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Direct Oral Anticoagulants Decrease Treatment Failure For Acute Lower Extremity DVT

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Background

Optimal medical therapy for acute lower extremity deep venous thrombosis (DVT) remains an enigma. While clinical trials demonstrate non-inferiority with an oral anti-Xa inhibitor, or direct oral anticoagulant (DOAC), versus combined low molecular weight heparin (LMWH) and oral vitamin K agonist (VKA), the most effective regimen remains to be determined.

Methods

This study is a single-center retrospective cohort study from October 2014-December 2015 of patients with a diagnosis of acute DVT and subsequent serial lower extremity venous duplex. Demographics, medical history, medications, serial ultrasound findings as well as the primary anticoagulant used for treatment were collected and analyzed by two independent data extractors. Treatment failure was defined as any new DVT or progression of an existing DVT within 3 months of diagnosis of the index clot. Risk factors for treatment failure were assessed using standard odds ratios and Fischer's exact test.

Acute DVT	Chronic DVT
Vein often dilated compared to companion artery	Vein typically equal to or smaller than companion artery
Vein partially or not at all compressible	Vein usually at least partially compressible
Soft echoes, may be only loosely attached to vein wall	Bright echoes, typically along vein walls
May lose respiratory variation	Maintains respiratory variation
Augmentation is reduced or diminished	

Table 1: **Criteria to distinguish acute versus chronic DVT**. All duplex studies were performed in the same accredited vascular laboratory with the listed criteria to distinguish acute from chronic DVT.

Results I: Demographics

Factor	Frequency % (n)
Ethnicity	
Caucasian	46% (221)[a]
Black	19.8% (98)[a]
Asian	0.8% (4)[a]
Hispanic	2.8% (14)[a]
Other	25.6% (127)[a]
Declined	3.2% (16)[a]
Prior DVT	28.3% (140)[b]
Prior pulmonary embolism	14.1% (70)[c]
Thrombophilia (Inherited or acquired)	7.1% (35)[c]
Renal insufficiency (Acute or chronic)	21.8% (108)[c]
Hepatic insufficiency (Acute or chronic)	3.6% (18)[c]
Cancer	36.1% (179)[c]
Cerebrovascular accident	11.3% (56)[c]
GI bleeding	8.7% (43)[c]
Pre-existing antiplatelet therapy	29% (144)[c]
Pre-existing anticoagulation therapy	13.9% (69)[d]
Proximal segment involved	35% (174)[c]

Table 2: **Demographic and medical history.** The distribution of ethnicity and the frequency of prior medical conditions for the cohort is presented.
[a]Total N=480. [b]Total N=495. [c] Total N=496. [d] Total N=488

Results II: DOAC was the most commonly used treatment

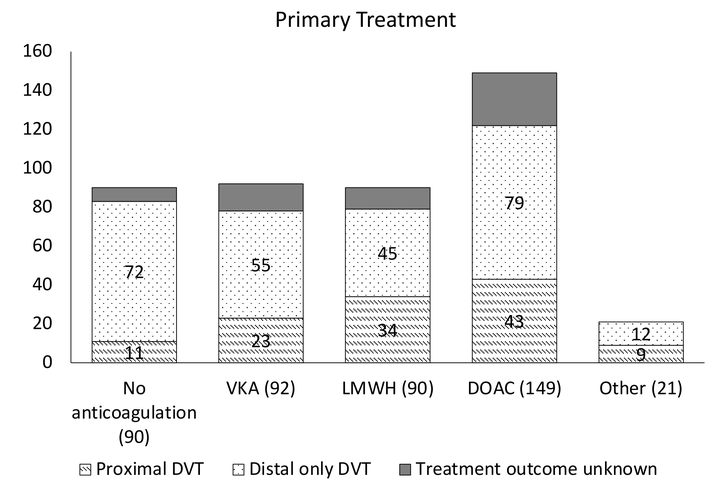

Figure 1: **Distribution of treatment choices utilized by DVT location.** DOACs were the most commonly used treatment, followed by VKA, LMWH and no anticoagulation.
DOAC = Direct oral anticoagulant. VKA = Vitamin K agonist. LMWH = Low molecular weight heparin.

Results III: DOACs were protective against treatment failure

Factor	Risk of treatment failure OR [95% CI]	p-value
Any anticoagulation	0.90 [0.49, 1.66]	0.74
Anticoagulation duration <3 months	1.31 [0.69, 2.50]	0.42
0-2 anticoagulation agents	1.67 [0.90, 3.11]	0.10
VKA	1.31 [0.73, 2.37]	0.37
LMWH	0.78 [0.43, 1.40]	0.41
Other class of anticoagulant	3.86 [1.58, 9.45]	0.0032
DOAC	0.43 [0.23, 0.79]	0.0069
DOAC vs VKA	0.44 [0.21, 0.92]	0.029

Table 3: **Risk factors for treatment failure**. Risk factors for treatment failure were assessed with univariate odds ratios with 95% confidence intervals and p-values. The use of DOACs was protective against treatment failure.
DOAC = Direct oral anticoagulant.

Conclusions

Patients treated with a DOAC were less likely to experience treatment failure when compared with any other treatment (odds ratio 0.43; 95% confidence intervals [0.23, 0.79]; p=0.0069), and when compared with traditional oral VKA (OR 0.44; 95% CI [0.21, 0.92]; p=0.029). None of prior history of DVT, pulmonary embolism, thrombophilia, renal insufficiency, hepatic insufficiency, cancer, or antiplatelet therapy correlated with treatment failure. Treatment outcome did not correlate with being on any anticoagulation versus none (p=0.74), nor did it correlate with the duration of treatment (<3 months versus ≥3 months) (p=0.42).

In summary, the use of a DOAC for acute lower extremity DVT yielded better overall outcomes and fewer treatment failures at 3 months as compared to traditional oral VKA therapy based on serial duplex imaging.

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Grant Support
- Ruth L. Kirschstein NRSA Post-doctoral fellowship award, NHLBI, 1F32HL137292

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