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Hemostatic variability among anemic peripheral artery disease patients using comprehensive viscoelastic testing

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Ethical Approval
Approval was obtained from the Mass General Brigham Institutional Review Board before study initiation (Protocol No. 2022P001918; approval date: September 19, 2022).

Informed Consent
Written informed consent was obtained from all participants before data collection.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Peripheral arterial disease (PAD) often requires revascularization, but postprocedural thrombotic complications can lead to adverse limb and survival outcomes. Anemia is common among older patients with PAD and may alter coagulation, yet its association with peri-revascularization hemostatic profiles remains unclear. This study evaluated whether anemia was associated with differences in coagulation profiles before and after lower extremity revascularization.

Methods: This prospective, single-center study included patients with PAD who underwent revascularization from December 2022 to December 2024. Blood samples obtained before and one month after revascularization were analyzed using thromboelastography with platelet mapping (TEG-PM). Patients were categorized as anemic or non-anemic using prespecified hemoglobin thresholds. Continuous variables were compared using the Mann-Whitney U test, and categorical variables were analyzed using Fisher's exact test.

Results: Among 344 patients, 62.8% were anemic. Compared with non-anemic patients, anemic patients were older (70 vs. 67 years, $P = 0.004$), had higher prevalences of diabetes mellitus (60.3% vs. 46.0%, $P = 0.013$) and coronary artery disease (60.8% vs. 43.7%, $P = 0.002$), and had lower hemoglobin levels (10.7 (1.6) vs. 14.4 (1.3) g/dL, $P < 0.001$). At baseline, anemic patients had greater clot strength, including higher MA-CK (65.0 (6.7) vs. 61.3 (6.3) mm, $P < 0.001$) and MA-CFF (29.1 (10.7) vs. 21.4 (7.7) mm, $P < 0.001$), as well as higher CFF-FLEV values (515 (201) vs. 400 (145) mg/dL, $P < 0.001$). Differences in selected fibrin-related parameters persisted at one month. Longitudinally, non-anemic patients showed larger increases in MA-CFF (4.4 (8.4) vs. -0.2 (9.5) mm, $P = 0.002$) and MA-ActF (3.1 (7.4) vs. -1.6 (8.2) mm, $P < 0.001$). Iron-deficient anemic patients had the highest clot-strength and fibrinogen-related values at both time points.

Conclusion: Anemic patients with PAD demonstrated higher clot strength and fibrin activity on TEG-PM before and after revascularization. These findings identify anemia as a marker of a more prothrombotic viscoelastic profile and warrant further study of its role in thrombotic risk stratification.

Keywords: peripheral artery disease, thromboelastography, anemia, thrombosis, anticoagulants, thromboprophylaxis

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Introduction

Peripheral arterial disease (PAD) is a chronic condition affecting more than 8.5 million Americans and more than 200 million people worldwide [1, 2], yet it remains underrecognized compared with other vascular conditions [3]. PAD is often asymptomatic and is associated with increased mortality, cardiovascular events, and a substantial burden of amputation [3, 4]. These challenges underscore the need to identify additional risk factors that may worsen PAD outcomes.

Anemia is a common condition characterized by a reduced concentration of hemoglobin or red blood cells and is frequently observed in older adults and patients with chronic medical conditions. Its etiology in patients with PAD is often multifactorial and may involve chronic inflammation and comorbid conditions such as chronic kidney disease (CKD) [5]. Anemia has been independently associated with increased mortality and, among patients undergoing revascularization, with increased risks of amputation and death [6]. A better understanding of the mechanisms by which anemia contributes to these outcomes may provide clinically useful information and improve management of this high-risk population.

Thromboelastography (TEG) assesses the viscoelastic properties of whole blood and provides a dynamic representation of clot formation. Hemostatic responses measured by TEG can vary substantially among patients [7]. TEG with platelet mapping (TEG-PM) enables detailed characterization of clot strength and platelet-related pathways and therefore provides an opportunity to examine how anemia may influence coagulation in patients with PAD. The aim of this study was to evaluate whether anemia is associated with distinct coagulation profiles measured by TEG-PM. We hypothesized that anemic and non-anemic patients would differ significantly in hemostatic parameters.

Materials and methods

Study design and ethics

We conducted a prospective, single-institution study of adults aged >18 years undergoing lower extremity revascularization for PAD from December 2022 to December 2024. Approval was obtained from the Mass General Brigham Institutional Review Board before study initiation (Protocol No. 2022P001918; approved September 19, 2022), and the study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients before data collection.

Exclusion criteria included pregnancy, absence of atherosclerotic disease, contraindications or allergies to antiplatelet therapy, concurrent anticoagulant use, inability to provide informed consent, or inability to undergo serial blood draws.

Revascularization was considered successful when adequate blood flow was restored to the ischemic area immediately after angioplasty, stenting, or bypass surgery.

Patient data

Baseline demographics, comorbidities, medical history, and intervention-related data were collected from the electronic medical record. Variables included age at intervention, race, body mass index (BMI), hypertension, hyperlipidemia, coronary artery disease (CAD), myocardial infarction (MI), diabetes mellitus, chronic kidney disease (CKD), and deep venous thrombosis (DVT). Medication regimens, coagulation test results, and complete blood count results were also obtained from the medical record. Interventions were categorized as open surgical, endovascular, or combined procedures.

Sample collection and processing

Blood samples for TEG-PM analysis were collected in 4.0-mL non-gel sodium heparin Vacutainers at four time points: baseline (before revascularization) and one, three, and six months after the procedure. According to the manufacturer's instructions, samples underwent a mandatory 30-minute incubation period and were analyzed within two hours of collection. Only baseline and one-month postoperative time points were included in the present analysis.

Thromboelastography with platelet mapping assay

Coagulation profiles were generated using the TEG® 6s Hemostasis Analyzer (Haemonetics Corporation, Boston, MA, USA). The TEG PlateletMapping® 6s system uses PlateletMapping® cartridges to measure kinetic changes during clotting of heparinized whole-blood samples and provide a qualitative assessment of platelet function.

The PlateletMapping® cartridge evaluates maximum amplitude (MA) under four conditions: heparinized kaolin with heparinase activation (MA-HKH), which stimulates a maximal thrombin response to assess overall clot strength and stability despite antiplatelet therapy; fibrin-only activation (MA-ActF), in which reptilase converts fibrinogen to fibrin while thrombin is inhibited; adenosine diphosphate stimulation (MA-ADP); and arachidonic acid stimulation (MA-AA). Reduced MA responses to ADP or AA indicate P2Y12 inhibitor or aspirin activity, respectively, and results are calculated as the percentage of platelet aggregation or inhibition for the ADP and AA pathways.

Subgroup analysis

Patients were classified as anemic or non-anemic using prespecified hemoglobin thresholds (<13.5 g/dL for men and <12 g/dL for women). Additional analyses evaluated iron deficiency anemia (IDA) by categorizing patients as non-anemic, anemic without iron deficiency, or anemic with iron deficiency (IDA-A). A separate analysis excluded patients with CKD to assess whether coagulation differences between anemic and non-anemic patients persisted in the absence of renal impairment.

Statistical analysis

Descriptive statistics were calculated for all variables. Continuous variables are reported as mean (SD), including age, BMI, and hemoglobin A1c. Categorical variables are presented as frequencies and percentages. Groups were compared using the Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables. Analyses were performed using GraphPad Prism (GraphPad Software; version 11.0.2). $P < 0.05$ was considered statistically significant.

Results

Patient characteristics and comorbidities

Of 344 patients, 216 (62.8%) were anemic. As shown in Table 1, the anemic group was older (70 (11) vs. 67 (11) years, $P = 0.004$) and had higher prevalences of diabetes mellitus (60.3% vs. 46.0%, $P = 0.013$) and coronary artery disease (60.8% vs.

43.7%, $P = 0.002$) than the non-anemic group. Anemic patients also had a lower BMI (26.6 (5.3) vs. 28.3 (6.5) kg/m², $P = 0.013$) and lower eGFR (65 (27) vs. 76 (21) mL/min/1.73 m², $P = 0.017$).

Table 1. Demographics and medical history of anemic and non-anemic patients.

Variable	Non-anemic	Anemic	*P*-value
Demographics	n = 124	n = 211	
Age (years)	67 (11)	70 (11)	**0.004**
Male (%)	57.3	73.4	**0.003**
White (%)	78.2	64.0	**0.007**
Comorbidities	n = 126	n = 209	
Body mass index (BMI) (kg/m²)	28.3 (6.5)	26.6 (5.3)	**0.013**
eGFR (mL/min/1.73 m²)	76 (21)	65 (27)	**0.017**
Diabetes mellitus (%)	46.0	60.3	**0.013**
Hypertension (%)	84.1	88.5	0.249
Hyperlipidemia (%)	81.8	88.5	0.104
Current smoker (%)	33.3	19.6	**0.006**
Coronary artery disease (%)	43.7	60.8	**0.002**
Previous myocardial infarction (%)	23.2	31.1	0.135

Data are presented as mean (SD) or percentage, as applicable. Abbreviations: BMI: body mass index, eGFR: estimated glomerular filtration rate. $P < 0.05$ was considered statistically significant.

Laboratory and coagulation profiles

As shown in Table S1, anemic patients had lower red blood cell counts (3.69 (0.6) vs. 4.75 (0.5) million/mcL, $P < 0.001$), hemoglobin levels (10.7 (1.6) vs. 14.4 (1.3) g/dL, $P < 0.001$), and hematocrit values (33.1 (5.1)% vs. 43.4 (3.7)%, $P < 0.001$). Mean corpuscular volume ($P = 0.697$), white blood cell count ($P = 0.787$), and platelet count ($P = 0.451$) did not differ significantly between groups. Conventional coagulation tests showed longer values in anemic patients, including PT (16.0 (7.7) vs. 15.3 (5.7) seconds, $P = 0.002$), INR (1.28 (0.42) vs. 1.19 (0.49), $P < 0.001$), and aPTT (50 (27) vs. 35 (14) seconds, $P < 0.001$).

Table S1. Baseline laboratory values in anemic and non-anemic patients.

CBC and clotting laboratory values	Non-anemic (n = 128)	Anemic (n = 216)	*P*-value
White blood cell count (k/mcL)	8.9 (5.7)	8.3 (2.7)	0.787
Red blood cell count (million/mcL)	4.75 (0.5)	3.69 (0.6)	**<0.001**
Hematocrit (%)	43.4 (3.7)	33.1 (5.1)	**<0.001**
Hemoglobin (g/dL)	14.4 (1.3)	10.7 (1.6)	**<0.001**
Mean corpuscular volume (fL)	91.4 (5.0)	91.9 (8.0)	0.697
Platelet count (k/mcL)	249 (91)	265 (129)	0.451
INR	1.19 (0.49)	1.28 (0.42)	**<0.001**
PT (seconds)	15.3 (5.7)	16.0 (7.7)	**0.002**
aPTT (seconds)	35 (14)	50 (27)	**<0.001**

Data are presented as mean (SD). Abbreviations: CBC: complete blood count, INR: international normalized ratio, PT: prothrombin time, aPTT: activated partial thromboplastin time. $P < 0.05$ was considered statistically significant.

TEG-PM findings at baseline and 1-month follow-up

At baseline (Table 2), anemic patients had higher MA-CK (65.0 (6.7) vs. 61.3 (6.3) mm, $P < 0.001$), MA-CFF (29.1 (10.7) vs. 21.4 (7.7) mm, $P < 0.001$), MA-HKH (62.9 (8.2) vs. 58.2 (7.3) mm, $P < 0.001$), MA-ActF (16.1 (7.5) vs. 10.3 (5.4) mm, $P < 0.001$), MA-ADP (52.8 (15.0) vs. 44.6 (15.4) mm, $P < 0.001$), and MA-AA (41.4 (19.7) vs. 35.3 (17.0) mm, $P = 0.007$). Anemic patients also had shorter CK-K times (1.32 (0.70) vs. 1.61 (0.63) minutes, $P < 0.001$), larger CK angles (71.0 (10.5)° vs. 68.6 (8.9)°, $P < 0.001$), and higher CFF-FLEV values (515 (201) vs. 400 (145) mg/dL, $P < 0.001$). R time ($P = 0.199$), lysis-30 ($P = 0.207$), ADP inhibition ($P = 0.395$), and AA inhibition ($P = 0.313$) were not significantly different.

At one month (Table 2), anemic patients continued to have higher MA-CK (67.3 (5.2) vs. 64.9 (5.7) mm, $P = 0.001$), MA-CFF (30.8 (10.8) vs. 26.2 (8.1) mm, $P = 0.008$), CK angle (72.1 (9.6)° vs. 69.8 (9.7)°, $P = 0.016$), and CFF-FLEV (552 (213) vs. 466 (145) mg/dL, $P = 0.008$), as well as a shorter CK-K time (1.34 (0.76) vs. 1.48 (0.74) minutes, $P = 0.047$). No significant differences were observed for R time ($P = 0.182$), lysis-30 ($P = 0.154$), MA-HKH ($P = 0.203$), MA-ActF ($P = 0.177$), MA-ADP ($P = 0.257$), MA-AA ($P = 0.252$), ADP inhibition ($P = 0.660$), or AA inhibition ($P = 0.516$).

Longitudinal changes in TEG-PM

Longitudinal comparisons (Table S2) showed larger changes in non-anemic patients for MA-CK (3.5 (5.2) vs. 2.0 (6.2) mm, $P = 0.012$), MA-CFF (4.4 (8.4) vs. -0.2 (9.5) mm, $P = 0.002$), MA-HKH (4.2 (10.2) vs. -2.0 (6.8) mm, $P < 0.001$), and MA-ActF (3.1 (7.4) vs. -1.6 (8.2) mm, $P < 0.001$). The change in CK-K also differed between groups (-0.14 (0.90) vs. 0.05 (0.81) minutes, $P = 0.010$).

Table 2. Preoperative and 1-month postoperative TEG-PM values in non-anemic and anemic patients.

Variable	Non-anemic (n = 108)	Anemic (n = 180)	*P*-value
Preoperative			
R time (minutes)	6.4 (2.5)	6.9 (4.6)	0.199
Lysis-30 (minutes)	0.48 (0.92)	0.65 (1.52)	0.207
MA-CK (mm)	61.3 (6.3)	65.0 (6.7)	**<0.001**
MA-CFF (mm)	21.4 (7.7)	29.1 (10.7)	**<0.001**
MA-HKH (mm)	58.2 (7.3)	62.9 (8.2)	**<0.001**
MA-ActF (mm)	10.3 (5.4)	16.1 (7.5)	**<0.001**
MA-ADP (mm)	44.6 (15.4)	52.8 (15.0)	**<0.001**
MA-AA (mm)	35.3 (17.0)	41.4 (19.7)	**0.007**
ADP inhibition (%)	21.9 (26.4)	20.4 (21.0)	0.395
AA inhibition (%)	43.7 (36.0)	49.5 (37.5)	0.313
CK-K (minutes)	1.61 (0.63)	1.32 (0.70)	**<0.001**
CK angle (degrees)	68.6 (8.9)	71.0 (10.5)	**<0.001**
CFF-FLEV (mg/dL)	400 (145)	515 (201)	**<0.001**
1-month postoperative			
R time (minutes)	6.8 (1.7)	7.4 (2.3)	0.182
Lysis-30 (minutes)	0.72 (0.89)	0.84 (2.31)	0.154
MA-CK (mm)	64.9 (5.7)	67.3 (5.2)	**0.001**
MA-CFF (mm)	26.2 (8.1)	30.8 (10.8)	**0.008**
MA-HKH (mm)	61.3 (7.2)	62.5 (7.5)	0.203
MA-ActF (mm)	13.8 (6.7)	15.3 (7.2)	0.177
MA-ADP (mm)	41.4 (17.9)	44.0 (18.5)	0.257
MA-AA (mm)	34.9 (18.8)	37.5 (19.2)	0.252
ADP inhibition (%)	44 (36)	40 (34)	0.660
AA inhibition (%)	56 (40)	59 (39)	0.516
CK-K (minutes)	1.48 (0.74)	1.34 (0.76)	**0.047**
CK angle (degrees)	69.8 (9.7)	72.1 (9.6)	**0.016**
CFF-FLEV (mg/dL)	466 (145)	552 (213)	**0.008**

Data are presented as mean (SD). Abbreviations: TEG-PM: thromboelastography with platelet mapping, MA: maximum amplitude, CK: citrated kaolin, CFF: citrated functional fibrinogen, HKH: heparinized kaolin with heparinase, ActF: activator F, ADP: adenosine diphosphate, AA: arachidonic acid, FLEV: functional fibrinogen level. $P < 0.05$ was considered statistically significant.

Table S2. Changes in TEG-PM values between preoperative and postoperative time points (paired differences).

Variable	Non-anemic (n = 54)	Anemic (n = 95)	*P*-value
R time (minutes)	0.3 (2.6)	0.2 (6.1)	0.297
Lysis-30 (minutes)	0.04 (1.06)	0.22 (2.55)	0.243
MA (mm)	3.5 (5.2)	2.0 (6.2)	**0.012**
MA-CFF (mm)	4.4 (8.4)	-0.2 (9.5)	**0.002**
MA-HKH (mm)	4.2 (10.2)	-2.0 (6.8)	**<0.001**
MA-ActF (mm)	3.1 (7.4)	-1.6 (8.2)	**<0.001**
MA-ADP (mm)	-4.7 (21.5)	-11.2 (19.2)	0.113
MA-AA (mm)	1.0 (22.0)	-7.5 (21.6)	0.131
ADP inhibition (%)	25 (39)	21 (35)	0.305
AA inhibition (%)	17 (41)	14 (46)	0.488
CK-K (minutes)	-0.14 (0.90)	0.05 (0.81)	**0.010**
CK angle (degrees)	1.8 (11.6)	1.2 (11.7)	0.547
CFF-FLEV (mg/dL)	53 (157)	4 (213)	0.135

Data are presented as mean (SD). Abbreviations: TEG-PM: thromboelastography with platelet mapping, MA: maximum amplitude, CK: citrated kaolin, CFF: citrated functional fibrinogen, HKH: heparinized kaolin with heparinase, ActF: activator F, ADP: adenosine diphosphate, AA: arachidonic acid, FLEV: functional fibrinogen level. $P < 0.05$ was considered statistically significant.

Subgroup analysis: iron deficiency and CKD status

Among anemic patients, those with iron deficiency had the most pronounced hypercoagulable profile (Table 3). At baseline, IDA-A patients had higher MA-CK, MA-CFF, MA-HKH, MA-ActF, MA-ADP, and MA-AA values than non-anemic patients (all $P < 0.001$), as well as a shorter CK-K time ($P < 0.001$), a larger CK angle ($P = 0.002$), and a higher CFF-FLEV value ($P < 0.001$). At one month, IDA-A patients continued to have higher MA-CK ($P < 0.001$), MA-CFF ($P < 0.001$), MA-ActF ($P = 0.025$), MA-AA ($P = 0.033$), CK angle ($P = 0.011$), and CFF-FLEV ($P = 0.005$), with a longer R time ($P = 0.004$).

Among patients without CKD (Table 4), anemia remained associated with higher MA-CK (64.1 (5.5) vs. 62.0 (6.6) mm, P = 0.017), MA-CFF (26.4 (9.4) vs. 22.0 (9.1) mm, P < 0.001), MA-HKH (62.8 (5.9) vs. 59.2 (7.1) mm, P < 0.001), MA-ActF (14.1 (7.3) vs. 10.2 (5.2) mm, P < 0.001), MA-ADP (51.5 (15.6) vs. 45.3 (15.8) mm, P = 0.003), and CFF-FLEV (447 (194) vs. 391 (164) mg/dL, P = 0.017).

Table 3. TEG-PM values in iron-deficient anemic and non-anemic patients.

Variable	Non-anemic (n = 124)	Iron-deficient anemic (n = 73)	*P*-value
Baseline			
R time (minutes)	6.3 (2.4)	7.0 (2.8)	0.148
Lysis-30 (minutes)	0.47 (0.90)	0.91 (2.25)	0.100
MA (mm)	61.4 (6.2)	65.9 (7.4)	**<0.001**
MA-CFF (mm)	21.5 (7.7)	31.8 (11.1)	**<0.001**
MA-HKH (mm)	58.6 (7.3)	64.7 (7.7)	**<0.001**
MA-ActF (mm)	10.4 (5.4)	16.7 (7.8)	**<0.001**
MA-ADP (mm)	45.4 (15.4)	53.1 (17.9)	**<0.001**
MA-AA (mm)	35.6 (17.1)	47.7 (18.6)	**<0.001**
ADP inhibition (%)	21.0 (25.8)	23.7 (26.8)	0.432
AA inhibition (%)	43.5 (36.2)	37.4 (36.2)	0.520
CK-K (minutes)	1.58 (0.62)	1.30 (0.81)	**<0.001**
CK angle (degrees)	68.9 (8.8)	70.3 (12.3)	**0.002**
CFF-FLEV (mg/dL)	401 (143)	555 (218)	**<0.001**
1-month postoperative			
R time (minutes)	6.8 (1.7)	8.3 (2.8)	**0.004**
Lysis-30 (minutes)	0.72 (0.89)	1.47 (3.80)	0.400
MA (mm)	64.9 (5.7)	68.8 (5.1)	**<0.001**
MA-CFF (mm)	26.2 (8.1)	34.8 (11.3)	**<0.001**
MA-HKH (mm)	61.3 (7.2)	64.1 (6.7)	0.056
MA-ActF (mm)	13.8 (6.7)	16.9 (7.4)	**0.025**
MA-ADP (mm)	41.4 (17.9)	47.0 (18.6)	0.078
MA-AA (mm)	34.9 (18.8)	42.3 (19.7)	**0.033**
ADP inhibition (%)	43.9 (36.4)	38.1 (29.8)	0.564
AA inhibition (%)	59.1 (38.6)	52.1 (39.9)	0.221
CK-K (minutes)	1.48 (0.74)	1.46 (1.10)	0.051
CK angle (degrees)	69.8 (9.7)	72.3 (11.3)	**0.011**
CFF-FLEV (mg/dL)	466 (145)	607 (239)	**0.005**

Data are presented as mean (SD). Abbreviations: IDA: iron deficiency anemia, TEG-PM: thromboelastography with platelet mapping, MA: maximum amplitude, CK: citrated kaolin, CFF: citrated functional fibrinogen, HKH: heparinized kaolin with heparinase, ActF: activator F, ADP: adenosine diphosphate, AA: arachidonic acid, FLEV: functional fibrinogen level. P < 0.05 was considered statistically significant.

Table 4. TEG-PM assay results in non-anemic and anemic patients without chronic kidney disease.

Variable	Non-anemic, no CKD (n = 55)	Anemic, no CKD (n = 58)	*P*-value
R time (minutes)	6.0 (2.4)	6.6 (1.7)	0.058
Lysis-30 (minutes)	0.48 (0.97)	0.547 (0.88)	0.589
MA (mm)	62.0 (6.6)	64.1 (5.5)	**0.017**
MA-CFF (mm)	22.0 (9.1)	26.4 (9.4)	**<0.001**
MA-HKH (mm)	59.2 (7.1)	62.8 (5.9)	**<0.001**
MA-ActF (mm)	10.2 (5.2)	14.1 (7.3)	**<0.001**
MA-ADP (mm)	45.3 (15.8)	51.5 (15.6)	**0.003**
MA-AA (mm)	36.6 (17.2)	39.8 (22.4)	0.210
ADP inhibition (%)	23.1 (29.0)	21.3 (23.0)	0.616
AA inhibition (%)	23.1 (36.0)	21.3 (42.6)	0.616
CK-K (minutes)	1.53 (0.63)	1.40 (0.72)	0.142
CK angle (degrees)	68.8 (9.6)	68.6 (12.0)	0.853
CFF-FLEV (mg/dL)	391 (164)	447 (194)	**0.017**

Data are presented as mean (SD). Abbreviations: CKD: chronic kidney disease, TEG-PM: thromboelastography with platelet mapping, MA: maximum amplitude, CK: citrated kaolin, CFF: citrated functional fibrinogen, HKH: heparinized kaolin with heparinase, ActF: activator F, ADP: adenosine diphosphate, AA: arachidonic acid, FLEV: functional fibrinogen level. P < 0.05 was considered statistically significant.

Discussion

Fibrin-driven hypercoagulability

This study identified distinct TEG-PM profiles in anemic and non-anemic patients with PAD. Anemic patients were older and had a greater burden of comorbidity, consistent with previous reports [8-11]. The most notable differences involved clot-strength and fibrin-related measures, suggesting that anemia is associated with a more procoagulant whole-blood phenotype in this population.

Longitudinal changes after revascularization

Before revascularization, anemic patients demonstrated greater clot strength and fibrin activity, reflected by higher MA-CK and MA-CFF values, faster clot propagation, and higher CFF-FLEV values. Because platelet-specific inhibition measures were not consistently different between groups, the higher overall clot strength may reflect a larger fibrin contribution rather than platelet function alone. After revascularization, coagulation parameters changed in both groups; non-anemic patients showed larger increases in several clot-strength measures, whereas anemic patients maintained higher absolute values for selected fibrin-related parameters. This pattern supports persistent between-group differences rather than uniformly greater postoperative increases in anemic patients.

Contrast with conventional coagulation tests

Conventional coagulation tests (INR, PT, and aPTT) showed longer clotting times in anemic patients, in contrast to the more hypercoagulable TEG-PM profile. This discrepancy highlights the limitations of standard plasma-based assays and the complementary information provided by whole-blood viscoelastic testing [12]. TEG-PM evaluates clot formation under conditions that incorporate cellular and fibrin components and may therefore characterize hemostatic function more comprehensively than conventional clotting times alone.

The pathophysiology of anemia in PAD is often multifactorial, with chronic inflammation contributing through hepcidin-mediated iron sequestration and impaired erythropoiesis. White blood cell counts were similar between groups, although this finding alone does not exclude differences in systemic inflammation. Platelet counts were numerically higher in anemic patients but were not significantly different, making an erythropoietin-mediated effect on platelet production a possible but unproven mechanism [13].

Iron deficiency anemia subgroup

The IDA-A subgroup demonstrated a particularly pronounced hypercoagulable profile. These observations suggest that iron deficiency may accentuate the coagulation abnormalities associated with anemia and warrant further investigation. Excluding patients with CKD did not eliminate most of the observed TEG-PM differences, suggesting that renal dysfunction alone does not explain the association. These findings extend previous reports of altered hemostasis in anemia [14, 15] by applying detailed TEG-PM measurements in patients with PAD. The observed fibrin activity and clot strength may be relevant to thrombotic risk, although clinical thrombotic outcomes were not evaluated in the presented analyses. The findings also remain compatible with proposed interactions between erythropoiesis and platelet biology [13].

Limitations

This single-center study included a predominantly male and White population, limiting generalizability across sex and racial groups. Sample availability varied across analyses and follow-up time points, which may introduce selection bias and should be considered when interpreting between-group comparisons. The analyses were primarily unadjusted and therefore do not establish anemia as an independent causal determinant of the observed TEG-PM differences. In addition, TEG-PM parameters are surrogate hemostatic measures, and clinical thrombotic outcomes were not reported. Further studies should assess whether anemia correction, including treatment of

iron deficiency, modifies viscoelastic profiles and clinically relevant thrombotic outcomes.

Conclusion

TEG-PM findings indicate that anemia is associated with increased clot strength and fibrin activity before and after revascularization in patients with PAD, consistent with a more prothrombotic laboratory profile. These findings support further investigation of anemia as a factor in thrombotic risk stratification and individualized antithrombotic management.

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