Distal deep vein thrombosis: is there a way out of this dark forest?

Matteo Guarascio,[1] Gerardo Nicola Pititto,[2] Alessia Abenante,[3] Marco Paolo Donadini[4]

[1]Internal Medicine Unit, Vito Fazzi Hospital, Lecce; [2]Internal Medicine Residency Program, School of Medicine, University of Insubria, Varese and Como; [3]Internal Medicine Department, ASST Settelaghi, Varese; [4]Research Center on Thromboembolic Diseases and Antithrombotic Therapies, University of Insubria, Varese, Italy

ABSTRACT

Isolated distal deep vein thrombosis (IDDVT) represents a common manifestation of venous thromboembolism (VTE), accounting for up to 50% of cases involving lower-extremity deep vein thrombosis (DVT). In contrast to proximal DVT, IDDVT exhibits a higher association with transient risk factors and less frequently occurs spontaneously. IDDVT generally entails a substantially lower risk of proximal extension, pulmonary embolism, post-thrombotic syndrome, and recurrence compared to proximal DVT. Nevertheless, specific patient subgroups, including those with active cancer, prior VTE, unprovoked IDDVT, and involvement of more than one vein, demonstrate a noteworthy recurrence risk. Unlike proximal DVT, the optimal therapeutic management of IDDVT remains uncertain. In clinical practice, the predominant approach for managing IDDVT involves anticoagulation rather than ultrasound imaging surveillance, due to a significant reduction in the risk of proximal extension and recurrence. Conversely, serial imaging is typically preferred for individuals without risk factors for extension or at high risk for bleeding. Finally, anticoagulant duration relies on the different risk of VTE recurrence within the specific patient subgroups considered. This review offers an updated overview of the epidemiology, risk factors, and natural history of IDDVT, emphasizing therapeutic management in accordance with current guideline recommendations and the latest evidence, trying to provide a way out of this dark forest.

Correspondence: Matteo Guarascio, Internal Medicine Unit, Vito Fazzi Hospital, Lecce, Italy.
E-mail: guarasciomatteo@gmail.com

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Introduction

Isolated distal deep vein thrombosis (IDDVT) is a thrombotic event that involves the axial veins (posterior tibial, peroneal, and anterior tibial) or the muscular veins (soleal and gastrocnemius) of the calf. This condition occurs independently, without concurrent thrombosis in other venous districts.

Among individuals evaluated for suspected pulmonary embolism (PE) or deep vein thrombosis (DVT) of the lower extremities, the incidence of IDDVT ranges from 7% to 11% in situations with suspected PE and from 4% to 15% in cases with suspected DVT. Instead, among patients who received a confirmed diagnosis of DVT, the prevalence of IDDVT varied between 23% and 59%.[1] The variability in the prevalence of IDDVT is due to the differences in the cohorts of patients studied, the inclusion or absence of calf veins in routine ultrasound (US) examination, the US technique used, and the operator's expertise. A systematic review and meta-analysis conducted by Goodacre *et al.* compared various US techniques to venography in patients with suspected DVT. Compressive ultrasound (CUS) alone demonstrated a considerably low sensitivity for IDDVT compared to proximal DVT (56.8% *versus* 93.8%), with a similar high specificity. A slight increase in sensitivity was observed with duplex US (71.2% *versus* 96.5%) and triplex US (75.2% *versus* 96.4%), denoting the importance of selecting the US method based on the patient's estimated risk.[2] Moreover, a study in which the US imaging was performed by highly skilled ultrasonographers reported a much superior accuracy, showing a more reliable diagnosis of distal DVT in experienced hands.[3] Another adopted method is the so-called serial proximal CUS strategy: symptomatic patients with a first negative proximal CUS would receive a second examination after 1 week to detect the possible extension of a distal DVT.[4] To avoid misdi-

agnosis in this wide heterogeneity, the *Society of Radiologists in Ultrasound Consensus Conference* recommended a standardization of the ultrasound methods, suggesting a complete duplex US from the inguinal ligament to the ankle of both legs, with compression performed at 2-cm intervals.[5] Furthermore, it should be noted that incidentally detected IDDVT emerges as the predominant observation among asymptomatic individuals when investigating the occurrence of DVT within high-risk contexts.[1,6]

IDDVT is generally perceived as a non-threatening and self-limited condition, even though several studies reported a non-negligible rate of complications, including recurrent venous thromboembolism (VTE), proximal extension, and post-thrombotic syndrome (PTS).[7]

IDDVT is more frequently associated with transient risk factors, such as recent surgery, trauma, hospitalization, travel, immobilization, or hormonal therapy.[8] Moreover, the risk of progression or recurrence may appear to be increased only in *high-risk* patients, defined by the coexistence of major underlying and/or permanent risk factors.[9] In this context, cancer-associated IDDVT has a similar natural history to cancer-associated proximal DVT, with substantially less favorable outcomes than noncancer-associated IDDVT.[7,10] Recent guidelines have identified risk factors for VTE recurrence in individuals with IDDVTs. Patients are categorized as high or low risk based on factors such as previous VTE, age over 50, active cancer, unprovoked IDDVT, persistently limited mobility, IDDVT in the popliteal trifurcation, and/or involvement of more than one calf vein. This categorization can aid physicians in determining the most effective treatment and its duration.[11]

Despite its quite high frequency, the optimal management remains controversial. This is mostly linked to its debatable clinical relevance that leads to highly heterogeneous management, ranging from anticoagulant treatment to clinical and ultrasonographic follow-up, as reflected by scarce and dissimilar guideline recommendations.[11,12]

Natural history and complications

Although IDDVTs are commonly perceived as carrying a low risk of complications due to their location, they still present relevant potential risks and complications.[13]

Between 1% and 22% of untreated IDDVTs are expected to extend into the proximal veins or embolize into the pulmonary arteries, underscoring the clinical relevance of this condition.[14] In the prospective CALTHRO study, untreated isolated calf DVTs were extended into proximal veins in 3.1% of cases.[15] Similarly, in the study conducted by Schwarz *et al*., isolated calf muscle vein thrombosis progressed to DVT in 3.8% of cases at 90 days in the group without anticoagulation.[9] In the ACT pilot study, patients with IDDVT assigned to the conservative treatment group experienced severe thromboembolic complications in 11.4% of cases (4/35), including three symptomatic popliteal propagations and one symptomatic pulmonary embolism.[16] In the CACTUS trial, seven patients with calf DVT in the placebo group (5.4%) were diagnosed with proximal extension during the 6-week follow-up period.[17]

Also, IDDVT carries a non-negligible risk of VTE recurrence, which is further increased by the presence of specific risk factors.[8,18-22]

In a multi-centre prospective cohort study enrolling 490 patients (OPTIMEV study), those with an IDDVT had a lower annualized incidence of overall VTE recurrence compared with patients with proximal DVT (2.7% *vs* 5.2%, respectively) but a similar incidence of PE recurrence (0.9% *vs* 1.0%, respectively), after stopping anticoagulation. Patients aged over 50 years, those with an unprovoked IDDVT, or those with involvement of more than one vein exhibited a threefold higher risk of VTE recurrence compared to patients lacking these characteristics.[18]

In a retrospective study of 280 patients with IDDVT treated with a short-term protocol of low molecular weight heparin (LMWH), the incidence rate of recurrent VTE was 4.4 per 100 patient-years; notably, proximal DVT or PE accounted for half of the recurrences. The absence of provoking factors and previous history of VTE were significantly associated with recurrent VTE.[19]

Based on the analysis of patients included in the XALIA study, the occurrence of recurrent VTE after treatment cessation was numerically lower in individuals with IDDVT compared to those with proximal DVT. However, this difference did not reach statistical significance after adjusting for differences in baseline characteristics.[20]

In the GARFIELD VTE registry, one-year VTE recurrence rates were 4.8, 6.5, and 4.2 per 100 person-years for patients with IDDVT, proximal DVT, and PE, respectively. Over 12 months of follow-up, the incidence rate for recurrent VTE was significantly lower in patients with IDDVT compared to those with proximal DVT. This difference was not observed when compared to patients with PE.[21]

An analysis of the RIETE registry, found VTE deterioration events, defined as PE, PE-related mortality, or new proximal DVT, in 246 cases (4.5%) in patients with IDDVT and in 1688 cases in patients with proximal DVT (6.8%) at 1-year follow-up.[8]

Recently, in a cohort of more than 400 patients with IDDVT, the cumulative incidences of VTE recurrence at 1, 5, and 10 years after discontinuing anticoagulation were 6%, 15%, and 27%, respectively. Among the recurrent events, 29% were PE and 33% were proximal DVT. Notably, patients with unprovoked IDDVT experienced higher rates of recurrence compared to those with provoked IDDVT.[22]

Additionally, cancer patients with IDDVT are at high risk of recurrent VTE, irrespective of the type and duration of anticoagulant therapy as showed by a recent meta-analysis.[23]

Notably, rate of VTE recurrence is also influenced by location of IDDVT distinguishing axial and muscular thrombosis. In a recent meta-analysis including twelve studies, axial group showed a higher rate of primary composite outcome of recurrent VTE, defined as recurrent non-propagation of calf DVT, increased thrombus burden within the same named vessel, proximal propagation of calf DVT, and PE, compared to the muscular one.[24]

IDDVTs are also associated with the development of PTS, although to a lesser extent than DVTs. PTS represents a potentially debilitating and costly consequence of DVT due to the combination of symptoms and signs including leg pain, heaviness, edema, redness, telangiectasias, thickening of the skin, and, in severe cases, leg ulcers.[25] In the analysis of the RIETE registry, individuals with IDDVT exhibited lower occurrence of signs and symptoms related to PTS in comparison to those with proximal DVT at 2-year follow-up (36.8% *vs* 62.5%).[8]

In a meta-analysis of seven studies including a total of 1105

participants, one in five patients with IDDVT developed long-term symptoms, and one in 50 experienced severe PTS.[26]

Recently, Prandoni *et al.* found that 21.2% of patients with IDDVT developed PTS over a 3-year follow-up period. Factors identified as contributing to an increased risk of PTS include chronic heart failure, prolonged immobilization, and previous episodes of DVT and/or PE.[27]

Finally, patients with IDDVT exhibit a lower rate of 1-year all-cause mortality compared to those with proximal DVT, as observed in both RIETE and GARFIELD registries.[8,21]

Treatment

Despite several observational and randomized controlled trials (RCT), the optimal therapeutic management of IDDVT remains uncertain. Some randomized trials have investigated the need for anticoagulant treatment in individuals with IDDVT.[9,16,17,28] Table 1 reports the main characteristics of the cited studies.[9,16,17,28-35]

Historically, the management approach towards IDDVT has been based on the findings of a small randomized controlled trial.[28] In the landmark trial conducted by Lagerstedt *et al.* in 1985, 51 individuals with symptomatic IDDVT were randomized to either receive warfarin for 3 months or no anticoagulation following an initial course of unfractionated heparin. Anticoagulation significantly reduced the rate of recurrent VTE at 3 and 12 months without increasing bleeding risk. Of the 28 patients with calf DVT diagnosed by venography who did not receive anticoagulation, eight experienced complications: one developed a PE, while the others had recurrences identified through physical examination and serial isotopic tests.[28]

In a subsequent study, focused on muscular vein thrombosis, Schwarz *et al.* conducted a randomized open-label trial comparing nadroparin administration for a duration of 10 days against no anticoagulation in 107 patients, most of them defined at low thrombotic risk, with symptomatic muscular IDDVT. The results revealed no difference between the two groups in progression to DVT at 90 days.[9]

In the anticoagulation of calf thrombosis (ACT) trial, the ad-

Table 1. Characteristics of the included studies.

Author, year [study design]	Population [No.]	Main exclusion criteria	Method for IDDVT diagnosis	Treatment	Principal VTE outcomes	Main bleeding outcomes
Anticoagulant treatment *versus* no anticoagulant treatment						
Lagerstedt *et al.*, 1985 [RCT open][28]	Symptomatic IDDVT [51]	Malignancy, and a history of recurrent thrombosis	^{99}Tc-plasmin, venography	UFH --> warfarin for 3 months *vs* no warfarin	Recurrence within 90 days: 0% *vs* 29% (p<0.01) Recurrence within one year: 4.3% *vs* 32.1% (p<0.02)	NA
Schwartz *et al.*, 2010 [RCT open][9]	Symptomatic muscular IDDVT [107]	Previous muscular IDDVT and remaining thrombotic material	US	Nadroparin (10 days) + compression therapy (3 months) *vs* compression therapy (3 months)	Progression to DVT at 90 days: 3.7% *vs* 3.8% (p=0.99). No PE in both groups	No MB in both arms
Horner *et al.*, 2014 [RCT open][16]	Symptomatic IDDVT [70]	Active cancer, and prior above knee DVT/PE	US	Dalteparin --> warfarin + compression therapy (3 months) *vs* compression therapy (3 months)	Symptomatic popliteal propagation and symptomatic PE at 90 days: 0% *vs* 11.4% (p=0.11)	No MB in both arms
Righini *et al.*, 2016 [RCT blind][17]	Symptomatic IDDVT [259]	Previous VTE, and active or recent malignancy	US	Nadroparin + compression therapy *vs* placebo + compression therapy (for 42 days)	Composite of progression to DVT, contralateral proximal DVT, or symptomatic PE at day 42 and at day 90 after randomisation: 3.3% *vs* 5.4% (p=0.54) and 3.3% *vs* 6.2% (p=0.28)	MB or CRNMB at day 42: 4% *vs* 0% (p=0.025)
Different anticoagulant treatment and/or duration						
Schulman *et al.*, 1995 [RCT open][30]	Acute PE and/or DVT [DDVT 347]	Cancer	Venography	UFH/LMWH (at least 5 days) --> VKA (6 wks) + compression therapy (at least 1 year) *vs* VKA (6 months) + compression therapy (at least 1 year)	Two-year incidence of recurrent thromboembolism in DDVT subgroup: 1.4% *vs* 5.8% (p=0.1)	NA

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Table 1. Continued from previous page.

Author, year [study design]	Population [No.]	Main exclusion criteria	Method for IDDVT diagnosis	Treatment	Principal VTE outcomes	Main bleeding outcomes
Pinede *et al.*, 2001 [RCT open][32]	Symptomatic DVT and/or PE [IDDVT 197]	Previous VTE, evolutive cancer or malignant hematological disease, known biological thrombophilia	US, venography	LMWH/UFH at least 5 days) --> (VKA (for 6 wks) *vs* VKA (for 12 wks)	Recurrent VTE: 2% *vs* 3.4% (RR 0.58; 95% CI, 0.10, 3.36)	MB: 1 *vs* 3.4% (RR 0.29; 95% CI, 0.03, 2.72)
Ferrara *et al.*, 2006 [RCT open][31]	DDVT in post-surgical patients. Group 1 (involving one collecting vein) and group 2 (involving more than one collecting vein) [68/124]	Neoplasia, malignant hematologic diseases, and inherited coagulopathies	US	Nadroparin (5-6 days) --> warfarin for 12 wks (subgroup A) *vs* warfarin for 6 wks (subgroup B)	Proximal extension at 12 wks: subgroup 1A - 1/34 *vs* subgroup 1B - 5/34 (p=0.197) and subgroup 2A - 6/62 *vs* subgroup 2B - 22/62 (p=0.001)	No severe bleeding in both arms
Ageno *et al.*, 2022 [RCT blind][33]	Symptomatic IDDVT [402]	Active cancer	US	Rivaroxaban 15 mg twice daily (3 wks) followed by rivaroxaban 20 mg once daily (3 wks) --> rivaroxaban 20 mg *vs* placebo once daily (6 wks)	Recurrent VTE (composite of progression of IDDVT, recurrent IDDVT, proximal DVT, symptomatic PE, or fatal PE) during follow-up after randomization: 11% *vs* 19% (p 0.03)	No MB in both arms after randomization 1 CRNMB in each arm after randomisation
Yamashita *et al.*, 2023 [RCT open][34]	IDDVT and active cancer [604]	Life expectancy of 3 months or less	US	Edoxaban (12 months) *vs* edoxaban (3 months)	Composite of symptomatic recurrent VTE or VTE-related death at 12 months: 1.0% *vs* 7.2% (OR, 0.13; 95% CI, 0.03 to 0.44)	MB at 12 months: 9.5% *vs* 7.2% (OR, 1.34; 95% CI, 0.75 to 2.41)
Sartori *et al.*, 2024 [RCT open][35]	Symptomatic IDDVT [260]	Active cancer and/or prior VTE	US	LMWH 1 mg/kg subcutaneously twice a day (2 wks) followed by 1 mg/kg subcutaneously once a day (4 wks) + compression therapy *vs* enoxaparin 1 mg/kg subcutaneously twice a day and concurrent warfarin (3 months) + compression therapy	Composite of progression to the proximal veins, recurrent IDDVT, extension of IDDVT, proximal DVT, symptomatic PE, and fatal PE at day 90 and day 180: 6.9% *vs* 0.8% (p=0.01) and 10.8% *vs* 3.8%(p=0.032)	1 MB in LMWH arm (0.7%) and 0 MB in warfarin arm. 1 CRNMB in each arm

VTE, venous thromboembolism; IDDVT, isolated distal deep vein thrombosis; DDVT, distal deep vein thrombosis; DVT, deep vein thrombosis; PE, pulmonary embolism; MB, major bleeding; UFH, unfractionated heparin; VKA, vitamin K antagonist; CRNMB, clinically relevant non major bleeding; LMWH, low molecular weight heparin; RCT, randomised-controlled trial; NA, not applicable; US, ultrasound.

ministration of warfarin after dalteparin for a duration of 3 months showed a non-significant trend toward lower proximal extension and symptomatic PE compared to no anticoagulation.[16]

The CACTUS trial, involving 259 low-risk patients experiencing symptomatic acute IDDVT, compared the efficacy of 6-week nadroparin treatment versus placebo. The use of nadroparin showed a trend in reducing the composite outcome of progression to DVT, contralateral proximal DVT, or symptomatic PE at 6 weeks and at 3 months after randomisation, without reaching statistical significance. Notably, the study was interrupted prematurely due to slow recruitment, reaching less than 50% of the original sample size. Additionally, the study found an increased bleeding risk in the nadroparin group.[17]

Franco *et al*. conducted a meta-analysis encompassing 2936 patients diagnosed with IDDVT across 20 distinct studies. The use of anticoagulation, at either prophylactic or therapeutic doses, was associated with a noteworthy reduction in the recurrence of VTE compared to no anticoagulation (OR: 0.50; 95%CI: 0.31-

0.79), without a statistically significant elevation in the risk of major bleeding (OR: 0.64; 95% CI: 0.15-2.73).[14]

The prospective, multicenter TWISTER study included low-risk ambulatory IDDVT patients who received therapeutic-dose anticoagulation (enoxaparin or rivaroxaban) for 2 weeks. If complete symptom resolution occurred without proximal extension, treatment was discontinued; otherwise, it was extended for additional 4 weeks. Although the study's findings were limited by a small number of events and lack of randomization, they indicated that this approach could be safe for low-risk patients.[29] Moreover, the optimal treatment duration has been investigated by several RCTs.[30-35]

In the study conducted by Ferrara *et al.*, there were two groups consisting of 68 patients with post-surgical IDDVT involving a single vein, and 124 patients with post-surgical IDDVT involving 2 or more veins. Each group was divided into two subgroups receiving nadroparin followed by warfarin for 6 or 12 weeks, respectively. A significant difference was observed only in subgroup of IDDVT involving 2 or more veins: proximal extension at 12 weeks was less frequent in patient treated with a longer duration of anticoagulation. No major bleeding was registered.[31]

On the other hand, the DOTAVK study showed that short-term anticoagulation (6 weeks) was sufficient in preventing VTE recurrence compared to long-term anticoagulation (3 months) after IDDVT in patients without cancer and/or previous VTE.[32]

Two recent studies evaluated the duration of anticoagulant therapy with DOACs in different IDDVT patient categories.[33,34]

In the RIDTS study, outpatients diagnosed with symptomatic acute IDDVT were treated with rivaroxaban 15 mg twice a day for 3 weeks, followed by 20 mg once a day for another 3 weeks. Subsequently, they were randomized to receive either 20 mg of rivaroxaban or placebo once a day for additional 6 weeks. The primary outcome was to assess the recurrence of VTE after randomization, while the primary safety outcome was the occurrence of major bleeding. Recurrent VTE was observed in 11% and 19% of patients in the rivaroxaban and placebo groups, respectively (RR 0.59, 95%CI 0.36-0.95; p=0.03). Notably, this result persisted across different subgroups, including patients with muscular vein thrombosis. No major bleeding events were registered in both arms after randomization.[33]

The ONCO-DVT study randomly assigned 604 Japanese patients with cancer and IDDVT to receive either a 12-month or 3-month edoxaban treatment. Primary composite outcome consisting of symptomatic recurrent VTE, or VTE-related death occurred in 1.0% of patients receiving 12 months edoxaban and in 7.2% of patients receiving three months edoxaban (OR 0.13; 95%CI: 0.03-0.44). Although there was a slightly higher incidence of major bleeding with the longer duration of anticoagulant treatment, the difference was not statistically significant.[34]

The recently published TODI study enrolled 260 patients with symptomatic IDDVT without active cancer or prior VTE and randomized them to LMWH followed by vitamin K antagonist (VKA) for 3 months or LMWH at a dose of 1 mg/kg subcutaneously twice daily for 2 weeks, followed by 1 mg/kg subcutaneously once daily for 4 weeks. The primary composite endpoint included recurrence or extension of IDDVT, proximal DVT and PE, and was assessed over a 6-month follow-up period. Results demonstrated a lower rate of recurrent VTE in patients who received 3-month warfarin compared to those who received 6-weeks of LMWH (3.8% *vs* 10.8%, p=0.032). Treatment with VKA did not result in increased bleeding risk. Notably, the study was interrupted prematurely before reaching the targeted number of participants.[35]

Elastic compression stockings (ECS) are commonly prescribed for individuals diagnosed with DVT to mitigate pain and edema during the acute phase and to reduce the risk of PTS.[36]

Due to insufficient evidence to guide clinical practice, the use of compression therapy after acute DVT remains controversial. The uncertainty is even greater regarding IDDVT, as most randomized trials assessing compression therapies were carried out on patients with proximal DVT.

Consequently, guideline recommendations primarily refer to acute proximal DVT, with unclear application to acute IDDVT, highlighting the need for further research in this population.[37]

Thus, there is currently no evidence to support the need for prescribing ECS for after calf DVT.

Finally, international guidelines on the management of IDDVT often provide weak recommendations with low to moderate certainty, reflecting the lack of a solid clinical basis.[11,12,37] Additionally, some major international guidelines on VTE do not offer specific recommendations for IDDVT, or do not include the latest research findings published.

The American College of Chest Physicians 2021 guidelines recommend serial US imaging for two weeks for patients with acute IDDVT without severe symptoms or risk factors for extension. They suggest starting anticoagulation, the same therapeutic regimen and duration used for acute proximal DVT, only if it extends proximally. In patients with acute IDDVT who have severe symptoms or risk factors for extension, anticoagulation is preferred to serial imaging.[12]

The European Society of Cardiology also suggests that IDDVT patients at high risk of recurrence receive at least three months of full anticoagulation, while those at low risk may benefit of a shorter LMWH regimen.[11]

According to the guidelines of the European Society for Vascular Surgery, patients with symptomatic IDDVT who are not receiving anticoagulation should undergo clinical reassessment and repeated whole-leg ultrasonography after one week. Patients with symptomatic IDDVT who require anticoagulation should be treated for three months or more, with direct oral anticoagulation (DOAC) preferred to LMWH followed by VKA. Finally, in patients with symptomatic IDDVT associated with active cancer, extension of anticoagulation beyond 3 months should be considered.[37]

Management of isolated distal deep vein thrombosis: *how I treat*

Symptomatic IDDVT outpatients should receive anticoagulant treatment. Large real-life registries indicate that up to 95% of IDDVT patients receive anticoagulation.[20,38,39]

In our experience, it is crucial to assess patients' thrombotic and bleeding risks before starting anticoagulation. This involves carefully evaluating acquired and inherited bleeding risk factors and patient characteristics such as renal function, platelet count, and body mass index. In the absence of bleeding risk factors, IDDVT patients should be treated with therapeutic-dose anticoagulation for 3 months, using the same approach as proximal DVT.

In patients with a high risk of bleeding, repeated US testing is a viable alternative. Anticoagulation should be started if proximal propagation or recurrent VTE is detected through serial imaging.

As previously mentioned, cancer-associated IDDVT has clinical outcomes that are like those of cancer-associated proximal DVT. Therefore, if there is no increased risk of bleeding, we typically treat these patients with extended-duration full-dose anticoagulation for as long as the cancer remains active.

According to 2022 ESC Guidelines, low thrombotic risk patients may benefit from a shorter LMWH regimen (*e.g.* 4-6 weeks), but the benefits of this strategy remain uncertain.[11]

Regarding the choice of anticoagulant, DOACs seem to be a safe and effective alternative to LMWH followed by VKAs.

Conclusions

Isolated distal deep vein thrombosis represents a common and clinically significant manifestation of VTE. Compared to proximal DVT, IDDVT is generally associated with a lower incidence of proximal propagation, VTE recurrence, PTS, and mortality. Nonetheless, certain subgroups of patients, such as those with active cancer, prior VTE, unprovoked IDDVT, and involvement of more than one vein, exhibit a non-negligible rate of these outcomes. Hence, risk stratification is imperative and should be conducted on an individualized basis.

The approaches recommended for managing symptomatic acute IDDVT are either anticoagulation for three months or six weeks or surveillance imaging only, based on the individual thrombotic and hemorrhagic risk. In real-world clinical practice, the predominant approach for managing IDDVT is the use of anticoagulant therapy. DOACs appear to be both safe and effective in this context. In cases of IDDVT associated with cancer, an extended-duration anticoagulation regimen is preferable.

The management of IDDVT remains challenging and requiring tailored therapeutic decisions. Further research is imperative to refine risk stratification and management protocols, encompassing considerations such as the type, intensity, and duration of anticoagulation, to provide physicians a way out of this dark forest.

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