EDITORIAL

European Society for Vascular Surgery (ESVS) 2021 Clinical Practice Guidelines on the Management of Venous Thrombosis

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The European Society for Vascular Surgery (ESVS) has developed a series of clinical practice guidelines for the care of patients with vascular diseases[1]. Their aim is to provide an evidence-based standard that helps clinicians in selecting the best management strategies to achieve optimal patient outcomes. Until now, the American College of Chest Physicians (ACCP) clinical guidelines for venous thromboembolism (VTE) management[2], the International Union of Angiology (IUA),[3] and more recently the American Society of Hematology (ASH) guidelines[4,5], have been used for such patients. These are the first ESVS guidelines on venous thrombosis (VT). The ESVS VT guidelines address acute deep vein thrombosis (DVT) of the lower extremity, upper extremity DVT (UEDVT), superficial vein thrombosis (SVT), thrombosis in unusual sites and catheter related thrombosis (CRT).

A literature search to 31 March 2018 was performed, as well as reference checking and hand searches by individual members of the Guideline Writing Committee (GWC). Aggregated evidence studies including meta-analyses, randomized controlled trials (RCTs), and observational studies were analyzed. The strength of recommendations were based on the quality of the studies relating to the specific recommendation. The level of available evidence for each section was used to guide the class of each recommendation in the guideline. The ESVS 2021 includes 72 recommendations, 33 of them are Class I, 21 are Class IIa, 7 are Class IIb recommendations, and 11 are Class III recommendations. The strength of evidence on which these recommendations were based was relatively weak, similar to the ACCP and ASH guidelines, with the vast majority of the recommendations being based on levels of evidence B and C which are considered to be moderate levels of evidence. The GWC also included some flowcharts of recommendations for the diagnosis and investigation of DVT, treatment for provoked and unprovoked DVT, and treatment for superficial vein thrombosis, promoting greater understanding of the sequence of steps for ideal management of the vascular disease.

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ISSN 2732-7175 / 2022 Hellenic Society of Vascular and Endovascular Surgery Published by Rotonda Publications

As expected ESVS VT 2021 guidelines have provided some novel recommendations compared with older guidelines. First, they highlight the significant need for including specific types of venous thrombosis and patient populations, as children, pregnant women, and cancer associated thrombosis (CAT). Secondly, the duration of principal - primary anticoagulation treatment for DVT is recommended for 3 months, contrary to ASH guidelines which proposed the period of 3 to 6 months as primary treatment. In this field, for patients with a provoked proximal DVT and a major transient risk factor, ESVS guidelines recommend anticoagulation therapy for three months over a shorter duration as a Class I recommendation, while ASH guidelines recommend a more extended period of three to six months. In contrary, the updated ACCP guidelines suggest against extending treatment more than 3 months for patients with VTE and major transient risk, while they have included recommendations for an extended phase therapy only in the absence of transient risk.

Moreover, according to ESVS 2021 VT guidelines initial and principal treatment of unprovoked proximal DVT is generally the same as with provoked DVT, with a direct oral anticoagulant (DOAC) being recommended over a vitamin K antagonist (VKA), as strong Class I recommendation and level of evidence A. Also in the same context, the recently updated ACCP guidelines suggested dabigatran, rivaroxaban, apixaban, or edoxaban over VKA therapy as anticoagulant therapy for a 3-month treatment phase with a strong recommendation, while ASH 2020 also agreed but with only moderate certainty[2,3]. A thorough discussion of the optimal anticoagulant therapy in cases needed extended therapy is also included in ESVS guidelines.

The authors of ESVS guidelines attempted to include the concept of patient status re-assessment when anticoagulation therapy is suggested. For patients with provoked proximal DVT and a persistent risk factor other than malignancy, ESVS guidelines are comparable to ACCP and ASH suggesting that anticoagulation beyond three months should be considered after evaluation of thrombotic and bleeding risks. Similarly, for patients with unprovoked DVT, continuing anticoagulation be-

yond three months is strongly recommended as Class I in ESVS guidelines, while both updated ACCP and ASH guidelines also include the recommendation of extended treatment in such cases. All guidelines have suggested reassessment of bleeding risk in such patients before deciding to proceed with, or continue, the extended-phase anticoagulation therapy.

For patients with unprovoked proximal DVT requiring extended anticoagulation beyond three months, a recommendation (Class IIa) with Level of Evidence B is included in ESVS guidelines for treatment with DOAC over VKA, as it is similarly suggested by updated ACCP. Although the same suggestion is supported by ASH guidelines, it is referred to as a Grade 2C, a weaker grade of recommendation. The ESVS guidelines diverge from ASH in respect to the patients with unprovoked proximal DVT requiring extended anticoagulation beyond six months, suggesting that a reduced dose of the DOAC apixaban (2.5mg twice daily) or rivaroxaban (10mg once daily) should be considered, as Class IIa, level B recommendation when ASH guideline panel less strictly suggests using either a standard-dose DOAC or a lower-dose DOAC. Recently, the updated ACCP also included the same suggestion as ESVS with a weaker level of recommendation.

In the field of Catheter-Directed Thrombolysis (CDT) for Acute DVT of the Leg, ESVS guidelines made an impactful change compared to ACCP and ASH which both suggest anticoagulant therapy alone over CDT. ESVS guidelines suggest that early thrombus removal strategies should be considered (Class IIa), especially in patients who are at highest risk of developing post-thrombotic syndrome (PTS), such as those with symptomatic iliofemoral deep vein thrombosis. The early thrombus removal reduces moderate to severe PTS, as referred by the authors, but also increases major bleeding.

An important suggestion in respect to the use of elastic stockings for acute DVT of the leg has been included in the ESVS guidelines. For patients with proximal DVT, early compression at 30 - 40 mmHg with either multilayer bandaging or compression hosiery, applied within 24 hours, is recommended to reduce pain, oedema, and residual venous obstruction, with a strong recommendation (Class I, level A). Moreover, in proximal DVT, use of below knee compression stockings should be considered to reduce the risk of post-thrombotic syndrome, as Class IIa. In proximal DVT with limited symptoms and signs, as described in the Villalta score, it is recommended as Class I, to limit the use of below knee stockings to six or 12 months. This guidance supporting the use of elastic stockings from ESVS contrast with both ACCP and ASH guidelines which suggest against using compression stockings routinely to prevent PTS (Grade 2B). Prevention of PTS has been discussed in ESVS guidelines although the clinical effectiveness of ECS in PTS prevention has yet to be identified.

Recommendations for patients with calf vein DVT have been included in ESVS guidelines as specified patient population although there is a lack of RCTs specific for different clinical scenarios. With this in mind, the authors suggested use of anticoagulation based on low level evidence (level C) as anticoagulation has been proved to be superior to no anticoagulation. Precisely, in patients with calf DVT, a decision for anticoagulation based on symptoms, risk factors for progression and bleeding risk should be considered as Class IIa, level C recommendation. What is more, for those with symptomatic calf DVT requiring anticoagulant treatment, three months of therapy is strongly recommended over shorter durations, as Class I, level A recommendation.

For patients with cancer-associated DVT, a low-molecular weight heparin (LMWH) is recommended for initial and principal phase anticoagulation (Class I, level A) as they are more effective than VKA. This contrasts the updated ACCP, which suggest the use of oral Xa inhibitor (apixaban, edoxaban, rivaroxaban) over LMWH for the initiation and treatment phases of therapy, as a strong recommendation. However, it is noticed by the authors that both apixaban and LMWH may be the preferred option in patients with luminal GI malignancies who place higher value on avoiding GI major bleeding, since edoxaban and rivaroxaban appear to be associated with a higher risk of gastrointestinal major bleeding compared to LMWH. Recently ASH guidelines specific for cancer patients are also in contrast with ESVS suggesting either apixaban, rivaroxaban or LMWH for initial treatment of VTE as a conditional recommendation with very low certainty of evidence. ESVS guidelines have suggested that for patients with malignancy not located in the gastrointestinal or genitourinary systems, an approved DOAC for initial, principal and extended treatment should be considered as Class IIa, level of evidence A, based on studies reporting effectiveness of DOAC over the LMWH dalteparin in preventing VTE recurrence. However, it is noticed that a non-significant trend for a higher risk for major bleeding accompany DOAC rather than the LMWH dalteparin.

ESVS has included some key points regarding to use of the Inferior Vena Cava (IVC) filters. While ACCP recommends against the use of an IVC filter in addition to anticoagulants (Grade 1B) and ASH suggests anticoagulation alone rather than anticoagulation plus insertion of an IVC filter (Grade 2B), the ESVS VT guidelines report that during the initial or principal treatment phase, temporary IVC filter insertion is recommended, as Class IC recommendation, for patients with proximal DVT who have contraindications to anticoagulation. In the same context, the updated ACCP has also included the same suggestion with strong recommendation grade, while the updated ASH for cancer patients included the use of an IVC filter as a remark suggesting that it may be required in such cases as well. For patients who are anticoagulated for DVT, all three guidelines' panels agree against the routine use of IVC filters.

In conclusion, some key points and initiatives in comparison to other guideline panels have been identified to help clinicians improve their practice, underlying the need for high-quality comparative effectiveness research in the venous thrombosis field in order to improve healthcare. Meticulous evaluation of the published literature made it possible for the ESVS VT authors to develop well justified recommendations for optimal clinical practice and ultimately improvement of the outcomes of patients with venous thrombosis. Although some uncertainty remains regarding management of special patient populations, ESVS VT 2021 have provided lucid guidelines for

Venous Thrombosis based on the latest data for management of vascular disease.

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