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SURVEY OF PHARMACOLOGIC THROMBOPROPHYLAXIS IN CRITICALLY ILL CHILDREN

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Abstract

Objective—There is lack of evidence to guide thromboprophylaxis in the pediatric intensive care unit (PICU). We aimed to assess current prescribing practice for pharmacologic thromboprophylaxis in critically ill children.

Setting—PICUs in the United States and Canada with at least 10 beds.

Design—Cross-sectional self-administered survey of pediatric intensivists using adolescent, child and infant scenarios.

Participants—PICU clinical directors or section heads.

Intervention—None.

Measurements and Main Results—Physician leaders from 97 of 151 (64.2%) PICUs or their designees responded to the survey. In mechanically ventilated children, 42.3% of the respondents would usually or always prescribe thromboprophylaxis for the adolescent but only 1.0% would prescribe it for the child and 1.1% for the infant. Considering all PICU patients, 3.1%, 32.0% and 44.2% of respondents would never prescribe thromboprophylaxis for the adolescent, child and infant scenarios, respectively. These findings were significant ($P<.001$ for the adolescent versus child and infant; $P=.002$ for child versus infant). Other patient factors that increased the likelihood of prescribing prophylaxis to a critically ill child for all 3 scenarios were the presence of hypercoagulability, prior deep venous thrombosis or a cavopulmonary anastomosis. Prophylaxis was less likely to be prescribed to patients with major bleeding or an anticipated invasive intervention. Low molecular weight heparin was the most commonly prescribed drug.

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Conclusions—In these scenarios, physician leaders in PICUs were more likely to prescribe thromboprophylaxis to adolescents compared to children or infants, but they prescribed it less often in adolescents than is recommended by evidence-based guidelines for adults. The heterogeneity in practice we documented underscores the need for rigorous randomized trials to determine the need for thromboprophylaxis in critically ill adolescents and children.

Keywords

venous thromboembolism; anticoagulants; prevention; risk factor; intensive care

INTRODUCTION

Venous thromboembolism (VTE), which includes deep venous thrombosis (DVT) and pulmonary embolism (PE), is a leading cause of excess mortality and morbidity in hospitalized adults (1, 2). In children, the annual rate of VTE increased from 34 to 58 cases per 10,000 hospitalized children between 2001 and 2007 (3). The incidence of VTE in children is bimodal and peaks during infancy and adolescence (3, 4). In contrast to adults who usually have unprovoked VTE, most episodes of VTE in children are associated with risk factors (4, 5), most commonly central venous catheter (CVC) use (4–10). Hypercoagulable states, immobility and life-sustaining interventions also predispose critically ill children to DVT (4, 5, 7, 10–15).

Although there is strong evidence that for adults, pharmacologic thromboprophylaxis decreases the incidence of DVT by 45–55% (16–18) and PE-related death by 31–100% (19–22), the risks and benefits of thromboprophylaxis in children are unclear and based on small trials and observational studies (23–29). Extrapolation from adult thromboprophylaxis studies may not be relevant for children because of the dynamic development of the coagulation system during childhood (30) and differences in the underlying diseases and medications in childhood that may affect the development of VTE (5).

In this study, we aim (1) to determine the reported frequency of pharmacologic thromboprophylaxis in critically ill children, (2) to determine patient factors considered important by pediatric intensivists in prescribing pharmacologic thromboprophylaxis, and (3) to determine the most common anticoagulants used.

METHODS

Research Design and Oversight

We performed a survey of physician leaders of pediatric intensive care units (PICU) in the United States and Canada sponsored by the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network, a collaboration of clinical pediatric critical care researchers across North America. The study was reviewed and approved by the Human Investigations Committee at Yale University School of Medicine. The survey was voluntary and anonymous, and participation implied consent.

Respondents

Recipients of the survey were PICU medical directors, heads of the section of pediatric critical care or their designees. There were 151 unique PICUs identified from the 2008 Annual Survey of the American Hospital Association, PALISI mailing list and American and Canadian PICU databases. We limited the survey to PICUs with at least 10 beds to provide the recipients with an adequate number of patients upon which their practice was

based. One recipient was chosen from each PICU. Respondents were requested to answer the questions on behalf of all critical care physicians in the unit.

Survey Development

The survey focused on pharmacologic thromboprophylaxis in preparation for a proposed pharmacologic prevention trial and did not include mechanical thromboprophylaxis. The survey instrument was case-based, structured around 3 patients reflecting different age-related VTE risk. These were a 17 year old adolescent, a 4 year old child and a 3 month old infant who were recently admitted to the PICU after intubation for mechanical ventilator support. We chose 17 years of age for the adolescent scenario because this is defined as an "adult" in the American College of Chest Physicians' (ACCP) guidelines for uses of thromboprophylaxis (5). For each patient, the recipients were asked to indicate, using a Likert scale (i.e., 1=never, 2=rarely, 3=sometimes, 4=usually, or 5=always), how often they would provide thromboprophylaxis. Respondents who answered rarely, sometimes or usually were asked, using a Likert scale (i.e., 1=less likely, 2=neither less nor more likely, or 3=more likely), how each of 20 patient factors would affect their decision to prescribe prophylaxis. Respondents who answered rarely, sometimes, usually and always to the first question were additionally asked, using a Likert scale (i.e., 1=never, 2=rarely, 3=sometimes, 4=usually, or 5=always), how often they would prescribe each of 7 anticoagulants as prophylaxis to the adolescent and child.

Items for the survey instrument were based on a literature review, investigator discussion, and suggestions from the PALISI Scientific Committee. The list of patient factors was the same for all respondents. However, some items differed depending on the respondent's type of PICU. For example, physicians working in cardiac PICUs had a modified instrument including items related to operative congenital heart disease patients, which were not included for physicians in a medical-surgical unit.

We collected the following data: number of years in practice, specialty background, country of practice, prior participation in a PALISI-supported study, size of the PICU (i.e., number of beds), type of PICU (i.e., medical-surgical, cardiac or mixed medical-surgical and cardiac) and availability of thromboprophylaxis implementation strategies (i.e., informal unit policies, written guidelines or preprinted orders). We pilot tested the instrument on 5 pediatric intensivists and revised it before final distribution.

Survey Administration

The survey, which was conducted from November 2009 to April 2010, was initially administered electronically using a commercial web-based survey tool (SurveyMonkey.com, Menlo Park, CA). Electronic reminders were sent twice to non-respondents every 2 weeks. Physicians who did not respond after the second reminder were sent paper copies of the survey monthly for 3 months to increase the response rate. Non-respondents were also contacted by phone.

Statistical Analysis

Descriptive data are presented as mean±SD, absolute counts and percentages. Unadjusted pair-wise comparisons of the distributions of the reported frequency of thromboprophylaxis by patient scenario were done using the Wilcoxon Signed Rank test, correcting for 3 comparisons with the Bonferroni approach (critical alpha of .05/3=.017). We adjusted for factors associated with the likelihood of prescribing thromboprophylaxis using nonlinear mixed effects modeling approach (31). The model accounted for the ordinal nature of the Likert scale and the repeated responses by each respondent. Covariates included the patient scenarios and the respondents' PICU characteristics (i.e., country, size, type and presence of

thromboprophylaxis implementation strategies). $P<.05$ was considered statistically significant for the nonlinear mixed effects model.

Responses for patient factors considered important by pediatric intensivists were reported descriptively. A patient factor was considered important if more than half of the respondents indicated that they were more or less likely to prescribe thromboprophylaxis in the presence of the factor.

The most prescribed anticoagulant was defined as having the largest combined percentages of being usually and always prescribed. The responses for the most often prescribed anticoagulant were compared with the other anticoagulants using the Wilcoxon Signed Rank test, correcting for 6 comparisons with the Bonferroni approach (critical alpha of .05/6=. 008).

Statistical tests were performed using SPSS 16.0 for Windows (SPSS, Inc., Chicago, IL) and SAS 9.2 (SAS Institute, Inc., Cary, NC).

RESULTS

The survey was sent to the physician leaders of all of the 151 PICUs, with at least 10 beds, in the United States and Canada. Of these, 130 (86.1%) PICUs were medical-surgical or mixed and 134 (88.7%) were from the United States.

Physician leaders from 97 (64.2%) PICUs, or their designees, responded to the survey (Table 1). The respondents had practiced critical care for 16±7 years. Most respondents were pediatricians (n=89, 91.8%) and from the United States (n=84, 86.6%). Most (n=55, 57.3%) had participated in at least one PALISI-supported research study and were working in a PICU with at most 20 beds (n=54, 55.7%). The majority of the PICUs (n=81, 83.5%) were medical-surgical or mixed. Approximately 60% of the PICUs had informal unit policies, written guidelines or preprinted orders on thromboprophylaxis.

Reported Frequency of Pharmacologic Thromboprophylaxis

Respondents would prescribe thromboprophylaxis more often for the adolescent compared to the child or infant (Figure 1). A total of 41 of the 97 (42.3%) respondents would usually or always prescribe prophylaxis to the adolescent compared to 1 of 97 (1.0%) respondents for the child ($P<.001$), and 1 of 95 (1.1%) respondents for the infant ($P<.001$), whereas 3.1%, 32.0% and 44.2% of the respondents would never prescribe thromboprophylaxis for the adolescent, child or infant, respectively. More respondents would never prescribe thromboprophylaxis to the child compared to the infant ($P=0.002$). These findings were confirmed in the nonlinear mixed effects model. In addition, respondents from PICUs with a thromboprophylaxis implementation strategy were 34 times more likely to prescribe prophylaxis compared to those with no strategy ($P<.001$). The likelihood of prescribing prophylaxis among respondents from the United States versus Canada, or from PICUs of different sizes or types was not different (data not shown).

Patient Factors Considered Important for Pharmacologic Thromboprophylaxis

The majority of the respondents who would rarely, sometimes or usually prescribe thromboprophylaxis indicated that the presence of hypercoagulability, prior DVT or a cavopulmonary anastomosis increased the likelihood of a prescription across all age groups, whereas major bleeding or an anticipated invasive intervention decreased its likelihood (Table 2). While more than half of the respondents indicated that myocardial dysfunction increased the likelihood of prophylaxis in the 3 patient scenarios, a similar number of respondents considered this factor neither less nor more likely to affect their decision,

particularly in the infant scenario. More than half of the respondents were more likely to prescribe thromboprophylaxis in the adolescent scenario, but not in the child or infant scenario, in the presence of obesity, immobility, use of oral contraceptives, spinal cord injury, underlying malignancy or lower extremity fracture. Polycythemia in an adolescent also increased the likelihood of prescribing prophylaxis. A similar number of respondents indicated that polycythemia in a child or cyanotic congenital heart disease in an infant either increased the likelihood of prophylaxis or did not affect their decision. The presence of a CVC did not affect the likelihood of thromboprophylaxis prescription.

Most Common Anticoagulant Used for Thromboprophylaxis

Among the respondents who would prescribe thromboprophylaxis, 66 of 94 (70.2%) and 40 of 71 (56.1%) would usually or always prescribe low molecular weight heparin (LMWH) to the adolescent or child, respectively (Figure 2). LMWH was prescribed more often than the other anticoagulants ($P<.001$ for adolescent and child scenarios).

DISCUSSION

We found wide variability in stated pharmacologic thromboprophylaxis practice among physician leaders of PICUs in North America. The responses are likely representative of the practice in North American PICUs with at least 10 beds. The proportion of the respondents' PICU types and locations are comparable to that of the entire survey target population. The critically ill adolescent was more likely than the child or infant to be prescribed thromboprophylaxis. The presence of hypercoagulability, prior DVT or a cavopulmonary anastomosis increased the reported likelihood of thromboprophylaxis regardless of patient age, whereas the presence of major bleeding or an anticipated invasive intervention decreased its likelihood. The commonest drug prescribed was LMWH. Although this variation in physician practice is consistent with previous thromboprophylaxis surveys of internists, adult critical care specialists, pediatric trauma nurses and pediatric intensivists (32–37), this is the first survey to show broad variability in the likelihood of thromboprophylaxis for critically ill children of different ages.

The ACCP evidence-based clinical practice guidelines on antithrombosis provided separate recommendations for children and adults (Table 3) (1, 5). An adult defined as anyone 16 years and older was arbitrarily determined based on the age when children are transitioned to adult services and not on physiologic characteristics such as pubertal status and physical development (5). The adult guidelines strongly recommend pharmacologic thromboprophylaxis in acutely ill adults, similar to the adolescent in our scenario, unless there is a contraindication such as increased risk of bleeding (Table 3) (1). Although over 40% of the respondents stated that they would usually or always prescribe pharmacologic thromboprophylaxis to this patient, this is significantly less than the 85% to 90% endorsement of internists and adult ICU specialists surveyed about patients with similar illnesses (32, 35). The lack of data on the true burden of illness of VTE in adolescents, uncertainty of the risks and benefits of thromboprophylaxis in this age group, absence of a thromboprophylaxis implementation strategy, and unfamiliarity with the adult age threshold may have influenced the reported practice.

A smaller proportion of respondents in this survey reported that they would prescribe thromboprophylaxis for the younger patients. O'Brien et al. found that only about 5% of trauma practitioners would provide pharmacologic thromboprophylaxis to children below 10 years old (33). The practice variation does not seem to be due to the risks of bleeding as there was no age-dependent difference in thromboprophylaxis prescription in patients with major bleeding or anticipated invasive intervention. While the likelihood of thromboprophylaxis is increased in all 3 patient scenarios in the presence of

hypercoagulability, prior DVT or a cavopulmonary anastomosis, the overall likelihood of prophylaxis in younger patients remained significantly lower than in the adolescent. Only respondents who stated that they rarely, sometimes or usually prescribe thromboprophylaxis were surveyed on the influence of patient factors on their decision to prescribe thromboprophylaxis. In the absence of high quality evidence, it is unclear whether the perceived burden of illness, such as the morbidity from DVT, outweighs the risks of complications of thromboprophylaxis in particular groups of children.

Some of the patient factors increased the likelihood of prophylaxis for specific age groups. Pre-PICU characteristics (obesity, oral contraceptive pills and malignancy), current conditions (myocardial dysfunction, immobility, spinal cord injury and lower extremity fracture) and laboratory abnormality (polycythemia) were associated with higher likelihood of prescribing prophylaxis to adolescents but not to younger patients. These responses are consistent with the ACCP guidelines and reflect adult risk factors for DVT (Table 3) (1).

Regardless of age, majority of the respondents reported that the presence of a CVC did not affect their decision to prescribe prophylaxis. Clarke et al. reported that only 45% of the pediatric intensivists who responded to their survey regularly used heparin prophylaxis for CVC (36). Unfractionated heparin (UFH) at 5–10 units/kg/hr was continuously infused to mitigate CVC complications such as thrombosis and occlusion. Randomized trials in children with CVC failed to prove that thromboprophylaxis reduces CVC-related DVT (23–25). While these trials were not adequately powered, they formed the basis of the pediatric ACCP recommendation that the risks of thromboprophylaxis for CVC-related DVT do not outweigh the benefits (5) which we hypothesize precludes most intensivists we surveyed from providing prophylaxis in patients with CVC.

LMWH was the most commonly prescribed anticoagulant, which is consistent with adult and pediatric guidelines (1, 5). LMWH has become the preferred anticoagulant in the treatment of VTE in children (7, 9) despite its unproven efficacy in children due to lack of formal studies (5). The reason for the greater use of LMWH may be related to potential advantages (5) including minimal monitoring requirements which is typically not the case for UFH, lack of interference by other drugs or diet, and marketing influences.

Our study has several strengths. Our respondents come from the United States and Canada and represent a wide range of PICU types and sizes. The use of close-ended items in our questionnaire increased the accuracy and completeness of the survey (38). We combined electronic and postal strategies to maximize the response rate (38). Our rate of 64.2% is typical (38) and somewhat higher than the response rates achieved in other physician surveys on DVT in children (39, 40). Our results reflect current views of the largest number of pediatric respondents to a survey on DVT in children (33, 36, 39, 40).

Certain limitations should also be noted. Our focus was pharmacologic rather than mechanical thromboprophylaxis. The responding physician leaders may not reflect the practice of the entire PICU team (33, 34). Our respondents reported practice in medium to large size PICUs, and approaches may be different in smaller PICUs. Further, actual practice may differ from reported practice, as is the case for all surveys (33). Other risk factors may increase the likelihood of thrombosis and may have affected the decision to provide prophylaxis (5). However, in order to maximize the responses, we limited the number of factors to include in the survey. Lastly, we did not inquire on the perceived morbidity of DVT in the different patient scenarios which may have affected the likelihood of thromboprophylaxis in these patients.

Surveys provide a snapshot of current practitioners' practice patterns and opinions (33). They are instrumental in the development of a research agenda and in the conduct of

successful trials (34, 41). Observational studies have identified risk factors for DVT (4, 7–10) while our survey indicates factors considered important by practitioners. Other surveys have also reported patient factors and radiologic features that make VTE clinically significant (39, 42). Before conducting a randomized trial of thromboprophylaxis in children, it is essential to perform a prospective multicenter observational study to examine the burden of illness of DVT. Participation of sites that may enroll patients in a future randomized trial (e.g., PALISI or Canadian Critical Care Trials Group sites) will provide key data, engage the community, and potentially improve the success of the trial. Due to the low incidence of DVT in children, we suggest that specific high risk patient populations should be targeted for future DVT research. Randomized trials should evaluate the risks and benefits of different pharmacologic approaches, particularly LMWH.

CONCLUSION

In this survey of physician leaders of PICUs in North America, we found wide variation in reported prescribing of pharmacologic thromboprophylaxis for critically ill children. Although physician leaders in PICUs are markedly more likely to prescribe thromboprophylaxis to adolescents compared to younger patients, prescribing appears to be less frequent than is recommended by evidence-based adult guidelines. Thromboprophylaxis is likely to be prescribed for younger patients only in the presence of certain risk factors. This variability exposes the paucity of rigorous research on which to base practice. Although guidelines may increase the consistency of care, advancing this field requires high quality observational studies to inform the burden of illness, and randomized trials to identify optimal approaches to thromboprophylaxis.

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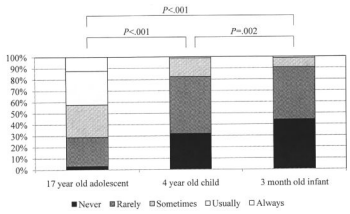

Figure 1.
Frequency of responses (in percent) to the question of how often a respondent prescribes pharmacologic prophylaxis against DVT to a critically ill patient by patient scenario (n=97).

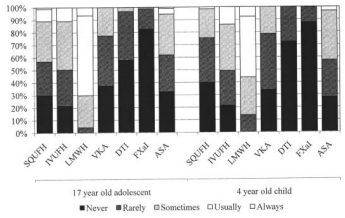

Figure 2.

Frequency of responses (in percent) to the question of how often a particular pharmacologic thromboprophylaxis approach will be prescribed for a critically ill patient. Only respondents who rarely, sometimes, usually and always prescribe thromboprophylaxis were asked about the choice of anticoagulant (n=94 for adolescent scenario; n=71 for child scenario). For each patient scenario, all pair-wise comparisons between low molecular weight heparin (LMWH) and the other anticoagulants are statistically significant at $P<.001$. SQUFH – subcutaneous unfractionated heparin, IVUFH – intravenous unfractionated heparin, VKA – vitamin K antagonists, DTI – direct thrombin inhibitors, FXaI – factor Xa inhibitors, and ASA – aspirin.

Table 1

Characteristics of the 97 survey respondents and their pediatric intensive care units (PICU).

Years in practice, mean ± SD	**16 ± 7**
Specialty background, no. (%)	
Pediatrics	89 (91.8%)
Internal medicine-pediatrics	3 (3.1%)
Anesthesia	3 (3.1%)
Emergency medicine	1 (1.0%)
Pharmacy	1 (1.0%)
Country of practice, no. (%)	
United States	84 (86.6%)
Canada	13 (13.4%)
Prior participation in a PALISI-supported study, no. (%)	
Yes	55 (57.3%)
No	35 (36.5%)
Not known to the respondent	6 (6.3%)
Size of the PICU, no. (%)	
≤ 20 beds	54 (55.7%)
21–30 beds	24 (24.7%)
31–40 beds	10 (10.3%)
> 40 beds	9 (9.3%)
Type of PICU, no. (%)	
Medical-surgical	27 (27.8%)
Cardiac	16 (16.5%)
Mixed medical-surgical and cardiac	54 (55.7%)
Thromboprophylaxis implementation strategies, no. (%)[a]	
Informal unit policy	29 (29.9%)
Written guideline	19 (19.6%)
Preprinted order	18 (18.6%)
None of the above	40 (41.2%)

[a]The percentages do not total 100% as some units use more than one approach. PALISI – Pediatric Acute Lung Injury and Sepsis Investigators.

Table 2

Patient factors and likelihood of prescribing thromboprophylaxis among respondents who indicated that they would rarely, sometimes or usually prescribe pharmacologic thromboprophylaxis. Data are presented as number of responses (frequency in percent). N/A – not applicable.

Patient Factor	17 Year old Adolescent (n=82)			4 Year Old Child (n=66)			3 Month Old Infant (n=53)		
	Less Likely	Neither Less nor More Likely	More Likely	Less Likely	Neither Less nor More Likely	More Likely	Less Likely	Neither Less nor More Likely	More Likely
Hypercoagulability	0 (0)	1 (1.2)	80 (98.8)	0 (0)	4 (6.1)	62 (93.9)	0 (0)	4 (7.5)	49 (92.5)
Prior deep vein thrombosis	0 (0)	3 (3.7)	79 (96.3)	0 (0)	4 (6.1)	62 (93.9)	0 (0)	4 (7.5)	49 (92.5)
Obesity	0 (0)	9 (11.0)	73 (89.0)	0 (0)	34 (51.5)	32 (48.5)	N/A	N/A	N/A
Immobility	2 (2.4)	9 (11.0)	71 (86.6)	2 (3.0)	37 (56.1)	27 (40.9)	6 (11.3)	35 (66.0)	12 (22.6)
Oral contraceptives	1 (1.2)	13 (15.9)	68 (82.9)	N/A	N/A	N/A	N/A	N/A	N/A
Cavopulmonary anastomosis	1 (1.6)	15 (24.6)	45 (73.8)	1 (2.0)	14 (27.5)	36 (70.6)	1 (2.3)	11 (25.6)	31 (72.1)
Spinal cord injury	3 (4.3)	18 (26.1)	48 (69.6)	4 (7.3)	24 (43.6)	27 (49.1)	N/A	N/A	N/A
Myocardial dysfunction	0 (0)	25 (36.2)	44 (63.8)	0 (0)	30 (45.5)	36 (54.5)	0 (0)	26 (49.1)	27 (50.9)
Polycythemia	1 (1.6)	25 (41.0)	35 (57.4)	3 (5.9)	22 (43.1)	26 (51.0)	4 (9.3)	19 (44.2)	20 (46.5)
Malignancy	0 (0)	31 (44.9)	38 (55.1)	0 (0)	35 (63.6)	20 (36.4)	N/A	N/A	N/A
Lower extremity fracture	5 (7.2)	26 (37.7)	38 (55.1)	5 (9.1)	35 (63.6)	15 (27.3)	N/A	N/A	N/A
Pulmonary hypertension	0 (0)	30 (49.2)	31 (50.8)	1 (2.0)	31 (60.8)	19 (37.3)	0 (0)	28 (65.1)	15 (34.9)
Cyanotic congenital heart disease	1 (1.3)	40 (50.0)	39 (48.8)	1 (1.5)	37 (56.1)	28 (42.4)	1 (1.9)	24 (46.2)	27 (51.9)
Central venous catheter	2 (2.4)	46 (56.1)	34 (41.5)	2 (4.5)	40 (60.6)	23 (34.8)	3 (5.7)	30 (56.6)	20 (37.7)
Complex cardiac repair	2 (3.3)	35 (57.4)	24 (39.3)	2 (3.9)	34 (66.7)	15 (29.4)	2 (4.7)	30 (69.8)	11 (25.6)
Pulmonary artery catheter	1 (1.6)	38 (62.3)	22 (36.1)	2 (3.9)	37 (72.5)	12 (23.5)	2 (4.7)	26 (60.5)	15 (34.9)
Multiple cardiac catheterization	0 (0)	43 (70.5)	18 (29.5)	1 (2.0)	38 (74.5)	12 (23.5)	2 (4.7)	29 (67.4)	12 (27.9)
Sepsis	17 (20.7)	55 (67.1)	10 (12.2)	13 (19.7)	48 (72.7)	5 (7.6)	7 (13.2)	41 (77.4)	5 (9.4)
Invasive intervention	68 (82.9)	14 (17.1)	0 (0)	54 (81.8)	11 (16.7)	1 (1.5)	42 (79.2)	11 (20.8)	0 (0)
Major bleeding	78 (95.1)	4 (4.9)	0 (0)	58 (87.9)	7 (10.6)	1 (1.5)	46 (86.8)	7 (13.2)	0 (0)

Table 3

Summary of Antithrombotic Consensus Conference recommendations from the American College of Chest Physicians on pharmacologic thromboprophylaxis (1, 5).

Patient Factor	Adult Guidelines	Pediatric Guidelines
Severe respiratory illness	SR	—
Hypercoagulability	—	—
Prior deep vein thrombosis	SR	—
Obesity	SR	—
Immobility	SR	—
Oral contraceptives	SR	—
Cavopulmonary anastomosis	—	R
Spinal cord injury	SR	—
Myocardial dysfunction	SR	R
Polycythemia	—	—
Malignancy	NR	NR
Lower extremity fracture	SR	—
Pulmonary hypertension	—	R
Cyanotic congenital heart disease	—	R
Central venous catheter	NR	NR
Complex cardiac repair	—	—
Pulmonary artery catheter	—	—
Multiple cardiac catheterization	—	—
Sepsis	SR	—
Invasive intervention	NR	NR
Major bleeding	NR	NR

SR – strongly recommended, R – recommended, NR – not recommend