Recent Advances in Anticoagulation Duration for Deep Vein Thrombosis at Different Sites of the Lower Limb: Postprint

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Abstract

Lower extremity deep vein thrombosis (LEDVT) represents a common vascular disease with increasing incidence. While extensive research has been conducted on its treatment, personalized optimal management remains limited. This article systematically examines anticoagulation duration for thrombosis at different anatomical sites of the lower extremity and, through comprehensive literature review, summarizes evidence-based recommendations for anticoagulation regimens in various locations including calf muscular veins, calf axial veins, femoropopliteal veins, and iliofemoral veins. This article posits that among deep veins at different lower extremity locations, distal deep vein thrombosis (DDVT) exhibits a high incidence, whereas proximal deep vein thrombosis (PDVT) is associated with higher probabilities of pulmonary embolism (PE) and post-thrombotic syndrome (PTS). Short-term anticoagulation (2–6 weeks) is recommended for DDVT, as extended duration provides no additional benefit and instead increases bleeding risk. PDVT and mixed-type LEDVT should receive medium- to long-term anticoagulation ($ $3 months), particularly femoropopliteal deep vein thrombosis (FDVT) that does not meet criteria for interventional therapy. Indefinite anticoagulation therapy merely postpones thromboembolism recurrence without truly reducing the risk of recurrent thrombosis. This article may serve as a reference for deepening understanding of LEDVT, optimizing anticoagulation regimens, and facilitating personalized anticoagulation therapy for LEDVT.

Full Text

Research Progress on Anticoagulant Therapy for Deep Vein Thrombosis in Different Parts of the Lower Extremity

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Abstract

Lower extremity deep vein thrombosis (LEDVT) is one of the common vascular diseases with its incidence increasing annually. Although extensive research has focused on treating LEDVT, personalized management strategies remain limited. This review systematically discussed the recommended duration of anticoagulant therapy for LEDVT in various locations of the lower extremities and summarized the evidence-based recommendations for the anticoagulation treatment of different parts of the calf intermuscular vein, calf axial vein, femoropopliteal vein, and iliofemoral vein. This review further emphasized that in different parts of the lower extremities, the incidence of distal deep vein thrombosis (DDVT) was high, while the probability of proximal deep vein thrombosis (PDVT) complicated with pulmonary embolism (PE) and post-thrombotic syndrome (PTS) is greater. Short-term anticoagulation (2-6 weeks) is recommended for DDVT. A prolonged anticoagulation course will not bring more benefits, whereas increases the risk of bleeding. PDVT and mixed LEDVT of lower extremities should be treated with medium and long-term anticoagulation ($\geq$ 3 months), especially for femoropopliteal deep vein thrombosis (FDVT) that does not meet the indications of interventional treatment. Indefinite anticoagulation treatment only delays the recurrence of thromboembolism, but does not really reduce the risk of thrombosis recurrence. The results of this review can provide reference for further understanding of LEDVT and optimization of anticoagulation course, as well as for personalized anticoagulation treatment of LEDVT.

Keywords: Lower extremity deep vein thrombosis; Anticoagulation therapy; Pulmonary embolism; Distal deep vein thrombosis; Proximal deep vein thrombosis

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1. Literature Search Strategy

Computer searches were conducted in CNKI, Wanfang Data Knowledge Service Platform, and PubMed databases from inception to May 2024. Chinese

search terms included "lower extremity deep vein thrombosis," "anticoagulation," "pulmonary embolism," "distal deep vein thrombosis," "proximal deep vein thrombosis," "calf muscular vein," "calf axial vein," "proximal deep vein thrombosis," "femoropopliteal vein," "iliofemoral vein," and "mixed LEDVT." English search terms included "Lower extremity deep venous thrombosis," "Anticoagulation therapy," "Distal deep vein thrombosis," "Calf muscular vein," "Axial calf vein," "Proximal deep vein thrombosis," "Femoropopliteal vein," "Proximal vein," and "Mixed LEDVT." Inclusion criteria comprised studies addressing anticoagulation efficacy in lower extremity DVT at different sites, including reduction of thrombosis recurrence, decreased complication rates, and occurrence of major bleeding during anticoagulation. Exclusion criteria included literature unrelated to the topic, unpublished studies, and articles where full text was unavailable. A total of 59 articles were ultimately included.

2. Distal Deep Vein Thrombosis (DDVT)

DDVT is confined to the deep veins below the knee joint. LEDVT can be classified as one of the five common vascular diseases and represents the third leading cause of death globally [1]. LEDVT typically arises from abnormal blood coagulation in lower extremity deep veins, constituting a venous system disease associated with pulmonary embolism (PE), collectively termed venous thromboembolism (VTE) [2]. LEDVT is categorized into distal deep vein thrombosis (DDVT) and proximal DVT (PDVT), with the former involving calf axial and muscular veins and the latter involving popliteal, femoral, and iliac veins [3], where the embolism risk is significantly greater in PDVT [4-6]. One study demonstrated that the 30-day VTE mortality rate was 2.6% for DDVT patients, 3.3% for PDVT, and 5.2% for PE [2]. In European and American countries, VTE incidence is 1-2 cases per 1,000 person-years, slightly higher than in Asian countries [2]. With current population aging trends, LEDVT incidence continues to rise annually, making its prevention and treatment a formidable task in healthcare. Thrombi formed by abnormal blood coagulation account for approximately half of all LEDVT cases [7]. DDVT can be further subdivided into calf axial DVT (thrombosis of peroneal, anterior tibial, and posterior tibial veins) and calf muscular DVT (thrombosis of soleal and gastrocnemius veins) [2,5], with the former exhibiting higher recurrence rates, propagation rates, and risk profiles than the latter [5,8-9]. This discrepancy may relate to anatomical and pathophysiological differences [10-11]. Calf axial veins primarily accompany their corresponding arteries, with blood return mainly facilitated by continuous arterial pulsation. Compared with muscular veins, calf axial veins have larger diameters, are closer to proximal veins, and receive numerous branches from soleal veins [10]. In contrast, calf muscular veins travel within the gastrocnemius and soleal muscles, where venous vessels are slender with slow blood flow, relying primarily on muscle pumps and venous valves to promote return [12]. However, some experts consider these merely different stages of the same disease [5,10]. Currently, domestic and international guidelines do not distinguish between the two in terms of anticoagulation duration [8,13]. Therefore,

whether patients with DDVT at different locations should receive identical anticoagulation courses or differentiated treatment remains fundamental to LEDVT prevention and management, though LEDVT anticoagulation duration has long been controversial. Current anticoagulation courses primarily reference acute or subacute triggers (e.g., surgery, fracture, hospitalization, inflammation, or oral contraceptives) and baseline or acquired risk factors (e.g., age, sex, body weight, genetic disease, or cancer) [2], rarely using thrombus location to guide anticoagulation. This article summarizes relevant literature to elaborate on anticoagulation duration and efficacy for LEDVT patients at different lower extremity sites.

2.1 Calf Muscular Vein Thrombosis (CMVT)

CMVT refers to thrombi formed by abnormal blood coagulation in gastrocnemius and soleal veins [12], occurring in 47%-79% of LEDVT patients [14].

2.1.1 CMVT Should Receive Anticoagulation Therapy Early concerns focused on whether CMVT patients required anticoagulation. SCHWARZ et al. [15] demonstrated in a prospective cohort study that short-term anticoagulation (10 days) showed no significant difference in efficacy and safety compared with compression therapy alone. Analyzing 107 patients with isolated CMVT divided into heparin group (n=54) and compression-only group (n=53), they found venous thrombus progression in 4 cases (3.7%) total: 3.7% (2/54) in the heparin group and 3.8% (2/53) in the compression-only group, with no major bleeding or PE in either group. At 3-month follow-up, thrombus recanalization rates showed no statistical difference [15]. Additionally, SALES et al. [16] reported that anticoagulation appeared to have no significant effect on thrombus progression in CMVT patients, with 76 of 141 CMVT patients (54%) receiving anticoagulation, yet 43 patients (30%) still experienced venous thrombus progression: 33% (25/76) in the anticoagulation group versus 28% (18/65) in the non-anticoagulation group (P=0.50) [16].

Conversely, MERRIMAN et al. [17] found that discontinuing anticoagulation after 2 weeks yielded only a 1.3% recurrence rate in DDVT patients. Their prospective study enrolled 241 DDVT patients, with 112 (46%) involving only muscular veins, followed up at 3 and 6 months. Among them, 167 patients (69%) received 2 weeks of anticoagulation, with 2 recurrences within $ $3 months; VTE recurrence occurred in 2 cases (2/156) (1.3% recurrence rate, 95%CI=0.05%-4.85%) within 3 months, with 11 patients lost to follow-up; 69% of patients experienced complete symptom resolution within two weeks; 8 patients (8/184) developed post-thrombotic syndrome (PTS) within $ $6 months (4.4% PTS rate, 95%CI=2.1%-8.5%), with no major bleeding reported, leading to the conclusion that stopping anticoagulation after 2 weeks is safe and effective [17]. Additionally, studies have shown that untreated CMVT may progress, with 16.3% potentially extending to adjacent calf axial veins and 2.9% progressing to proximal DVT [14], and severe cases may develop PE and PTS [12]. Therefore,

domestic and international experts increasingly recommend anticoagulation for CMVT patients [8,18].

2.1.2 Anticoagulation Treatment for CMVT In a retrospective study by GUO Yuanyuan et al. [19], 154 CMVT patients were randomly divided by anticoagulation duration into three groups: 4 weeks (n=52), 12 weeks (n=48), and 24 weeks (n=54). Results showed that 4-week short-term anticoagulation was non-inferior to medium- and long-term anticoagulation (12, 24 weeks) in terms of venous recanalization rate, recurrence rate, and post-discontinuation thrombosis recurrence. Among 62 patients who received 6-18 months of follow-up (40.1% follow-up rate), no statistical differences were found in recurrence rates or LEDVT incidence among the three groups (P>0.05) [19]. Furthermore, RIGHINI et al. [20] found in a randomized controlled trial that extending anticoagulation to 6 weeks did not benefit CMVT patients but increased bleeding risk. In their study of 259 CMVT patients randomized to 6 weeks of nadroparin or placebo, no significant difference was observed in reducing proximal extension or VTE events, while 5 patients (4%) in the nadroparin group experienced bleeding versus none in the placebo group (Risk difference=4.1, 95%CI=0.4-9.2; P=0.0255). KRET et al. [21] advocated active anticoagulation for CMVT patients but not long-term therapy, with the optimal duration being 2-4 weeks, as this is sufficient for DVT resolution. MA Yulin et al. [22] recommended at least 2 months of continuous anticoagulation for CMVT patients, dividing 87 patients into three groups: Group A (<1-2 months), Group B (2-3 months), and Group C ($ $3 months). After 1-year follow-up, 17 patients (19.5%) experienced LEDVT recurrence: 9 in Group A, 4 in Group B, and 4 in Group C. Comparing bleeding complications and recurrence rates among the three groups, Group B had slightly higher bleeding complications (7.4%) but without statistical difference (P>0.05); Group A had the highest recurrence rate (29.0%), followed by Group B, with Group C having the lowest, though no statistical differences were observed among groups (P>0.05).

2.2 Axial Calf Vein Thrombosis (ACVT)

ACVT refers to venous thrombi formed by abnormal blood coagulation in anterior/posterior tibial and peroneal veins [23]. The vast majority of ACVT patients have primary thrombosis, though some develop from CMVT progression.

2.2.1 ACVT Requires Longer Anticoagulation Than CMVT GALANAUD et al. [24] compared anticoagulation efficacy between 267 ACVT and 457 CMVT patients in a multicenter prospective study, finding similar outcomes in mortality (3.8% vs 4.1%), VTE recurrence (1.5% vs 1.4%), and major bleeding (0 vs 0.5%). However, treatment duration was significantly longer for ACVT patients [24]. SARTORI et al. [25] reached the same conclusion in a prospective trial, finding during 2-year follow-up after anticoagulation cessation that VTE recurrence in 90 DDVT patients was

unrelated to anatomical characteristics. Therefore, from an anticoagulation perspective, the treatment courses differ; from an outcomes perspective, both belong to DDVT. KUCZMIK et al. [4] standardized anticoagulation duration at 3 months, analyzing 647 calf DVT patients from the Gonda Vascular Center ultrasound database, divided into axial group (n=321) and muscular group (n=326). With 85.5% of patients receiving 3-month anticoagulation (median), 300-day follow-up revealed more frequent VTE recurrence in the axial group (15.9% vs 7.1%, P<0.0015), including more frequent DVT propagation (9.4% vs 3.1%, P<0.0017) and PE (3.4% vs 0.6%, P<0.0168). No differences were observed in major bleeding, clinically relevant non-major bleeding, or mortality between groups. Thrombus propagation was more frequent after anticoagulation cessation in the axial group (3.4% vs 0.9%, P<0.029). Thus, when ACVT patients receive the same treatment as CMVT, the former may have higher recurrence, resolution, and proximal propagation rates, while bleeding outcomes remain similar [5].

2.2.2 Anticoagulation Treatment for ACVT WOULFE et al. [26] retrospectively analyzed patients divided into three groups: <6 weeks, 6 weeks, and >6 weeks. Three cases of proximal propagation occurred, all in the <6 weeks group; 6 cases of VTE recurrence occurred, 3 in the <6 weeks group and 3 in the >6 weeks group. Researchers concluded that 6-week anticoagulation was non-inferior to >6 weeks, with similar proximal propagation and VTE recurrence rates. Significant differences in proximal propagation rates existed between <6 weeks and $ $6 weeks groups, leading to the recommendation against shorter courses. A retrospective study showed that when ACVT patients received 4-12 weeks of anticoagulation, recanalization rates for CMVT and ACVT were 41% [27]. SARTORI et al. [28] conducted a prospective, multicenter cohort study demonstrating 51% recanalization rate with 6-week anticoagulation for ACVT, enrolling 172 patients (76.7% CMVT, 14% ACVT, 9.3% with both). All received 6 weeks of low molecular weight heparin, with 51% achieving vascular recanalization, independent of distal DVT type [28].

3. Proximal Deep Vein Thrombosis (PDVT)

PDVT refers to thrombi formed by abnormal blood coagulation in deep veins at or above the popliteal vein [6], often leading to venous insufficiency and chronic venous hypertension [29]. Compared with DDVT, PDVT carries higher risks of PE and PTS [5]. Studies have shown that anatomical involvement site correlates with recurrence risk and PTS severity [30]. To optimize treatment, BOCHANEN et al. [6] proposed subdividing PDVT into iliofemoral and femoropopliteal DVT based on thrombus distribution differences, as significant variations exist in vascular anatomy, lower extremity muscle pump function, and gravitational effects [31]. This classification appears frequently in literature [32-33] and will be used herein. Furthermore, treatment selection differs between iliofemoral and femoropopliteal segments. Iliofemoral segment patients have more definitive treatment approaches favoring endovascular intervention [33], such as catheter-

directed thrombolysis and percutaneous mechanical thrombectomy, though effective iliofemoral treatments may not suit femoropopliteal segments. Both segments require anticoagulation, but because PDVT risk factors are typically chronic and persistent [34], long-cycle anticoagulation is necessary to improve prognosis [9].

3.1 Femoropopliteal Deep Vein Thrombosis (FDVT)

FDVT involves thrombi formed by abnormal blood coagulation in deep veins at or above the popliteal vein, typically not involving the common femoral or iliac veins [6,32]. Compared with iliofemoral segments, FDVT patients have lower PTS rates (0.6/0.4) [35], though more FDVT-related PTS patients may present clinically because femoropopliteal thrombosis occurs three times more frequently than iliac system thrombosis [35]. Current treatment for FDVT remains controversial due to thrombus extent and location.

3.1.1 Endovascular Therapy Is Not First-Line for FDVT With medical advances, physician perspectives have shifted from actively preventing complications to early complete thrombus clearance, with endovascular therapy increasingly applied to FDVT patients [36]. LIU et al. [37] reported 87% complete recanalization of femoropopliteal segments with endovascular therapy and only 17% PTS incidence during mean 20-month follow-up. However, KEARON et al. [38] found suboptimal endovascular outcomes, randomizing 300 FDVT patients to pharmacomechanical catheter-directed thrombolysis (PCDT) plus anticoagulation versus anticoagulation alone (no PCDT) with 24-month follow-up. No differences were observed in PTS incidence (27% PCDT vs 32% no PCDT) or recurrent VTE (16 PCDT vs 12 non-PCDT, P=0.24) [38]. MAGNUSON et al. [39] also concluded that endovascular intervention is not preferred for FDVT, with standard anticoagulation being the economically dominant strategy, showing only moderate value when FDVT involves iliofemoral segments [40].

3.1.2 Anticoagulation Treatment for FDVT DOUKETIS et al. [41] analyzed PDVT patients at different proximal locations, finding FDVT recurrence rates of 5.1% (57/1,098) during the first 3 months of anticoagulation, similar to the overall recurrent VTE rate of 5.5% (63/1,149). Conversely, iliofemoral DVT patients had 11.8% recurrence (6/51), double the FDVT rate. Thus, anticoagulation appears more effective for FDVT than iliofemoral DVT. Additionally, KEARON et al. [38] found that 88% of PDVT patients receiving anticoagulation alone chose 6-month courses, while only 46% continued for 24 months. COUTURAUD et al. [42] randomized 104 first-time unprovoked PDVT patients to 6-month placebo (n=54) versus extended 18-month anticoagulation (n=50). During treatment, the extended group had no VTE recurrence or major bleeding, while 16 placebo patients (29.6%) had VTE recurrence (HR=0.03, 95%CI=0.01-0.09, P<0.001). However, post-treatment follow-up showed similar outcomes: 14 extended-group patients (36.8%) and 17 placebo patients (31.5%) experienced VTE recurrence (HR=0.72, 95%CI=0.35-1.46). Multiple studies

demonstrate that continuous anticoagulation prevents recurrence and reduces complications, but effects do not persist after discontinuation, with bleeding risk increasing proportionally to treatment duration [42-43]. Due to limited literature on FDVT treatment, whether medium- to long-term (3-6 months) anticoagulation is superior to indefinite anticoagulation or intervention remains unclear. Current domestic consensus recommends at least 3 months of anticoagulation for PDVT patients, extending to at least 6 months postoperatively if receiving vascular intervention [33-44].

3.2 Iliofemoral Deep Vein Thrombosis (IDVT)

IDVT involves thrombi formed by abnormal blood coagulation in iliac and common femoral veins, with or without inferior vena cava involvement [6]. Compared with other segments, iliofemoral veins carry the highest risk for PE and PTS [35-36]. The 2014 AHA scientific statement noted that anticoagulation alone for IDVT yields poor prognosis [45], with over 50% developing PTS [46]. Current evidence supports endovascular therapy for IDVT to achieve early thrombus clearance and reduce PTS incidence [47], with anticoagulation primarily used post-intervention to reduce recurrence [36].

3.2.1 Endovascular Therapy Is Preferred for IDVT Anticoagulation alone appears inadequate for preventing PTS and protecting venous valves. ABRAMOWITZ et al. [48] found mechanical thrombectomy significantly reduced PTS compared with guideline-recommended anticoagulation (3-6 months), with PTS rates reduced by 27% and 21% at 6 and 12 months postoperatively, respectively, and significantly lower mean Villalta scores at 30 days. TSAI et al. [49] compared catheter-directed thrombolysis (CDT) plus anticoagulation versus anticoagulation alone for acute IDVT, with anticoagulation durations of 10 (3-25) months and 12 (3-48) months, respectively (P=0.124). Thrombus resolution rates at 1, 3, 6, and 9 months were 75.2%, 84.5%, 89.4%, and 91.7% in the CDT group versus 22.9%, 52%, 71.6%, and 81.6% in the anticoagulation group. The anticoagulation group only reached significant resolution at 6 months (71.6%), approximating the CDT group' s initial efficacy (75.2%). No significant difference was found in the anticoagulation group before and after the 5-month subgroup cutoff (>5 months vs $ $5 months, P=0.627) [49]. Consequently, endovascular therapy has become the preferred treatment for IDVT [34], with postoperative completion of 3 months of standard anticoagulation encouraged rather than indefinite extension, which shows no clear improvement in adverse thrombotic outcomes.

3.2.2 Indefinite Anticoagulation Extension BRADBURY et al. [50] randomized 281 PDVT patients to non-extended (3 months anticoagulation, n=140) versus extended (3 months plus continuation, n=141) groups. At 2-year follow-up, extended anticoagulation significantly reduced VTE recurrence (2.75 events/100 patient-years vs 13.54 events/100 patient-years, aHR=0.20, 95%CI=0.09-0.46, P<0.001), with no differences in PTS or major bleeding.

Similarly, SCHULMAN et al. [51] treated 545 LEDVT patients with 6 weeks or 6 months of anticoagulation, following them for 10 years and finding no differences in 10-year PTS incidence or VET recurrence rates (31% in 6-week group vs 27% in 6-month group). For idiopathic PDVT patients, increased anticoagulation duration merely delays rather than reduces recurrence risk, with similar recurrence rates observed in the first year after discontinuation [43]. Moreover, extended anticoagulation shows suboptimal effects in preventing PTS regardless of duration.

4. Mixed LEDVT

LEDVT is a common vascular disease with considerable controversy regarding treatment selection and anticoagulation duration across different anatomical locations. When thrombi involve two or more non-coagulating vessels or limbs throughout the lower extremity deep venous system, it is termed mixed lower extremity deep vein thrombosis, which presents more severe symptoms and prognosis than isolated thrombosis. Studies show patients with bilateral limbs or multiple distal veins have >3-fold increased VTE recurrence risk after anticoagulation cessation [52], with thrombus quantity correlating with prognosis [53]. GALANAUD et al. [24] demonstrated worse prognosis for bilateral CMVT, with 17.4% mortality at 3 months, even higher than unilateral proximal DVT (6.1%). Currently, no unified treatment protocol exists for mixed LEDVT in clinical practice. Some studies suggest 6-week anticoagulation appears effective for isolated calf DVT [18], while patients with multiple DDVT, malignant tumors, permanent risk factors, or idiopathic causes require >12 weeks [23]. FERRARA et al. [54] evaluated optimal anticoagulation duration for patients with one or more DDVT, enrolling 192 calf DVT patients (124 with $ 2 veins involved) randomized to 6 or 12 weeks of anticoagulation. No significant differences were found between
0.197). However, significant differences existed between subgroups 2A(2 veins, 12 weeks) and 2B($2
veins, 6 weeks) (P=0.01). Researchers concluded that 6 weeks suffices for isolated single distal vein thrombosis, with 12 weeks required only when $ $2 calf veins are involved, though these findings alone cannot unify treatment standards and require further investigation. When mixed LEDVT involves vessels above the popliteal vein, treatment favors endovascular therapy [55], with prompt intervention recommended for proximal mixed LEDVT to facilitate early thrombus clearance, protect venous valve function, and reduce PTS incidence. HAIG et al. [55] enrolled 176 PDVT patients (87 thrombolysis, 89 anticoagulation), finding at 5-year follow-up that recurrent VTE occurred in 13 thrombolysis patients (15%) versus 21 anticoagulation patients (24%). PTS developed in 37 thrombolysis patients (43%, 95%CI=33%-53%) versus 63 anticoagulation patients (71%, 95%CI=61%-79%) (P<0.0001), representing absolute risk reduction of 28% (95%CI=14%-42%). ZHANG Mingzhao et al. [56] demonstrated that postoperative adjuvant anticoagulation for 12 weeks after endovascular treatment for acute mixed unilateral LEDVT was effective, with only 1 recurrence during 10-14 months of follow-up.

In summary, CMVT may receive regular follow-up or short-term anticoagulation for 2-4 weeks, with duration appropriately extended when disease progression or chronic, persistent high-risk factors are present. ACVT patients are recommended to receive 2-4 weeks additional anticoagulation beyond CMVT protocols. Current domestic and international guidelines [8,13] do not clearly distinguish between the two, partly because calf DVT anticoagulation duration remains controversial and ACVT literature is limited. IDVT and proximal mixed LEDVT should prefer endovascular therapy with at least 3 months of postoperative standard anticoagulation. As endovascular techniques advance, FDVT treatment is no longer limited to anticoagulation alone, though whether endovascular therapy is superior requires further validation. Currently, cancer and postoperative bedridden patients are high-risk LEDVT populations who should receive extended anticoagulation.

The advent of novel oral anticoagulants has eliminated the need for real-time monitoring of prothrombin time (PT) and international normalized ratio (INR), largely paving the way for indefinite anticoagulation extension. However, this does not imply uniform anticoagulation for all LEDVT patients. With precision medicine concepts deepening, existing treatment guidelines require further refinement to provide targeted guidance for different LEDVT locations. For instance, whether distal DVT anticoagulation duration can be discussed separately for axial versus muscular veins to provide more precise treatment protocols, and whether FDVT as a proximal DVT should prefer anticoagulation or endovascular therapy requires more clinical trials. Additionally, D-dimer, an important indicator for excluding and screening thrombosis, has limitations in guiding anticoagulation discontinuation. Developing scientifically reasonable discontinuation scoring criteria combined with D-dimer warrants exploration.

As primary care providers offering comprehensive diagnosis and treatment, general practitioners play crucial roles in LEDVT patient management, diagnosis, treatment, and long-term care. Thoughtful management approaches remain priority options for patients requiring long-term or permanent anticoagulation, particularly in elderly populations with multiple chronic diseases (e.g., hypertension, diabetes, heart disease) that directly or indirectly influence anticoagulation decisions. Based on understanding individual patient characteristics and chronic conditions, general practitioners should develop effective and reasonable thrombosis prevention and treatment protocols to ensure anticoagulation efficacy and safety while helping patients improve disease awareness, closely monitoring coagulation function and bleeding tendency, and providing timely, effective referrals when conditions deteriorate.

In conclusion, regardless of how anatomical classification is refined, all constitute factors within LEDVT. Different anticoagulants have varying courses, though this article does not further categorize drug types because multiple studies show direct oral anticoagulants and other agents have VTE recurrence rates $ $3.5% in clinical trials without statistical differences [2,57-59]. Only by fully understanding reversible and irreversible LEDVT risk factors, thrombus anatomical

location, size, and morphology can we comprehensively understand the disease, avoid treatment risks, develop effective individualized prevention strategies, and improve patient prognosis. Therefore, deeper clinical research in this field remains necessary.

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