Cochrane for Clinicians

Putting Evidence Into Practice

Antiplatelet Agents for the Treatment of Deep Venous Thrombosis

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Author disclosure: No relevant financial relationships.

Clinical Question

Is adding an antiplatelet agent for the treatment of deep venous thrombosis (DVT) safe and effective for preventing future complications?

Evidence-Based Answer

Best medical practices for the initial treatment of uncomplicated DVT include anticoagulation, compression stockings, and physical exercise. In the management of DVT (both acute [i.e., treatment started within 21 days of symptom onset] and chronic [i.e., treatment started after 21 days of symptom onset]), adding an antiplatelet agent to standard practices does not show clear benefits or cause significant adverse effects.[1] (Strength of Recommendation: B, inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

After stroke and myocardial infarction, venous thromboembolism (VTE; includes pulmonary embolism [PE] and DVT) is the third most common cardiovascular disease diagnosed worldwide. The incidence of DVT (the most common VTE) is increasing with the aging population, and there are more than 100,000 PE-related deaths in the United States per year.[2]

Anticoagulation with direct oral anticoagulants, warfarin, or heparin is part of the standard initial treatment for DVT. Secondary treatment options include thrombolysis, mechanical thrombectomy, inferior vena cava filter, angioplasty, and stenting. Several studies have been done to assess whether adding antiplatelet agents to standard anticoagulation decreases the risk of recurrent VTE and mortality.

The Cochrane review included six randomized controlled trials (RCTs) with 1,625 adult participants from the United States, Canada, Europe, India, Argentina, Australia, and New Zealand.[1] Two groups were studied: participants with acute DVT and participants with chronic DVT. The length of treatment with antiplatelet agents varied from six months to two years. Treatment with antiplatelets varied from six to 24 months, but some studies presented follow-up data up to 37.2 months (exceeding treatment time). All studies used best medical practices or best medical practices plus placebo for comparison. Best medical practices were sometimes mentioned in the studies but were not comprehensively defined. Each comparison investigated the effects of antiplatelets on the recurrence of DVT, PE, mortality, and adverse effects. Four studies used various antiplatelet agents: dipyridamole; aspirin, 300 mg four times per day; sulfinpyrazone (Anturane), 800 mg per day; and indobufen (not available in the United States), 200 mg twice per day. Two trials used aspirin in a dosage of 100 mg per day. The authors considered all RCTs that used antiplatelet therapy at the same time as or after anticoagulation and analyzed the two groups separately.

There was no meta-analysis of patients treated with antiplatelet agents in acute DVT. Only one study addressed acute DVT, which yielded results of very low certainty.

The meta-analysis did not reveal a statistically significant benefit for the outcomes of mortality or progression to PE, and there was no increased risk of bleeding or other adverse effects in patients with chronic DVT who were receiving antiplatelet therapy. Use of antiplatelet therapy in addition to best practices decreased the risk of recurrent VTE compared with placebo (number needed to treat = 14; 95% CI, 8 to 125; four studies; 901 participants). However, when only PE was studied, antiplatelet agents did not achieve a difference between the groups.

The 2021 CHEST guidelines from the American College of Chest Physicians for the management of VTE recommend the use of direct oral anticoagulants as first-line treatment for acute

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This series is coordinated by Corey D. Fogleman, MD, assistant medical editor.

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DVT or PE.[3] For patients with VTE and otherwise stable cardiovascular disease, the CHEST guidelines suggest suspending aspirin therapy when initiating anticoagulation. The combination of anticoagulation plus aspirin does not seem to decrease mortality risk.

Editor's Note: The number needed to treat and related CI reported in this Cochrane for Clinicians were calculated by the authors based on raw data provided in the original Cochrane review.

The practice recommendations in this activity are available at https://www.cochrane.org/CD012369.

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Foot Orthoses for Treating Flat Feet in Children

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Author disclosure: No relevant financial relationships.

Clinical Question

Does treatment with customized or prefabricated foot orthoses improve pain, function, or quality-of-life scores in children with flat feet (pes planus)?

Evidence-Based Answer

Customized or prefabricated foot orthoses do not result in significant improvements in pain, function, or parent and child quality-of-life scores. Importantly, quality-of-life scores were not reported in patients who were asymptomatic. There is a need for further targeted studies to identify the clinical utility of foot orthoses in children with flat feet that are associated with underlying conditions; however, asymptomatic flat feet in children should not be routinely treated.[1] (Strength of Recommendation: C, consensus, disease-oriented evidence, usual practice, expert opinion, or case series.)

Practice Pointers

Flatfoot is a common condition estimated to affect 44% to 70% of children three to six years of age.[1] Historically, foot orthoses have been suggested as treatment to promote postural stability and efficient gait function. However, recent data suggest that the use of foot orthoses in childhood flatfoot may not be necessary.[2,3] Flat feet develop as a child ages and usually self-correct without the need for intervention.[4] This Cochrane review evaluated whether customized or prefabricated foot orthoses provided benefits to children with flat feet in patient-reported pain levels, functional status, or parent and child quality-of-life scores.

The Cochrane review included 16 trials with a total of 1,058 participants ranging from 11 months to 19 years of age, all with flexible flat feet. The trials were conducted in outpatient clinics in nine countries (Australia, United States, United Kingdom, Iran, Egypt, Turkey, Republic of Korea, India, and Taiwan). The authors included studies that evaluated one of several major outcomes, including pain measures, gait and function assessment, and health-related quality-of-life scores. Trials that included validated outcome measures in which multiple measures were evaluated were preferentially included. Several well-validated childhood pain scales assessed pain outcomes and provided objective measures, such as functional data scales, including the Foot Function Index, timed walking, timed up and go test, six-minute walk test, and vertical jump height. The Pediatric Quality of Life Inventory assessed child- and parent-rated quality of life.

Patients who experienced little pain at the beginning of the trial showed little improvement in pain scores. Custom and prefabricated foot orthoses, compared with each other and with shoes, resulted in little to no reduction in the proportion of children reporting pain. There were no statistically significant benefits, and all included studies were considered low to very low quality on the GRADE scale.

Some improvements were noted when children with symptoms, specifically those with juvenile idiopathic arthritis, were included in the studies. In these patients, customized foot orthoses compared with shoes resulted in a small improvement in clinical function and child- and parent-rated

quality of life. Prefabricated foot orthoses compared with shoes showed no significant change in these outcomes. When comparing customized foot orthoses with prefabricated foot orthoses, there were no differences in improvement in pain or function.

None of the trials were at low risk of bias; many trials were at risk for selection, performance, detection, and selective reporting biases. The review authors further downgraded the data due to small sample size and small effects across scaled outcome measures. The authors of this Cochrane review encourage further research but only in relevant childhood foot conditions that cause symptoms.

Current practice guidelines from the American Academy of Family Physicians and the American Academy of Pediatrics suggest that painless childhood flat feet, which are flexible in nature, should be monitored without the need for intervention.[5,6] There is no routine recommendation if the condition is symptomatic; however, both organizations mention the limited data to support the use of foot orthoses to modify symptom burden. Family physicians should carefully consider the need for intervention in childhood flat feet on a case-by-case basis.

The practice recommendations in this activity are available at https://www.cochrane.org/CD006311.

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GLOSSARY OF EVIDENCE-BASED MEDICINE AND STATISTICAL TERMS

Term	Abbreviation	Definition
Sensitivity	Sn	Percentage of patients with disease who have a positive test for the disease in question
Specificity	Sp	Percentage of patients without disease who have a negative test for the disease in question
Predictive value (positive and negative)	PV+ PV-	Percentage of patients with a positive or negative test for a disease who do or do not have the disease in question
Pretest probability		Probability of disease before a test is performed
Post-test probability		Probability of disease after a test is performed
Likelihood ratio	LR	LR >1 indicates an increased likelihood of disease, LR <1 indicates a decreased likelihood of disease. The most helpful tests generally have a ratio of less than 0.2 or greater than 5.
Relative risk reduction	RRR	The percentage difference in risk or outcomes between treatment and control groups. Example: if mortality is 30% in controls and 20% with treatment, RRR is (30 - 20)/30 = 33%.
Absolute risk reduction	ARR	The arithmetic difference in risk or outcomes between treatment and control groups. Example: if mortality is 30% in controls and 20% with treatment, ARR is 30 - 20 = 10%.
Number needed to treat	NNT	The number of patients who need to receive an intervention instead of the alternative in order for one additional patient to benefit. The NNT is calculated as: 1/ARR. Example: if the ARR is 4%, the NNT = 1/4% = 1/0.04 = 25.
Number needed to harm	NNH	The number of patients who need to receive an intervention instead of the alternative in order for one additional patient to experience an adverse event.
95% confidence interval	95% CI	An estimate of certainty. It is 95% certain that the true value lies within the given range. A narrow CI is good. A CI that spans 1.0 calls into question the validity of the result.
Systematic review		A type of review article that uses explicit methods to comprehensively analyze and qualitatively synthesize information from multiple studies
Meta-analysis		A type of systematic review that uses rigorous statistical methods to quantitatively synthesize the results of multiple similar studies