheters, such as in the study by Miruna A. Popa et al[20]. In our PFA group, postoperative free hemoglobin levels were 210.01 ± 74.93 mg/L versus 158.54 ±

108.44 mg/L in the RFA group (P = 0.037), and TBIL levels were 13.86 ± 5.19 μmol/L versus 8.99 ± 3.38 μmol/L (P < 0.001). In contrast, the study by Miruna A. Popa et al[20]. Reported free hemoglobin levels of 592.8 ± 330.6 mg/L versus 147.8 ± 183.0 mg/L (P < 0.001) and bilirubin levels of 21.3 ± 11.3 μmol/L versus 14.8 ± 8.8 μmol/L (P < 0.001). This suggests that the Circular PFA catheter used in our study may cause less hemolytic damage. Additionally, beyond conventional hemolysis indicators, we further measured the Apoptotic Cell Percentage, which was significantly higher in the PFA group (8.14 ± 4.00% vs. 5.28 ± 2.18% in the RFA group, P = 0.007). This metric, not previously reported in other studies, may more accurately reflect the extent of hemolytic damage. We found that both traditional hemolysis indices and the newly adopted Apoptotic Cells Percentage demonstrated significantly higher hemolysis in the PFA group compared to the RFA group.

Although hemolysis indicators were elevated, none of the patients in our study exhibited clinical symptoms such as cola-colored urine or renal function decline, suggesting that the degree of hemolysis did not lead to severe clinical consequences.

4.2 Hemolysis and Number of Applications

Unlike the study by Miruna A. Popa et al[20], our research found no significant correlation between the number of discharges and hemolysis-related indicators (TBIL, DBIL, IBIL, Free Hemoglobin) in the PFA group. This discrepancy may be attributed to the specific PFA catheter used in our study. The circular PFA catheter employed here was manufactured in China (by Sichuan Jinjiang Electronic Science and Technology Co., Ltd.) and utilized a tissue-contact-specific discharge strategy, where energy was delivered only through electrodes in contact with cardiac tissue. This approach minimizes unnecessary electric field exposure and optimizes energy delivery efficiency, which may explain the lack of correlation between hemolysis and the number of discharges. Additionally, the relatively small sample size in our study may have limited statistical power, potentially contributing to the absence of a significant observed relationship. Further studies with larger sample sizes are needed to validate whether a correlation exists between the number of discharges and hemolysis when using circular PFA catheters.

4.3 The PFA group had lower myocardial injury

Our study found that postoperative hs-TnT levels in the RFA group (1341.13 ± 657.61 ng/L) were significantly higher than those in the PFA group (866.13 ± 318.57 ng/L, P < 0.001). This contrasts with the findings of Osmancik et al[21], whose study reported that hs-TnT levels in the PFA group (10,102 ng/L [IQR: 8,272 – 14,207 ng/L]) were substantially greater than those in the RFA group (1,006 ng/L [IQR: 603-1,433 ng/L]). This discrepancy may be attributed to the use of a circular PFA ablation catheter in our study, which features a circular electrode and employs a tissue-contact-specific discharge strategy at 1800V, potentially reducing myocardial injury. Future studies could explore altering voltage parameters, discharge locations, or conducting multicenter comparisons with different PFA catheters to further elucidate the relationship between PFA and the extent of myocardial injury.

By comparing the difference in hemolysis between the PFA and RFA groups in AF patients, this study demonstrated that PFA using a circular PFA catheter produces significantly greater hemolysis than RFA, however, compared with RFA, it has obvious advantages of low myocardial injury. This fills the gap in comparative hemolysis data for circular PFA catheters, thereby aiding in better selection of ablation modalities for AF patients, providing a basis for choosing safer AF ablation strategies in clinical practice, and ultimately optimizing patient treatment plans and improving long-term prognosis.

4.4 Study Limitations

Firstly, this single-center randomized study had a modest sample and focused on peri-procedural assessments; longer-term outcomes were outside the scope. Secondly, patient enrollment occurred after hospital admission and scheduling of ablation therapy, rather than at the initial treatment decision-making stage in the outpatient setting. While this approach aligns with the real-world scenario of this study (which evaluates perioperative management in patients already scheduled for ablation), and measures such as an independent informed consent process and strict inclusion criteria were implemented to mitigate bias, this design may still introduce a degree of selection bias. Furthermore, it may limit the generalizability of the study findings to patient populations at earlier stages of the therapeutic decision-making pathway. Thirdly, the biomarker panel was pragmatic rather than exhaustive, and analyses by detailed energy/voltage strata were exploratory. Results reflect the studied circular PFA platform and may not generalize to all systems. These factors do not change the direction of the observed effects but suggest that confirmation in larger, multicenter cohorts with extended follow-up would be informative.

4.5 Conclusion

Among patients with paroxysmal AF, circular PFA catheters were associated with greater hemolysis but lower myocardial injury than RFA.

Declarations

Ethics approval and consent

This study was approved by the Ethics Committee of the Affiliated Hospital of Xuzhou Medical University and conducted in accordance with the Declaration of Helsinki. Each participant signed an informed consent form. Ethics approval number: XYFY2024-KL351-01.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated during and/or analyzed during the current study are available by request from the correspondence (chen.wensu@163.com).

Competing interest

The authors declare that the study was conducted without any commercial or financial relationships construed as a potential conflict of interest.

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Author contribution

MCD, and PL performed the experiments and analyzed the data. MCD and PL were involved in data collection. MCD wrote the manuscript. ZQZ and WSC directed the entire research work and corrected the articles. All authors read and approve the manuscript and agree to be accountable for all aspects of the research in ensuring that the accuracy or integrity of any part of the work is appropriately investigated and resolved.

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Not applicable.

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Figures

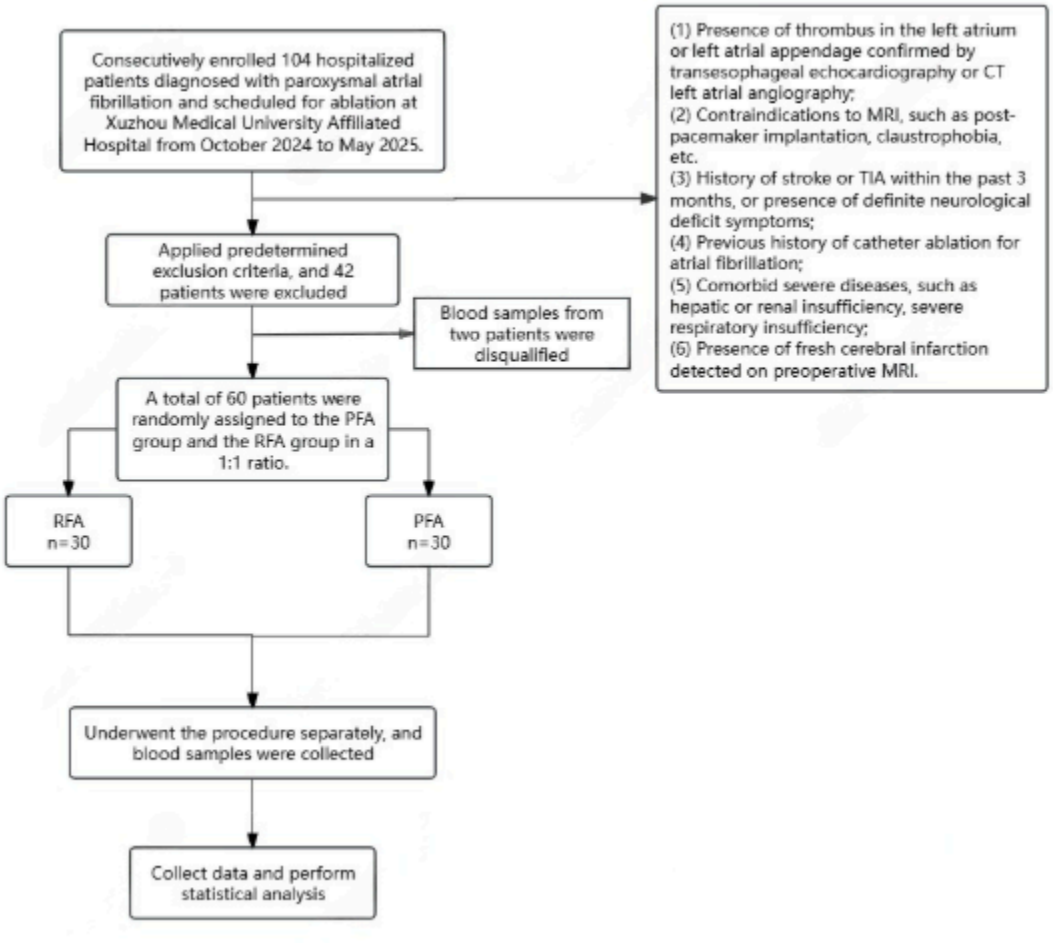


Figure 1

Flowchart

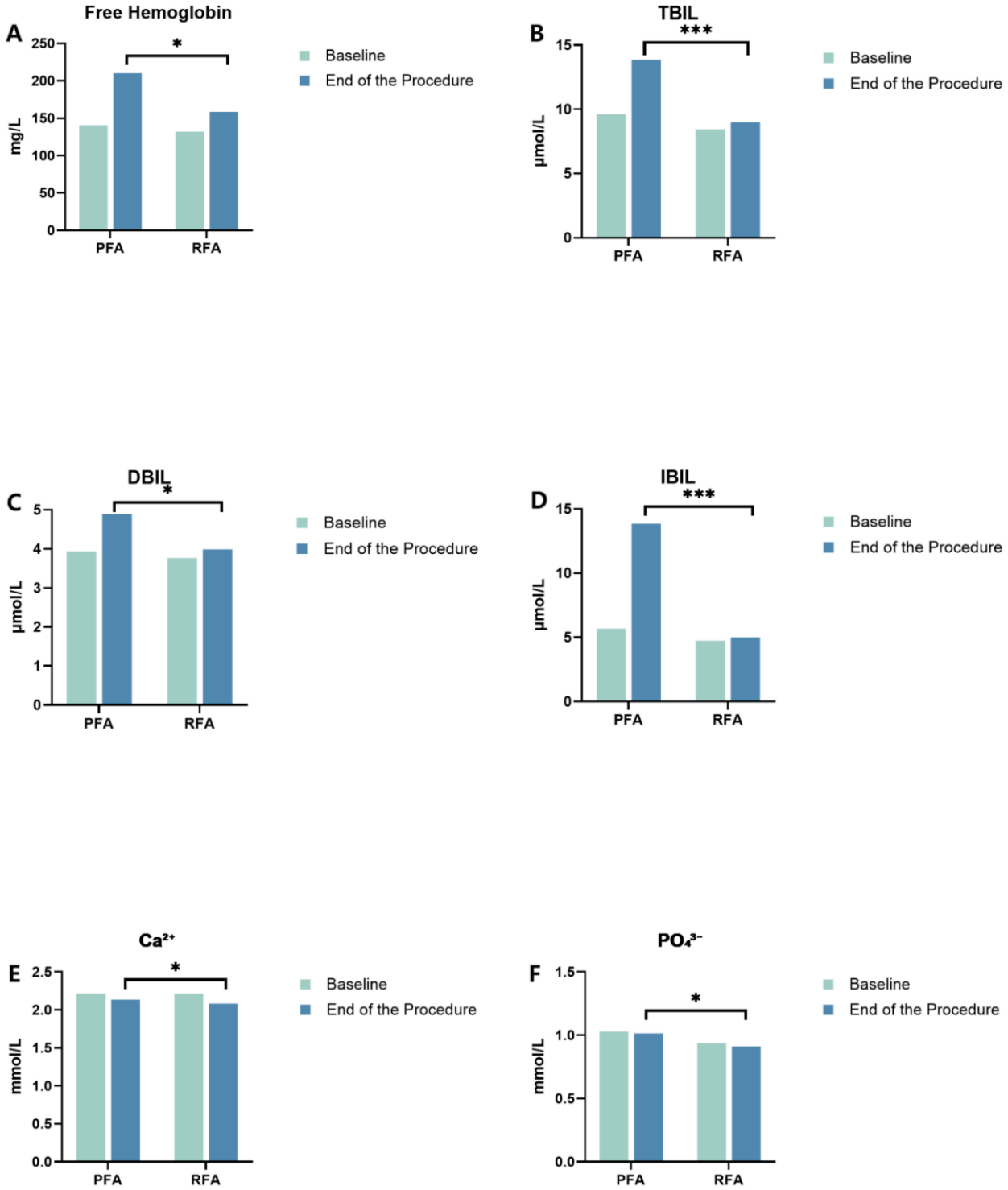


Figure 2

Comparison of hemolysis related indicators

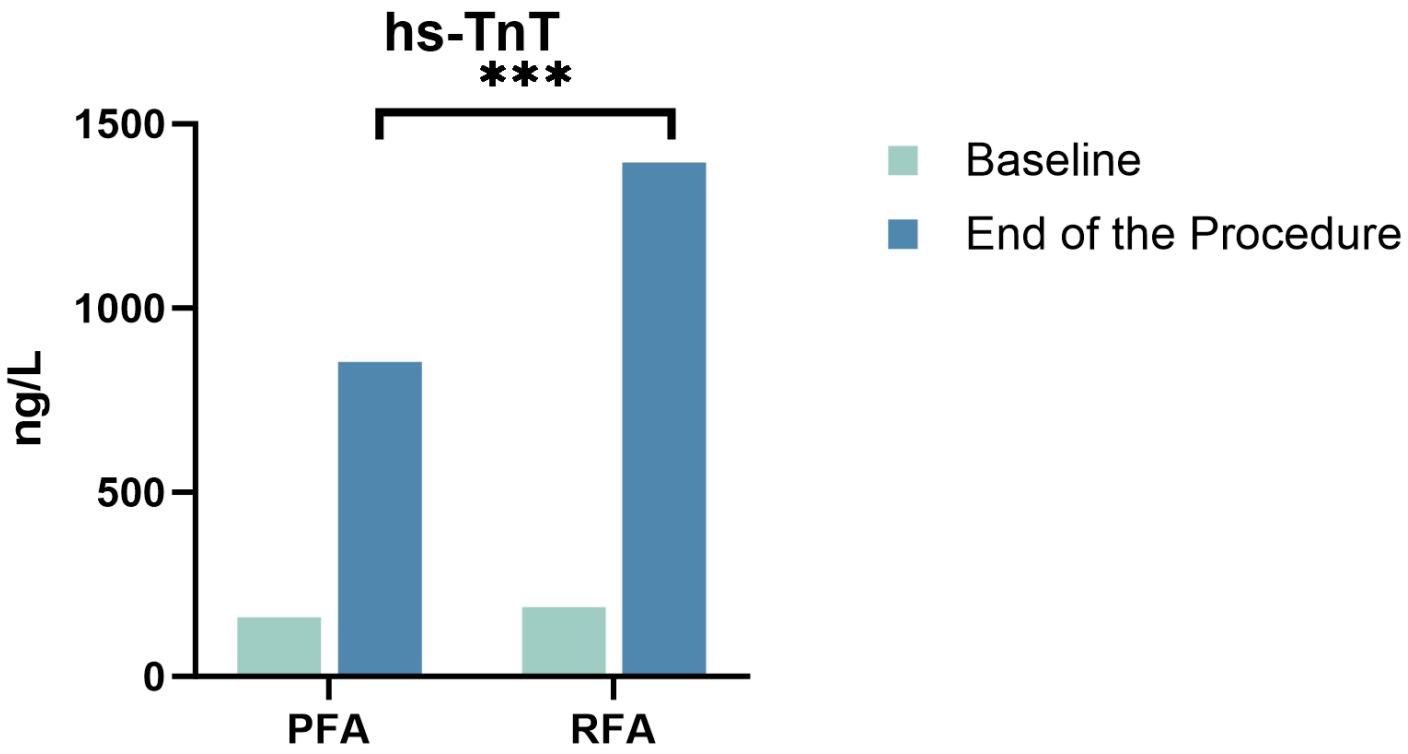


Figure 3

Comparison of hs-TnT between PFA and RFA groups

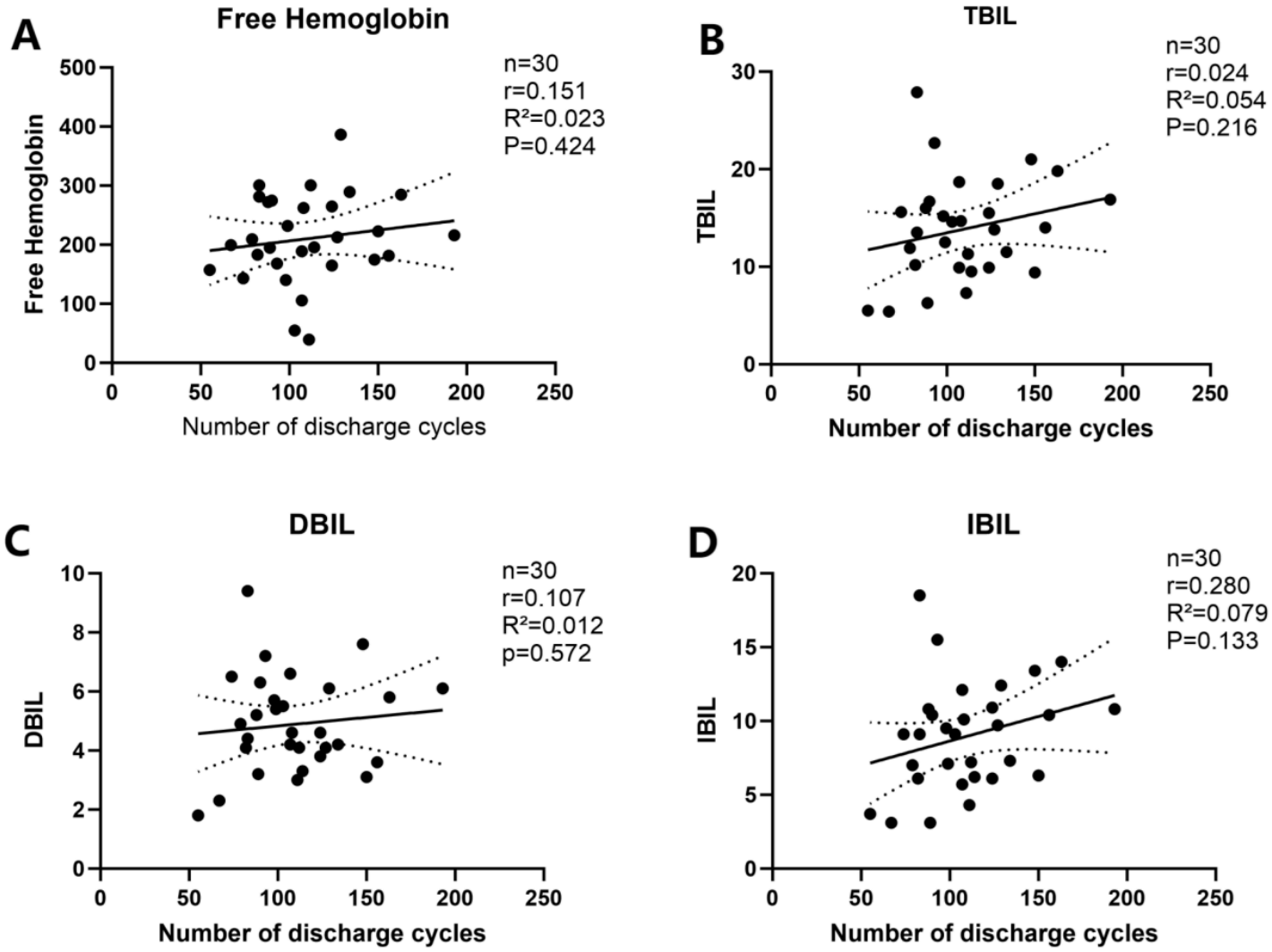


Figure 4

Correlation between number of discharges and hemolysis

Supplementary Files

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