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Optimizing Heparin and Protamine Dosing During Cardiopulmonary Bypass Using Activated Clotting Time-Guided Protocols: A Single-Centre Prospective Randomized Controlled Trial

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Graphical abstract

Optimizing Heparin and Protamine Dosing During Cardiopulmonary Bypass Using Activated Clotting Time-Guided Protocols: A Single-Center Prospective Randomized Controlled Trial in CABG Patients

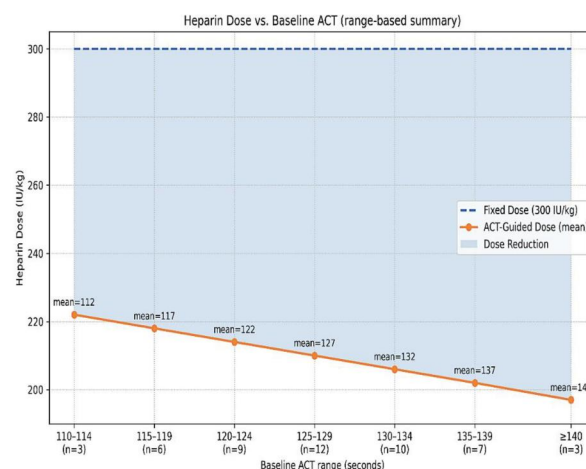
Summary

Study Design and Population:

- Single-Centre, Prospective, Randomized Study
- 100 Isolated CABG with CPB (50 patients per group)
- ACT-Guided versus Standard Anticoagulation Management

ACT-Guided Group Key Results:

- Lower Intra-Operative Need of Heparin Adjuncts & Better ACT Values within the Therapeutic Ranges
- Reduced Total Heparin Exposure
- ROTEM-Based Improved Clot Strength & Reduced Hypocoagulability
- Lower 24-hour Chest Drainage Blood Loss
- Reduced Platelet Decline
- Reduced Postoperative Transfusion Rate (28% vs. 52%)
- Reduced Total Allogenic Transfused Units (0.6 vs. 1.4)
- No Difference in Thrombotic Events



Legend: CABG: coronary artery bypass grafting; ACT: activated clotting time; CPB: cardiopulmonary bypass; ROTEM: Rotational Thromboelastometry.

Abstract

Objectives: To evaluate whether an activated clotting time (ACT)-guided, formula-based anticoagulation strategy supported by viscoelastic coagulation monitoring (ROTEM) improves perioperative coagulation management and reduces bleeding compared with standard weight-based heparin dosing in patients undergoing coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB).

Methods: In this single-centre prospective, randomized controlled trial, 100 adults undergoing isolated CABG with CPB were allocated to ACT-guided management ($n = 50$) or standard care ($n = 50$). The ACT-guided group received individualized heparin and protamine dosing calculated using predefined ACT-based formulas targeting ACT ≥ 400 seconds. The control group received a fixed heparin bolus (300 IU/kg) with empirical protamine reversal. ROTEM was performed preoperatively, intraoperatively, and postoperatively. The primary end-point was total chest drain output at 24 hours. Secondary end-points included transfusion requirements, thrombotic events, platelet count variation, oxygenator performance, additional heparin or protamine use, ROTEM-derived parameters, and perioperative clinical outcomes.

Results: The ACT-guided group had lower 24-hour chest drain bleeding and reduced total exposure to heparin and protamine. Intraoperative ACT values were more consistently within target range, with fewer supplemental heparin doses required. ROTEM demonstrated shorter clotting times and improved clot firmness, indicating reduced postoperative hypocoagulability. Platelet decline during CPB was attenuated. Transfusion rates (28% vs 52%, $P = .01$) and total allogeneic units transfused (0.6 ± 1.0 vs 1.4 ± 1.6 , $P = .003$) were significantly lower, with no observed increase in thrombotic events.

Conclusions: Activated clotting time-guided, formula-based anticoagulation supported by ROTEM was associated with more favourable coagulation parameters and reduced bleeding without evidence of increased thrombotic complications within the limitations of the study sample size. Larger prospective studies are warranted to confirm these findings.

Keywords: activated clotting time; cardiopulmonary bypass; coronary artery bypass grafting; heparin dosing; protamine reversal; viscoelastic coagulation monitoring.

INTRODUCTION

Effective anticoagulation management during cardiopulmonary bypass (CPB) is essential to ensure circuit patency while minimizing perioperative bleeding in patients undergoing coronary artery bypass grafting (CABG). Unfractionated heparin, followed by protamine sulphate for reversal, remains the cornerstone of anticoagulation in cardiac surgery.^{1,2} Despite its long-standing use, defining the optimal dose of both agents continues to represent a major clinical challenge. Conventional anticoagulation strategies are largely based on fixed, weight-adjusted heparin dosing most commonly 300 IU/kg with protamine administered empirically in a 1:1 or near-equimolar ratio.³ This simplified approach fails to account for the substantial interindividual variability in heparin responsiveness, antithrombin levels, platelet function, and inflammatory activation associated with CPB.⁴ As a consequence, both under- and over-anticoagulation remain frequent, exposing patients to potentially avoidable complications.^{4,5} These constraints restrict their availability to well-resourced centres and limit widespread adoption, particularly in healthcare systems with constrained economic resources. In everyday clinical practice, excessive heparin administration may result in persistently elevated activated clotting time (ACT) values, increased postoperative bleeding, and higher transfusion requirements.⁶ Conversely, protamine overdosing is increasingly recognized as an independent contributor to coagulopathy, platelet dysfunction, hypotension, and paradoxical anticoagulant effects.⁷⁻¹¹ Against this background, the present study evaluates an ACT-guided, formula-based strategy for heparin and protamine dosing, supported by viscoelastic coagulation monitoring, in patients undergoing isolated CABG with CPB. We hypothesized that this

approach could reduce perioperative bleeding and drug exposure compared with standard weight-based anticoagulation, without increasing thrombotic risk, while remaining feasible and potentially cost-efficient in routine clinical practice.

METHODS

Study design

This single-centre prospective, randomized controlled trial was conducted in adult patients undergoing isolated CABG with CPB. The study aimed to compare a conventional weight-based anticoagulation strategy with an individualized, ACT-guided, formula-based approach for both heparin administration and protamine reversal. The protocol was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines, received approval from the local Institutional Review Board, and required written informed consent from all participants prior to enrolment (University Institutional Review Board of K.Kale; 2024.11.27). Patient recruitment was conducted between December 2024 and July 2025, with 30-day postoperative follow-up completed for all participants. Although the study received institutional review board approval, due to its investigator-initiated single-centre design, formal prospective registration in a public clinical trial registry was not performed.

Study population

Adult patients aged 18 years or older scheduled for elective or urgent isolated CABG requiring CPB were considered eligible for inclusion. All patients were required to

have a baseline ACT measurement available before heparin administration and to be able to provide written informed consent. Patients were excluded if any of the following conditions were present: known hypersensitivity or adverse reactions to unfractionated heparin or protamine sulphate, allergy to fish or neutral protamine Hagedorn (NPH) insulin, preoperative treatment with low-molecular-weight heparins or antiplatelet and/or anticoagulant agents not adequately discontinued according to current guidelines, including ticagrelor (Brilique) and other P2Y₁₂ inhibitors, known congenital or acquired coagulation disorders such as thrombocytopaenia or qualitative platelet dysfunction, baseline antithrombin III activity <80% or severe antithrombin deficiency not correctable with supplementation, uncorrected preoperative coagulopathy, international normalized ratio (INR) >1.8 not correctable before surgery, inadequate discontinuation of direct oral anticoagulants, emergency surgery, pregnancy, or participation in other interventional clinical trials potentially affecting coagulation status or bleeding outcomes.

Randomization and allocation

Patients were randomized in a 1:1 ratio to either the ACT-guided anticoagulation group or the standard anticoagulation group using a computer-generated randomization sequence with block randomization to ensure balanced group sizes. Allocation concealment was maintained through sealed, opaque envelopes opened immediately before induction of anaesthesia. Due to the nature of the intervention, blinding of anaesthesia and perfusion teams was not feasible; however, investigators responsible for postoperative outcome assessment and statistical analysis were blinded to group allocation.

Cardiopulmonary bypass configuration and normothermic perfusion strategy

Cardiopulmonary bypass was established using a standardized extracorporeal circuit consisting of a roller pump, a membrane oxygenator (Spectrum Medical LTD, United Kingdom), circuits both coated with phosphorilcoline and a crystalloid priming solution. All procedures were conducted under normothermic conditions, with core body temperature actively maintained between 36.0 and 37.0°C throughout CPB using integrated heat exchangers and continuous temperature monitoring. A goal-directed perfusion strategy was applied uniformly in both study groups. Pump flow was indexed to body surface area and adjusted to achieve an indexed oxygen delivery (DO_{2i}) of at least 280 mL/min/m². Mean arterial pressure during CPB was maintained between 60 and 70 mmHg. Arterial blood gas analysis and haemoglobin concentration were assessed at regular intervals to ensure adequate oxygenation and metabolic control.

Surgical technique

All surgical procedures were performed via median sternotomy by experienced cardiac surgeons using standardized operative techniques. After systemic heparinization, arterial and venous cannulation was achieved in a conventional manner. Myocardial protection was provided using intermittent cold blood cardioplegia administered to institutional practice. Coronary revascularization was completed using standard microsurgical techniques. The number and type of grafts were determined by the operating surgeon and were not influenced by study group allocation.

Anticoagulation management and ACT monitoring

Activated clotting time was measured using a point-of-care ACT monitoring system (Hemochron Signature Elite, Werfen, Bedford, MA, United States). ACT measurements were obtained after anaesthesia induction (baseline ACT), after initial heparin administration, at regular intervals during CPB, and following protamine administration. In the ACT-guided group, unfractionated heparin dosing was individualized using predefined ACT-based formulas.¹ Based on institutional experience and published data, it was assumed that 1 IU/kg of unfractionated heparin increases ACT by approximately 1.3 seconds. The target ACT before initiation of CPB was set at ≥400 seconds. This assumption was derived from previously published pharmacodynamic models and institutional observational data; however, substantial interindividual variability in heparin responsiveness is recognized, and the relationship should be interpreted as an approximate operational estimate rather than a fixed biological constant.

The initial heparin dose was calculated according to the following formula:

$$\begin{aligned} &\text{Initial heparin dose (IU)} \\ &= [(\text{Target ACT} - \text{Baseline ACT})/1.3] \times \text{body weight (kg)} \end{aligned}$$

During CPB, if ACT values decreased below the predefined target threshold, supplemental ("top-up") heparin doses were administered using the same ACT-based approach:

$$\begin{aligned} &\text{Heparin top-up dose (IU)} \\ &= [(\text{Target ACT} - \text{Current ACT})/1.3] \times \text{body weight (kg)} \end{aligned}$$

At the conclusion of CPB, protamine sulphate was administered to reverse residual heparin anticoagulation. The amount of residual heparin was estimated based on the difference between measured ACT after CPB and baseline ACT:

$$\begin{aligned} &\text{Residual heparin (IU/kg)} \\ &= (\text{Measured ACT} - \text{Baseline ACT})/1.3 \end{aligned}$$

The protamine dose was then calculated assuming that 1 mg of protamine neutralizes approximately 100 IU of heparin, according to the following formula:

$$\text{Protamine dose (mg)} = \text{residual heparin (IU)} \times 0.01$$

Protamine was administered as a slow intravenous infusion at a rate of approximately 10-15 mg/min. ACT was reassessed 5-10 min after completion of protamine infusion, and additional protamine was administered only if ACT values remained significantly above baseline. In the standard anticoagulation group, patients received a fixed initial bolus of unfractionated heparin at a dose of 300 IU/kg. Additional heparin dosing and protamine reversal were performed according to institutional standard practice, typically using an empirical ratio of approximately 1 mg of protamine per 100 IU of heparin administered, guided by ACT measurements.

Viscoelastic coagulation monitoring

Global coagulation status was assessed using rotational thromboelastometry (ROTEM delta system, TEM Innovations GmbH, Munich, Germany) at predefined perioperative time points. Standard EXTEM, INTEM, and FIBTEM assays were performed according to manufacturer recommendations. Recorded parameters included clotting time (CT), clot formation time (CFT), alpha angle (α), maximum clot firmness (MCF), and maximum lysis (ML). ROTEM findings were used to support postoperative haemostatic management and transfusion decisions when clinically indicated, but did not directly guide intraoperative heparin or protamine dosing (Table 1).

Data collection, endpoints, and statistical analysis

Perioperative data were prospectively collected using a standardized electronic case-report form. The primary end-point was total chest drain output within the first 24

postoperative hours. Secondary end-points included transfusion requirements, thrombotic events, platelet count variation, additional heparin or protamine use, ROTEM-derived parameters, ICU stay, and hospital length of stay. Sample size calculation was based on an expected 24-hour chest drain output of 800 mL in the standard group and a clinically relevant 20% reduction in the ACT-guided group, requiring at least 45 patients per group to achieve 80% power with a 2-sided alpha of .05. To account for possible incomplete data, 50 patients were enrolled in each group. Continuous variables are presented as mean $\pm$ SD and categorical variables as counts and percentages. Comparisons between the groups were performed using Student's *t*-test, chi-square test, Fisher's exact test, or Mann-Whitney *U*-test, as appropriate. Because the study was powered for the primary end-point only, secondary outcome analyses should be considered exploratory. Statistical analyses were performed using IBM SPSS Statistics Version 29.0 (IBM Corp., Armonk, NY, United States). The study was reported according to CONSORT recommendations.

RESULTS

A total of 100 patients undergoing isolated CABG with CPB were prospectively enrolled and randomized equally to the ACT-guided anticoagulation group or the standard anticoagulation group. No patients were lost to follow-up or excluded after randomization. All randomized patients were included in the final analysis according to the intention-to-treat principle. Baseline demographic, clinical, and operative characteristics were well balanced between the groups, including CPB duration, aortic cross-clamp time, and surgical complexity (Table 2). ACT-guided management significantly reduced both initial and total heparin exposure compared with standard

Table 1. ROTEM Parameters, Interpretation, and Clinical Implications

ROTEM assay	Parameter	Reference/target range	Interpretation of abnormal values	Clinical implications
INTEM	CT	100-240 s	Prolonged CT suggests residual heparin effect or intrinsic pathway factor deficiency	Compare with HEPTM to differentiate residual heparin from true coagulopathy
HEPTM	CT	100-240 s	Correction of INTEM CT indicates heparin effect	If HEPTM CT normalizes, residual heparin is likely present
EXTEM	CT	38-79 s	Prolonged CT indicates deficiency of clotting factors (extrinsic pathway)	Consider plasma or factor replacement if clinically indicated
EXTEM	CFT	≤ 100 s	Prolonged CFT reflects impaired clot propagation	Suggests platelet dysfunction or hypofibrinogenemia
EXTEM	α -angle	$\geq 60^\circ$	Reduced α -angle indicates delayed fibrin polymerization	Consider platelet or fibrinogen support
EXTEM	MCF	≥ 50 mm	Low MCF reflects reduced clot strength	Suggests platelet and/or fibrinogen deficiency
FIBTEM	MCF	≥ 7 mm	Low values indicate hypofibrinogenemia	Consider fibrinogen concentrate or cryoprecipitate
APTEM	ML	$\leq 15\%$	Increased ML compared with EXTEM indicates hyperfibrinolysis	Consider antifibrinolytic therapy (eg, tranexamic acid)

Abbreviations: α -angle (α), alpha angle; APTEM, aprotinin-modified thromboelastometry; CFT, clot formation time; CT, clotting time; EXTEM, extrinsic pathway thromboelastometry; FIBTEM, fibrin-based thromboelastometry; HEPTM, heparinase-modified intrinsic thromboelastometry; INTEM, intrinsic pathway thromboelastometry; MCF, maximum clot firmness; ML, maximum lysis; ROTEM, rotational thromboelastometry.

weight-based dosing, while maintaining ACT values above the predefined target throughout CPB. ACT control was more consistent, with a higher proportion of values within target range and fewer supplemental heparin boluses. Protamine exposure was also significantly lower, with fewer patients requiring additional protamine after initial reversal (Table 3). Within the ACT-guided group, baseline ACT-stratified analysis showed a progressive reduction in heparin requirements with increasing baseline ACT values. This corresponded to a graded increase in dose reduction compared with the fixed 300 IU/kg regimen, supporting the dose-adjustment behaviour of the protocol (Table 4; Figure 1A). After protamine administration, ROTEM demonstrated a more favourable coagulation profile in the ACT-guided group, with shorter clotting and clot formation times and greater clot firmness. Hyperfibrinolysis was numerically less frequent in the ACT-guided group, although the difference was not

statistically significant. Although not statistically significant, the absolute numerical reduction in hyperfibrinolysis may still be clinically relevant and should be interpreted cautiously given the limited sample size (Table 5; Figure 1B and C). Postoperative bleeding was significantly reduced in the ACT-guided group, as shown by lower 24-hour chest drain output. The absolute mean reduction in 24-hour chest tube output was 260 mL (95% CI 160-360 mL). This was accompanied by lower red blood cell transfusion requirements, fewer patients receiving any allogeneic blood product, and a smaller perioperative platelet count decline. The absolute reduction in transfusion exposure was 24%. Surgical re-exploration for bleeding and thrombotic events was infrequent and did not differ significantly between the groups. Review of the re-exploration cases did not identify protocol-related coagulation management failure as the primary cause of bleeding. ACT-guided management was also associated with shorter ICU and hospital length of stay, with no 30-day mortality in either group (Table 6).

Table 2. Study Population and Perioperative Characteristics

Variable	ACT-guided group (n = 50)	Standard care group (n = 50)	P-value
Age, years	67 ± 9	68 ± 8	.52
Male sex, n (%)	38 (76%)	36 (72%)	.64
Female sex, n (%)	12 (24%)	14 (28%)	
Body weight, kg	78 ± 11	80 ± 12	.41
Body surface area, m ²	1.92 ± 0.18	1.94 ± 0.17	.58
Diabetes mellitus, n (%)	18 (36%)	20 (40%)	.68
Hypertension, n (%)	41 (82%)	43 (86%)	.58
Baseline platelet count (×10 ⁹ /L)	225 ± 48	218 ± 52	.47
ATIII preoperative, %	98 ± 8	97 ± 9	.55
Baseline ACT, s	128 ± 9	130 ± 10	.29
CPB duration, minutes	92 ± 18	95 ± 21	.43
Aortic cross-clamp time, minutes	68 ± 14	71 ± 16	.39

Abbreviations: ACT, activated clotting time; ATIII, antithrombin III; CPB, cardiopulmonary bypass.

Table 3. Heparin and Protamine Dosing and ACT Control

Variable	ACT-guided group	Standard care group	P-value
Initial heparin dose, IU/kg	214 ± 22	300 ± 0	<.001
Total heparin dose, IU/kg	248 ± 34	332 ± 41	<.001
Supplemental heparin boluses, n	0.6 ± 0.8	1.4 ± 1.1	.002
ACT during CPB (mean), s	432 ± 38	486 ± 61	<.001
ACT values within target range, %	84 ± 9	62 ± 14	<.001
Total protamine dose, mg	178 ± 32	246 ± 45	<.001
Additional protamine required, n (%)	6 (12)	18 (36)	.006

Abbreviations: ACT, activated clotting time; CPB, cardiopulmonary bypass; IU, international units.

DISCUSSION

In this prospective randomized study, an ACT-guided, formula-based strategy for heparin and protamine management during CPB was associated with more consistent anticoagulation control, reduced postoperative bleeding, and favourable coagulation profiles without evidence of increased thrombotic complications within the limitations of the study sample size.¹⁻³ Compared with historical strategies based on empirical ACT thresholds and fixed anticoagulation dosing, the present protocol incorporated individualized ACT-guided formulas allowing adjustment according to baseline coagulation status and intraoperative variability.¹² Unlike the approach described by Cuenca et al, this protocol also integrated viscoelastic coagulation assessment, potentially providing a more comprehensive evaluation of perioperative haemostasis and postoperative coagulation competence.¹³ Importantly, the present findings should not be interpreted as demonstrating superiority of ACT-guided monitoring alone, but rather as evidence that a protocolized ACT-guided strategy enabling lower anticoagulation exposure may improve perioperative haemostatic outcomes compared with conventional fixed-dose anticoagulation. Since the ACT-guided algorithm resulted in lower total heparin administration, part of the observed reduction in bleeding and transfusion may reflect differences in anticoagulation intensity rather than monitoring methodology alone.⁶⁻⁸ The ACT-guided strategy also provided more stable anticoagulation management, with fewer excursions beyond the target range and reduced need for supplemental dosing. Bauer et al demonstrated that maintaining ACT values around 300 seconds during MiECC procedures was feasible and not associated with increased thrombotic complications.⁹ In the present study, despite maintaining ACT values above 400 seconds, the ACT-guided approach was associated with reduced chest tube output and lower transfusion requirements. ROTEM analysis demonstrated improved clot formation and clot firmness without increased

Table 4. ACT-Guided Heparin Dosing by Baseline ACT Ranges (ACT-Guided Group, *n* = 50)

Baseline ACT range (s)	Patients (n)	Mean baseline ACT (s)	Fixed dose (IU/kg)	Mean ACT-guided dose (IU/kg)	Mean dose reduction (IU/kg)	Mean reduction (%)
110-114	3	112	300	222	78	26
115-119	6	117	300	218	82	27
120-124	9	122	300	214	86	29
125-129	12	127	300	210	90	30
130-134	10	132	300	206	94	31
135-139	7	137	300	202	98	33
≥140	3	143	300	197	103	34

Abbreviation: ACT, activated clotting time.

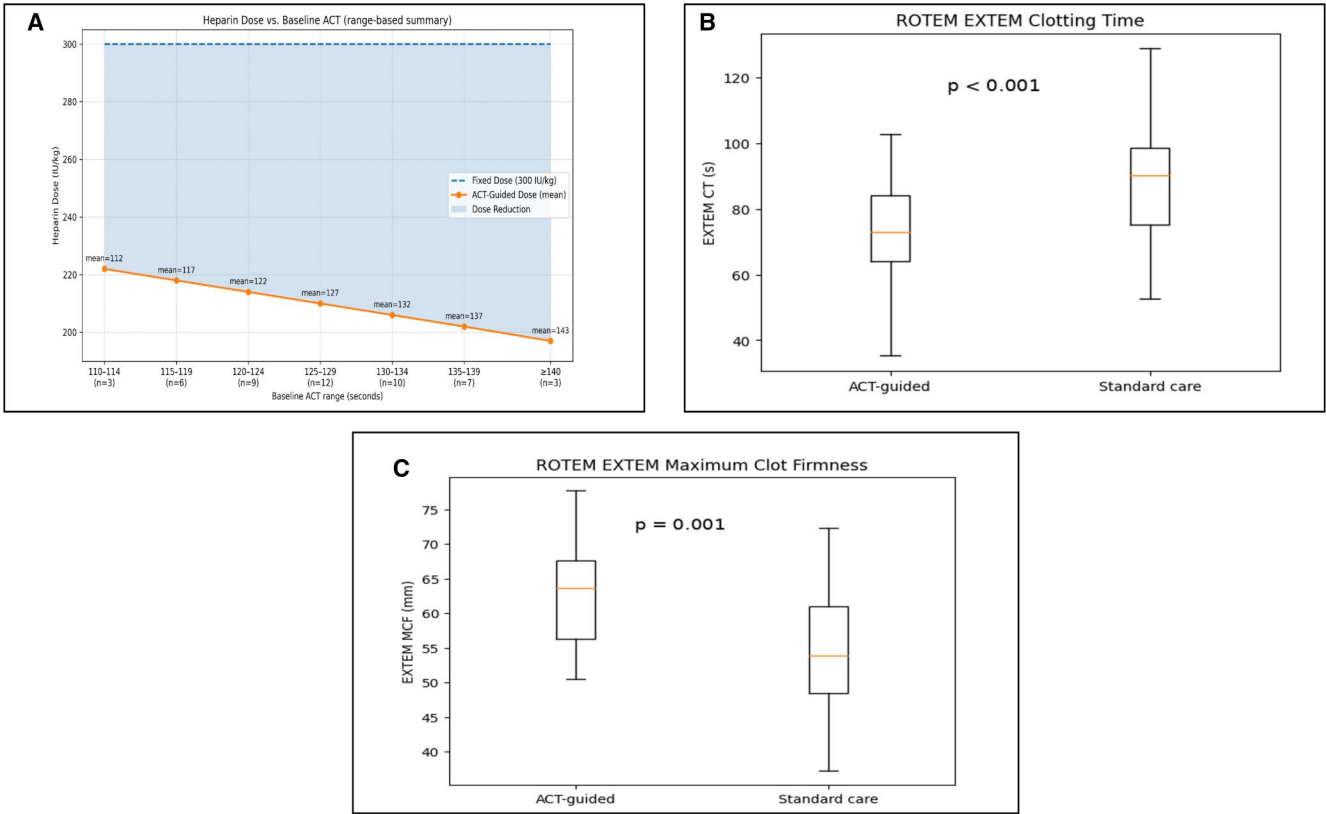


Figure 1. (A) Heparin dose vs baseline ACT (range-based summary). (B) ROTEM EXTEM clotting time. (C) ROTEM FIBTEM maximum clot firmness

hyperfibrinolysis, suggesting that lower anticoagulant exposure did not predispose patients to dysregulated fibrinolysis or thrombotic complications.¹⁴⁻¹⁸ Reduced bleeding also translated into lower transfusion exposure.^{19,20} Although a formal cost-analysis was not performed, lower heparin and protamine consumption together with reduced transfusion requirements may support improved cost-efficiency and broader applicability in routine clinical practice.^{12,13,20,21} Postoperative bleeding quantified by chest tube output is a widely accepted surrogate marker of bleeding severity after cardiac surgery and has been associated with increased transfusion requirements, prolonged ICU and hospital stay, and mortality. Although the reduction in chest tube output observed in the present study was moderate (260 mL), it was accompanied by lower transfusion

exposure and shorter ICU and hospital length of stay, supporting its potential clinical relevance.²²

Limitations

This study has several limitations. First, although randomized, it was a single-centre study with a relatively small sample size and was not powered to establish thrombotic safety equivalence; therefore, the absence of increased thrombotic events should be interpreted cautiously. Second, blinding of anaesthesia and perfusion teams was not feasible, although objective end-points and blinded outcome assessment were used to reduce bias. Third, ROTEM was incorporated into perioperative coagulation monitoring but not into a fully goal-directed

Table 5. ROTEM Parameters After Protamine Administration

Parameter	ACT-guided group	Standard care group	P-value
EXTEM CT, s	71 ± 14	89 ± 21	<.001
EXTEM CFT, s	89 ± 23	118 ± 31	<.001
EXTEM α -angle, °	67 ± 6	60 ± 7	<.001
EXTEM MCF, mm	61 ± 7	55 ± 8	.001
FIBTEM MCF, mm	11.2 ± 3.1	8.6 ± 2.9	<.001
Hyperfibrinolysis (ML >15%), n (%)	2 (4)	7 (14)	.08

Abbreviations: ACT, activated clotting time; α -angle, alpha angle; CT, clotting time; CFT, clot formation time; EXTEM, extrinsic pathway thromboelastometry assay; FIBTEM, fibrin-based thromboelastometry assay; MCF, maximum clot firmness; ML, maximum lysis; ROTEM, rotational thromboelastometry.

Table 6. Postoperative Bleeding, Transfusion, and Clinical Outcomes

Outcome	ACT-guided group	Standard care group	P-value
Chest drain output 24 h, mL	560 ± 210	820 ± 310	<.001
RBC transfusion, units	0.6 ± 1.0	1.4 ± 1.6	.003
Any blood product transfusion, n (%)	14 (28)	26 (52)	.01
Platelet count reduction, %	22 ± 9	31 ± 11	<.001
ATIII postoperative, %	81 ± 10	75 ± 12	.01
Surgical re-exploration for bleeding, n (%)	1 (2)	4 (8)	.17
Thrombotic events, n (%)	0 (0)	1 (2)	.31
ICU length of stay, days	1.9 ± 0.8	2.6 ± 1.2	.002
Hospital length of stay, days	7.1 ± 1.9	8.4 ± 2.3	.004
30-day mortality, n (%)	0 (0)	0 (0)	Ns

Abbreviations: ACT, activated clotting time; ATIII, antithrombin III; ICU, intensive care unit; RBC, red blood cells.

anticoagulation or transfusion algorithm, and its availability may have influenced transfusion decisions. Fourth, the study population was limited to isolated CABG procedures, which may reduce generalizability to broader cardiac surgical populations. Finally, secondary endpoints should be considered exploratory because the study was powered for the primary bleeding outcome only. Larger multicentre studies are warranted to validate these findings and further assess ACT-guided anticoagulation strategies.

CONCLUSIONS

This study suggests that an ACT-guided, formula-based approach to heparin administration and protamine reversal during CPB enables more precise anticoagulation management in patients undergoing isolated CABG. Compared with conventional weight-based dosing, this strategy reduces exposure to both anticoagulant and reversal agents, improves intraoperative ACT stability,

and is associated with more favourable viscoelastic coagulation profiles and a clinically relevant reduction in postoperative bleeding and transfusion requirements, while no increase in thrombotic events was observed within the limitations of the study sample size. These findings support further validation in larger, multicentre trials and suggest a potential role for ACT-guided dosing algorithms within integrated, goal-directed coagulation management strategies in cardiac surgery.

AUTHOR CONTRIBUTIONS

Youssef El Dsouki, Serdar Gunaydin, and Ignazio Condello (Conceptualization, Methodology, Data Analysis, Writing Original Draft), Orhan Eren Gunerter, Abducelil Yildirim (Support in the revision and literature review), Roberto Lorusso (Supervision, Validation, Clinical Interpretation). All authors have read and approved the final article.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *ICVTS* online.

FUNDING

None declared.

CONFLICTS OF INTEREST

The authors Youssef el Dsouki and Ignazio Condello are employees of Spectrum Medical Ltd. However, the present work was conducted independently as part of the authors' academic activity. Spectrum Medical did not provide any financial or material support and had no influence on the content of this article. Roberto Lorusso is consultant for Medtronic, LivaNova (past), Spectrum Medical, and J&J MedTech, member of the Xenios, Hemocue, ChinaBridge Medical and Eurosets (past) Medical Advisory Board.

DATA AVAILABILITY

The datasets analysed during the current study are available from the corresponding author upon reasonable request and subject to institutional approval and applicable data protection regulations.

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