



ASH CLINICAL PRACTICE GUIDELINES VENOUS THROMBOEMBOLISM (VTE)



Venous Thromboembolism Diagnosis and Management of Special Populations in Latin America

Educational Slide Sets

American Society of Hematology 2022 for the Management of Venous Thromboembolism Disease

Author:

Dr Juan Carlos Serrano Casas, MD, Central University of Venezuela
Clínica Cancerológica de Norte de Santander (North Santander Oncology Clinic)



Clinical Practice Guidelines

ASH, ABHH, ACHO, CAHT Group, CLAHT Group, SAH, SBHH, SHU, SOCHIHEM, SOMETH, Panamenian Society of Hematology, SPH, SVH.

2022 guidelines for venous thromboembolism diagnosis and management of Special Populations in Latin America

Ignacio Neumann, Ariel Izcovich, Ricardo Aguilar, Guillermo León Basantes, Patricia Casais, Cecilia Colorio, Cecilia Guillermo, Pedro Garcia Lazaro, Jaime Pereira, Luis Meillon, Suely Meireles Rezende, Juan Carlos Serrano, Mario Luis Tejerina Valle, Felipe Vera, Lorena Karzulovic, Gabriel Rada, Holger Schunemann.



Latin American ADOLOPMENT project

- The Latin American ADOLOPMENT project is a pilot collaborative effort of the following institutions
- Argentinian Society of Hematology (Sociedad Argentina de Hematología, SAH), Cecilia Colorio, MD
- Bolivian Society of Hematology and Hemotherapy (Sociedad Boliviana de Hematología y Hemoterapia, SBHH), Mario Luis Tejerina Valle, MD
- Brazilian Association of Hematology, Hemotherapy and Cellular Therapy (Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular, ABHH), Suely Meireles Rezende, MD PhD
- Chilean Society of Hematology (Sociedad Chilena de Hematología), Jaime Pereira, MD
- Peruvian Society of Hematology (Sociedad Peruana de Hematología, SPH), Pedro García Lázaro, MD
- Uruguay's Society of Hematology (Sociedad de Hematología del Uruguay, SHU), Cecilia Guillermo, MD
- Venezuelan Society of Hematology (Sociedad Venezolana de Hematología, SVH), Juan Carlos Serrano, MD
- Latin American Cooperative for Hemostasis and Thrombosis (Grupo Cooperativo Latinoamericano de Hemostasis y Trombosis, CLAHT), Patricia Casais, MD
- Mexican Association of Hematology (Asociación Mexicana de Hematología), Luis Meillon, MD
- Colombian Association of Hematology and Oncology (Asociación Colombiana de Hematología y Oncología), Guillermo Basantes, MD
- American Society of Hematology
- MacGRADE Center



GRADE-ADOLOPMENT is an explicit and systematic method for adoption, adaptation, or development of evidence-based recommendations derived from the existing GRADE-focused recommendation.



ASH Clinical Practice Guidelines on VTE

1. VTE prevention in surgical hospitalized patients
2. VTE prevention in VTE prevention in medical hospitalized patients
3. Acute VTE treatment (DVT and PE)
4. **Optimal management of anticoagulation therapy**
5. VTE prevention and treatment in cancer patients
6. Heparin-Induced Thrombocytopenia (HIT)
7. Thrombophilia
8. **VTE diagnosis**
9. **Pediatric VTE**
10. **VTE in the context of pregnancy surgical hospitalized patients**



How were the ASH guidelines were developed?

PANEL FORMATION

Each panel was formed following these key criteria:

- Balance of expertise (including disciplines beyond hematology, and patients)
- Attention to minimization and management of COI

CLINICAL QUESTIONS

10 to 20 clinically-relevant questions generated in PICO format (population, intervention, comparison, and outcome)

PICO QUESTION EXAMPLE

In a population of patients with low clinical probability of PTE, what is the best diagnostic strategy to assess a PTE hypothesis?

EVIDENCE SYNTHESIS

Evidence analysis for each PICO question x systematic review of effects:

- Desirable and undesirable effects
- Resource use
- Feasibility
- Acceptability
- Accessibility
- Patient values and preferences

MAKING RECOMMENDATIONS

Recommendations made by panel members based on evidence for all factors

ASH guidelines are reviewed annually by expert work groups convened by ASH. Resources, such as this slide set, derived from guidelines that require updating are removed from the ASH website.



How should patients and clinicians use these guidelines?

	STRONG Recommendation ("The panel recommends...")	CONDITIONAL Recommendation ("The panel suggests ...")
For patients	Most individuals would want the intervention.	Most individuals would want the intervention, but many would not.
For clinicians	Most individuals should receive the intervention.	Different choices will be appropriate for different patients, depending on their values and preferences. Use shared decision making.



OBJECTIVES:

To provide evidence-based guidelines on the diagnosis of VTE/PE and the treatment of VTE in children and during pregnancy.

METHODS

The GRADE ADOLOPMENT SYSTEM has allowed the adaptation of 3 ASH guidelines on VTE (Diagnosis, Pregnancy, and Pediatric chapters.)

- 12 local hematology societies formed a panel of guidelines made up of medical professionals from 10 Latin American countries.
- We have prioritized 10 questions about VTE diagnosis and 18 about management for special populations relevant in a Latin American context.
- Evidence analysis, benefits, and damages; also, to be considered are values and preferences, resources, accessibility, feasibility, impact, and equity in health.



Prevalence and Probability Pretest

- The diagnosis of venous thromboembolism (VTE) is based on an assessment of the clinical probability of VTE in a population before diagnostic tests (pretest probability, PTP)
- Patients are identified as low/intermediate/high probability or likely/unlikely to have VTE
- Low PTP (unlikely) = low VTE prevalence
(Intermediate)/high PTP (likely) = high VTE prevalence
- VTE prevalence in a population influences the predictive value of diagnostic tests



RESULTS OF THE LATIN AMERICAN GUIDELINES ANALYSIS

- Compared to the original guidelines,
- Significant changes have been made to 2/10 diagnostic recommendations
- And to 9/18 management recommendations
- (4 guidance changes and 5 strength changes).



Pretest PE probability based on clinical prediction rules



Revised Geneva score	
Component	Score
Pain on deep palpation	4
Previous DVT or PE	3
Unilateral lower limb pain	3
Tachycardia	0 / 3 / 5
Active malignant condition	2
Recent surgery or fracture	2
Hemoptysis	2
Age ≥ 65	1

Score ≥ 11: High PTP:
Score 4 to 10: Intermediate PTP
Score 0 to 3: Low PTP

Wells score for PE	
Component	Score
DVT Signs / Symptoms	3
No alternate diagnosis	3
Tachycardia	1.5
Immobilization / Surgery	1.5
Previous DVT or PE	1.5
Hemoptysis	1
Active malignant condition	1

Score > 6: High PTP:
Score ≥ 2 and ≤ 6: Intermediate PTP
Score < 2: Low PTP

Prevalence per PTP:
High PTP: ≥ 50%
Intermediate PTP: ~20%
Low PTP: ≤ 5%



Clinical prediction rules (PPT) for DVT:

Wells score for lower limb DVT

Component	Score
Active malignant condition	1
Localized sensitivity	1
Whole leg swollen	1
Calf swelling > 3 cm	1
Insect bite edema	1
Collateral superficial veins	1
Previous DVT	1
Bedridden/surgery	1
Paralysis	1
Alternate diagnosis	-2

Score ≥ 3 : high PTP ($\geq 50\%$ prevalence)

Score: 1 to 2: Intermediate PTP ($\sim 25\%$)

Score: 0 or less: low PTP ($\leq 10\%$)

Geneva score for PE

Component	Score
Age 65+	1
Previous PTE or DVT	3
Surgery or fracture within 1 month	2
Malignancy	2
Unilateral lower limb pain	3
Hemoptysis	2
Heart rate 75 to 94 per min	3
Heart rate 95 or more per min	5
Pain on deep palpation of lower limb and unilateral edema	4

Low probability 8% (score 0 to 3)

Intermediate probability 28% (score 4 to 10)

High probability 74% (score ≥ 11)

Wells NEJM 2003

Le Gal G, Ann Intern Med 2006

Kleinjan Ann Intern Med 2014



DIAGNOSTIC TEST ACCURACY



Studies that assess diagnostic tests (CTPA, D-Dimer, etc.) compared to the reference standard

	Sick	Healthy
Positive	TP	FP
Negative	FN	TN

$$S = TP / (TP + FN)$$

$$SP = TN / (TN + FP)$$

$$PPV = TP / (TP + FP)$$

$$NPV = TN / (TN + FN)$$

$$PPQ = S / (1 - SP)$$

$$NPQ = (1 - S) / SP$$

$$AI = (TP + TN) / (TP + TN + FP + FN)$$

$$YI = S + SP - 1$$

S = sensitivity; SP = specificity; PPV = positive predictive value; NPV = negative predictive value; PPQ = positive probability quotient; NPQ = negative probability quotient; AI = accuracy index; YI = Youden index

Pretest Probability
(VTE prevalence in a group)



Test Accuracy



VTE Post-Test Probability



Case 1: SUSPECTED PULMONARY EMBOLISM

64-year-old male

History: HBP, ischemic heart disease

Medication: Losartan, Carvedilol, Atorvastatin, Aspirin.

Arrives at E.R. with: chest pain, dyspnea, palpitations

- No data suggesting VTE, no cancer, QX, surgeries
- Recent mild bronchopneumonia in outpatient care

Examination: Heart rate of 93 per min, 90% saturation in ambient air, grade I/IV edema in lower limbs

Chest X-ray: Cardiomegaly

Clinical pretest probability (revised Geneva score)**low 3 pts**



Your patient's pretest probability for PE is low or intermediate.

Which of the following tests would you recommend to exclude PE diagnosis?

- A. Pulmonary angiography
- B. High-sensitivity d-dimer
- C. Bilateral leg compression ultrasound
- D. Electrocardiogram
- E. Chest X-ray



Recommendation 1 and 2

For patients with low pretest probability of a first episode or recurring PE ($\leq 5\%$), the Latin American ASH guidelines panel recommends the use of D-dimer to exclude PE (strong evidence-based recommendation due to high certainty about the effects $\oplus\oplus\oplus\oplus$), followed by a CT pulmonary angiogram (CTPA) in patients with positive D-dimer (conditional recommendation based on very low certainty about the effects $\oplus\bigcirc\bigcirc\bigcirc$).

Notes:

If CTPA is not available, an alternative could be a VQ scan followed by a proximal compression ultrasound (CUS,) if the VQ scan fails to discard or confirm the PE (conditional).

- Recommendation based on very low certainty about the effects $\oplus\bigcirc\bigcirc\bigcirc$)

The same diagnostic strategy is recommended for intermediate PTP patients (starting with D-dimer)



D-dimer diagnostic threshold

D-dimer has limited use in the following patient groups, due to the high frequency of positive results with standard thresholds:

- Hospitalized
- Post-surgery
- Pregnant

The use of "age-adjusted" D-dimer cutoff in 50+ outpatients is as safe as the standard cutoff and increases diagnostic usefulness

- Age-adjusted threshold = age (years) x 10 $\mu\text{g/L}$ (using d-dimer tests with a 500 $\mu\text{g/L}$ threshold)



Recommendations for Latin American Guidelines

- A change has been made to the Original Guidelines: D-dimer was used, followed by VP scintigraphy (VPS) and CT angiography should it not be available. The purpose is to lower exposure to radiation.
- The Latin American panel considered that D-dimer was affordable and generally available in the region; therefore, it was considered a reasonable first step to rule out PE.
- There is very limited VPS availability in Latin America, *therefore the choice to suggest a CT angiography instead of VP as a follow-up test in case of a positive D-dimer.*

SCINTIGRAPHY LIMITATIONS

Probability of a diagnostic result (normal or high probability)
Less feasible in case of: older people, preexisting pulmonary disease, abnormal chest X-ray.



Imaging considerations for VQ and CTPA scans in case of suspected PE



Limited institutional access or experience in Nuclear Medicine	VQ Scan	CTPA
At risk of reaction to contrast media requiring premedication	+	-
Concern about radiation issues in female breasts	+	-
Renal insufficiency	+	-
Suspected VTE recurrence or treatment failure with PE index diagnosed by VP scintigraphy	+	-
Suspected VTE recurrence or treatment failure with PE index diagnosed by CTPA	+	+/-
Concern about radiation affecting the fetus (especially in the first trimester)	+/-	+/-
Minimizing undiscovered VTE risk at 3 months	+/-	+/-
Requirement of timely result and both modalities accessible	-	+
Actively sought alternative or concomitant diagnoses (such as cancer)	-	+
Abnormalities present in plain radiography (hyperinflation, effusion)	-	+
Limited institutional access or experience in Nuclear Medicine	-	+



Case continued

- Due to low PESI score, the patient was placed on anticoagulation with Rivaroxaban 15 mg every 12 hours on an outpatient basis for 21 days, then Rivaroxaban 20 mg per day for 3 to 6 months due to symptoms caused by previous bronchopneumonia; patient took only one more month and abandoned treatment because another physician told them to.
- After 15 days, the patient had chest pain again with dyspnea and also an increase in the volume of the right leg with pain. Recurrent PTE is suspected.

What type of test would you recommend?

- A. Pulmonary angiotachy
- B. High-sensitivity d-dimer
- C. Bilateral leg compression ultrasound
- D. Electrocardiogram
- E. Chest X-ray



HIGH PROBABILITY OF RECURRENT PTE



- Recommendations 4 and 5
- For patients with high pretest probability of a first episode or recurring PE ($\geq 50\%$), the Latin American ASH guidelines panel recommends a strategy starting with CTPA (both conditional recommendations based on very low certainty about the effects $\oplus\bigcirc\bigcirc\bigcirc$)

Notes:

If clinical suspicion of PTE remains high after a negative CTPA, a follow-up with compression ultrasound or D-dimer may help rule out the diagnosis.

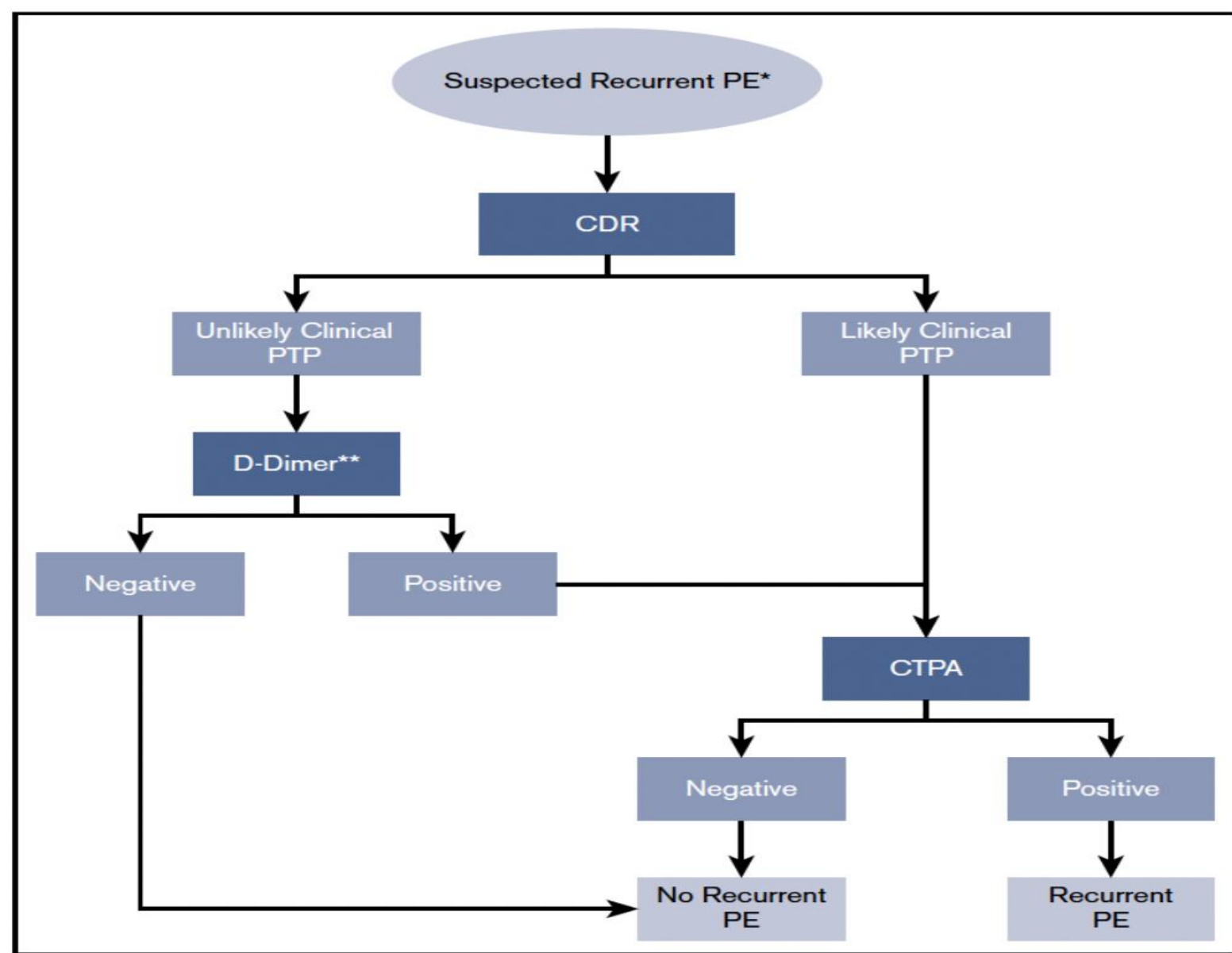
Conclusions:

- A pretest probability $\geq 50\%$ indicates that PE is the most likely diagnosis.
- Under such circumstances, the D-dimer can no longer safely discard PE.
- Many of the region's cases may require transfer to a center where CT angiography is available.
- The crucial decision to be made is whether to start empirical anticoagulation or wait for test results.
- When deciding, consider CT angiography delay, risk of death from PTE, bleeding, patient values and preferences.



PTE diagnosis flowchart for patients with pretest probability of recurrent episode

CDR = clinical decision rule (i.e., Wells or Geneva score)



PE: pulmonary embolism, CDR: clinical decision rule
CTPA: CT pulmonary angiogram, PTP: pretest probability

* Dynamically stable hemo ** High-sensitivity D-dimer



Case 1: Summary

In patients with low or intermediate PTP for PE, a negative high-sensitivity D-dimer may safely discard PE without the need for additional tests.

Latin American Guidelines for CT Angiography on VP Scintigraphy, especially for older patients or those with pre-existing lung disease.

Patients with suspected recurrent PE should be categorized between likely or unlikely PTP to determine further testing, despite the fact that clinical prediction rules have not been widely validated for recurrent PE.



VTE During Pregnancy



Objectives

When you finish this section, you should be able to:

1. Describe the recommendations for acute VTE management during pregnancy.
2. Identify pregnant patients who need VTE prophylaxis antepartum and/or postpartum



VTE is one of the main causes of morbidity and mortality during pregnancy

Venous thrombosis causes complications in roughly 1.2 in every 1,000 births

VTE incidence is similar during antepartum and postpartum periods, but **the postpartum period is shorter, thus increasing the daily risk of VTE**

Such increased risk persists until 12 weeks postpartum, **with higher risk during the first 6 weeks postpartum**

VTE diagnosis, prevention, and treatment during pregnancy must consider **fetal and maternal well-being**



Case 1: Deep vein thrombosis during pregnancy

28-year-old female patient, first pregnancy, 32 weeks, lives close to the city.

Personal History: Deep vein thrombosis at age 22, while taking oral contraceptives.

Medication: Vitamins, her doctor did not prescribe antithrombotic prophylaxis.

Arrives at E.R.:

With increased volume on the right leg over the past few days, chest pain and associated dyspnea. Fr 91 x mm, 91% sat.

Lower limb venous echo doppler:

Shows evidence of right femur DVT and analysis of the pulmonary CT angiography evidences bilateral subsegmental pulmonary embolism.

Pesi score 28 pts very low risk



Patient is 29 weeks pregnant and low-risk acute proximal DVT with pulmonary embolism, hemodynamically stable.

Where would you recommend this patient be treated?

- A. In hospital for at least 15 days
- B. In hospital for 48 hours and in outpatient care for the rest of the time
- C. Outpatient care for the entire period
- D. ICU admission

B and C are Correct



Recommendation 15

For pregnant women with DVT or TPE, and low-risk pregnancies (maternal or fetal factors), the Latin American ASH Guidelines recommends home treatment instead of hospitals (conditional recommendation based on a low probability on the evidence over the effects ⊕⊕○○)

PROS

- Patients value most the comfort of receiving home treatment
- This can lower health system costs
- Less functional and emotional impact

CAUTION:

Invalid option in high-risk cases:

Abnormal vital signs, analgesic needs, extensive VTE, advanced maternal age, maternal comorbidities

LMWH contraindications

CONS

- Evidence in pregnant women is limited (inconsistent data)
- Access to outpatient LMWH or FNH can be difficult in some countries
- Occasionally, pregnant women may feel safer in the hospital and prefer this option



Question 2

What anticoagulant would you suggest for his DVT?

(UFH = Unfractionated heparin, LMWH = Low molecular weight heparin)

- A. Subcutaneous UFH
- B. Direct oral anticoagulant
- C. UFH 1 or 2x a day, with anti-Xa monitoring
- D. LMWH 1 or 2x a day, with anti-Xa monitoring



Which anticoagulant can be used safely during pregnancy?

Anticoagulant	Acceptability in pregnancy	Comments
LMWH	YES	<ul style="list-style-type: none"> Does not cross the placenta LMWH is preferred over UFH due to maternal security profile (less risk of TIH, reduced bone mineral density); Does not cross the placenta
UFH	YES	<ul style="list-style-type: none"> Does not cross the placenta
Fondaparinux	Not preferred	<ul style="list-style-type: none"> Has been reported to cross the placenta in small amounts Very limited clinical experience with fondaparinux
Vitamin K antagonists (VKAs)	No	<ul style="list-style-type: none"> Crosses the placenta Teratogenicity potential, pregnancy loss, fetal bleeding, neurodevelopmental disorders
Direct oral anticoagulants	No	<ul style="list-style-type: none"> Probably dabigatran and Xa inhibitors cross the placenta Reproductive effects in humans are unknown.



Recommendation 12

For pregnant women with acute VTE, the Latin American ASH panel suggests LMWH 1x or 2x a day, based on clinical circumstances and patients' values and preferences (conditional recommendation based on low certainty on the evidence about the effects ⊕⊕○○)

LMWH doses prescribed 2x a day compared to 1x a day.

Event	Number of studies	Impact of dose regimens
● Recurrent PE	2 observational studies	Low general incidence of VTE (<1 %), without difference between the dose regimens
● Recurrent DVT	2 observational studies	Low general incidence of VTE (<1 %), without difference between the dose regimens
● Major bleeding (antenatal or postpartum)	2 observational studies	Low general incidence of a major bleeding (<1 %), without difference between the dose regimens

Notes:

- *LMWH 1x a day may lead to a higher maximum concentration and lower minimum level. The impact of pharmacokinetics in patients is uncertain.*
- *Women who value most avoiding injections may choose LMWH once a day.*
- *While women who value most possible complications from LMWH pharmacokinetics, may prefer LMWH 2x a day.*



Case 2 continued: Decision about Thromboprophylaxis

28-year-old woman with first pregnancy of 32 weeks with DVT and PE, and low risk, treated during entire pregnancy and puerperium with LMWH 1x a day; Gave birth to a healthy child in excellent conditions.

Medical evaluation after 3 months

- Complete thrombophilia profile study:
- It is possible to determine protein S levels in repeated 15% antigenic method
- Their relatives were studied
 - Mother: with protein level S: 12%
 - Younger sister with S protein: 10%



The relatives were confirmed with **Deficiency of S protein**, the younger sister is 12 weeks pregnant, having developed obesity before the pregnancy, and lives far away from the city center; **do you want to know the plan for thromboprophylaxis in your case?**

What is recommended to prevent VTE associated to pregnancy during the first pregnancy of the sister?

- A. Anticoagulant prophylaxis is not recommended in antepartum, but in postpartum
- B. Lower extremity duplex ultrasound examinations and treatment only if recurrent DVT is diagnosed
- C. Only antepartum anticoagulant prophylaxis
- D. Antepartum anticoagulant prophylaxis is not recommended postpartum
- E. Antepartum and postpartum anticoagulant prophylaxis are recommended



Recommendation 22

- For pregnant women with inherited thrombophilia, the ASH guideline panel suggests against administering anticoagulant prophylaxis (conditional recommendation based on the low certainty about the evidence of the effects ⊕○○○).

Notes:

- *Women with high-risk thrombophilia: family history of thrombosis, homozygous factor V Leiden mutation, PT G20210A, combined thrombophilia (double heterozygous), and AT III deficiency, may be at increased risk of VTE during pregnancy. The benefits of prophylaxis may outweigh the risk of bleeding.*
- *Women at low risk: No family history or heterozygous for factor V Leiden or PT G20210A mutation. The risk of bleeding outweighs the benefits.*
- *Between these two groups, there is an intermediate risk of thrombosis.*
- *Therefore, doctors and patients can analyze additional risk factors to decide.*

The original panel pointed out 3 factors:

1. Recommendation against antepartum prophylaxis in women with low-risk thrombophilia
2. Recommendation against prophylaxis in women with high-risk thrombophilia
3. Recommends prophylaxis in women with thrombophilia and previous VTE events.

The Latin American Panel recommended the same for low-risk and high-risk women with thrombophilia, but they were combined into a single recommendation statement.



Recommendation 22



For pregnant women with inherited thrombophilia, the ASH Guidelines for Latin American panel suggests postpartum anticoagulant prophylaxis over no prophylaxis (conditional recommendation based on very low-certainty evidence on the effects ⊕○○○).

Notes:

- **Probably the risk of thrombosis increases in postpartum compared to prepartum. Therefore, most women with a family history of thrombosis and thrombophilia can benefit from prophylaxis.**
- **In women heterozygous for factor V Leiden or the PT G20210A mutation, with no family history of VTE, the risk of thrombosis may be low enough to be safely treated without prophylaxis.**
- **Clinicians and patients may consider additional risk factors for DVT to decide.**



Recommendation 22

For pregnant women with inherited thrombophilia, the ASH Guidelines for Latin American panel suggests postpartum anticoagulant prophylaxis over no prophylaxis (conditional recommendation based on very low-certainty evidence on the effects ⊕○○○).

This recommendation partially changed its guidance and strength

THE ORIGINAL PANEL RAISED:

- Two conditional recommendations in favor of postpartum prophylaxis in women with a family history of VTE + protein C or S deficiency, in addition to cases with combined thrombophilia and homozygotes for factor V Leiden or prothrombin G20210A
- A strong recommendation for postpartum prophylaxis in women with a family history of VTE, and antithrombin II deficiency
- Two recommendations against postpartum prophylaxis in women without a family history of VTE, heterozygous for factor V Leiden or prothrombin G20210A mutation, or with AT III, Protein C or S deficiency, and in women with a family history of VTE who are heterozygous for factor V Leiden or PTG20210A.

THE LATIN AMERICAN PANEL HAS A DIFFERENT APPROACH

- Due to the increased risk of thrombosis during the postpartum period, most women may be better off with prophylaxis.
- A single recommendation was issued suggesting this course of action, while contextualizing different clinical scenarios on the comments.



Recommendation 22



For women with no VTE personal history, the panel recommends:

Inherited thrombophilia patient	Family history of VTE	Antepartum prophylaxis	Postpartum prophylaxis
Homozygous PGM	(+)	● No formal recommendation**	● Yes
	(-)	● No	● Yes
Homozygous factor V Leiden	(+)	● Yes	● Yes
	(-)	● No	● Yes
Combined thrombophilia	(+)	● Yes	● Yes
	(-)	● No	● Yes

**There are no formal recommendation as there are no family studies on homozygous PGM available. However, panel members are in favor of an antepartum prophylaxis considering the VTE risk estimates.



Recommendation



For women with no VTE personal history, the panel recommends:

Inherited thrombophilia patient	Family history of VTE	Antepartum prophylaxis	Postpartum prophylaxis
Heterozygous PGM O	(+)	● No	● No
Heterozygous Factor V Leiden	(-)	● No	● No
Protein S Deficiency O	(+)	● No	● Yes
Protein C Deficiency	(-)	● No	● No
Antithrombin Deficiency	(+)	● Yes	● Yes
	(-)	● No	● No

These recommendations were based on a VTE risk threshold of 2% antepartum and 1% postpartum to recommend LMWH prophylaxis

Our patient:
Protein S deficiency with family history (+).
The patient's estimated VTE risk is 1.8% postpartum but increases with additional risk factors (obesity).



The patient receives a daily prophylactic dose of LMWH. She is 32 weeks pregnant, and her estimated due date is in 7 weeks. She would rather have a vaginal delivery with epidural anesthesia.

What do you suggest for managing her prophylaxis around the time of delivery?

- A. Change anticoagulation to intravenous heparin, then elective (induced) delivery with interruption of IV heparin 6 hours prior to delivery
- B. Planned (induced) labor with interruption of LMWH 24 hours prior to delivery**
- C. Allow spontaneous labor before discontinuing LMWH anticoagulation
- D. Elective cesarean section with suspension of LMWH 48 hours prior to delivery
- E. Maintain LMWH now as it requires anticoagulation



Recommendation

For pregnant women taking prophylactic LMWH doses, **the Latin American ASH panel suggests the elective delivery with prior suspension of LMWH over LMWH interruption with the spontaneous onset of labor** (conditional recommendation based on low evidence of the effects ⊕○○○).

Notes:

- Although most women receiving prophylactic doses of LMWH may have a safe spontaneous labor, many women in Latin American have limited access to a qualified delivery care.
- In this scenario, a scheduled induction in a hospital may be safer for women taking LMWH.
- In this scenario, a scheduled induction in a hospital may be safer for women taking LMWH.

A scheduled induction may facilitate neuraxial anesthesia and reduce maternal bleeding risk (*very low certainty of evidence*)



Summary: Back to the objectives of VTE in pregnant women

1. Describe the recommendations for acute VTE management during pregnancy. Place of care, anticoagulation scheme, planning in childbirth
2. Identify pregnant patients who need prophylaxis antepartum and/or postpartum: Classification of inherited thrombophilia risk, use of thromboprophylaxis in patients with and without a DVT history, use of prophylaxis before delivery in high-risk thrombophilias and postpartum in most thrombophilias.



Objectives

At the end of this section, you will be able to:

1. Describe the recommendations for treating asymptomatic VTE in children.
2. Manage children with PTE and hemodynamic failure.



Pediatric VTE is a disease primarily of hospitalized children

VTE in the general pediatric population is **rare** (0.07 to 0.14 per 10,000 children)

The VTE rate in children increases from **100 to 1000 times** in hospitalized children

The presence of a **central venous catheter** (90 % of all VTE) and other children (more than 60 %)

There are no anticoagulants approved for use in children, and very **little specific research on pediatric VTE.**



Case 3: Asymptomatic DVT.

6-year-old boy

Patient is taken to surgery to correct intestinal stenosis. Due to the need for a , central venous catheter placement was performed. The postoperative evolution was excellent, free of infection or bleeding.

The catheter was removed after 8 days without problems. Before discharge, the pediatrician noted that there was a mitral murmur not heard before and an echocardiogram was done. A slight mitral stenosis was observed, as well as an internal jugular vein thrombosis without cardiac involvement that was asymptomatic



You have diagnosed your patient with an asymptomatic non-occlusive DVT in the internal jugular vein and superior vena cava, which was probably caused by a removed central venous catheter.

What treatment would you suggest for this patient's asymptomatic DVT?

- A. Therapeutic anticoagulation
- B. No anticoagulation, as it was an incidental finding**
- C. Without anticoagulation, repeat ultrasound in 1 week to ensure it has not extended
- D. Graduated compression stockings
- E. Intermittent pneumatic compression devices



For children with asymptomatic VTE, the Latin American ASH guidelines panel suggests against anticoagulation (conditional recommendation based on the very low certainty of evidence over the effects ⊕○○○).

Comments

- For most children with asymptomatic VTE, the risk of anticoagulation probably outweighs the benefits. Some patients at high risk of thrombosis recurrence or those who may require multiple central venous access devices during their lifetime may benefit from anticoagulation.
- The final decision must consider individual risk factors, as well as parent and child values and preferences.

This recommendation changed guidance. The original ASH panel made a conditional recommendation of anticoagulation or no anticoagulation. The Latin American panel considered that in most children with asymptomatic VTE the risk of bleeding exceeds potential benefits.



Case 4

6-year-old female preschool patient diagnosed with stage IIB diffuse large cell non-Hodgkin lymphoma and a large mediastinal mass. After biopsy surgery, presents dyspnea, with severe low blood pressure, requiring medical management with vasopressors. Her chest CT angiography revealed large thrombi in the pulmonary arteries, with severe right ventricular dysfunction on echocardiography.

Idx: Massive pulmonary thromboembolism with hemodynamic compromise



The girl has a massive pulmonary embolism with hemodynamic compromise. What do you recommend in this case?

- A. No anticoagulation, since the risk of bleeding is high.
- B. Anticoagulation therapy with low molecular weight heparin
- C. Catheter-directed thrombolysis (CDT) followed by anticoagulation
- D. Surgical thrombectomy followed by anticoagulation
- E. Prophylactic IVC filter placement
- F. Prescribe Rivaroxaban in anticoagulant dose.



Recommendation 24

For children with PE and hemodynamic failure, ASH Latin American recommends thrombolytic therapy in addition to anticoagulation (strong recommendation based on low-certainty evidence on effects ⊕⊕○○).

Comments

- There is uncertainty regarding the effect of thrombolytics in children due to the lack of studies with the adequate statistical power and design.
 - The available evidence in adults suggests a positive effect of thrombolytics in preserving life in a condition of high mortality.
 - This scenario justifies a strong recommendation in favor of intervention following the ASH GRADE rules.
-
- This recommendation changed its strength. The original panel made a conditional recommendation in favor of thrombolytic therapy.
 - The Latin American panel considered the changes in baseline mortality risk identified in the update (22% vs. 4.5%) and issued a strong recommendation.



Pulmonary embolism with hemodynamic failure is a serious condition associated with high mortality

New evidence.

In an additional study (n=5654), overall mortality in children with PE was 8.6%, with a bimodal distribution with a first peak in children under 1 year of age and a second peak in adolescents aged 16-17 years. The first peak in young children was largely explained by congenital conditions such as underlying heart diseases.

The second study identified (n=170), showed a similar overall mortality of 6%, but also independently reported a mortality risk of 22% in children with PE and hemodynamic failure.



FINAL CONSIDERATIONS



- Although there are no direct data from randomized trials conducted in children, indirect evidence from the adult population suggests a potential life-preserving benefit.
- Given the high mortality observed in children with PE and hemodynamic failure, thrombolytic therapy should be routinely offered.
- Implementation of this recommendation may be hampered by a lack of appropriate facilities and human resources to deliver critical care in some settings within the regions.
- Efforts must be made to ensure timely access to specialized care for children with PE and hemodynamic failure.



Summary of changes in the pediatric section

Treatment of asymptomatic VTE is generally not indicated, however the decision must be individualized based on the patient's specific risks of recurrent VTE and bleeding

Thrombolysis in pulmonary embolism and hemodynamic failure is an appropriate measure in the pediatric setting



Acknowledgements

Team members of the ASH Guidelines Panel
Knowledge Synthesis team members
McMaster University GRADE Center

Author of the presentation: Juan Carlos Serrano Casas, MD,
Central University of Venezuela
Clínica Cancerológica de Norte de Santander (North
Santander Oncology Clinic)

Learn more about the ASH VTE guidelines at
<http://www.hematology.org/VTEguidelines>