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ASH Guidelines for prevention of VTE in Latin America

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Abstract

- We studied the ASH guidelines for prevention of VTE in Latin America.
- The Latin American population appears to have certain differences compared to the general population.
- A variety of countries within Latin America and a total of 12 societies contributed to these guidelines.
- Comments from anyone were solicited and accepted if found appropriate.
- After analyzing these guidelines, we concluded that these guidelines are slightly different since the facilitators used the GRADE ADOLOPMENT method which was used to provide specific but general advice pertaining to localized standards.

Introduction

We undertook this project since we have the privilege of making this presentation in Porto Alegre, a part of Latin America, in an attempt to provide evidence-based guidelines about VTE prevention for Latin American patients, clinicians, and decision makers.

There's a separate set of guidelines for Hispanic patients as their bodies act slightly different to those in other parts of the world, causing them to require a different treatment than others.

Background

- Between 2017 and 2020, the American Society of Hematology (ASH) sought comments on draft recommendations for the ASH VTE guidelines for patient populations with varying probabilities of PE and lower extremity DVT in Latin America.
- ASH partnered with 12 societies to adapt the ASH VTE Clinical Practice Guidelines for Latin America.
- The panel selected questions from the original ASH VTE guidelines that are clinically significant and pertinent in Latin America and reviewed evidence to form recommendations.
- Anyone was welcome to comment.

Why Focus on Latin America?

There are several reasons why ASH decided to focus on Latin America:

- Although multiple studies have evaluated the epidemiology of venous thromboembolism (VTE) in European and American populations, there is limited evidence on the prevalence of VTE and the burden of disease in Latin America.
- Evidence from a study in the United States suggests that there are differences in the incidence of VTE among white, black, Hispanic, and Asian populations.
- Thus, it may not be appropriate to simply extrapolate the prevalence of VTE in Latin America from data obtained from European and U.S. populations.

Why Focus on Latin America? (cont'd)

- There are various regional challenges to effective VTE diagnosis and treatment in Latin America.
- A significant proportion of patients diagnosed with VTE in Latin American countries may not receive appropriate anticoagulation and some patients at risk of VTE do not receive appropriate prophylaxis.

Are the ASH guidelines acceptable to the societies in Latin America?

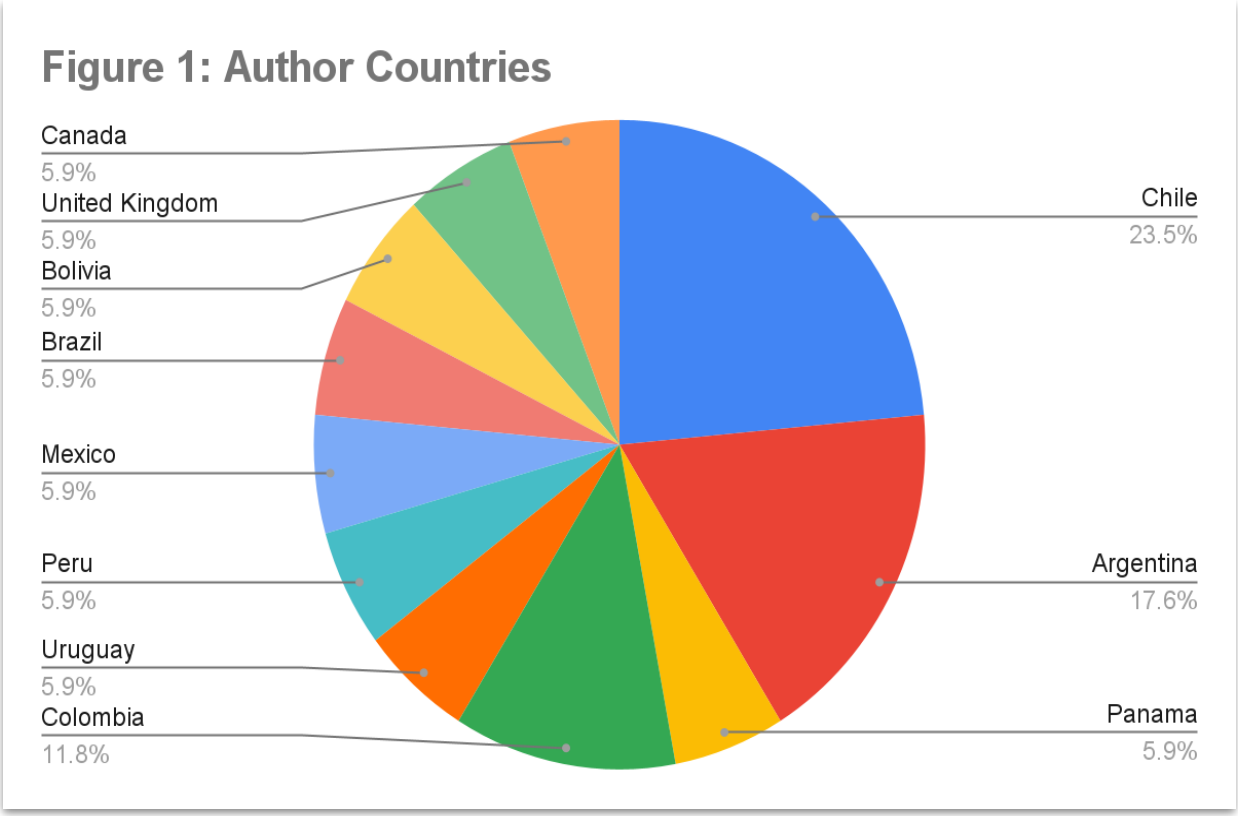
The ASH guidelines on venous thromboembolism (VTE), published in 2018 and 2020 in *Blood Advances*, were developed for a global audience and were endorsed by the following organizations in Latin America.

Table 1: Society Participants from Latin America

- Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular
- Asociación Colombiana de Hematología y Oncología
- Grupo Cooperativo Argentino de Hemostasia y Trombosis
- Grupo Cooperativo Latinoamericano de Hemostasia y Trombosis
- Sociedad Argentina de Hematología
- Sociedad Boliviana de Hematología y Hemoterapia
- Sociedad Chilena de Hematología
- Sociedad de Hematología del Uruguay
- Sociedad Mexicana de Trombosis y Hemostasia
- Sociedad Panameña de Hematología
- Sociedad Peruana de Hematología
- Sociedad Venezolana de Hematología

The Author Countries

The authors of the ASH Guidelines were from several different countries, a majority of which were in Latin America.



The Process

A 6-step process was created to ensure that the guidelines were accurate and appropriate.

#	Steps
1	Each society nominated 1 individual to serve on the guideline panel
2	The work of the panel was facilitated by 2 methodologists
3	The team selected 4 of the original VTE guidelines for a first round
4	To select the most relevant questions, a 2 step prioritization process was conducted through an online survey and then through an in-person discussion.
5	During an in-person meeting in Rio de Janeiro, Brazil, from April 23rd to April 26th, 2018, the panel developed recommendations using the ADOLOPMENT approach.
6	Evidence about health effects from the original guidelines was reused, but important data about the resource use, accessibility, feasibility, and impact on health equity was added.

The Topics

The adaptation of the VTE guidelines covered the following topics:

- Prevention of VTE: Prophylaxis in medical and surgical patients and long-distance travelers.
- Management of VTE: Treatment and anticoagulation therapy.

Methods

- For many recommendations, the most important criteria are the health effects of interventions (i.e., the balance of the most important health benefits and harms, such as prevention of clots vs risk of bleeding).
- Other criteria considered by ASH guideline panels under the GRADE Evidence to Decision (EtD) framework include the values and preferences of patients, resource use, accessibility, feasibility, and impact on health equity.

Methods (cont'd)

- The GRADE ADOLOPMENT method to adapt recommendations from two American Society of Hematology (ASH) VTE guidelines (Prevention of VTE in Surgical Patients and Prophylaxis for Medical Patients) were used.
- ADOLOPMENT requires involvement of local stakeholders and experts throughout the guideline development process to ensure that the questions, evidence, and recommendations are contextualized to address local needs and the health care system structure.

Methods (cont'd)

- The "GRADE-ADOLOPMENT" approach to guideline production combines adoption, adaptation, and, as needed, de novo development of recommendations. If developers of guidelines follow EtD criteria more widely and make their work publicly available, this approach should prove even more useful.
- International standards require clinical practice guidelines to be transparent about the evidence that informs recommendations.
- The ASH guidelines were developed using the GRADE Evidence to Decision (EtD) framework, a system intended to maximize transparency around the criteria that drive each recommendation.

Process for Consideration of Comments

- All comments received during the open comment period were provided to the guideline panel for review prior to finalizing the guidelines for publication.
- Guideline panels were obligated to consider all comments received.
- The panelists were told that infrequently, ASH guideline panels may change judgments or decisions because of comments.
- More commonly, panels may provide additional explanations within the final guideline report to explain judgments or decisions.
- Comments may also inform ASH's communication and implementation plan for the guidelines, as well as future updates or revisions of the guidelines.

GRADE Evidence to Decision (EtD) Frameworks

- Clinicians, guideline developers, and policymakers sometimes neglect important criteria, give undue weight to criteria, and do not use the best available evidence to inform their judgments.
- Explicit and transparent systems for decision making can help to ensure that all important criteria are considered and that decisions are informed by the best available research evidence.
- The purpose of Evidence to Decision (EtD) frameworks is to help people use evidence in a structured and transparent way to inform decisions in the context of clinical recommendations, coverage decisions, and health system or public health recommendations and decisions.

GRADE Evidence to Decision (EtD) Frameworks (cont'd)

- EtD frameworks have a common structure that includes formulation of the question, an assessment of the evidence, and drawing conclusions, though there are some differences between frameworks for each type of decision.
- EtD frameworks inform users about the judgments that were made and the evidence supporting those judgments by making the basis for decisions transparent to target audiences.
- EtD frameworks also facilitate dissemination of recommendations and enable decision makers in other jurisdictions to adopt recommendations or decisions or adapt them to their context.

Panel Training

- During the first in-person meeting (question prioritization), the methodologists conducted a half-day training workshop.
- The GRADE methodology used in the original VTE guidelines and the ADOLOPMENT approach were introduced.
- During the second part of the workshop, panelists simulated the adaptation of a recommendation following the methods introduced with real information about the values and preferences of patients, resource use, accessibility, feasibility, and impact on health equity in Latin America.

Development of Recommendations

- During an in-person meeting that took place in Rio de Janeiro, Brazil, from April 23 to 26, 2018, the panel developed recommendations based on the evidence summarized in the EtD tables.
- The panel agreed on the direction and strength of recommendations through group discussion 233 and deliberation.
- In such 234 circumstances, the result of the voting was recorded on the respective EtD table. The direction 235 of the recommendation was decided by simple majority, whereas an 80% majority was required by 236 to issue a strong recommendation.

How to use the Recommendations?

- The recommendations are labeled as “strong” or “conditional” according to the GRADE 258 approach.
- The words “the ASH Latin American guideline panel recommends” are used for 259 strong recommendations and “the ASH Latin American guideline panel suggests” for conditional 260 recommendations.

Conflicts of Interest in Guideline Funding and Management

- No conflict of interest was found because the ideas from all Latin American countries were solicited.
- The source guidelines and these adapted guidelines were wholly funded by ASH.

Interpretation of Certainty of the Evidence about Effects

High certainty ⊕⊕⊕⊕	There is almost no uncertainty regarding where the true effect of the intervention lies.
Moderate certainty ⊕⊕⊕◯	There is little uncertainty regarding where the true effect of the intervention lies.
Low certainty ⊕⊕◯◯	There is uncertainty regarding where the true effect of the intervention lies.
Very-low certainty ⊕◯◯◯	There is considerable uncertainty regarding where the true effect of the intervention lies.

Recommendations

In surgical patients in whom pharmacological thromboprophylaxis is preferred, the ASH Latin American Guideline Panel suggests delayed prophylaxis (12 hours after surgery) over early administration (before surgery or within 12 hours post-surgery) (conditional recommendation based on very low certainty in the evidence about effects).

Note: For details, please see Appendix (I)

Table 4. Summary of recommendations for prevention of VTE in surgical patients.

Population	Preferred alternative	Proposed treatment	Specific strategy
Patients undergoing major general surgery **Patients undergoing surgery following major trauma** **Patients undergoing major neurosurgical procedures**	**Use thromboprophylaxis** (recommendations 1, 2, and 6)	**High risk of bleeding:** Mechanical prophylaxis **Average risk of bleeding:** Pharmacological prophylaxis	**If pharmacological prophylaxis is preferred:** A short scheme (7–10 days) initiated 12 hours after surgery (recommendations 9 and 10)
Patients undergoing laparoscopic cholecystectomy **Patients undergoing transurethral resection of the prostate** **Patients undergoing radical prostatectomy**	**No thromboprophylaxis** (recommendations 3–5)	**High risk of VTE:** Mechanical prophylaxis **Average risk of VTE:** No prophylaxis	**If mechanical prophylaxis Is preferred:** mechanical compression devices when available. Compression stockings may be a reasonable alternative if there are barriers to access compression devices (recommendation 8)

VTE, venous thromboembolism.

Recommendations (cont'd)

Population	Preferred alternative	Proposed treatment
Critically ill inpatients	**Use thromboprophylaxis** (recommendation 12)	**If prophylaxis is preferred:** Short scheme (inpatient only) of LMWH or UFH. (recommendations 13, 16, 17, and 18) **Patients who cannot receive pharmacological prophylaxis:** Mechanical prophylaxis with either compression devices or compression stockings (recommendations 14 and 15)
Acutely ill inpatients	**No thromboprophylaxis** (recommendation 11)	
Chronically ill patients	**No thromboprophylaxis** (recommendation 16)	
Long-distance travelers	**Average risk of VTE:** No prophylaxis **High risk of VTE:** Use thromboprophylaxis (recommendations 19 and 20)	**If prophylaxis is preferred:** Either compression stockings or LMWH

Note: For details, please see Appendix (II)

Deficiencies in Guidelines for Latin America

The Latin American ASH Guideline panel used the GRADE ADOLOPMENT approach which focuses on economically challenged areas.

Limitations

- The project aim was limited by practical considerations; to offer sensible recommendations, all panels were instructed to assume the perspective of high-resource settings.
- Implementation of some of these recommendations may not be straightforward in other contexts and may require additional considerations.
- Multiple recommendations are regarded as under low certainty due to the fact that they required consideration in multiple contexts.

What is the message in the provided guidelines?

- The words “the ASH Latin American guideline panel recommends” are used for strong recommendations and “the ASH Latin American guideline panel suggests” for conditional recommendations.
- The guidelines suggest that the large majority of long-distance travelers have a minimal risk of VTE. Hence, harms, cost, and inconvenience likely outweigh any potential benefit.
- In contrast, patients with an increased risk of VTE, for example, individuals with a recent surgery or history of VTE, postpartum women, and individuals with an active malignancy, may experience a thrombotic event as a consequence of the travel.

What is the message in the provided guidelines? (cont'd)

- Therefore, the use of thromboprophylaxis may be justified. Regarding the options for thromboprophylaxis, plenty of indirect evidence supports the use of LMWH or compression stockings.
- The evidence with aspirin is very limited, and there is no evidence of the potential effect of DOACs.

Conclusions

Latin America is one of the biggest continents in the world, and its population varies from other continents in many respects. It was therefore important to create some specific guidelines for the management of VTE in this continent.

The guidelines suggest that the large majority of long-distance travelers have a minimal risk of VTE. Hence, harms, cost, and inconvenience likely outweigh any potential benefit. Use of thromboprophylaxis in many VTE conditions is strongly recommended. The guidelines, although not mandatory, have covered the best recommendations for patients who suffer from VTE.

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Appendix (I) - Recommendations

- For patients undergoing major general surgery, the ASH Latin American Guideline Panel suggests thromboprophylaxis over no prophylaxis (conditional recommendation based on low certainty in the evidence about effects).
- In patients undergoing surgery following major trauma, the ASH Latin American Guideline Panel suggests thromboprophylaxis over no prophylaxis (conditional recommendation based on very low certainty in the evidence about effects).
- In patients undergoing laparoscopic cholecystectomy, the ASH Latin American Guideline Panel suggests against thromboprophylaxis (conditional recommendation based on very low certainty in the evidence about effects).

Appendix (I) - Recommendations (cont'd)

- In patients undergoing transurethral resection of the prostate or radical prostatectomy, the ASH Latin American Guideline Panel suggests against thromboprophylaxis (both conditional recommendations based on very low certainty in the evidence about effects).
- In patients undergoing major neurosurgical procedures, the ASH Latin American Guideline Panel suggests thromboprophylaxis over no prophylaxis (conditional recommendation based on very low certainty in the evidence about effects).
- In surgical patients in whom thromboprophylaxis is preferred, the ASH Latin American Guideline Panel suggests either mechanical or pharmacological prophylaxis (conditional recommendation based on low certainty in the evidence about effects).

Appendix (I) - Recommendations (cont'd)

- For surgical patients in whom mechanical thromboprophylaxis is preferred, the ASH Latin American Guideline Panel suggests mechanical compression devices over compression stockings (conditional recommendation based on low certainty in the evidence about effects).
- In surgical patients in whom pharmacological thromboprophylaxis is preferred, the ASH Latin American Guideline Panel suggests short prophylaxis (7 to 10 days) over extended prophylaxis (30 days) (conditional recommendation based on very low certainty in the evidence about effects).

Appendix (II) - Recommendations

- In acutely medically ill patients, the Guideline Panel suggests against routinely use of heparins (unfractionated heparin or low-molecular-weight heparin).
- In acutely critically ill patients, the use of heparins (unfractionated heparin or low-molecular-weight heparin) over no use (conditional recommendation based on moderate certainty in the evidence about effects) is recommended.
- In acutely critically and medically ill patients who require pharmacologic prophylaxis, either unfractionated heparin (UFH) or low molecular-weight heparin (LMWH) is recommended (conditional recommendation based on low certainty in the evidence about effects).

Appendix (II) - Recommendations (cont'd)

- In acutely critically and medically ill patients who cannot receive pharmacological prophylaxis, use of mechanical prophylaxis over no prophylaxis is recommended (conditional recommendation based on moderate certainty in the 766 evidence about effects).
- In acutely critically and medically ill patients who need mechanical prophylaxis, either pneumatic compression devices or graduated compression stockings are recommended (conditional recommendation based on very low certainty in the evidence about effects).
- In acutely critically and medically ill patients who require pharmacological thromboprophylaxis, using a short period of prophylaxis (inpatients) over an extended period (inpatients and extended-duration outpatients) is often recommended.

Appendix (II) - Recommendations (cont'd)

- In chronically ill patients, the recommendation is against using thromboprophylaxis.
- In acutely ill patients who require pharmacological thromboprophylaxis, using LMWH over direct oral anticoagulants (DOACs) is preferred (conditional recommendation based on moderate certainty in the evidence about effects).
- In long-distance travelers (>4 hours) with low risk of VTE, the panel suggests against thromboprophylaxis. However, for long-distance travelers with high risk of VTE, thromboprophylaxis with compression stockings or LMWH is recommended.

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