TEG-Guided Anticoagulation Assessment in Deep Vein Arterialization: A Prospective Analysis

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Background: Deep vein arterialization (DVA) is an innovative surgical technique aimed at enhancing blood flow in compromised limbs facing amputation. Maintenance of flow postrevascularization is crucial to limb salvage. As this is a new technique, no standardized thromboprophylaxis regime is currently established, and postprocedure thromboprophylaxis is at the discretion of the proceduralist. This study aims to evaluate coagulation profiles using viscoelastic studies in peripheral artery disease patients who underwent DVA, assessing the impact of various postprocedure thromboprophylaxis regimens.

Methods: Patients (aged $>$ 60 years) undergoing DVA were prospectively evaluated using thromboelastography at baseline, 1, 3, and 6 months (2020–2024). Postprocedure thromboprophylaxis included mono antiplatelet therapy (MAPT), MAPT + direct oral anticoagulant (DOAC), dual antiplatelet therapy (DAPT), or DAPT + DOAC. Coagulation profiles were analyzed using descriptive statistics.

Results: Among 16 patients (mean age 66.6 years, 75% male/Caucasian), hypertension and hyperlipidemia were present in 91%, and diabetes in 88%. The DAPT + DOAC group showed consistently superior platelet inhibition with the lowest adenosine diphosphate maximum amplitude values throughout baseline (35.65 mm vs. 42.2–65.03 mm in other groups), 1 month (26.7 mm vs. 32.14–69.4 mm), 3 months (27.36 mm vs. 32.2–39.97 mm), and 6 months (43.7 mm vs. 50.2–50.5 mm). MAPT demonstrated the slowest clot strengthening (citrated kaolin angle 65.25° vs. 68.7–71.55°).

Conclusion: Thromboelastography with platelet mapping demonstrated enhanced platelet inhibition and reduced clot formation in the DAPT + DOAC group, suggesting the importance of coagulation monitoring.

INTRODUCTION

Peripheral arterial disease (PAD) affects more than 200 million individuals worldwide, with a particularly high prevalence among older adults.[1,2] PAD is a progressive atherosclerotic condition where arterial narrowing reduces blood flow to the lower extremities, ranging from asymptomatic to chronic limb-threatening ischemia (CLTI), which carries a 1-year amputation rate of 30% and mortality rate of 25% if untreated.[3]

The management of PAD has evolved to include endovascular and surgical revascularization, yet ''no-option'' CLTI patients—those with extensive calcification, unsuitable target vessels, or failed previous interventions—face limited alternatives and higher amputation rates than standard CLTI patients.

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Deep vein arterialization (DVA) with the LimFlow system (Inari Medical, Irvine, CA) has emerged as an innovative and promising solution for these otherwise untreatable cases.[4,5] This technique involves creating an arteriovenous connection to redirect arterial blood flow into the venous system of the affected limb, effectively bypassing the occluded arteries while using the existing venous network as a conduit for tissue perfusion. Clinical outcomes with DVA have been consistently encouraging across studies, with reported technical success rates of 56−100%, limb salvage rates of 83−100%, and major amputation-free survival rates of 71−100% at 1 year.[6,7] These encouraging results were further validated in the UK National Health Service setting through the PROMISE-UK study, a prospective multicenter trial evaluating the LimFlow system in no-option CLTI patients. In this study of 28 patients across 6 National Health System centers, Zayed et al.[8] reported a technical success rate of 96% (27/28 patients), with a 67% amputation-free survival rate and 81% limb salvage rate at 1 year. Notably, all surviving patients achieved complete or near-complete wound healing by the 1-year follow-up. These results were achieved in a high-risk population of patients with Rutherford class 5−6 disease who had been deemed unsuitable for conventional revascularization approaches, suggesting DVA may offer a viable limb salvage option for patients who would otherwise face major amputation.[9]

Unlike conventional arterial revascularization, DVA creates unique hemodynamic challenges as veins must adapt to arterial pressure and flow patterns, potentially increasing thrombotic risk through altered endothelial responses and flow dynamics. The optimal antithrombotic regimen for DVA patients remains undefined, with current approaches ranging from single antiplatelet therapy to combinations of dual antiplatelet therapy (DAPT) and direct oral anticoagulants (DOACs), highlighting the need for standardized guidelines.

Thromboelastography with platelet mapping (TEG-PM) offers a sophisticated approach to understanding and monitoring the complex hemostatic changes in these patients.[10,11] Unlike conventional coagulation tests that assess isolated components of the clotting cascade, TEG-PM provides a comprehensive, real-time evaluation of clot formation dynamics, strength, and stability.[12] The technique's ability to measure both the viscoelastic properties of forming clots and specific platelet responses to agonists such as adenosine diphosphate (ADP) and arachidonic acid (AA) makes it particularly valuable for monitoring patients on complex antithrombotic regimens.[13]

Integrating TEG-PM into post-DVA management could potentially provide crucial insights into the effectiveness of various thromboprophylaxis strategies. The present study aims to optimize postprocedural thromboprophylaxis in DVA patients by evaluating antithrombotic strategies through TEG-PM monitoring, representing a critical step toward improving outcomes in this unique population.

METHODS

Study Design and Patient Population

We conducted a prospective, observational study from 2020 to 2024 at a single large tertiary institution. The study protocol was approved by the institutional review board (Protocol Number: 2022P002264), and written informed consent was obtained from all participants. Patient eligibility criteria included age 60 years or more, diagnosis of PAD with CLTI, and scheduled DVA using the LimFlow system. Additionally, patients were required to demonstrate the ability to comply with follow-up requirements. We excluded patients with known coagulation disorders, active bleeding, contraindications to antiplatelet or anticoagulant therapy, life expectancy less than 1 year, or inability to provide informed consent.

DVA Procedure

All DVA procedures were performed according to standardized institutional protocols.[14,15] The procedures were conducted under appropriate anesthesia, with continuous monitoring of vital parameters. We defined technical success as the successful creation of an arteriovenous connection with demonstrated flow through the target vessel on completion of angiography.

Thromboprophylaxis Regimens

Patients were classified to 1 of 4 antithrombotic regimens, according to the medication regimen they were on. The first group received mono antiplatelet therapy (MAPT), consisting of either aspirin 81 mg daily or clopidogrel 75 mg daily. The second group received MAPT and a DOAC (MAPT + DOAC), which included either apixaban 5 mg twice daily or rivaroxaban 20 mg daily. The third group

received DAPT, comprising aspirin 81 mg daily and either clopidogrel 75 mg daily or ticagrelor 90 mg twice daily. The fourth group received DAPT and a DOAC (DAPT + DOAC), combining the dual antiplatelet regimen with either apixaban or rivaroxaban at the previously specified doses.

Our thromboprophylaxis approach evolved based on outcomes and clinical considerations. Initially, patients received MAPT or DAPT based on medical history and cardiologist recommendations. After encountering thrombotic complications and concerns about neovascularization patency, we modified our protocol to include anticoagulation. For patients on DOACs for cardiac indications, we continued their DOAC and added DAPT if there were procedural concerns about outflow issues or imminent thrombosis. We used thromboelastography to monitor platelet function and clot strength, ensuring safety with combination antithrombotic therapy. The final regimen was individualized based on patient factors including cardiac history, procedural findings, antiplatelet tolerance, and objective coagulation measurements.

TEG-PM Analysis

TEG-PM was performed using the TEG 6s system (Haemonetics Corporation, Boston, MA) at 4 time points: pre-DVA procedure (baseline [BL]) and at 1, 3, and 6 months postprocedure. Blood samples were collected using a standardized venipuncture technique and processed within 30 min of collection according to manufacturer specifications.

Clinical Follow-Up and Outcome Assessment

Patients underwent systematic follow-up with weekly visits during the first month, followed by monthly visits until 6 months, with additional visits scheduled as clinically indicated. The primary outcomes comprised changes in TEG-PM parameters across time points and their correlation with clinical events. Secondary outcomes included technical success, stenosis or occlusion at the intervention site, wound healing, amputation events, mortality, and bleeding complications. Thrombotic events were documented based on any clinical or imaging evidence of thrombosis.

Clinically significant events in this study were defined as stenosis or occlusion of the DVA within 3 months of the surgery requiring intervention, major amputations (below-knee or above-knee amputations) within 6 months of surgery, and/or death within a year of surgery. We did not include occlusion of the DVA stent post 3 months because after 3 months occlusion of the DVA stent is not uncommon and does not result in the need for intervention to reopen the stent. Minor amputations such as transmetatarsal amputation (TMA) are also expected as a part of the limb salvage process. TMA is not performed for up to 3 months post to allow for maturation of the DVA and neorevascularization. All DVA patients undergo ultrasound surveillance and there are still no definitive data to delineate how much flow is necessary through the circuit to be considered appropriate, although the accepted flow volume is approximately 300 cc/min. Hence, even if an ultrasound-based stenosis is recognized through peak systolic velocities whether that stenosis is clinically significant is based on whether flow volumes are impacted.

Analytical Approach

Our analytical approach consisted of 2 main steps: (1) analyzing changes in all TEG-PM parameters across time points (BL, 1, 3, and 6 months) blinded to stratification by medication regimen to establish overall temporal trends and (2) stratifying samples according to the 4 medication regimens (MAPT, MAPT + DOAC, DAPT, and DAPT + DOAC) and comparing the main TEG-PM parameters between groups at each time point to determine which antithrombotic regimen demonstrated superior efficacy.

Statistical Analysis

Sample size was determined by the total number of DVA patients available in our database ($n = 16$). Descriptive statistics were performed for demographic and clinical characteristics. We used chi-squared or Fisher's exact test for categorical variables and Mann-Whitney U test for continuous variables, depending on data distribution. Kruskal-Wallis tests were used for between-group comparisons of TEG-PM parameters at each time point given the nonparametric nature of the data.

Statistical significance was set at $P < 0.05$, and missing data were handled using multiple imputation techniques when appropriate. We performed statistical analysis using SPSS version 27.0 (IBM Corp., Armonk, NY).

RESULTS

Patient Demographics and Clinical Characteristics

A total of 16 patients were enrolled with a mean age of 66.56 ± 11.3 years, with males comprising 75% of the cohort (Table I). The majority of patients were Caucasian (75%), followed by Hispanic (19%) and Black (6%), with a mean body mass index of 25.35 ± 3.2 kg/m^2. Active tobacco use was reported in 64% of patients.

The study population demonstrated a high prevalence of cardiovascular risk factors, with hypertension and hyperlipidemia each present in 91% of patients, while diabetes mellitus was documented in 88%. Previous myocardial infarction was reported in 50% and coronary artery disease in 44% of patients. Other significant medical history included prior stroke in 19%, deep vein thrombosis in 13% (2 patients had DVT—1 ipsilateral and 1 contralateral to the affected CLTI limb. The patient with ipsilateral DVT was cleared for DVA treatment after consultation with the device company, as the DVT was remote and had resolved prior to the procedure. We included this patient since they had no active DVT during treatment and pulmonary embolism in 6% of patients. Half of the patients could perform activities of daily living without impairment, while one-quarter required assistance with medical devices, and 13% were impaired but could perform activities without assistance.

Table I. Demographic characteristics of DVA patients ($N = 16$)

Variables	Results
Age (years), mean ± SD	66.56 ± 11.3
Gender, *n*(%)	
Female	4 (25)
Male	12 (75)
Race, *n* (%)	
White	(75)
Black	1 (6)
Hispanic	3 (19)
BMI (kg/m^2), mean ± SD	25.35 ± 3.2
Hypertension, *n* (%)	10 (91)
Hyperlipidemia, *n* (%)	10 (91)
Tobacco use, *n* (%)	7 (64)
Diabetes, *n* (%)	14 (88)
Coronary artery disease, *n* (%)	7 (44)
History of MI, *n* (%)	8 (50)
Functional status, *n* (%)	
Impaired—perform ADL without assistance	2 (13)
Impaired—assistance of medical device	2 (13)
Impaired—no assistance	4 (25)
No impairment	8 (50)
Cancer, *n* (%)	2 (13)
History of cancer, *n* (%)	2 (13)
History of PE, *n* (%)	1 (6)
History of DVT, *n* (%)	2 (13)
History of stroke, *n* (%)	3 (19)

ADL, activities of daily living; BMI, body mass index; MI, myocardial infarction; PE, pulmonary embolism; SD, standard deviation.

Patient Follow-Up

Patient retention varied throughout the follow-up period, with 14 patients (88%) completing the 1-month follow-up, 6 patients (38%) completing the 3-month follow-up, and 9 patients (56%) completing the 6-month follow-up. Reasons for loss of follow-up include patient withdrawal from the study, geographic distance/inability to attend follow-up appointments, and death in 2 cases.

Treatment Regimens and Distribution

The initial distribution of antithrombotic regimens showed that 25% of patients received MAPT, 25% received MAPT + DOAC, 37.5% received DAPT, and 12.5% received DAPT + DOAC. Treatment patterns evolved over the follow-up period, with a notable shift toward more intensive anticoagulation. By the 6-month follow-up, no patients remained on MAPT alone; 11% were on MAPT + DOAC, 22% were on DAPT alone, and 67% were on DAPT + DOAC (Tables II and III and Table SI).

Temporal Changes

Analysis of TEG parameters in DVA patients, examining the overall cohort without stratification by medication regimens, revealed significant changes across study intervals through 6 months. The lysis at 30 mins showed variable results without a clear trend (BL: 0.64%, 1 month: 5.91%, 3 months: 0.06%, and 6 months: 0.27%; $P = 0.307$). Reaction time demonstrated a gradual increase from BL to 3 months (8.17 mins, 8.94 mins, and 9.67 mins, respectively) before decreasing at 6 months to 6.9 mins ($P < 0.001$). The citrated rapid thromboelastography maximum amplitude (CRT MA) fluctuated slightly (BL: 65.98 mm, 1 month: 67.73 mm, 3 months: 64.11 mm, and 6 months: 64.39 mm; $P < 0.0001$), while citrated functional fibrinogen (CFF) MA showed initial increase followed by decline (BL: 29.14 mm, 1 month: 35.36 mm, 3 months: 23.77 mm, and 6 months: 23.06 mm; $P < 0.001$). HKH MA

Table II. Medications regimens across time points

Medications, *n* (%)	BL (*n* = 16)	1 month (*n* = 14)	3 months (*n* = 6)	6 months (*n* = 9)
MAPT	4 (25)	0 (0)	1 (17)	0 (0)
MAPT + DOAC	4 (25)	1 (7)	0 (0)	1 (11)
DAPT	6 (37.5)	5 (36)	3 (50)	2 (22)
DAPT + DOAC	2 (12.5)	8 (57)	2 (33)	6 (67)

The sample size (*N*) varies at each visit due to patients missing follow-up appointments.
BL, baseline; DAPT, dual antiplatelet therapy (Aspirin + Clopidogrel, Aspirin + Ticagrelor); DAPT + DOAC, dual antiplatelet therapy and direct oral anticoagulant (Aspirin + Clopidogrel + Ticagrelor, Aspirin + Clopidogrel + Rivaroxaban, Aspirin + Clopidogrel + Apixaban); MAPT, mono antiplatelet therapy (aspirin/clopidogrel); MAPT + DOAC, mono antiplatelet therapy and direct oral anticoagulant (Aspirin + Apixaban, Aspirin + Rivaroxaban, Clopidogrel + Rivaroxaban).

Table III. Analysis of TEG parameters across time points

Variables	BL	1 month	3 months	6 months	*P* value[a]
Lysis at 30 mins (%), mean	0.64	5.91	0.06	0.27	0.307
Reaction time (mins), mean	8.17	8.94	9.67	6.9	<0.001
CRT maximum amplitude (MA) in mm, mean	65.98	67.73	64.11	64.39	<0.0001
CFF maximum amplitude (MA) in mm, mean	29.14	35.36	23.77	23.06	<0.001
HKH MA (mm), mean	61.4	62.86	61.48	63.12	<0.0001
ActF MA (mm), mean	19.33	18.67	15.06	13.57	<0.001
ADP MA (mm), mean	52.69	40.96	39.83	45.18	<0.0001
AA MA (mm), mean	38.03	30.43	30.86	24.27	<0.001
ADP% aggregation, mean	74.27	42.1	52.24	63.94	<0.001
ADP% inhibition, mean	25.73	57.9	47.76	36.06	<0.001
AA % aggregation, mean	42.39	9.38	37.64	21.76	<0.001
AA % inhibition, mean	57.61	90.62	62.36	78.24	<0.001
CK R (min), mean	8.37	8.82	8.65	6.67	<0.001
CK K (min), mean	2.01	1.3	1.7	1.27	<0.0001
CK angle (degree), mean	67.69	71.76	70.63	72.78	<0.001
CK MA (mm), mean	61.51	64.89	63.33	64.11	<0.0001
CRT MA (mm), mean	63.48	64.49	66.8	65.68	<0.0001
CKH R (min), mean	11.23	12.25	7.24	6.23	< 0.001
CFF MA (mm), mean	27.27	34.73	29.83	24.22	<0.001
CFF FLEV (mg/dL), mean	500.66	612.17	544.34	442.01	<0.001

BL, baseline; CK, citrated kaolin; CFF, citrated functional fibrinogen; ActF, activator F; FLEV, functional fibrinogen.
[a]Statistical analysis conducted with repeated measures ANOVA.

remained relatively stable (ranging from 61.4 to 63.12 mm; $P < 0.0001$), whereas activator F MA showed a consistent decreasing trend (from 19.33 to 13.57 mm; $P < 0.001$).

ADP Parameters

Notably, ADP parameters demonstrated significant variations throughout the study period. The ADP MA showed a BL value of 52.69 mm, which decreased to 40.96 mm at 1 month and 39.83 mm at 3 months, before slightly increasing to 45.18 mm at 6 months ($P < 0.0001$). Similarly, ADP% aggregation started at 74.27% at BL, dropping substantially to 42.1% at 1 month, and then showing a gradual increase to 52.24% at 3 months and 63.94% at 6 months ($P < 0.001$). Correspondingly, ADP% inhibition showed an inverse pattern, starting at 25.73% at BL, peaking at 57.9% at 1 month, and then decreasing to 47.76% at 3 months and further to 36.06% at 6 months ($P < 0.001$) (Fig. 1).

AA Parameters

AA parameters also showed significant changes, with AA MA demonstrating a steady decline from BL to 6 months (38.03 to 24.27 mm; $P < 0.001$), aggregation decreasing from 42.39% to 21.76%, and inhibition increasing from 57.61% to 78.24% at 6 months (both $P < 0.001$). The citrated kaolin (CK) parameters, including reaction time (R-time), K time, angle, and MA, all showed significant changes

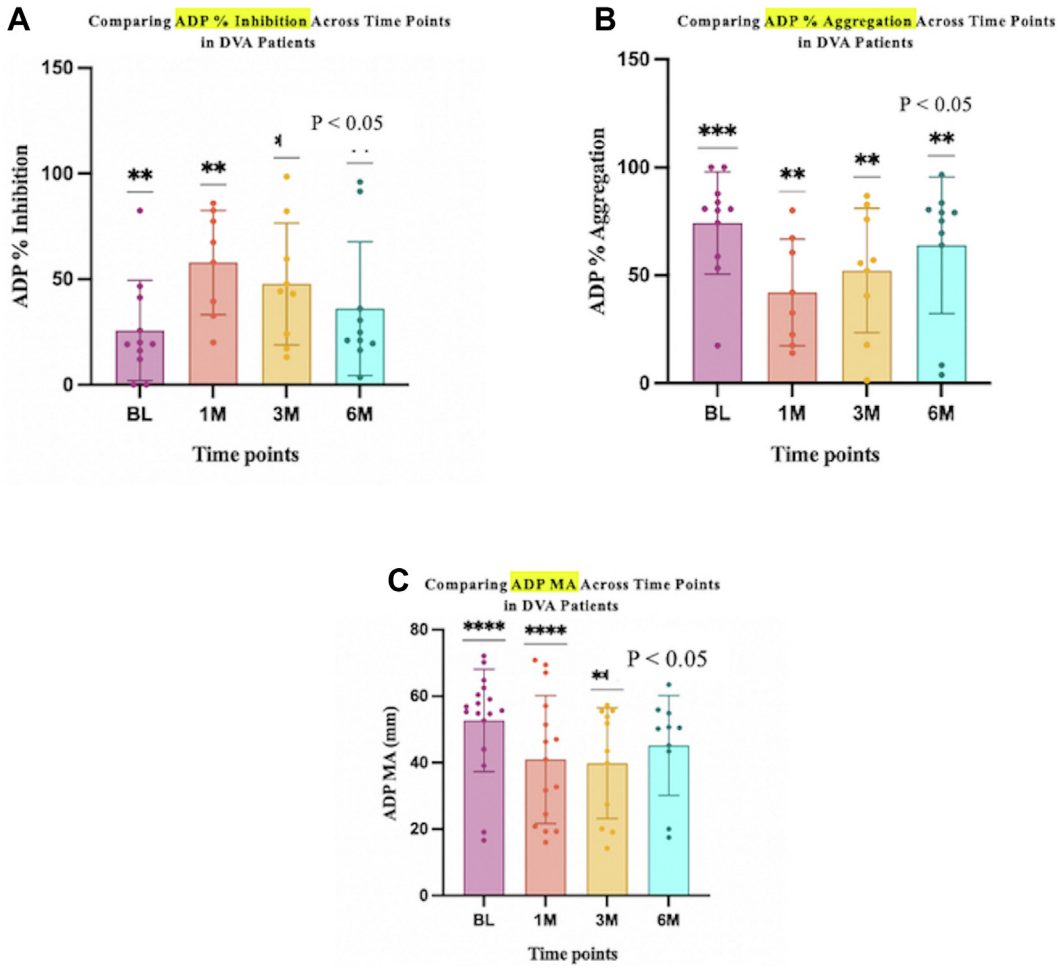

Fig. 1. TEG-PM parameters in DVA patients across different time points. **(A)** ADP% inhibition (mm), significant increase in the ADP inhibition of DVA patients across the follow-up visits. This indicates that the degree to which platelet aggregation is inhibited by adding ADP has improved. This hypocoagulable state benefits DVA patients, as it reduces the risk of thrombotic events. **(B)** ADP% aggregation among DVA patients across the follow-up visits. This suggests that their ability to aggregate and form clots in response to ADP stimulation has diminished. This hypocoagulable state is advantageous for DVA patients as it lowers the risk of thrombotic events. **(C)** ADP MA (mm), significant decrease of patients across the follow-up visits, indicating a reduced effectiveness of platelets in forming clots in response to ADP. However, at the 6-month visit, there was a slight increase.

($P < 0.001$), with CK angle showing an upward trend from 67.69° to 72.78°. Finally, CFF functional fibrinogen values fluctuated significantly, peaking at 1 month (612.17 mg/dL) before decreasing to 442.01 mg/dL at 6 months ($P < 0.001$).

TEG-PM Parameters Across Treatment Groups

Analysis of R-time revealed that the MAPT group demonstrated the shortest BL R-time at 6.3 mins, while the DAPT + DOAC group showed consistently longer R-times, beginning at 9.1 mins at BL and measuring 7.07 mins at 6 months (Table SII). This difference in R-times across treatment groups was statistically significant ($P = 0.027$).

Clot Lysis

Regarding clot lysis, treatment groups showed notable variations. The MAPT + DOAC group demonstrated the highest BL lysis (1.68%), while other groups had lower initial values (MAPT = 0.2%, DAPT = 0.16%, DAPT + DOAC = 0.2%). The DAPT + DOAC group showed interesting patterns: a marked increase to 7.7% at 1 month,

followed by a complete reduction to 0% at 3 months, and a slight rise to 0.19% at 6 months. Meanwhile, the MAPT + DOAC group maintained stable values at 1 and 3 months (0.2%), with a minor increase to 1.1% at 6 months. These differences between treatment groups reached statistical significance ($P = 0.038$), indicating that antiplatelet regimen choice significantly influences clot breakdown patterns (Table SIII).

Citrated Rapid Thromboelastography Maximum Amplitude

Dynamic changes in CRT MA were observed throughout the study period. BL values were comparable across regimens, with DAPT showing the highest CRT MA (66.9 mm), followed by MAPT + DOAC (65.43 mm), DAPT + DOAC (63.05 mm), and MAPT (61.25 mm). At 1 month, the DAPT + DOAC group peaked at 70.43 mm, while DAPT decreased to 60.3 mm, and MAPT + DOAC remained stable at 63.1 mm. Values converged by 3 months, ranging from 59.15 mm to 64.8 mm, suggesting stabilization. This stability continued through 6 months, with similar values across DAPT + DOAC, DAPT, and MAPT + DOAC groups (64.1 mm, 63.85 mm, and 62.2 mm, respectively). MAPT measurements were unavailable at 1 and 6 months due to patient absence ($P = 0.452$) (Table SIV).

Maximum Amplitude Parameters

MA parameters exhibited significant variations ($P < 0.0001$). The DAPT + DOAC group consistently showed the lowest values, with ADP MA decreasing from 35.65 mm at BL to 26.7 mm at 1 month and 27.36 mm at 3 months, before rising to 43.7 mm at 6 months ($P < 0.001$). Similarly, their AA MA values started at 49.9 mm, dropped to 24.84 mm at 1 month and 10.12 mm at 3 months, ending at 23.43 mm at 6 months ($P = 0.041$).

Platelet Function

Platelet function measurements revealed distinct patterns across regimens. For ADP% aggregation, MAPT showed the highest BL (83.8%), while MAPT + DOAC showed the lowest (6.4%). DAPT and DAPT + DOAC groups started at intermediate values (47.1% and 41.3%, respectively). By 1 month, DAPT decreased significantly to 17.05%, while DAPT + DOAC maintained moderate inhibition at 34.84%. The MAPT + DOAC group showed an unexpected rise to 59.7%, although this finding warrants careful interpretation given varying sample sizes. Three-month measurements showed convergence among MAPT, MAPT + DOAC, and DAPT (12.7%, 12.2%, and 24.2%, respectively), while DAPT + DOAC remained higher at 40.12%. At 6 months, both DAPT groups achieved enhanced platelet inhibition, while MAPT + DOAC showed increased aggregation ($P = 0.008$).

In terms of platelet inhibition, the DAPT + DOAC group achieved the highest ADP% inhibition, starting at 41.3% and peaking at 57.9% at 1 month, before stabilizing around 45% for the remaining period. The MAPT group, conversely, showed the lowest BL ADP inhibition (18.1%). For AA inhibition, the DAPT group achieved the highest BL at 86.4% ($P = 0.015$).

Clot Kinetics

Finally, the analysis of clot kinetics showed that the DAPT + DOAC group demonstrated the slowest rate of clot formation, with CK angles measuring 65.25° at BL, increasing to 70.47° at 1 month, slightly decreasing to 68.7° at 3 months, and reaching 71.55° at 6 months. However, analysis revealed no statistically significant differences in CK angles between treatment groups ($P = 0.384$).

Clinical Outcomes

Over the follow-up period of 16 patients at our institute, stenosis or occlusion at the intervention site attributed to 61.1% of the total events (11/18). Most stenoses or occlusions (10/11) were detected by ultrasound, while only 1 case was clinically diagnosed. Among these patients, 4/11 required reintervention. Amputations accounted to 27.8% of the total events (5/18), including 3 TMAs (16.7%), 1 above-knee amputation (5.5%), and 1 below-knee amputation (5.5%) (Table IV).

The clinically significant events during follow-up at our institute that included stenosis/occlusion of the area of intervention requiring reintervention within 3 months of DVA procedure, amputations (other than TMA), and death are depicted in Table V. Overall, there were 7 significant events, of which 3 (43%) were due to stenosis/occlusion at the intervention site, while 2 (28.5%) were amputations. Both the deaths that occurred were due to sepsis (28.5%). Within the 4 antithrombotic regimens studied, the distribution of patients at the time of clinical events was as follows: 1 patient was receiving MAPT, 1 patient was on MAPT + DOAC, 1 patient was on DAPT, and 3 patients were receiving DAPT + DOAC.

Table IV. Clinical events across antithrombotic regimen

Events, *n* (%)	Total (*n* = 7)	MAPT (*n* = 1)	MAPT + DOAC (*n* = 1)	DAPT (*n* = 2)	DAPT + DOAC (*n* = 3)
Stenosis/occlusion at the intervention site	3 (42.8)	-	-		3 (100)
Amputations	2 (28.5)		-		-
AKA	1 (14.3)	-		1 (50)	-
BKA	1 (14.3)	1 (100)		-	-
Death (all-cause mortality)	2 (28.5)	-	1 (100)	1 (50)	-

AKA, above-knee amputation; BKA, below-knee amputation.AKA, above-knee amputation; BKA, below-knee amputation.
BKA was performed due to osteomyelitis and sepsis. All patients died from septic shock. Clinical events in this study were defined as stenosis or occlusion of the DVA that required intervention within 3 months of the surgery.

Table V. Overall events across time points

Events, *n* (%)	Overall (*N* = 18)	BL (*N* = 2)	1 month (*N* = 9)	3 months (*N* = 4)	6 months (*N* = 3)
Stenosis/occlusion at the intervention site	11 (61.1)	1 (50)	7 (77.8)	2 (50)	1 (33.3)
USG	10 (55.5)	1 (50)	6 (66.7)	2 (50)	1 (33.3)
Clinically diagnosed	1 (5.5)	-	1 (11.1)	-	-
Required reintervention[a]	4 (22.2)	1 (50)	1 (11.1)	1 (25)	1 (33.3)
Amputation	5 (27.8)	-	2 (22.2)	1 (25)	2 (66.7)
TMA	3 (16.7)	-	1 (11.1)	-	2 (66.7)
AKA	1 (5.5)	-	1 (11.1)	-	-
BKA	1 (5.5)	-	-	1 (25)	-
Death (all-cause mortality)[b]	2 (11.1)	1 (50)	-	1 (25)	-

AKA, above-knee amputation; BKA, below-knee amputation; BL, baseline; USG, ultrasound guided.
[a]Only 4 patients who were found to have stenosis/occlusion required reintervention.
[b]Cause of death in both cases was septic shock.

DISCUSSION

CLTI annual incidence is 50 to 100 cases per 100,000 and mortality rates are 20% at 6 months after onset. Endovascular revascularization is often used as first-line for this condition. However, when this approach fails, it may result in a major amputation. In such cases, DVA can be an alternative approach to prevent limb loss, demonstrating a 71% limb savage rate and 46% secondary patency at 12 months.[5] This prospective study provides novel insights into the coagulation profiles of patients undergoing DVA and demonstrates the utility of TEG-PM in monitoring various thromboprophylaxis regimen. Our investigation revealed several pivotal findings that advance understanding of anticoagulation management in this patient population.

The DAPT + DOAC group exhibited consistently superior anticoagulation parameters throughout the study period, characterized by prolonged reaction times and reduced MA values. These parameters suggest more effective inhibition of clot formation compared to other antithrombotic regimens. Particularly notable were the significantly lower ADP MA values in the DAPT + DOAC group, which progressed from 35.65 mm at BL to 43.7 mm at 6 months, indicating substantial and sustained platelet inhibition. While graft survival was not directly tracked in this study, these favorable platelet inhibition parameters align with recent evidence from the COMPASS PAD substudy, which demonstrated significant long-term benefits of combined antiplatelet and anticoagulant therapy in PAD patients.[16,17] Our TEG-PM findings, when considered alongside the COMPASS PAD outcomes,[16,17] may suggest a possible relationship between sustained platelet inhibition through DAPT + DOAC therapy and graft patency in DVA patients, although larger studies would be needed to further explore this potential association.

The temporal analysis of coagulation parameters revealed distinct phases of hemostatic adaptation following DVA. Early postprocedure measurements

showed heightened platelet reactivity and accelerated clot formation, suggesting an initial prothrombotic state. This gradually transitioned to a more stable coagulation profile by 3 months, although with persistent elevations in certain parameters compared to BL. The maintenance of therapeutic anticoagulation proved particularly challenging during this initial period, with TEG-PM measurements highlighting the need for careful monitoring and potential dose adjustments. Notably, patients who maintained consistent DAPT + DOAC therapy showed more stable TEG parameters throughout this critical phase.

The pattern of TEG-PM changes also provided insights into the underlying mechanisms of thrombotic risk in DVA procedures. The combination of elevated MA values and accelerated clot formation kinetics suggests a complex interplay between platelet activation and the coagulation cascade. This observation aligns with the theoretical framework of venous arterialization, where altered flow dynamics and endothelial adaptation may create unique prothrombotic conditions.[18] The sustained elevation in certain TEG parameters, even in well-anticoagulated patients, suggests persistent alterations in the local hemostatic environment that may require long-term management strategies.

Beyond the coagulation dynamics, our study population's characteristics underscore the complexity of DVA patient management. Our cohort predominantly comprised high-risk patients with a mean age of 66.6 years and multiple comorbidities. The prevalence of cardiovascular risk factors in our population notably exceeded that reported in contemporary PAD trials, with diabetes affecting 88%, hypertension 91%, and hyperlipidemia 91% of patients. This increased risk factor burden, combined with significant functional impairment in half of our cohort, emphasizes the need for carefully tailored antithrombotic strategies that balance efficacy with safety.

The clinically significant events during follow-up at our institute included stenosis/occlusion of the area of intervention, amputations (other than TMA), and death (Table V). Overall there were 7 events, of which 3 (43%) were due to stenosis/occlusion at the intervention site, while 2 (28.5%) were amputations. All deaths were due to sepsis (28.5%). Within the 4 antithrombotic regimens studied, the distribution of patients at the time of clinical events was as follows: 1 patient was receiving MAPT, 1 patient was on MAPT + DOAC, 1 patient was on DAPT, and 3 patients were receiving DAPT + DOAC.

However, it is important to note that not only is this a small sample size but that in DVA especially the mechanical and patient factors in terms of inflow, distal venous outflow, donor vessel preparation, and wound stage are especially contributory to outcome. For example, in some patients, the posterior tibial (PT) donor vessel was free from atherosclerosis at the origin and the superficial femoral artery inflow was sound. In such a case, the patients' laminar inflow will lend itself nicely to keeping the graft flowing. The same patient with stenosis at the PT donor site take-off who may require balloon angioplasty of this inflow vessel to even deliver the crossing stent may thrombose but not because of the anticoagulation rather because of the turbulent flow or restenosis at the inflow site. Overall, while we are reporting our overall all-cause thrombosis/stenotic and amputation rates here broken down by anticoagulant regimen, these results need to be interpreted with caution given the myriad of other factors that contribute to thrombosis.

Although we found ultrasound imaging evidence of occlusion/stenosis in 10 patients (Table IV), only 3 patients had volume flow values that necessitated intervention. As per the natural course post DVA procedure, we found worsening of wounds or tarsometatarsal amputation in some patients. There was no significant number of patients on each anticoagulant group to warrant comparison as the regimen evolved toward DAPT + DOAC toward the 3-month follow-up.

While these rates might appear high, they are comparable to, or better than, those reported in other series of complex limb salvage procedures. Notably, the safety profile of the antithrombotic regimens was favorable, with no major bleeding complications recorded during the follow-up period. Although minor bleeding events were documented, none required discontinuation of therapy. The absence of thrombotic events in patients who maintained their prescribed antithrombotic regimen suggests adequate anticoagulation across all treatment groups, although larger studies are needed to confirm this safety profile.

The evolution of treatment patterns in our cohort, marked by a shift toward more intensive anticoagulation over time (67% on DAPT + DOAC at 6 months), reflects growing recognition of the unique thrombotic challenges posed by DVA procedures. This trend parallels developments in other areas of vascular intervention, where initial conservative approaches have given way to more aggressive antithrombotic strategies. The TEG-PM

parameters suggest that arterialization of venous segments creates a distinct procoagulant environment requiring specific antithrombotic approaches. This aligns with recent research demonstrating unique patterns of endothelial activation and platelet adhesion in arterialized veins.

Several important limitations of our study must be acknowledged. The relatively small sample size of 16 patients and variable follow-up rates throughout the study period limit our statistical power and may have introduced bias in longer-term outcomes. Study retention varied considerably, with 88% completing the 1-month follow-up, dropping to 38% at 3 months, and rising to 56% at 6 months. The nonrandomized nature of treatment assignment and observational design preclude definitive conclusions about causality between treatment regimens and outcomes. The data were collected using an electronic medical record and have limitations of potentially incorrect or missing diagnostic codes. As a single-center experience, the generalizability of our findings may be limited to similar practice settings. The evolution of antithrombotic regimens during the study period makes it challenging to isolate specific treatment effects, and we were unable to control for concurrent medications or other interventions that might affect coagulation.

Looking ahead, several important research directions emerge from our findings. Larger, randomized controlled trials comparing different antithrombotic strategies in DVA patients are needed to validate our observations. The correlation between technical aspects of DVA and coagulation profiles warrants further investigation, as does the influence of anatomical factors on thrombotic risk.[19] Development of predictive models incorporating both clinical and laboratory parameters could enhance our ability to identify patients at the highest risk for complications. Cost-effectiveness analyses of intensive antithrombotic strategies and TEG-PM–guided therapy versus empiric approaches would provide valuable information for healthcare resource allocation. Furthermore, investigation of patient-reported outcomes with different antithrombotic regimens would offer important insights into the real-world implementation of these strategies.[20]

The field of DVA continues to evolve rapidly, and our findings contribute to the growing understanding of optimal postprocedural care. As technical aspects of the procedure continue to be refined, parallel advancement in antithrombotic management strategies will be essential for maximizing the potential of this promising intervention for patients with limited revascularization options.[21]

CONCLUSION

While our preliminary data suggest improved outcomes with combined DAPT and DOAC therapy, larger studies are needed to confirm these findings and establish optimal antithrombotic strategies for DVA patients.

The outcomes achieved with DAPT + DOAC therapy highlight the importance of addressing multiple thrombotic pathways to optimize graft patency. While our findings support TEG-PM as a valuable tool for personalizing antithrombotic therapy in DVA patients, more extensive randomized trials are needed to definitively establish optimal protocols, determine ideal therapy duration, and validate these findings in larger cohorts.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Isabella F. Cieri: Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Adriana A. Rodriguez Alvarez:** Writing – review & editing, Validation, Investigation, Data curation. **Shiv Patel:** Writing – review & editing, Software, Data curation. **Mounika Boya:** Writing – review & editing, Investigation, Data curation. **Andrea Nurko:** Writing – review & editing, Validation, Data curation. **William Teeple:** Writing – review & editing, Software, Data curation. **Anahita Dua:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.avsg.2024.12.054.

REFERENCES

1. Eid MA, Mehta K, Barnes JA, et al. The global burden of peripheral artery disease. J Vasc Surg 2023;77:1119–1126.e1.
2. Aday AW, Matsushita K. Epidemiology of peripheral artery disease and polyvascular disease. Circ Res 2021;128:1818–32.
3. Beckman JA, Duncan MS, Damrauer SM, et al. Microvascular disease, peripheral artery disease, and amputation. Circulation 2019;140:449–58.
4. Huang I, Nakama T, Ichihashi S, et al. Technical aspects of percutaneous deep venous arterialization using off-the-shelf devices. J Endovasc Ther 2024;31:350–9.
5. Kum S, Tan YK, Schreve MA, et al. Midterm outcomes from a pilot study of percutaneous deep vein arterialization for

the treatment of No-option critical limb ischemia. J Endovasc Ther 2017;24:619–26.
6. Schreve MA, Vos CG, Vahl AC, et al. Venous arterialisation for salvage of critically ischaemic limbs: a systematic review and meta-analysis. Eur J Vasc Endovasc Surg 2017;53:387–402.
7. Beckman JA, Schneider PA, Conte MS. Advances in revascularization for peripheral artery disease: revascularization in PAD. Circ Res 2021;128:1885–912.
8. Clair DG, Mustapha JA, Shishehbor MH, et al. Promise I: early feasibility study of the LimFlow System for percutaneous deep vein arterialization in no-option chronic limb-threatening ischemia: 12-month results. J Vasc Surg 2021;74:1626–35.
9. Shishehbor MH, Powell RJ, Montero-Baker MF, et al. Transcatheter arterialization of deep veins in chronic limb-threatening ischemia. N Engl J Med 2023;388:1171–80.
10. Bolliger D, Tanaka KA. Point-of-Care coagulation testing in cardiac surgery. Semin Thromb Hemost 2017;43:386–96.
11. Dias JD, Sauaia A, Achneck HE, et al. Thromboelastography-guided therapy improves patient blood management and certain clinical outcomes in elective cardiac and liver surgery and emergency resuscitation: a systematic review and analysis. J Thromb Haemost 2019;17:984–94.
12. Tapia NM, Chang A, Norman M, et al. TEG-guided resuscitation is superior to standardized MTP resuscitation in massively transfused penetrating trauma patients. J Trauma Acute Care Surg 2013;74:378–86.
13. Weber CF, Görlinger K, Meininger D, et al. Point-of-care testing: a prospective, randomized clinical trial of efficacy in coagulopathic cardiac surgery patients. Anesthesiology 2012;117:531–47.
14. Kum S, Huizing E, Schreve MA, et al. Percutaneous deep venous arterialization in patients with critical limb ischemia. J Cardiovasc Surg 2018;59:665–9.
15. Zeller T, Micari A, Scheinert D, et al., IN.PACT DEEP Trial Investigators. The IN.PACT DEEP clinical drug-coated balloon trial: 5-year outcomes. JACC Cardiovasc Interv 2020;13:431–43.
16. Iida O, Takahara M, Soga Y, et al. One-year outcomes of heparin-bonded stent-graft therapy for real-world femoropopliteal lesions and the association of patency with the prothrombotic state based on the prospective, observational, multicenter *Via*bahn ste*n*t-graft placement for femoropopliteal diseases re*qui*ring endovas*c*ular t*h*erapy (VANQUISH) study. J Endovasc Ther 2021;28:123–31.
17. Nicklas JM, Diltz EA, O'Neill WW, et al. Quantitative measurement of coronary flow during medical revascularization (thrombolysis or angioplasty) in patients with acute infarction. J Am Coll Cardiol 1987;10:284–9.
18. Darling JD, McCallum JC, Soden PA, et al. Predictive ability of the Society for Vascular Surgery Wound, Ischemia, and foot Infection (WIfI) classification system after first-time lower extremity revascularizations. J Vasc Surg 2017;65:695–704.
19. Tan Y, Zhang Z, Zheng C, et al. Mechanisms of diabetic cardiomyopathy and potential therapeutic strategies: preclinical and clinical evidence. Nat Rev Cardiol 2020;17:585–607.
20. Mehran R, Baber U, Sharma SK, et al. Ticagrelor with or without aspirin in high-risk patients after PCI. N Engl J Med 2019;381:2032–42.
21. Gulpen AJW, Ten Cate H, Henskens YMC, et al. The daily practice of direct oral anticoagulant use in patients with atrial fibrillation; an observational cohort study. PLoS One 2019;14:e0217302.