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Pediatric Venous Thromboembolism in the United States: A Tertiary Care Complication of Chronic Diseases

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Abstract

Background—Pediatric venous thromboembolism (VTE) is an increasingly common problem. We hypothesized that VTE occurs most commonly in tertiary care settings and that the pattern of associated illnesses may have changed from earlier reports.

Methods—The Kids' Inpatient Database 2006 was utilized to identify children ≤18 years old with in-hospital VTE. Children were identified by the presence of thrombosis specific ICD-9-CM diagnosis or procedure codes. Remaining ICD-9-CM codes were utilized to categorize patients by acute or chronic illness. The incidence of in-hospital VTE by hospital type, age, gender, race, and disposition were estimated.

Results—Over 4,500 children met the inclusion criteria (188/100,000 discharges). Most VTE discharges (67.5%) were from children's hospitals (RR 5.09; 95% CI 4.76; 5.44). Underlying chronic illnesses were associated with most VTE (76.2%), most commonly: cardiovascular (18.4%), malignancy (15.7%), and neuromuscular disease (9.9%). VTE not associated with chronic illness were most often idiopathic (12.6%), followed by infections (9.5%) and trauma (9.1%). The greatest proportions of children with VTE were infants (23.1%) and adolescents (37.8%). However, when standardized against the entire database of discharges, infants were least likely to develop VTE (RR 0.48; 95% CI 0.43; 0.52), while adolescents were at highest risk (RR 1.89; 95% CI 1.73; 2.07). Hospitalizations ending with death were more likely to include VTE (RR 6.16; 95% CI 5.32; 7.13).

Conclusions—Pediatric VTE is most commonly seen in tertiary care. Adolescents are at greatest risk to develop in-hospital VTE. Patients whose hospitalization ended with death are at much greater risk to develop VTE.

Keywords

Thrombosis; Thromboembolism; Epidemiology; Pediatric; ICD-9-CM

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Introduction

Venous thromboembolism (VTE), which encompasses both deep venous thrombosis (DVT) and pulmonary embolism (PE), is an important cause of morbidity and mortality in adults. In contrast, VTE are considered to be relatively rare events in children [1]. Over the past 20 years, large epidemiological studies of pediatric VTE are sparse in comparison to those for adult VTE. Recent studies have shown that the incidence of VTE in children has been increasing over the last decade, creating a new epidemic in pediatric tertiary care [2,3]. The most commonly cited incidence among children is 53 per 100,000 admissions based on the Canadian Registry [1].

Raffini et al. utilized the Pediatric Health Information System (PHIS) database to define the rate of VTE among hospitalized children and evaluate how the rate has changed over time [2]. The PHIS database contains comprehensive inpatient data from throughout the United States, but is limited to free-standing children's hospitals. Approximately 11,000 pediatric VTE patients were included in the study which revealed an increasing incidence of VTE over time with the most recent estimate being 580 per 100,000 discharges. The recent development of large healthcare utilization databases enables a more comprehensive evaluation of the epidemiology of this increasingly important pediatric healthcare problem.

Pediatric VTE is a multifactorial disease, commonly seen in children with complex medical conditions. Most children with VTE have underlying disorders with associated predisposing factors, such as indwelling venous catheters, surgery, trauma, or malignancy [3–6]. Based on these risk factors for pediatric VTE, it has been postulated that the recent increase in incidence of VTE is related to advancements in treatment and supportive care for severely ill children [2,7]. The goal of this study is to refine the epidemiologic understanding of pediatric VTE association with acute and chronic diseases and to assess for differences in VTE prevalence between children hospitalized in community hospitals versus children's hospitals. We hypothesized that the spectrum of associated illnesses may have changed over the years as the incidence of VTE increased and that children hospitalized in children's hospitals would have a higher incidence of thrombosis.

Methods

Data source

The Healthcare Cost and Utilization Project (HCUP) Kids' Inpatient Database (KID) 2006, available from the Agency for Healthcare Research and Quality (AHRQ) was utilized [8]. KID is a dataset on hospital use, outcomes and charges designed to study children's use of hospital services in the United States. KID is a sample of discharges from all community, non-rehabilitation hospitals participating in HCUP, which include specialty hospitals such as obstetrics-gynecology, ear-nose-throat, short-term rehabilitation, orthopedic and pediatric institutions. Both public hospitals and academic medical centers are included. Participating hospitals provide charge information on all patients, regardless of payer, including persons covered by private insurance, Medicaid, Medicare and the uninsured. The KID has been released every three years since 1997. Inpatient stay records in the KID include clinical and resource use information available from discharge abstracts. The KID 2006 contains data from 38 State Inpatient Databases on children 20 years of age or younger who were discharged in the year 2006.

Patient population

Age, hospital type, hospital region, gender, race, median household income, and disposition were collected for all VTE discharges. Patients with a VTE were identified by discharge diagnoses using the International Classification of Diseases, 9th Revision, Clinical

Modification (ICD-9-CM). The following ICD-9-CM primary or secondary diagnosis or procedure codes were included: 325, 452, 453 (.0, .2–.42), 453 (.8–.9), 415 (.0–.11), 38 (.05, .07, .09), or 99.10. Thrombophlebitis codes (451.xx and 453.1) were not included as VTE because they do not distinguish between thrombosis and isolated phlebitis. Cases were reassigned to the control population if thrombolysis (99.10) appeared to have been used for a reason other than venous thromboembolism.

Age was classified into <1 year, 1–4 years, 5–9 years, 10–14 years, and 15–18 years. Only 32 of the 38 KID states provide age in 'days' for children less than 1 year of age. A sub-analysis of children <1 year old was performed from those 32 states. Patients with missing age data, age >18 years, and "uncomplicated birth" discharges were excluded from analysis. KID designates children's hospitals based upon self-reported NACHRI (National Association of Children's Hospitals and Related Institutions) definitions which include: "children's general hospital," "children's specialty hospital," "children's unit in a general hospital," or "not identified as a children's hospital by NACHRI." The hospitals in KID 2006 identified by the first 3 definitions are known by the investigators to include free-standing children's hospitals (children's general hospital), academic pediatric departments housed in academic medical centers (children's unit in a general hospital), or specialty children's hospitals (such as Shriners Hospitals for Children®). Therefore, for the purposes of this study, hospitals coded with the first 3 NACHRI definitions were grouped as "children's hospitals" while hospitals with the latter definition were grouped as "community hospitals."

Associated diagnostic categories

The remaining ICD-9-CM codes were used to assign an associated co-morbid diagnostic category for each VTE discharge. To identify chronic diseases, the Complex Chronic Conditions (CCC) categories were utilized based on previously published classification for pediatric patients, which includes the following categories: neuromuscular, cardiovascular, respiratory, renal, gastrointestinal, hematology and immunodeficiency, metabolic, other congenital or genetic defect, and malignancy [9]. The remaining patients were screened for trauma codes as defined by the American College of Surgeons National Trauma Data Bank (ICD-9-CM diagnosis codes: 800.00–904.9, 925.0–929.9 and 940.0–959.9) [10]. For patients without any CCC or trauma codes, one of the investigators (BAS or BAK) assigned a diagnostic category.

Some chronic conditions not included in the previously defined CCC, such as nephrotic syndrome, aplastic anemia, and diabetes mellitus were reassigned to appropriate CCC categories. The remaining patients were assigned to either an acute diagnostic category (such as infection, sick infant, pregnancy, or post-operative) or classified as idiopathic if there was no obvious precipitating illness for thrombosis based on the available ICD-9-CM codes. For the purposes of this study, acute illness occuring co-morbidly with (superimposed on) chronic conditions were not considered. Five percent of the VTE discharges were categorized by both investigators in a blinded fashion with >95% agreement.

Statistics

Descriptive statistics were used to demonstrate the distribution of VTE discharges by geography, hospital type, age, gender, race, household income, and disposition. For dichotomous and categorical variables, the χ^2 test was used to compare the VTE discharges with non-VTE discharges. The relative risk (RR) and 95% confidence intervals (95% CI) for VTE were also calculated for the dichotomous and categorical variables, using the non-VTE discharges as controls. Similarly, the relative risk of VTE-associated mortality was calculated using all other dispositions combined as a comparison group. SPSS Statistics 17.0

(IBM Corporation, Somers, NY) was used to abstract KID 2006 and for all statistical analyses.

Results

VTE discharges

KID 2006 includes 3,131,324 discharges made up of a 20% sampling of uncomplicated births and an 80% sampling of all other discharges in the KID 2006 hospital universe. After eliminating the uncomplicated birth records and limiting the data to those with a recorded admission age ≤18 years there were 2,410,351 discharges eligible for analysis. Of these, 4,708 included at least one VTE defining code; 170 of which had a thrombolysis code (99.10) without additional evidence of VTE (empyema/pleural effusion: 124, arterial thrombus: 31, CVA: 14, and fat embolism: 1), these cases were reassigned to the non-VTE group. Thus, 4,538 VTE discharges were identified (Figure 1).

Of the 4,538 VTE discharges, 427 (9.4%) had cerebral sinovenous thrombosis (ICD-9-CM: 325), 785 (17.3%) were associated with abdominal central venous thrombosis (codes: 452, 453.0, 453.2 453.3), 1,339 (29.5%) with lower extremity DVT (453.40, 453.41, 453.42), 1,536 (33.9%) with other DVT (453.8, 453.9), and 98 (2.2%) with pulmonary embolism (415.0, 415.1, 415.11). Thrombectomy codes (38.05, 38.07, and 38.09) were indicated for 149 (3.3%) cases and thrombolysis (99.10) for 751 (16.6%) cases.

Characteristics and demographics of VTE discharges

Of the 2,410,351 eligible discharges 4,538 were associated with VTE giving an estimated overall incidence of 188 VTE per 100,000 discharges (Table). Approximately 67.5% of the VTE occurred in discharges from children's hospitals, resulting in a significantly increased probability of VTE for children treated in these institutions.

The age pattern of the 4,538 VTE discharges reveals a bimodal distribution with the majority of VTE occurring in children >15 years old at admission with another lower peak in children <1 year of age at admission (Figure 2A). This distribution is consistent regardless of hospital type. However, when the data are standardized for the total number of discharges in each age category, the bimodal distribution disappears revealing an increasing incidence of VTE with increasing age (Figure 2B). Similarly, the relative risk of VTE increases with increasing age. Neonates (RR 0.29; 95% CI 0.26–0.4) and infants (RR 0.48; 95% CI 0.43–0.52) appear to be less likely to develop VTE in comparison to their reference groups (age 29–364 days or 1–4 years old; respectively), while early adolescents aged 10–14 (RR 1.62; 95% CI 1.45–1.80) and older teens (15–18 years; RR 1.89; 95% CI 1.73–2.07) were at greater risk compared to the 1–4 year old reference group.

Male gender is associated with a modestly increased risk of VTE (RR 1.20; 95% CI 1.13–1.27; Table). There were no significant race associations with the exception of an apparently lower likelihood of VTE for Hispanics (RR 0.61; 95% CI 0.55–0.67). Discharges ending with in-hospital death were significantly more likely to be associated with VTE (RR 6.16; 95% CI 5.32–7.13; Table).

Medical conditions associated with VTE discharges

Of the 4,538 VTE discharges, 76.2% were associated with at least one Complex Chronic Condition while 12.6% were idiopathic and 25% were associated with an acute disease process (Figure 3A). The most common CCCs associated with VTE were cardiovascular disease (18.4%), malignancies (15.7%), and neuromuscular disease (9.9%). Acute disease processes (in the absence of any chronic condition) most commonly associated with VTE

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were infectious (9.5%) and trauma or post-operative (9.1%). Sick infants (3.9%) and VTE associated with teen pregnancy (0.7%) were less common. Sick infants were children under 1 year of age at diagnosis with no clear VTE precipitating illness, most of these records included ICD-9-CM codes for electrolyte imbalance, nutrition issues, acute respiratory processes, and/or prematurity.

When considering acute versus chronic underlying medical conditions associated with VTE, chronic conditions predominate in early childhood with acute conditions becoming increasingly important in older children (Figure 3B). In fact, in adolescents aged 15–18 years at admission, acute medical conditions were nearly as likely to be present in association with VTE as were chronic conditions (acute:chronic ratio: 0.95). This trend was statistically significant ($P<0.00001$).

Discussion

In this study, VTE was identified in 188/100,000 discharges for children ≤18 years of age, utilizing the Kid's Inpatient Database (KID) 2006 which included over 2.4 million eligible discharges. The majority of patients with VTE (77.7%) also had at least one complex chronic condition (CCC). In fact, 11.5% of the cases were associated with the presence of more than one CCC. Similar to the PHIS report, the majority of VTE were associated with cardiovascular disease (18.4%) [2]. The evidence from this study and the PHIS survey strongly suggest that patients with chronic neuromuscular diseases (brain and spinal cord malformations, infantile cerebral palsy, mental retardation, epilepsy, and central nervous system degeneration) are the third largest group at risk for childhood VTE. These data are in contrast to the Canadian data that reported the most common associated conditions in descending order to be cancer, congenital heart disease, trauma/surgery, total parenteral nutrition dependence, infections, and nephrotic syndrome [1]. While sick infants may have an associated CCC, chronic conditions are not present in all cases.

For VTE not associated with chronic conditions, 12.6% appear to be idiopathic. However, our assessment of idiopathic causes is significantly limited by using healthcare utilization data. For instance, medication prescription patterns and family history of thrombosis are not recorded in KID. The Canadian registry reported a higher incidence of trauma/surgery (14.6%), compared to only 9.1% trauma/post-operative in this analysis [1]. This may potentially be explained by increased utilization of prophylactic anticoagulation in the adolescent trauma population having decreased the overall incidence of VTE in this group [7,11]. Acute disease appears to play an increasingly important role in VTE risk as children age.

As in previous studies, the majority of patients with VTE were infants and adolescents [1,2,12]. However, when the data were standardized for total discharges, infants were found to be at lowest risk while adolescents were at highest risk. In contrast, when the PHIS data were standardized for total admissions, the bimodal pattern persisted [2]. This difference is likely related to the source of the data, with the PHIS data coming from 43 children's hospitals who are members of the CHCA (Child Healthcare Corporation of America), while the KID pulls data from a much larger array of both children's and community hospitals. Thus, including discharge data from community hospitals, where the incidence of VTE is much lower, may alter the pattern of age related disease prevalence. Data from CDC surveillance reports higher incidences of fatal and nonfatal traumatic events in adolescents compared with children, with higher incidences in males compared to females [13]. In this study, males had a modestly higher risk for VTE. Thus, trauma epidemiology may explain much of this pattern. In contrast, adult data reports a higher standardized incidence of VTE in females [14]. In the National Hospital Discharge Survey, teenage females were reported

to have a diagnosis of VTE 2.1 times more commonly than males [12]. While a higher rate in females could be explained by pregnancy or oral contraceptive use, the KID dataset does not include data on medications [12,15]. The PHIS study demonstrated a non-significant predominance of male VTE [2].

In this cohort, the incidence of DVT was 188/100,000 discharges. This is notably lower than has been recently reported, but is likely secondary to differences in study design. Recent studies have estimated the incidence to be 420/100,000 discharges using data from KID 2003 and 580/100,000 admissions using the PHIS dataset [2,3]. Both of these studies included the codes for thrombophlebitis (451.xx), which we chose to eliminate from our data because isolated phlebitis may be included; resulting in a potentially higher false positive rate [16]. Other ICD-9-CM codes that may not be thrombus specific [(557.0-acute vascular insufficiency of intestine) and (572.1-portal pyemia)] were included in the PHIS study [2]. In contrast, our study included procedural codes specific to the care of thrombosis, which have not been used in previous VTE epidemiology studies. Unlike in the PHIS study, individual patients cannot be tracked in KID, further confounding incidence estimates in this analysis.

The majority (67.5%) of the cases were reported from children's hospitals. Nonetheless, about a quarter of VTE cases (26.0%) were recorded from community hospitals (i.e. non-tertiary care settings). Adolescents (15–18 years) and neonates represented the majority of community VTE (Figure 2A). This may reflect those VTEs occurring in community hospital neonatal units and/or in adolescents with acute conditions who present to community hospitals for initial care.

Hispanic children were found to be relatively protected from development of VTE in comparison to Caucasians and African Americans. Previous studies have also demonstrated this finding, but the mechanisms by which Hispanics are protected remain undefined [17,18].

Our data suggest that the relative risk of in-hospital death for children with VTE is about 6.27 (95% CI 5.41–7.25) compared to those without VTE. The Canadian registry estimated overall mortality in children with VTE to be 9.5%, of which ~2.2% was directly attributable to VTE, with the remainder dying from their underlying disease [1]. It is not possible to determine whether the children in the KID succumbed to VTE vs. an underlying disease, but the estimates from this analysis are in a similar range. Approximately 8% of the children with VTE in the PHIS analysis died; as with our study, the cause of death was not assessed [2]. Additional research examining patients with and without VTE matched for demographics and disease severity will likely refine the estimated risk of death associated with VTE.

Research involving the use of administrative data comes with several limitations. For example, VTE diagnoses cannot be confirmed with blinded readings of the imaging studies. Central venous catheters are thought to be the single greatest risk factor for VTE in children; however reliable information about whether the children had central venous catheters at the time of VTE is not available from KID [1,19–21]. Similarly, it is not possible to ascertain the role that thrombophilias may play in thrombotic risk [22]. The use of administrative data relies upon ICD-9-CM codes to identify cases. Recently the predictive value for ICD-9-CM coded administrative data to accurately identify VTE patients was assessed [16]. Adult patients with VTE ICD-9-CM codes were identified, VTE were then confirmed by review of radiology reports. The overall positive predictive values (PPV) were estimated to be 95% for VTE in the primary coding position and 75% for those coded in secondary positions. The more nebulous codes for thrombophlebitis (451.xx) had lower PPV of 86% and 50% in the

primary and secondary positions, respectively. Similar studies evaluating the PPV of ICD-9-CM codes for pediatric VTE have not been performed to date. Because most children with VTE appear to have an underlying health condition, we estimate from the adult data that the PPV estimates for the secondary positions are more reflective in the present analysis (~75%). Thus, it is possible that VTE are overestimated in this investigation as well as in the other recent studies [2,3]. Alternatively it is possible that VTE may be underestimated because of ommission coding errors.

Future pediatric VTE epidemiology research should focus on evaluating disease specific VTE epidemiology in order to further refine the understanding of which children are at greatest risk. Ideally this will lead to discovery of disease-related mechanisms and/or targeted thromboprophylactic strategies. Additional evaluation of adminstrative data may provide preliminary clues, but will continue to be limited by database design (as above) as well as the inability to examine candidate biomarkers. Meaningful progress will require the development of multi-institutional prospective cohort studies conducted in collaboration with subspecialty groups who care for children with the diseases of interest.

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Abbreviations

AHRQ	Agency for Healthcare Research and Quality
CCC	Complex Chronic Conditions
DVT	Deep Venous Thrombosis
HCUP	Healthcare Cost and Utilization Project
ICD-9-CM	International Classification of Diseases, 9th Revision, Clinical Modification
KID	Kids' Inpatient Database
PE	Pulmonary Embolism
PPV	Positive Predictive Value
VTE	Venous Thromboembolism

References

1. Andrew M, David M, Adams M, et al. Venous thromboembolic complications (VTE) in children: first analyses of the Canadian Registry of VTE. Blood. 1994; 83(5):1251–1257. [PubMed: 8118029]
2. Raffini L, Huang YS, Witmer C, et al. Dramatic increase in venous thromboembolism in children's hospitals in the United States from 2001 to 2007. Pediatrics. 2009; 124(4):1001–1008. [PubMed: 19736261]
3. Vu LT, Nobuhara KK, Lee H, et al. Determination of risk factors for deep venous thrombosis in hospitalized children. J Pediatr Surg. 2008; 43(6):1095–1099. [PubMed: 18558189]

4. Bajzar L, Chan AK, Massicotte MP, et al. Thrombosis in children with malignancy. Curr Opin Pediatr. 2006; 18(1):1–9. [PubMed: 16470154]

5. David M, Andrew M. Venous thromboembolic complications in children. J Pediatr. 1993; 123(3): 337–346. [PubMed: 8355108]

6. Male C, Chait P, Andrew M, et al. Central venous line-related thrombosis in children: association with central venous line location and insertion technique. Blood. 2003; 101(11):4273–4278. [PubMed: 12560228]

7. Manco-Johnson MJ. How I treat venous thrombosis in children. Blood. 2006; 107(1):21–29. [PubMed: 16099882]

8. HCUP Kids' Inpatient Database (KID). Healthcare Cost and Utilization Project (HCUP). Agency for Healthcare Research and Quality; Rockville, MD: 2006. www.hcup-us.ahrq.gov/kidoverview.jsp Accessed

9. Feudtner C, Hays RM, Haynes G, et al. Deaths attributed to pediatric complex chronic conditions: national trends and implications for supportive care services. Pediatrics. 2001; 107(6):E99. [PubMed: 11389297]

10. National Trauma Data Bank (NTBD). American College of Surgeons; Sep 2. 2009 http://www.facs.org/trauma/ntdb/index.html. Accessed September 2, 2009. <http://www.facs.org/trauma/ntdb/index.html

11. O'Brien SH, Haley K, Kelleher KJ, et al. Variation in DVT prophylaxis for adolescent trauma patients: a survey of the Society of Trauma Nurses. J Trauma Nurs. 2008; 15(2):53–57. [PubMed: 18690134]

12. Stein PD, Kayali F, Olson RE. Incidence of venous thromboembolism in infants and children: data from the National Hospital Discharge Survey. J Pediatr. 2004; 145(4):563–565. [PubMed: 15480387]

13. Vyrostek SB, Annest JL, Ryan GW. Surveillance for fatal and nonfatal injuries--United States, 2001. MMWR Surveill Summ. 2004; 53(7):1–57. [PubMed: 15343143]

14. White RH, Zhou H, Murin S, et al. Effect of ethnicity and gender on the incidence of venous thromboembolism in a diverse population in California in 1996. Thromb Haemost. 2005; 93(2): 298–305. [PubMed: 15711746]

15. Dietrich JE, Yee DL. Thrombophilic conditions in the adolescent: the gynecologic impact. Obstet Gynecol Clin North Am. 2009; 36(1):163–175. [PubMed: 19344854]

16. White RH, Garcia M, Sadeghi B, et al. Evaluation of the predictive value of ICD-9-CM coded administrative data for venous thromboembolism in the United States. Thromb Res. 2010; 126(1): 61–67. [PubMed: 20430419]

17. White RH, Zhou H, Romano PS. Incidence of idiopathic deep venous thrombosis and secondary thromboembolism among ethnic groups in California. Ann Intern Med. 1998; 128(9):737–740. [PubMed: 9556467]

18. White RH, Keenan CR. Effects of race and ethnicity on the incidence of venous thromboembolism. Thromb Res. 2009; 123 (Suppl 4):S11–17. [PubMed: 19303496]

19. Chan AK, Deveber G, Monagle P, et al. Venous thrombosis in children. J Thromb Haemost. 2003; 1(7):1443–1455. [PubMed: 12871279]

20. Monagle P, Adams M, Mahoney M, et al. Outcome of pediatric thromboembolic disease: a report from the Canadian Childhood Thrombophilia Registry. Pediatr Res. 2000; 47(6):763–766. [PubMed: 10832734]

21. van Ommen CH, Heijboer H, Buller HR, et al. Venous thromboembolism in childhood: a prospective two-year registry in The Netherlands. J Pediatr. 2001; 139(5):676–681. [PubMed: 11713446]

22. Young G, Albisetti M, Bonduel M, et al. Impact of inherited thrombophilia on venous thromboembolism in children: a systematic review and meta-analysis of observational studies. Circulation. 2008; 118(13):1373–1382. [PubMed: 18779442]

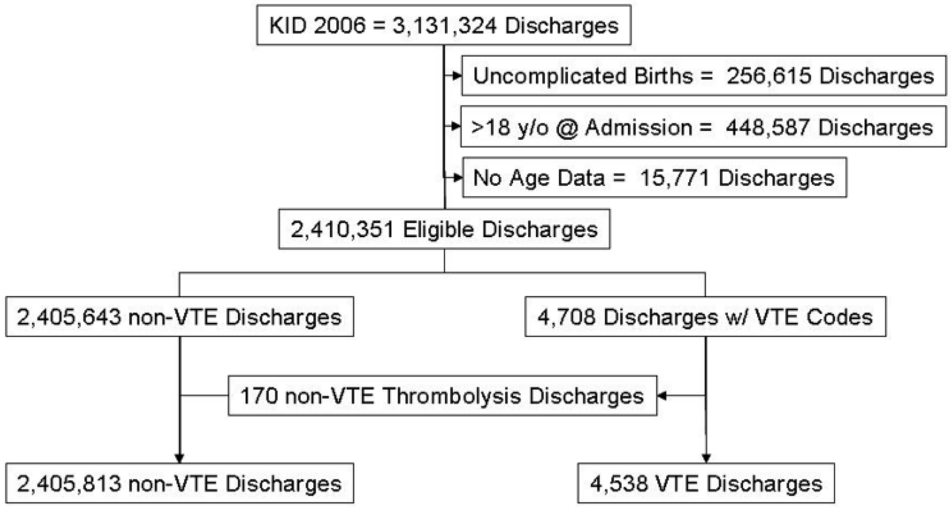

Figure 1.
KID 2006 VTE Case Selection Strategy.

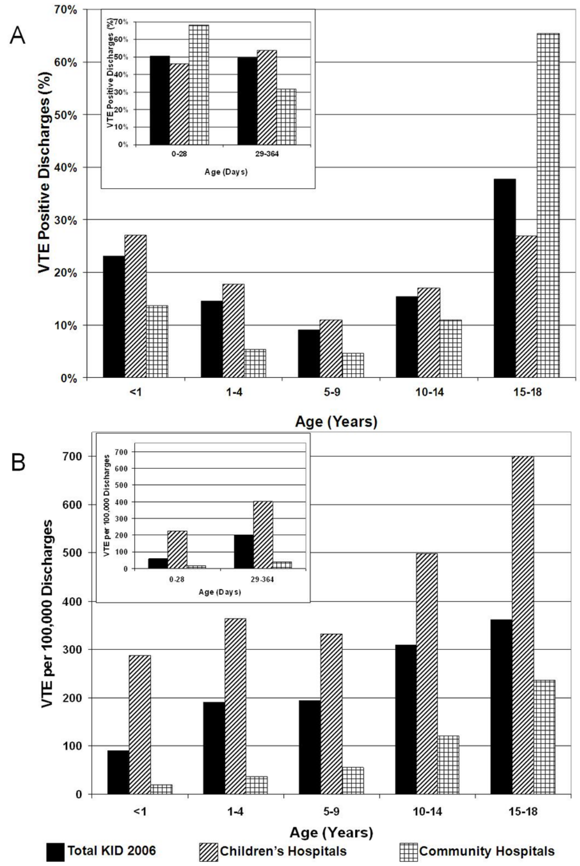

Figure 2.

The age distribution of KID 2006 VTE-positive discharges conforms to the well described bi-modal distribution **(A)**. However, when the age distribution is standardized for the number of discharges in each category, the youngest children (both infants and neonates) are least likely to develop VTE, while adolescents aged 15–18 years are most likely (categorical χ^2 P <0.00001) **(B)**. The differences in incidence of VTE between children's and community hospitals are significant (dichotomous χ^2 P <0.00001) in all age categories **(B)**. The age distribution for children <1 year of age from the 32 KID states that report age in days are shown in the **insets**.

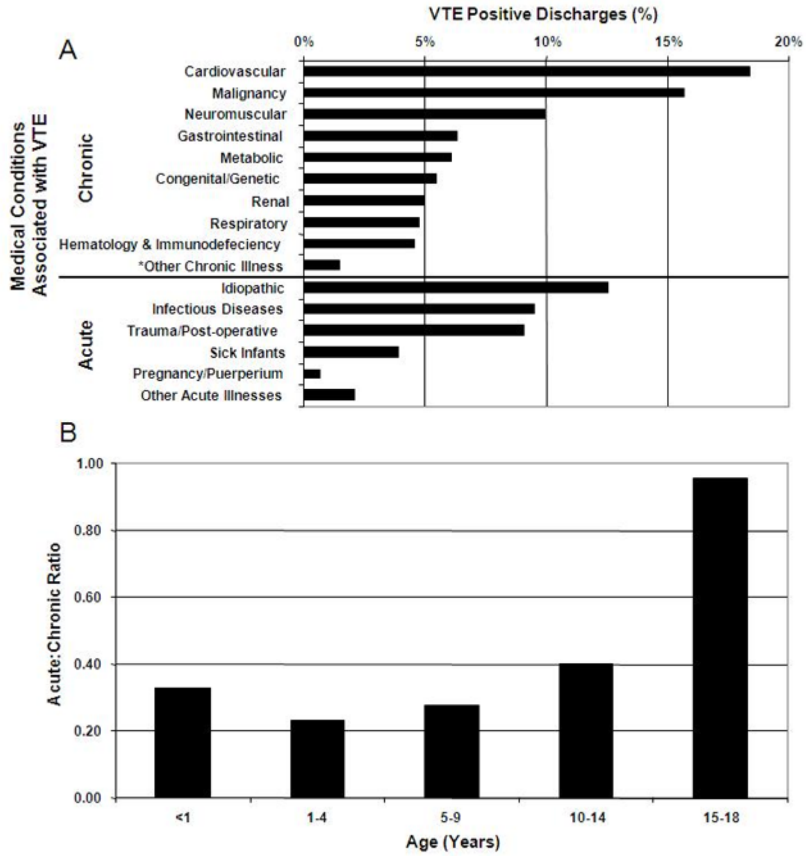

Figure 3.

The distribution of diseases associated with in-hospital VTE (>100% because some discharges were associated with more than one Complex Chronic Condition or had both a CCC and a trauma code) **(A)**. *Other Chronic Illness includes chronic pediatric diseases that are not included in the published CCC, such as histiocytosis, aplastic anemia, or diabetes mellitus. The ratio of acute to chronic conditions associated with in-hospital VTE changes with age (P<0.00001) **(B)**.

Table

VTE most commonly occurs in children discharged from children's hospitals and is associated with male gender and in-hospital death.

	Total Discharges	VTE Discharges	VTE per 100,000 Discharges	χ^2 Statistic	Relative Risk (95% CI)
KID 2006:	2,410,351	4,538	188	---	---
Hospital Type:					
[a]**Children's**	762,817	3,063	402	<0.00001	5.09 (4.76; 5.44)
Community	1,495,125	1,180	79		1 (Reference)
[b]**No Data**	152,409				
Gender:					
Male	1,202,803	2,484	207	<0.00001	1.20 (1.13; 1.27)
Female	1,190,354	2,047	172		1 (Reference)
[b]**No Data**	17,194				
Children's:					
Male	403,925	1,713	424	0.003	1.11 (1.04; 1.20)
Female	354,242	1,349	381		1 (Reference)
[b]**No Data**	4,650				
Community:					
Male	723,202	604	84	0.07	1.11 (0.99; 1.25)
Female	759,398	570	75		1 (Reference)
[b]**No Data**	12,524				
Race:					
White	886,597	1,892	213	<0.00001	1 (Reference)
Black	294,225	591	201		0.94 (0.86; 1.03)
Hispanic	423,054	549	130		0.61 (0.55; 0.67)
Other	159,304	334	210		0.98 (0.87; 1.10)
[b]**No Data**	647,171				
Region:					

	Total Discharges	VTE Discharges	VTE per 100,000 Discharges	χ^2 Statistic	Relative Risk (95% CI)
Northeast	367,467	623	170	<0.00001	0.91 (0.82; 1.00)
Midwest	583,510	1,314	225		1.20 (1.11; 1.31)
South	890,495	1,537	173		0.92 (0.85; 1.00)
West	568,879	1,064	187		1 (Reference)
[c]**Income:**					
0–25th %ile	714,142	1,243	174	0.00003	0.97 (0.89; 1.05)
26–50th %ile	585,034	1,048	179		1 (Reference)
51–75th %ile	554,346	1,112	201		1.12 (1.03; 1.22)
76–100th %ile	498,839	1,031	207		1.15 (1.06; 1.26)
[b]**No Data**	57,990				
Disposition:					
[d]**Alive**	2,393,055	4,346	182	<0.00001	1 (Reference)
Died in Hospital	16,979	190	1,119		6.16 (5.32; 7.13)
[b]**No Data**	317				

[a]Children's includes all NACHRI children's hospital types reported in KID.

[b]Not all KID states report all data elements. Data masking varies from state to state.

[c]Reported as median household income for patient's zip code.

[d]Includes all other possible disposition types reported in KID