Recommendations for venous thromboembolism prophylaxis in pediatric trauma patients: A national, multidisciplinary consensus study

Sheila J. Hanson, MD, MS, E. Vincent S. Faustino, MD, MHS, Arash Mahajerin, MD, MSCr, Sarah H. O'Brien, MD, Christian J. Streck, MD, A. Jill Thompson, PharmD, Toni M. Petrillo, MD, *and* **John K. Petty, MD,** *Winston-Salem, North Carolina*

The incidence of venous thromboembolism (VTE) has been increasing in children, although the incidence remains lower than the incidence in adults.[1] The incidence of VTE is higher in injured children than it is in the general population of uninjured hospitalized children, ranging from 0.02% to 0.33%.[2–8] Increasing scrutiny is given to hospital-acquired VTE, as quality initiatives to prevent VTE, such as Children's Hospitals Solutions for Patient Safety, gain national priority. Children with hospital-acquired VTE have increased length of stay and excess costs of $27,000.[9] Several risk factors have been associated with VTE in injured children, including older age, injury severity, obesity, central venous catheter (CVC) use, mechanical ventilation, inotrope use, blood transfusion, pelvic or lower extremity fracture, spinal cord injury, and intensive care unit stay.[2,4,7–13] However, it is not clear in any individual pediatric patient when the benefit of pharmacologic prophylaxis to reduce the risk of VTE outweighs the risk, particularly the risk of bleeding. The efficacy of anticoagulation to prevent VTE is unknown in this population. In addition, there are no pediatric studies on the effectiveness of mechanical prophylaxis to prevent VTE. In contrast, VTE prophylaxis with low-molecular-weight heparin (LMWH) is routinely recommended for injured adults.[14,15]

Despite the paucity of evidence, medical providers from different specialties are routinely called upon to make management decisions regarding the use of VTE prophylaxis in injured children. We proposed to survey experts in the field of pediatric trauma and thrombosis to develop consensus regarding the prevention of VTE in pediatric trauma patients.

PATIENTS AND METHODS

A modified Delphi method was used to develop consensus, according to previously published methodologies.[16–18] Institutional review board approval was obtained from a sponsoring institution. To provide the expert panel with current evidence on which to base their recommendations, a systematic review of the literature was performed. Three authors recently published systematic review articles on VTE prophylaxis in pediatric trauma.[19,20] Articles from 1995 to 2012 constituted the bibliography of the earlier published review.[19] A research librarian expanded and updated the literature search from 2012 to May 2014 according to previously published search parameters.[16] The authors reviewed and summarized the articles.

The Delphi survey was designed to gather expert opinion on the influence of patient-level risk factors for VTE and bleeding and on indications for mechanical prophylaxis, pharmacologic prophylaxis, and screening ultrasound (see Appendix, Supplemental Digital Content 1, http://links.lww.com/TA/A731). The pediatric age group was defined as patients 15 years or younger. The Delphi survey was designed to have a total of three rounds. The first two rounds were intended to allow fixed-option responses and open-ended comments to facilitate movement among the expert panel to components of decision making that would be most important. The third round identified areas of emerging agreement to create potential consensus statements with which the expert panel could agree or disagree (see Appendix, Digital Content 2, http://links.lww.com/TA/A732). Agreement of 80% or greater was determined a priori as the definition of consensus. *Near consensus* was defined as agreement of 70% to 79% on the statements from Round 3.[16–18,21]

Expert Panel

Participation of multiple different specialties is crucial to the validity of any consensus regarding VTE prophylaxis in pediatric trauma. The Pediatric Trauma Society (PTS) VTE workgroup was formed by members of the guidelines committee with specialty training in pediatric surgery and pediatric critical care medicine who recruited strategic nonmembers such that the workgroup would include specialists in pediatric hematology, pediatric pharmacy, pediatric critical care medicine, and pediatric surgery. It was a stated goal that the expert

Submitted: November 16, 2015, Accepted: December 4, 2015, Published online: February 13, 2016.

From the Division of Critical Care (S.J.H.), Department of Pediatrics, Medical College of Wisconsin, Milwaukee, Wisconsin; Division of Critical Care (E.V.S.F.), Department of Pediatrics, Yale School of Medicine, New Haven, Connecticut; Division of Hematology and Oncology (A.M.), Department of Pediatrics, University of California Irvine School of Medicine, Orange, California; Division of Hematology and Oncology (S.H.O.), Department of Pediatrics, The Ohio State University College of Medicine, Columbus, Ohio; Division of Pediatric Surgery (C.J.S.), Department of Surgery, and Department of Pharmacy Services (A.J.T.), Medical University of South Carolina, Charleston, South Carolina; Division of Critical Care (T.M.P.), Department of Pediatrics, Emory School of Medicine, Atlanta, Georgia; and Division of Pediatric Surgery (J.K.P.), Department of General Surgery, Wake Forest School of Medicine, Winston-Salem, North Carolina.

This study was presented at the 2nd annual meeting of the Pediatric Trauma Society, November 6–7, 2015, in Scottsdale, Arizona.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.jtrauma.com).

Address for reprints: John K. Petty, MD, Division of Pediatric Surgery, Department of General Surgery, Wake Forest School of Medicine, Medical Center Blvd, Winston-Salem, NC 27157; email: jpetty@wakehealth.edu.

DOI: 10.1097/TA.0000000000000962

panel for the Delphi process would include specialists from neurosurgery, orthopedic surgery, adult trauma surgery, pediatric hematology, pediatric pharmacy, pediatric critical care medicine, and pediatric surgery. The goal was to have between 15 and 60 expert panelists participate in the Delphi process.[18]

Experts were identified through a process of peer nomination. Nominations were recruited through a number of different organizations: PTS leadership, specialists at the authors ' institutions, Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) membership, Blood Research Network (Blood Net), the Pediatric Pharmacy Advocacy Group (PPAG), and the American College of Surgeons (ACS) list of verified Level 1 pediatric trauma centers. Members of these organizations were asked to nominate three to five individuals in their specialty that they consider expert in VTE prophylaxis for children. Additional nominees were sought, and invitations were extended to potential experts in the underrepresented fields of orthopedics and neurosurgery.

All nominees were contacted electronically. Consent to participate was obtained from each panelist before accessing the survey.

Survey Process

For the first round of the survey, expert panelists were provided the literature review summary table for ongoing review. Panelists were asked about age, ambulation, and the use of pharmacologic prophylaxis relative to patient risk factors and relative to potential bleeding situations. In addition, they were asked about mechanical prophylaxis, ultrasound, education, and future practice. They were then asked to describe their qualification as experts: specialty training, years of experience, clinical patient volume, publication, leadership, and national organization involvement. Potential expert panelists who did not respond were given additional electronic reminders.

Following completion of the first round, responses were collected and displayed graphically for expert panel review. Free-text answers for each question were edited for information that would potentially compromise the anonymity of the expert panelists and then fed back to the panel. Expert panelists who did not provide contact information were not able to be contacted for the second round survey.

The second round survey again provided the literature summary and invited the panelists to review the first round responses as they answered questions in the second round. The questions for the second round were identical in phrasing and format to the questions from the first round.

After completion of the second round, the responses were reviewed for areas of emerging consensus to construct the third round survey. Each component of the second round was examined for the range of responses. A potential consensus statement was generated based on a level of response that would capture at least 75% of the second round responses. For VTE risk factor categories, the 75th percentile was rounded down to the nearest whole category (i.e., the more conservative option). In a similar fashion, responses related to days of holding pharmacologic prophylaxis for potential bleeding were rounded up to the nearest whole day, again favoring the more conservative approach for potential consensus. Potential consensus statements were created as agree/disagree statements (see Appendix, Supplemental Digital 2, http://links.lww.com/TA/A732). During the third round, expert panelists were again provided the literature summary as well as the results of the second round as they considered potential consensus statements.

Statistical Analysis

The electronic surveys were conducted by the technology solutions team of Professional Relations and Research Institute (PRRI), the association management company contracted by PTS. The survey process was moderated by two of the authors, who reviewed responses, gave direction to the technology team, and contacted panelists who did not respond. Descriptive statistics for each item in each round were calculated by the survey software, MyPRRI. Results were presented graphically to display the range or responses for each item.

RESULTS

Thirty-nine respondents from the list of 96 potential experts participated in the first round. Of these, 33 (85%) participated in the second round and 32 (82%) in the third round (Fig. 1). Four respondents were lost between the first two rounds because there was no contact information provided for reminder follow-up.

Characteristics of the expert panel are shown in Table 1. Most panelists had more than 1 self-identified qualifications for VTE expertise. The panel was distributed among pediatric surgery, adult trauma surgery, neurosurgery, pediatric hematology, pediatric critical care, and pharmacy, with the distribution remaining similar between rounds (Fig. 1). Ninety-two percent of the expert panelists reported willingness to change their practice based on consensus findings.

The patient age for which it is recommended to consider routine VTE prophylaxis varied. Of the 33 respondents to this question in the second round, 42% agreed with the statement that "VTE prophylaxis should *not* routinely be considered for children age 15 years and younger," while 36% agreed with the statement that "VTE prophylaxis should routinely be considered for children age 15 years or younger." Another 21% of the respondents filled in an age for which to consider routine prophylaxis. Selected ages were 12 years (four respondents), 13 years (one respondent), and 14 years (one respondent).

Most expert respondents agreed that "injured children who can walk *may* need routine VTE prophylaxis based on other factors." A total of 23 respondents (59%) agreed with this statement in the first round, and 24 (73%) agreed in the second round.

Figure 2 summarizes the recommendations regarding the VTE risk factors and the need for pharmacologic prophylaxis. Personal history of VTE received the highest level of consensus (94%) and the highest strength of recommendation (strong), but this level of recommendation allows for interaction with other variables for the use of prophylaxis. The number of respondents who strongly or very strongly recommended VTE prophylaxis decreased after Round 1 for patients with spinal cord injury, traumatic brain injury, and personal history of VTE.

The recommendations for VTE prophylaxis in patients with increased risk of bleeding is summarized in Figure 3. The most common recommendation was to hold pharmacologic prophylaxis temporarily. The duration for holding prophylaxis

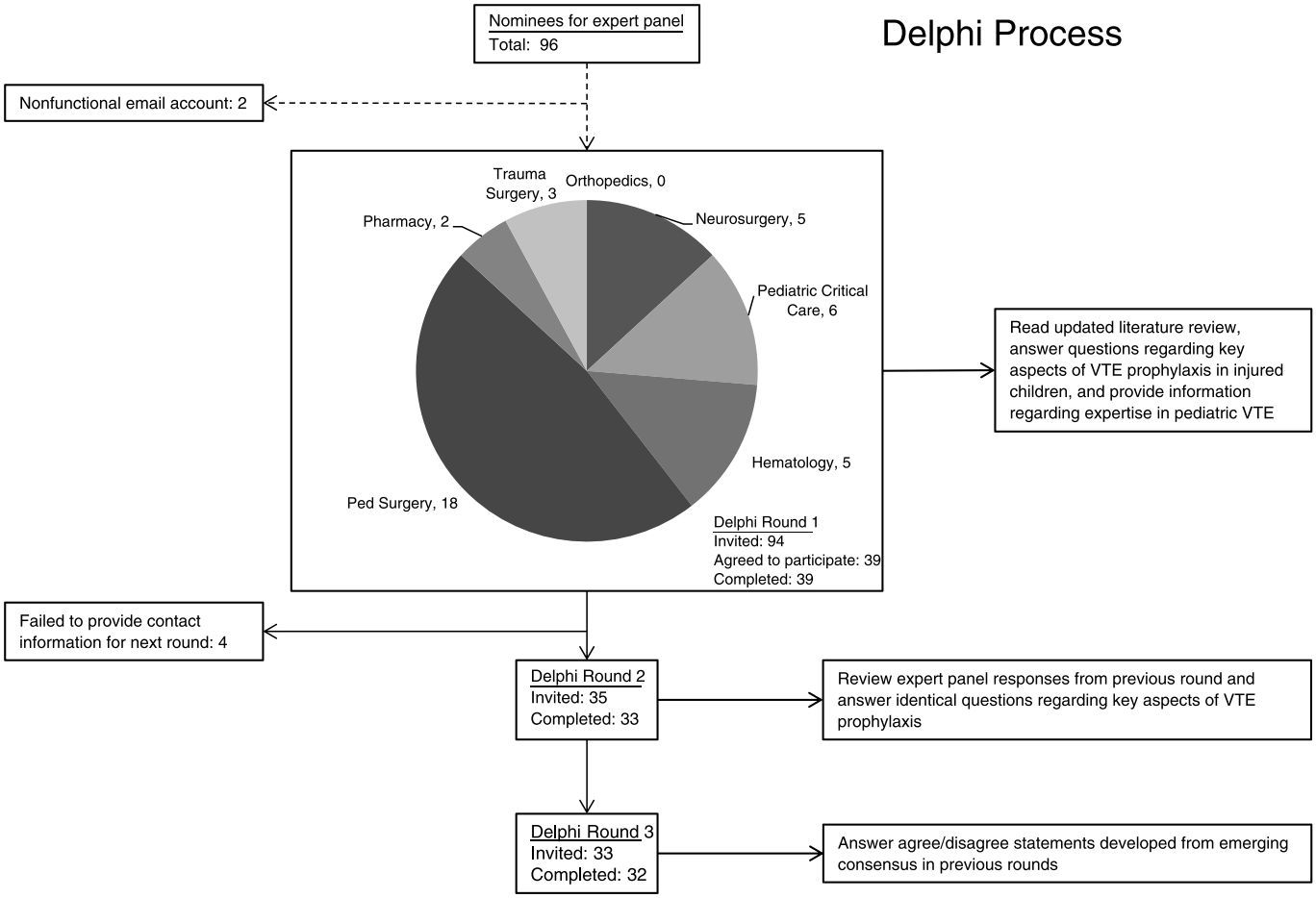

Figure 1. Applied Delphi process for building consensus, displaying respondents and three rounds of expert panelist surveys.

varied from a median of 1 day (range, 1–5 days) for orthopedic operations to 2 days (range, 1–5) for thoracic and abdominal operations, 2 days (range, 1–7 days) for major solid organ injury, and 3 days (range, 1–14 days) for neurosurgical operations and patients with intracranial hemorrhage.

Routine mechanical prophylaxis was recommended by most panel members (77% in Round 1 and 94% in Round 2). Reasons for use were "children with risk of VTE who have a sufficient risk of bleeding or other contraindication that prevents safe pharmacologic prophylaxis" (Round 1, n = 34/39; Round 2, n = 27/33), "children who are at risk for VTE but do not require pharmacologic prophylaxis" (Round 1, n = 26/39; Round 2 n = 27/31), and "children with risk of VTE, as an added level of prophylaxis" (Round 1, n = 18/39; Round 2, n = 13/31).

Routine screening ultrasounds were not recommended by most of the expert panel (73% in Round 1 and 64% in Round 2). In those who recommended screening ultrasound, most would initially screen at 5 days to 7 days after injury in high-risk patients not receiving pharmacologic prophylaxis.

From the iterative results of the second round, 22 potential consensus statements were provided for expert panel agreement or disagreement in the third round. Consensus was reached for 5 statements and near consensus for an additional 11 statements (Table 2).

TABLE 1. Self-Identified Qualifications of Panelists to Participate as Experts in the Delphi Consensus Process

	Total n = 39
Years in practice	
0–5	4
6–10	9
11–15	6
16–20	12
>20	8
Institution pediatric trauma patients, admissions per year	
0–100	3
101–200	6
>200	30
Expert qualifications, n	
Significant clinical experience	37
Institutional leadership related to care pediatric trauma and/or VTE	29
Publication in the field of pediatric trauma	25
Involvement in national organizations related to pediatric trauma and/or VTE	25
Publication in the field of VTE	17

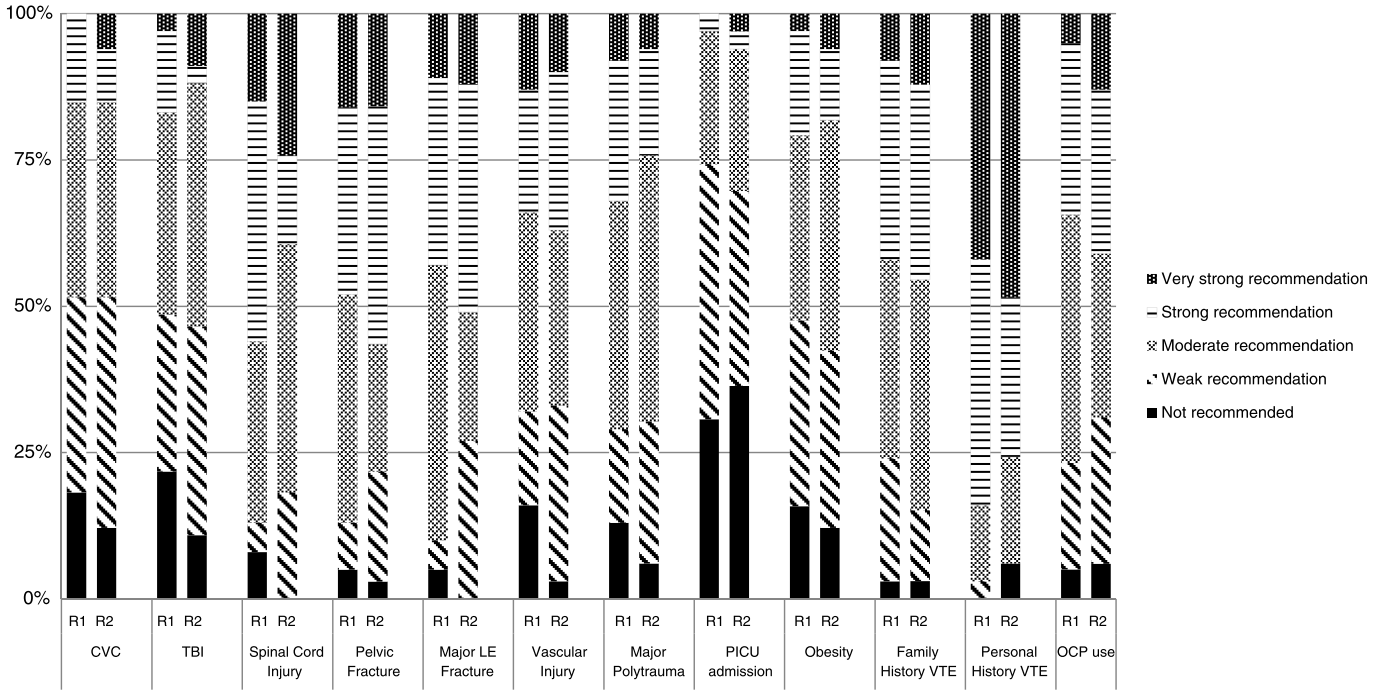

Figure 2. Expert panel recommendations for VTE prophylaxis by risk factor. Responses from Rounds 1 and 2 are compared.

DISCUSSION

The current work represents the first national expert consensus regarding the use of VTE prophylaxis in the setting of pediatric trauma. Important components of consensus methodology quality were achieved: defined goals of processes and outcomes, diverse representation of multiple specialties and institutions, anonymous feedback to panelists, process transparency, provision of updated relevant literature review, and high response rate. As such, the findings represent an important advance in the field of VTE prophylaxis decision making in injured children.

Decision making regarding the use of VTE prophylaxis involves a complex interaction of a number of variables. While retrospective data suggest risk factors for developing VTE in pediatric trauma and emerging data suggest a low bleeding risk with pharmacologic prophylaxis in children, almost no data exist to demonstrate the effectiveness of prophylaxis to prevent VTE in pediatric trauma.[5,6,10] The national expert panel achieved consensus in five key areas related to VTE prophylaxis in pediatric trauma, but in each of these key areas, an allowance was made for interactions with other variables. No single variable was identified as an isolated indication or

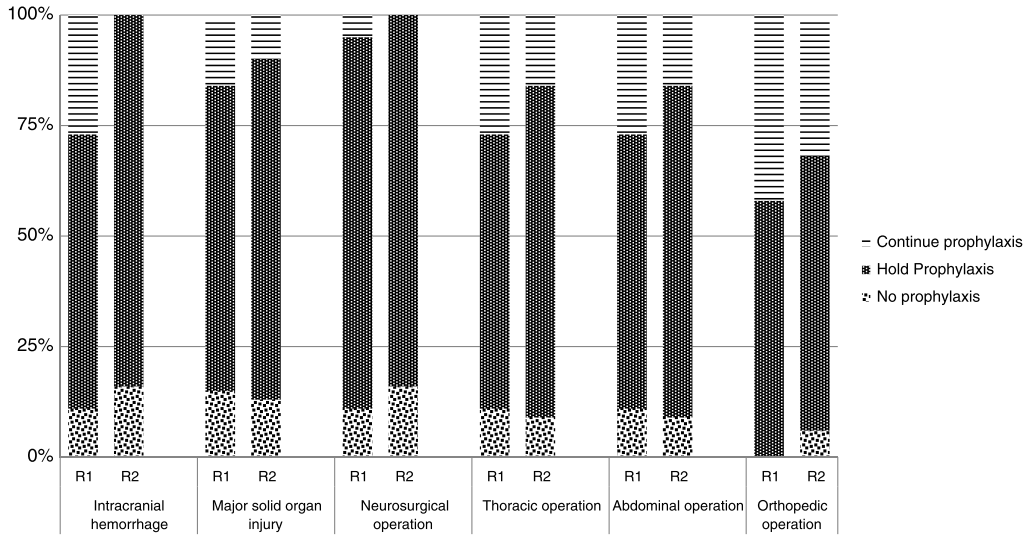

Figure 3. Recommendations for management of VTE prophylaxis in light of situations with a risk of bleeding. Responses from Rounds 1 and 2 are compared.

contraindication for the use of VTE prophylaxis. The panel agreed that most children 12 years and younger should not be given VTE prophylaxis. However, there was no consensus as to what age routine VTE prophylaxis should be started. Although the survey was limited to recommendations for patients 15 years or younger, the panel was nearly evenly split whether 15-year-olds should or should not receive VTE prophylaxis.

The ability to ambulate is often a reason to discontinue active VTE prophylaxis or as a reason not to initiate VTE prophylaxis. Interestingly, the expert panel reached consensus that children who can walk may still need VTE prophylaxis based on other factors. This is congruent with the American College of Chest Physicians (ACCP) recommendation of early ambulation alone as sufficient prophylaxis for adult patients at "very low" (<0.5%) risk of VTE, but not for patients at "low" risk (approximately 1.5%).[15] Mechanical VTE prophylaxis is of unproven effectiveness in the setting of pediatric trauma. The expert panel attained consensus that mechanical prophylaxis is appropriate for pediatric patients who are at risk for VTE but cannot safely receive pharmacologic prophylaxis.

A similar pattern was seen regarding risk factors for developing VTE. None of the risk factors achieved consensus for the use of prophylaxis as a stand-alone risk. Personal history of VTE received the highest level of consensus (94%) and the highest strength of recommendation (strong), but this level of recommendation allows for interaction with other variables for the use of prophylaxis. In addition, the presence of a CVC attained consensus for VTE prophylaxis but only at the level of a weak recommendation. This finding is noteworthy because CVC is the strongest risk factor for the development of VTE in

TABLE 2. Statements for VTE Prophylaxis in Injured Children With Consensus (>80% Agreement)

General	Agreement (%)
• For injured children ≤12 y, VTE prophylaxis should not routinely be given, although exceptions may apply.	91%
• Mechanical prophylaxis is appropriate to lower the risk of VTE in children with a significant risk of bleeding or other contraindication that would prevent safe pharmacologic prophylaxis.	91%
• Injured children who can walk may need VTE prophylaxis based on other factors.	84%
VTE risk factors	
• Strong recommendation for pharmacologic prophylaxis against VTE in injured children with a personal history of VTE.	94%
• Weak recommendation for pharmacologic prophylaxis against VTE in injured children with a CVC.	91%
Statements for VTE prophylaxis in injured children not reaching consensus	
Near-consensus statements (70–79% agreement)	
• Screening ultrasound should not be used routinely in children at risk for VTE.	75%
VTE risk factors	
• Strong recommendation for pharmacologic prophylaxis against VTE in injured children with a non–weight-bearing pelvic fracture.	75%
• Moderate recommendation for pharmacologic prophylaxis against VTE in injured children with a spinal cord injury.	78%
• Moderate recommendation for pharmacologic prophylaxis against VTE in injured children with obesity.	78%
• Moderate recommendation for pharmacologic prophylaxis against VTE in injured children with a vascular injury.	72%
• Moderate recommendation for pharmacologic prophylaxis against VTE in injured children with major polytrauma (ISS > 25).	72%
• Moderate recommendation for pharmacologic prophylaxis against VTE in injured children with a family history of VTE.	72%
• Moderate recommendation for pharmacologic prophylaxis against VTE in injured children with oral contraceptive use.	72%
Bleeding risks	
• For children whose risk of VTE requires pharmacologic prophylaxis, this prophylaxis should be held for 3 d following a neurosurgical operation (in the absence of active bleeding).	78%
• For children whose risk of VTE requires pharmacologic prophylaxis, this prophylaxis should be held for 4 d following intracranial hemorrhage (in the absence of active bleeding).	72%
• For children whose risk of VTE requires pharmacologic prophylaxis, this prophylaxis should be held for 3 d following major solid organ injury (in the absence of active bleeding).	72%
Statements without consensus (<70% agreement)	
• Moderate recommendation for pharmacologic prophylaxis against VTE in injured children with a major lower extremity fracture.	56%
• Moderate recommendation for pharmacologic prophylaxis against VTE in injured children with a traumatic brain injury.	59%
• Weak recommendation for pharmacologic prophylaxis against VTE in injured children who are admitted to the pediatric intensive care unit.	69%
Bleeding risks	
• For children whose risk of VTE requires pharmacologic prophylaxis, this prophylaxis should be held for 2 d following an abdominal operation (in the absence of active bleeding).	62%
• For children whose risk of VTE requires pharmacologic prophylaxis, this prophylaxis should be held for 2 d following a thoracic operation (in the absence of active bleeding).	59%
• For children whose risk of VTE requires pharmacologic prophylaxis, this prophylaxis should be held for 2 d following an orthopedic operation (in the absence of active bleeding).	47%

No recommendation: recommendations for routine VTE prophylaxis are not affected by the presence or absence of this factor.
Weak recommendation: weak recommendation in favor of routine VTE prophylaxis if other factor(s) are present.
Moderate recommendation: moderate recommendation in favor of routine VTE prophylaxis if other factor(s) are present.
Strong recommendation: strong recommendation in favor of routine VTE prophylaxis if other factor(s) are present.
Very strong recommendation: recommendation in favor of routine VTE prophylaxis even if *no additional* factor(s) are present.

children, increasing the risk between 2- and 20-fold.[12,19,22,23] It is not clear why the expert panel did not recommend VTE prophylaxis more strongly in this setting. In trials of LMWH to prevent VTE in children with CVC and malignancy, LMWH use has not been proven to prevent VTE.[24–26] Perhaps, this lack of proven effectiveness of LMWH prophylaxis against CVC-related deep venous thrombosis influenced the panel's recommendations. In addition, the risk associated with CVC in trauma patients is potentially reversible by removal of the CVC.

The recommendations of our expert panel differ somewhat from the current recommendations in adult trauma patients. The most recent practice management guidelines from the Eastern Association for the Surgery of Trauma (EAST) give a Level II recommendation for the use of LMWH for patients with pelvic fractures, lower extremity fractures, and spinal cord injury.[14] Although near-consensus agreement for pediatric spinal cord injury and pelvic fracture was achieved among our expert panel, the strength of recommendation would not warrant prophylaxis as stand-alone risk factors. This may reflect the proportionately lower incidence of these injuries in children in addition to the mitigating factor of young age as protective against VTE. In addition, EAST and the ACCP recommend prophylaxis for major trauma patients.[13,14] Major polytrauma (Injury Severity Score [v] > 25) was supported at the near-consensus level among the pediatric expert panel. Head injury is a primary driver of ISS in pediatric trauma, and it is possible that the perceived bleeding risk associated with head injury precluded a consensus.

Bleeding represents the other side of the pharmacologic prophylaxis coin. The expert panel did not reach consensus on the use of pharmacologic prophylaxis relative to potential bleeding. However, the consensus recommendation for mechanical prophylaxis when pharmacologic prophylaxis is felt to be unsafe implies recognition of some bleeding risk with chemical prophylaxis. Fewer than 20% of our experts recommended no pharmacologic prophylaxis whatsoever in the setting of different bleeding risks (Fig. 3). This suggests that for children with significant VTE risk, pharmacologic prophylaxis should still be pursued, although cautiously, in the face of a bleeding risk.

Limitations

Our study reports a consensus process rather than a patient outcome study. Consensus about the use of VTE prophylaxis does not prove its safety or efficacy in pediatric trauma. Accordingly, the findings of the current study should not discourage future scientific inquiry to provide better answers to the questions at hand.

Risk of VTE involves the interplay of multiple factors, and it is difficult to design a study that addresses the contribution of each factor individually. Terms such as *weak*, *moderate*, or *strong* carry a level of subjectivity among participants. The importance of a recommendation could be considered a function of both the strength of the recommendation and the level of consensus. For example, it is not clear which is more important for patient care, a consensus weak recommendation (such as CVC) or a near-consensus strong recommendation (such as pelvic fracture). If a lower threshold for consensus had been selected, additional factors would have been recognized at that level. The survey design did not address how differing recommendations from various specialists might influence the care of a patient. In addition, outcomes such as patient discomfort, therapeutic monitoring, cost, and patterns of diagnosis were not specifically addressed in the study design.

This study faced challenges with regard to the expert panel. Expertise in this arena is difficult to define. Both peer nomination and self-reported qualifications are limited with regard to identifying experts, and the combination of these two methods does not guarantee expertise. Despite efforts to recruit additional experts in the fields of orthopedics, neurosurgery, adult trauma surgery, and pharmacy, participation among these groups was underrepresented relative to the other disciplines. Although the overall response rate for completion of the three rounds of the Delphi process was very good at 82%, we had a loss of four participants between the first two rounds as a result of incomplete contact information reporting.

CONCLUSION

Current scientific data are insufficient to provide fully evidence-based guidance for the complex decisions regarding VTE prophylaxis in pediatric trauma. This study identifies consensus among a national panel of diverse experts in five key areas as follows: most patients 12 years and younger do not need VTE prophylaxis, patient ambulation is not exclusively protective against VTE, mechanical prophylaxis has a role in patients who cannot safely receive pharmacologic prophylaxis, pharmacologic prophylaxis should be strongly considered in patients with a personal history of VTE, and pharmacologic prophylaxis should be considered in patients with a CVC. These findings should guide future trial design to provide answers as to the best use of VTE prophylaxis in pediatric trauma. In addition, these findings may help with current decision making for injured children.

AUTHORSHIP

All authors designed the study, interpreted the data, and revised the manuscript. E.V.S.F., A.M., C.J.S., and A.J.T. conducted and updated the literature review. S.J.H. and J.K.P. acquired and analyzed the data. S.J.H. and J.K.P. drafted the initial manuscript.

ACKNOWLEDGMENT

We thank the PTS for its leadership as well as its organizational and administrative support of this project. We also thank members of the expert consensus panel for their ongoing participation: Randall Burd, Daniel Couture, Michele David, Peter Ehrlich, Rich Falcone, Ann Marie Flannery, Barbara Gaines, David Gourlay, Elliott Haut, Jeffrey Haynes, Joseph Iocono, Martin Keller, Nathaniel Kreykes, Sandi Lam, Francois Luks, Patti Massicotte, Paul Monagle, David Mooney, David Notrica, Robert Parker, D Dean Potter, David Procaccini, Leslie Raffini, Kenneth Remy, Edward Truemper, Marisa Tucci, David Wrubel, and Guy Young as well as other panelists who participated along the way.
We also acknowledge the PTS for supporting the work of the authors, who comprise the PTS VTE workgroup. PTS provided administrative, technical, and data management support for this project.

DISCLOSURE

The authors declare no conflicts of interest.

Dr. Hanson is a site investigator for an anticoagulation trial sponsored by Bristol-Myers Squibb. Dr. O'Brien is the principal investigator and a steering committee member for anticoagulation trials sponsored by Bristol-Myers Squibb and Pfizer. Dr. Faustino is a member of the data and safety monitoring board for an anticoagulation trial sponsored by Glaxo-Smith-Kline, and is partially supported by a grant from the American Heart Association.

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