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Original Article

Evaluation of Activated Clotting Time Response to Unfractionated Heparin in Vascular Surgery: An Observational Study

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Objectives: Activated clotting time (ACT) is widely used to monitor intraoperative anticoagulation with unfractionated heparin (UFH) during vascular surgery, but the most informative ACT-derived metric and the optimal approach for weight-based UFH dosing remain uncertain. The recent introduction of new point-of-care ACT analyzers has raised questions regarding the consistency of ACT response. This study aimed to assess the relationship between UFH dose and ACT response and to identify the most informative ACT-derived metric and the most appropriate body weight metric for dose normalization.

Design: Single-center retrospective observational study.

Setting: Tertiary university hospital.

Participants: Adult patients undergoing vascular surgery requiring intraoperative UFH administration.

Interventions: UFH was administered intraoperatively. ACT was measured before and 5 minutes after the first UFH bolus using the GEM Hemochron 100 system.

Measurements and Main Results: Anticoagulation response was assessed using post-UFH ACT and the ACT ratio (post/baseline). UFH dose was normalized to actual, adjusted, and ideal body weight. Associations were evaluated using Pearson correlation and multivariable linear regression adjusted for baseline ACT and sex. Weight-normalized UFH dose was significantly associated with both outcomes. Correlations were stronger for the ACT ratio than for post-UFH ACT. In multivariable models, UFH dose remained independently associated with both outcomes. Model performance was similar for actual and adjusted body weight, whereas ideal body weight did not improve fit.

Conclusions: Following implementation of a new point-of-care ACT analyzer, the expected UFH dose-response relationship was preserved. The ACT ratio showed stronger associations than absolute ACT values. Actual body weight appears sufficient for routine UFH dosing.

Key Words: activated clotting time (ACT); unfractionated heparin (UFH); dose-response relationship; intraoperative monitoring; point-of-care system; vascular surgical procedures

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Introduction

Systemic anticoagulation with unfractionated heparin (UFH) is routinely administered during vascular and endovascular procedures to prevent intraoperative thrombotic complications. Achieving an adequate balance between thrombosis prevention and bleeding risk remains a central challenge in vascular surgery. Although empiric standardized intravenous bolus dosing has been common practice, interindividual variability in heparin response may lead to substantial differences in achieved anticoagulation levels across patients.[1,2]

The activated clotting time (ACT), first described by Hattersley in 1966 as a rapid bedside whole-blood clotting assay, was developed to monitor high-dose heparinization during cardiopulmonary bypass.[3] Over subsequent decades, ACT monitoring became standard practice in cardiac surgery and interventional cardiology, where it is considered essential to ensure safe anticoagulation.[4] Its application in vascular surgery, however, has been more heterogeneous and remains subject to ongoing debate.[5]

ACT provides a point-of-care assessment of global clotting time after activation of the intrinsic pathway. Unlike laboratory-based assays such as activated partial thromboplastin time or anti−factor Xa activity, ACT gives immediate intraoperative results and can be repeated serially to guide additional heparin dosing.[6] It reflects a composite functional endpoint influenced not only by heparin-mediated antithrombin activity but also by hematocrit, platelet count and function, temperature, hemodilution, and device-specific characteristics.[7,8] Moreover, substantial interdevice variability has been documented, and ACT values obtained with different analyzers are not necessarily interchangeable.[9]

Despite growing interest in ACT-guided anticoagulation, important questions remain unresolved. The optimal ACT threshold during vascular surgery is not clearly established, and no large, randomized trials have definitively demonstrated that ACT-guided dosing improves clinical outcomes. The ongoing ACTION-1 randomized controlled trial aims to address this evidence gap in open abdominal aortic aneurysm repair.[10]

At the authors' institution, the Hemochron Jr Signature+ analyzer was recently replaced with the GEM Hemochron 100 point-of-care ACT system. ACT measurements are known to be device-dependent and not directly interchangeable across different platforms. Following this transition, clinicians observed that the increase in ACT after standard UFH boluses appeared less pronounced than expected based on prior experience. This observation raised a clinical question regarding the consistency of ACT response in this specific setting and prompted a systematic evaluation of ACT behavior during routine intraoperative heparin administration using the new monitoring platform.

The primary objective of this study was to characterize the pharmacodynamic relationship between UFH bolus dosing and ACT values obtained with the new system during vascular surgery, specifically assessing whether ACT measurements demonstrated a coherent dose-response relationship with administered UFH.

Secondary objectives were to determine which ACT-derived metric—absolute postheparin ACT or the ACT ratio (post/preheparin)—best reflects the anticoagulation response in routine clinical practice and to explore whether normalization of UFH dosing to different body weight metrics (actual, ideal, or adjusted body weight) influences the observed dose-response relationship.

Methods

Study Design and Setting

This retrospective observational study was conducted using prospectively collected intraoperative data from consecutive patients undergoing vascular surgery at the authors' institution between September 2024 and April 2025. ACT monitoring and UFH administration were performed according to routine clinical practice. No protocol changes were introduced for the purposes of this analysis.

During the study period, the institution replaced the previously adopted Hemochron Jr Signature+ analyzer with the GEM Hemochron 100 (Werfen), a next-generation point-of-care ACT system. All ACT measurements included in this study were obtained using the new device.

All data were fully anonymized prior to analysis. In accordance with local institutional regulations of the Fondazione IRCCS San Gerardo dei Tintori, retrospective analyses of anonymized data collected during routine clinical care do not require formal ethics committee approval or written informed consent. All patients provide a general consent at admission for the use of anonymized clinical data for research purposes. The study was conducted in compliance with the Declaration of Helsinki.

Participants

All consecutive adult patients (≥18 years) undergoing vascular procedures requiring intraoperative administration of UFH and at least 1 ACT measurement before and after the heparin bolus were considered eligible. For the purpose of this analysis, only the first intraoperative UFH bolus and the corresponding ACT measurement were considered; subsequent supplemental heparin doses were excluded. Patients were excluded if baseline or postheparin ACT values were missing, if the procedure represented a repeated or staged intervention during the same admission, if a known coagulation disorder or therapeutic anticoagulation was present at baseline, or if body weight or height data were incomplete.

Institutional Protocol for Heparin Administration and ACT Measurement

In all procedures, patients underwent standard anesthetic management according to institutional practice. Anticoagulation was achieved with an intravenous bolus of UFH according

to routine clinical protocols. ACT was measured immediately before UFH administration (baseline ACT) and repeated 5 minutes after the heparin bolus. Measurements were performed using a cartridge-based system with a temperature-controlled analytical chamber (37°C). Intraoperative monitoring included temperature control with maintenance of normothermia. UFH dosing was determined by the surgical team according to the intended intraoperative anticoagulation target.

ACT measurements were performed using the GEM Hemochron 100 system (Werfen) with low-range cartridges (ACT-LR), in accordance with routine clinical practice. All measurements included in this study were obtained using the same cartridge type, ensuring consistency across the cohort. The whole-blood sample was introduced into the cartridge immediately after collection, following the manufacturer's instructions to ensure accurate measurement. Within the study cohort, 2 different anticoagulation strategies were routinely applied in clinical practice. Most open and endovascular procedures were performed with a standard anticoagulation target, aiming for ACT values of approximately 180 to 220 seconds. In this setting, UFH boluses were generally individualized according to patient body weight and adjusted as needed. In contrast, carotid artery stenting procedures were managed with a higher anticoagulation target, typically aiming for ACT values of approximately 250 to 300 seconds to reduce the risk of thromboembolic complications during catheter manipulation within the carotid circulation. In these cases, UFH was usually administered using a more standardized bolus strategy (typically 5,000 IU).

To account for these differences in clinical practice, patients were stratified according to the intended anticoagulation target into standard-target and high-target groups. This stratification primarily reflects differences in the dosing approach. In procedures performed with the standard target, UFH dosing was more frequently tailored to individual patient characteristics. By contrast, in carotid stenting procedures, the use of a predefined high ACT target typically led to a more uniform dosing strategy. Distinguishing these 2 contexts allowed the analysis to better reflect the clinical rationale underlying UFH administration and to interpret the relationship between weight-normalized UFH dose and ACT response within comparable dosing frameworks.

Exposure and Outcomes

The primary exposure variable was the UFH bolus normalized to 3 different body weight metrics: actual body weight (ABW), ideal body weight (IBW), and adjusted body weight (AdjBW). IBW was calculated as height $(\text{cm}) - 100$ in males and height $(\text{cm}) - 110$ in females, while AdjBW was defined as $\text{IBW} + 0.4 * (\text{ABW} - \text{IBW})$.

The anticoagulation response to UFH was assessed using 2 ACT-derived measures: the absolute postheparin ACT value and the ACT ratio (postheparin ACT divided by baseline ACT). The ACT ratio was included to partially account for interindividual variability in baseline coagulation status and to provide a normalized estimate of the ACT response to heparin administration.

Statistical Analysis

Continuous variables were summarized as median and interquartile range, whereas categorical variables were reported as counts and percentages. Comparisons between the standard-target and high-target groups were performed using the Wilcoxon rank-sum test for continuous variables and the χ^2 test or Fisher exact test for categorical variables, as appropriate.

The relationship between weight-normalized UFH dose and ACT-derived outcomes was explored using Pearson correlation coefficients. Correlation analyses were performed separately for each UFH dose metric and for both ACT-derived outcomes in the overall cohort. Additional analyses were conducted in the standard-target subgroup, which represents the clinical setting in which UFH dosing is typically individualized according to patient characteristics.

To further evaluate the association between UFH dose and anticoagulation response while accounting for potential confounders, multivariable linear regression models were constructed. Separate models were fitted for each weight normalization metric. For postheparin ACT, models included UFH dose metric, baseline ACT, and sex as covariates. For ACT ratio, models included UFH dose metric and sex, as baseline ACT is intrinsically incorporated in the ratio definition. Sex was included because physiological differences in body composition and coagulation characteristics between males and females may influence the anticoagulant response to UFH independently of body weight−based dosing. Models within each outcome used identical covariates and differed only in the UFH weight normalization metric.

The comparative performance of the different UFH dose metrics was assessed using the Akaike information criterion corrected for small sample size (AICc), with lower values interpreted as indicating better model fit. Model explanatory power was also assessed using the coefficient of determination, R^2.

All analyses were performed using R statistical software (R Foundation for Statistical Computing). A 2-sided p value <0.05 was considered statistically significant.

Results

Study Population and Baseline Characteristics

A total of 117 patients were included in the overall cohort. Of these, 89 patients (76.1%) were managed according to a standard ACT target strategy, whereas 28 patients (23.9%) were treated using a high ACT target strategy. Baseline demographic, anthropometric, and procedural characteristics are summarized in Table 1.

Overall, 87 patients (74.4%) were male. The median (interquartile range) age of the study population was 74.5 (68.6-78.7) years. Patients managed with the standard-target strategy were significantly older than those in the high-target group

Table 1
Baseline Characteristics and Anticoagulation Parameters According to Anticoagulation Target Strategy

Variable	Overall (N = 117)	Standard Target (n = 89)	High Target (n = 28)	p Value
Male sex	87 (74.4)	65 (73)	22 (78.6)	0.736
Procedure				<0.001
Carotid endarterectomy	32 (27.4)	32 (36)	0 (0)	
Carotid stenting	28 (23.9)	0 (0)	28 (100)	
Endovascular aortic repair	16 (13.7)	16 (18)	0 (0)	
Open aortic surgery	4 (3.4)	4 (4.5)	0 (0)	
Lower limb bypass	8 (6.8)	8 (9)	0 (0)	
Femoral endarterectomy ± iliac stenting	16 (13.7)	16 (18)	0 (0)	
Iliac stenting	11 (9.4)	11 (12.4)	0 (0)	
Other	2 (1.7)	2 (2.2)	0 (0)	
Age, y	74.5 [68.6-78.7]	75.4 [69.1-79.3]	70.1 [66.6-74.1]	0.007
Height, cm	170 [165-175]	170 [165-175]	169 [162.8-175.8]	0.911
BMI, kg/m^2	25.4 [23.3-28.4]	25.3 [23.1-28.4]	26 [24.2-29]	0.466
Actual body weight, kg	75 [66-82]	75 [66-82]	75 [65.5-83.5]	0.749
Adjusted body weight, kg	71.4 [63.4-77]	70.4 [65-77]	73.2 [61.5-78.5]	0.704
Ideal body weight, kg	70 [60-75]	70 [60-75]	69 [61.5-75.8]	0.853
Baseline ACT, s	137 [131-144]	137 [133-142]	135.5 [127.5-145.5]	0.558
UFH/ABW, U/kg	40 [34.2-50.8]	37.9 [32.3-42.3]	65.4 [58.7-76.3]	<0.001
UFH/AdjBW, U/kg	41.7 [37-55.8]	39 [35.7-43.9]	67.9 [63.7-81.3]	<0.001
UFH/IBW, U/kg	42.9 [37.5-62.5]	40 [35.7-46.7]	75.2 [63.7-81.3]	<0.001
Post-UFH ACT, s	190 [176-224]	184 [174-203]	243.5 [220.5-266.8]	<0.001
Post-/pre-UFH ACT ratio	1.4 [1.3-1.6]	1.4 [1.3-1.5]	1.8 [1.6-1.9]	<0.001

NOTE. Baseline demographic characteristics, body composition metrics, procedural categories, and anticoagulation-related parameters are reported for the overall cohort and stratified by intended anticoagulation target (standard target *v* high target). Continuous variables are presented as median [interquartile range] and categorical variables as counts and percentages. The p values refer to comparisons between the standard-target and high-target groups.
Abbreviations: ABW, actual body weight; ACT, activated clotting time; AdjBW, adjusted body weight; BMI, body mass index; IBW, ideal body weight; Post-/pre-UFH ACT ratio, ratio between postheparin ACT and baseline ACT; UFH, unfractionated heparin; UFH/ABW, UFH dose normalized to actual body weight; UFH/AdjBW, UFH dose normalized to adjusted body weight; UFH/IBW, UFH dose normalized to ideal body weight.

(75.4 [69.1-79.3] *v* 70.1 [66.6-74.1] years, p = 0.007). No significant differences were observed between groups in terms of height, body mass index, actual body weight, adjusted body weight, ideal body weight, or baseline ACT.

Procedural distribution differed significantly between target strategies (p < 0.001). The standard-target group included a heterogeneous mix of procedures, including carotid endarterectomy, endovascular aortic repair, lower-limb bypass surgery, femoral endarterectomy with or without iliac stenting, and isolated iliac stenting. In contrast, the high-target group consisted exclusively of carotid stenting procedures.

Weight-normalized UFH dosing differed significantly between groups across all body weight metrics (all p < 0.001), consistent with the different anticoagulation targets applied in clinical practice, with higher doses administered in the high-target group. Correspondingly, both post-UFH ACT values and ACT ratios were significantly higher in the high-target group compared with the standard-target group (both p < 0.001), reflecting the intended differences in anticoagulation intensity between strategies.

To provide additional descriptive information, intraoperative anticoagulation management data are reported. No clinically significant intraoperative bleeding events were recorded in the study cohort. Protamine reversal at the end of the procedure was required in 3 patients, all belonging to the standard-target group. Additional UFH boluses were administered in 44 patients (42 in the standard-target group and 2 in the high-target group), and a third bolus was required in 10 patients, all in the standard-target group.

Correlation Between UFH Dose and ACT-Derived Outcomes

Pearson correlation analyses were performed to evaluate the association between weight-normalized UFH dose and ACT-derived outcomes (Supplementary Table S1).

In the overall cohort, UFH dose normalized to ABW, AdjBW, and IBW all showed significant positive correlations with post-UFH ACT. Correlation coefficients were broadly similar across dosing metrics, indicating that the method used to normalize UFH dose for body weight had a minimal impact on the observed dose-response relationship. AdjBW-normalized dosing showed a slightly higher correlation with post-UFH ACT (r = 0.64), whereas ABW and IBW demonstrated very similar correlation coefficients (both r = 0.61, p < 0.001) (Fig 1A-C). These findings suggest that alternative body weight normalization strategies provide limited additional value in predicting ACT response.

When the anticoagulation response was expressed as the ACT ratio, correlations with UFH dose were slightly stronger than those observed for postheparin ACT values, although the difference was small. Correlation coefficients were similar across dosing metrics, with values of r = 0.70 for AdjBW, r = 0.69 for ABW, and r = 0.69 for IBW (all p < 0.001) (Fig 1D-F).

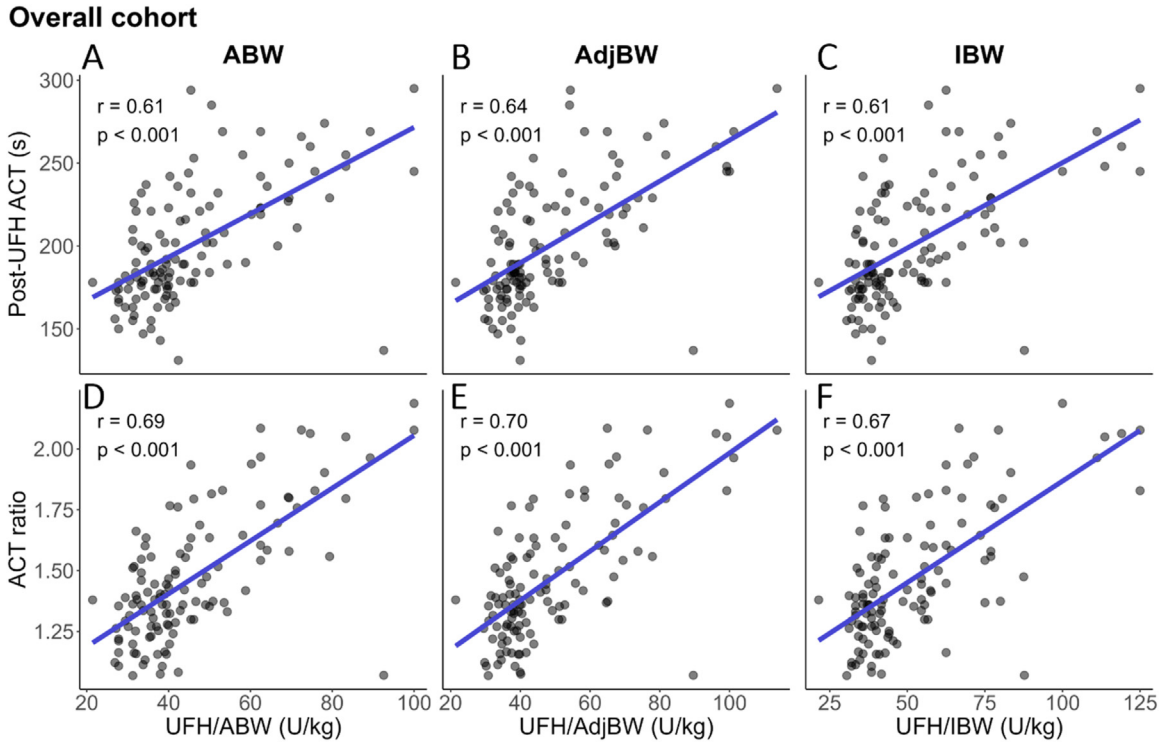

Fig 1. Association between weight-normalized unfractionated heparin (UFH) dose and activated clotting time (ACT) response in the overall cohort. Relationship between UFH dose normalized to actual body weight (ABW), adjusted body weight (AdjBW), and ideal body weight (IBW) and 2 ACT-derived outcomes: post-UFH ACT and ACT ratio (post-UFH ACT divided by baseline ACT). Each panel displays the relationship between weight-normalized UFH dose and the corresponding ACT outcome in the overall study cohort (n = 117). The solid line represents the fitted linear regression model. Pearson correlation coefficients (r) and p values are reported within each panel.

In the standard-target subgroup, correlations between UFH dose and ACT response were generally weaker compared with the overall cohort, with lower correlation coefficients across all body weight normalization strategies. For post-UFH ACT, correlation coefficients were r = 0.47 for ABW, r = 0.46 for AdjBW, and r = 0.40 for IBW (all $p < 0.001$) (Supplementary Fig S1A-C). For the ACT ratio, the corresponding correlations were r = 0.52 for ABW, r = 0.50 for AdjBW, and r = 0.43 for IBW (all $p < 0.001$) (Supplementary Fig S1D-F).

Multivariable Association Between UFH Dose Metrics and ACT Response

Multivariable linear regression models were constructed to evaluate the independent association between weight-normalized UFH dose and ACT-derived outcomes after adjustment for potential confounders. Detailed regression coefficients are reported in Supplementary Tables S2 to S5.

In the overall cohort, all weight-normalized UFH dose metrics were independently associated with post-UFH ACT (Supplementary Table S2). Coefficients of determination (R^2) ranged from 0.48 to 0.54 across the 3 weight descriptors, with the highest value observed for the model using adjusted body weight ($R^2 = 0.54$). Baseline ACT remained an independent predictor of post-UFH ACT across all models. The influence of baseline ACT on the dose-response relationship is illustrated using AdjBW-normalized dosing in Figure 2, which shows the association between weight-normalized UFH dose and ACT response across tertiles of baseline ACT.

For the ACT ratio, UFH dose normalized to each body weight metric was also independently associated with the outcome, with similar explanatory performance ($R^2 = 0.48$-0.54) (Supplementary Table S3).

When the analysis was restricted to the standard-target subgroup, the association between weight-normalized UFH dose and both ACT-derived outcomes remained statistically significant across all models (Supplementary Tables S4 and S5), with similar trends, although the relationship appeared weaker compared to the overall cohort (Supplementary Fig S2).

Notably, sex was associated with differences in ACT response in several models. In the overall cohort, male sex was significantly associated with higher post-UFH ACT values and higher ACT ratios in models using adjusted or ideal body weight, whereas this association was not statistically significant in models based on actual body weight. Similar patterns were observed in the standard-target subgroup. The relationship between weight-normalized UFH dose and ACT response according to sex is illustrated in Figure 3 for the overall cohort and in Supplementary Figure S3 for the standard-target subgroup.

Discussion

In this observational cohort of vascular surgery procedures, the relationship between intraoperative UFH bolus dosing and

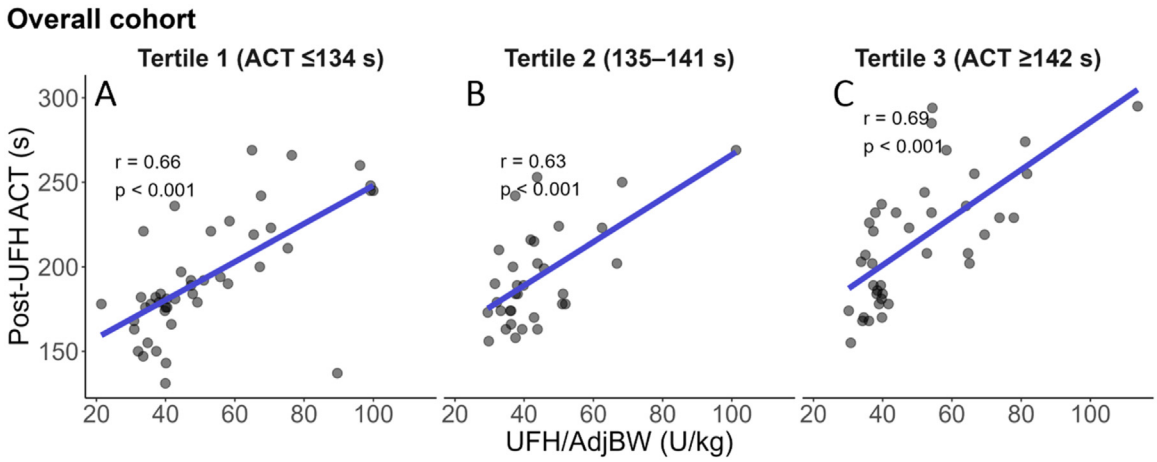

Fig 2. Relationship between unfractionated heparin (UFH) dose normalized to adjusted body weight and post-UFH activated clotting time (ACT) according to baseline ACT tertiles in the overall cohort. Association between UFH dose normalized to adjusted body weight (AdjBW) and post-UFH ACT in the overall cohort (n = 117), stratified according to tertiles of baseline ACT. Each panel represents 1 tertile of baseline ACT. The solid line represents the fitted linear regression model. Pearson correlation coefficients (r) and p values are reported within each panel.

ACT was characterized after implementation of a new point-of-care ACT analyzer. Three main findings emerged. First, a clear dose-response relationship between weight-normalized UFH dose and ACT response was observed. Second, ACT-derived metrics incorporating the baseline measurement, particularly the ACT ratio, showed stronger associations with UFH dose than absolute postheparin ACT values. Third, alternative body weight normalization strategies offered little additional predictive value, as UFH dosing normalized to actual and adjusted body weight produced nearly identical model performance, whereas ideal body weight provided no clear advantage.

UFH Dose-Response Relationship and ACT Variability

The introduction of a new ACT analyzer prompted a systematic evaluation of the relationship between UFH dosing and ACT response in routine vascular practice to better

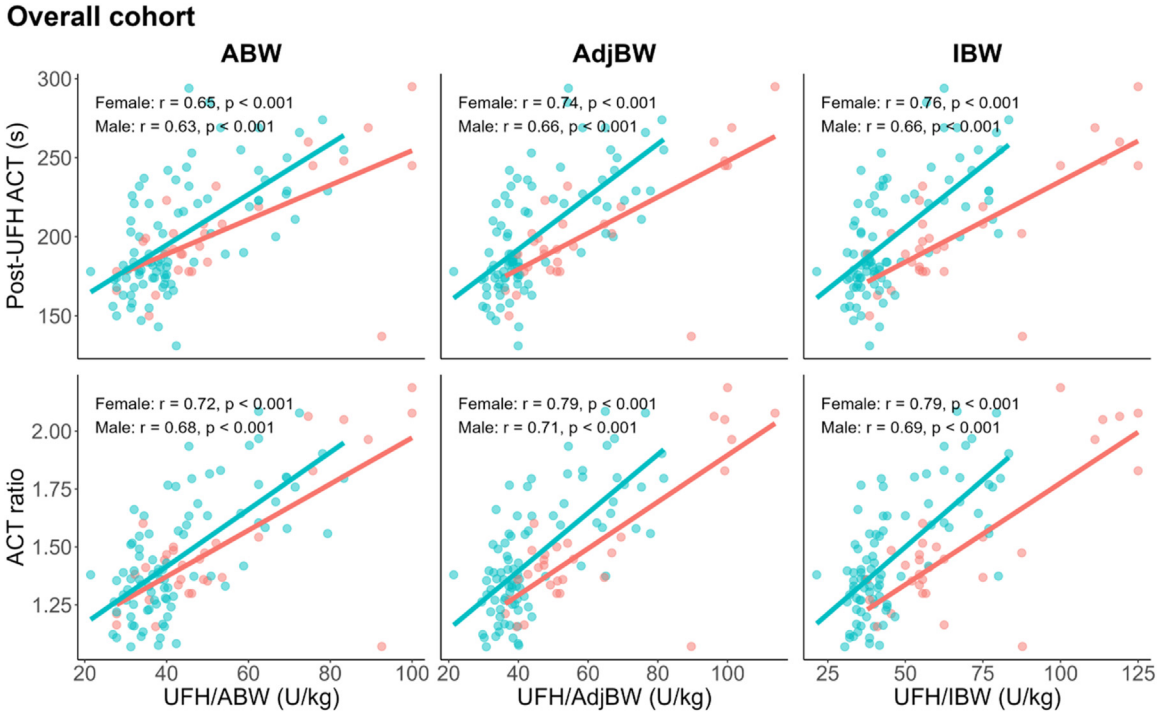

Fig 3. Association between weight-normalized unfractionated heparin (UFH) dose and activated clotting time (ACT) response according to sex in the overall cohort. Relationship between UFH dose normalized to actual body weight (ABW), adjusted body weight (AdjBW), and ideal body weight (IBW) and 2 ACT-derived outcomes (post-UFH ACT and ACT ratio, defined as post-UFH ACT divided by baseline ACT) in the overall cohort (n = 117), stratified by sex (87 males, 30 females). Each column represents 1 weight normalization strategy. Points represent individual patients. Blue points and regression lines correspond to male patients, whereas pink points and regression lines correspond to female patients. Solid lines represent fitted linear regression models within each sex subgroup. Pearson correlation coefficients (r) and p values are reported within each panel.

characterize the behavior of the new monitoring platform. Across the overall cohort, weight-normalized UFH dose demonstrated a consistent positive association with ACT response, with correlation coefficients ranging from approximately 0.61 to 0.70 depending on the outcome metric. Multivariable analyses confirmed UFH/kg as the primary determinant of ACT response after accounting for baseline ACT and sex.

The magnitude of these associations should be interpreted in light of the biological characteristics of ACT measurement. ACT does not directly quantify circulating heparin concentration but represents a whole-blood functional assay influenced by multiple physiological and technical factors, including platelet function, hematocrit, temperature, and hemodilution.[6-8] Consequently, only a proportion of ACT variability can be explained by the administered heparin dose alone.

Previous studies comparing ACT with anti−factor Xa activity have demonstrated similarly imperfect correlations between these measures of anticoagulation. For example, Dieplinger et al.[6] reported only a modest relationship between ACT values and anti-Xa levels during endovascular aortic procedures, highlighting that ACT reflects a composite coagulation response rather than a direct measure of heparin concentration.

Within this context, the moderate explanatory power observed in our models reflects the intrinsic variability of ACT as a global coagulation assay. ACT variability is known to arise from several biological and technical factors independent of UFH dose, including hematocrit, platelet function, inflammatory status, and device characteristics.[7-9] The proportion of ACT variability explained in our study, approximately 40% to 50%, is therefore consistent with the intrinsic complexity of ACT measurement and supports the presence of a dose-response relationship between UFH and ACT values after analyzer transition.

Interpretation of ACT-Derived Metrics

A second aim of the present study was to compare different ACT-derived endpoints for describing the anticoagulant response to UFH. In our cohort, the ACT ratio demonstrated slightly stronger associations with UFH dose than absolute postheparin ACT.

This finding is physiologically plausible. Baseline ACT varies substantially among patients due to intrinsic coagulation characteristics and perioperative factors unrelated to heparin exposure. As a global clotting assay, ACT reflects not only the pharmacologic effect of heparin but also patient-specific biological variability.[3,6,9] Expressing the response relative to baseline coagulation status may partially account for interindividual variability in baseline ACT values.

In clinical practice, anticoagulation monitoring during vascular procedures has traditionally relied on predefined absolute ACT thresholds.[2,11,12] However, absolute ACT values may be influenced by both device characteristics and baseline patient variability. Our findings suggest that baseline-adjusted metrics such as the ACT ratio may provide complementary information when interpreting intraoperative anticoagulation responses, particularly during transitions between monitoring systems when absolute ACT values may shift. This interpretation is further supported by our multivariable analyses, in which baseline ACT emerged as an independent predictor of postheparin ACT values.

Body Weight Normalization and Clinical Implications

In addition to evaluating the overall dose-response relationship, this study examined whether the body weight descriptor used to normalize UFH dose influences the observed association between UFH administration and ACT response. In vascular practice, weight-based heparin dosing is commonly used, and most studies proposing such regimens have normalized UFH dose to actual body weight.[2,11,12] However, it remains uncertain whether alternative weight descriptors provide a more appropriate representation of the relationship between UFH dose and anticoagulant effect.

In our analysis, normalization to actual body weight and adjusted body weight produced very similar correlations and multivariable model performance, whereas normalization to ideal body weight did not improve model fit. These findings suggest that alternative weight descriptors do not substantially improve the characterization of the UFH dose−ACT relationship within the dosing ranges typically used in vascular procedures. From a pragmatic perspective, normalization to actual body weight appears sufficient for routine UFH dosing in the population studied here. Importantly, however, our cohort had a median body mass index within the normal range and did not include substantial extremes of obesity. Accordingly, our findings may not be generalizable to severely obese patients, a subgroup in whom data from other procedural settings suggest that ABW dosing may lead to relative UFH overdosing.[13,14]

An additional observation was the different behavior of the sex variable across models using different weight normalization strategies. Male sex was associated with higher post-UFH ACT values and higher ACT ratios in models using adjusted or ideal body weight, whereas this association did not reach statistical significance when UFH dose was normalized to actual body weight. Previous studies of noncardiac arterial procedures have reported longer ACT values in women after periprocedural heparin administration, suggesting that sex-related variability in ACT response may exist.[2] In our models, however, the direction of the association differed and its statistical significance varied according to the weight descriptor used for dose normalization.

One possible explanation relates to differences in body composition and to the pharmacologic behavior of unfractionated heparin. UFH distributes predominantly within the intravascular compartment and interacts mainly with plasma proteins and endothelial surfaces rather than adipose tissue.[1,6] Because actual body weight incorporates total body mass, including adipose tissue, ABW-based normalization may partially absorb variability related to body size and composition. In contrast, weight descriptors such as adjusted or ideal body weight reduce the influence of adiposity and may therefore allow underlying variability between individuals, including sex-related differences, to appear more clearly in statistical models

of ACT response. This interpretation should remain cautious, as the present study was not designed to determine the mechanisms underlying potential sex differences in heparin response.

Limitations

This study has several limitations. First, this was an observational study based on routine clinical practice. The results therefore reflect associations observed in a real-world setting rather than effects under controlled experimental conditions. In addition, UFH dosing was not determined by a strictly standardized study protocol but by clinician judgment. The variability in clinical decision-making may have influenced the observed dose-response relationship.

Second, anti–factor Xa activity was not systematically measured. Given the imperfect correlation between ACT and anti-Xa described in prior studies, simultaneous measurement would have provided a more complete assessment of anticoagulant effect.

Third, this study did not systematically include variables known to influence ACT measurements, such as platelet count, hematocrit, or hemodilution. The potential contribution of these factors to ACT variability cannot be excluded.

Finally, clinical outcomes such as thromboembolic or bleeding events were not primary endpoints of this analysis. While this study describes the pharmacodynamic behavior of ACT after device transition, it does not determine whether 1 ACT-derived metric leads to better patient outcomes.

Conclusions

In this observational cohort of vascular surgery procedures, a dose-response relationship between weight-normalized UFH and ACT was observed after implementation of a new point-of-care analyzer. Although the strength of association was moderate, this magnitude is consistent with the known biological variability of ACT measurement. ACT ratio showed slightly better model performance compared with absolute postheparin ACT, while different body weight normalization strategies yielded similar results.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Roberta Garberi: Writing – original draft, Formal analysis, Data curation. **Manuela Milan:** Writing – review & editing, Data curation, Conceptualization. **Roberta Palermo:** Writing – review & editing. **Vittorio Maria Segramora:** Writing – review & editing, Methodology. **Marco Casati:** Writing – review & editing. **Matteo Pozzi:** Writing – review & editing, Methodology, Formal analysis. **Giuseppe Foti:** Writing – review & editing, Supervision. **Marco Giani:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1053/j.jvca.2026.05.018.

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