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What is This?
Pediatric Obesity and Safety in Inpatient Settings: A Systematic Literature Review

Elizabeth E. Halvorson, MD1, Megan B. Irby, MS1,2, and Joseph A. Skelton, MD, MS1,2,3

Abstract

Objective. Pediatric obesity affects more than 16% of American children and is associated with worse outcomes in hospitalized patients. A systematic literature review was performed to identify studies of adverse care events affecting obese pediatric patients in the emergency room, operating room, or inpatient wards. Evidence Review. We systematically searched Medline for articles published from 1970 to 2013 regarding obesity and patient safety events in pediatric acute care settings. We determined the study design, number of patients studied, definition and prevalence of obesity, the relevant acute care setting, the specific association with obesity addressed, and the results of each study. Results and Conclusion. Thirty-four studies documented both procedural complications and issues with general hospital care. Most were retrospective and focused on surgery or anesthesia. Obese patients may have increased risk for a variety of adverse events. Further study could improve institutional patient safety guidelines to enhance care for obese children.

Keywords

pediatric, obesity, safety, inpatient, surgery

Introduction

Pediatric obesity is a significant public health concern, as 16.9% of American children are currently obese, representing a tripling since 1980. Obese children are at higher risk for several chronic conditions, including diabetes, obstructive sleep apnea, nonalcoholic fatty liver disease, and gallbladder disease, both during childhood and into adulthood. Furthermore, obese children may become more ill if they have several common pediatric conditions, including asthma and influenza. One recent review demonstrated a trend toward increased mortality and increased rate of infections in obese patients who require hospitalization, and several studies report that obese inpatients have longer hospital length of stay and higher hospital charges than their normal-weight counterparts.

Patient safety, brought to national attention with the publication of the Institute of Medicine’s To Err is Human and Crossing the Quality Chasm, focuses on preventable measures that may adversely affect the outcomes discussed above. The Agency for Healthcare Research and Quality has defined a number of pediatric-specific quality indicator events. These focus on procedure-based complications including accidental punctures, iatrogenic pneumothoraces, hospital-acquired infections, and postoperative complications. A review of discharges from 38 children’s hospitals in the United States revealed that these events can prolong length of stay as long as 23.5 days in the case of postoperative sepsis and may result in up to $337,226 in excess hospital charges. Furthermore, obese patients may face issues with general hospital care unrelated to procedures. For example, medication dosing is typically weight-based in children; thus, appropriate dosing and pharmacokinetics for an obese patient may not be evident.

Although obese children are known to have poor clinical outcomes, it is unclear whether adverse patient-care
events are a contributing factor. This knowledge could change institutional patient safety protocols, many of which do not specifically address obese patients. In this systematic literature review, we identified studies of patient safety issues in obese children and asked whether obesity contributes to increased mortality, prolonged length of stay, and increased hospital charges. We hypothesize that obese inpatient children and adolescents are at greater risk for adverse patient-care events, which may contribute to overall poorer outcomes and increased medical costs.

Methods

We systematically searched Medline (PubMed) from 1970 to April 2013 for English-language manuscripts of children (birth to 18 years old), treated within acute care settings, specifically inpatient hospitalizations, emergency department visits, surgical operations, or other acute inpatient procedures. We focused on studies that identified overweight or obese children as a specific subpopulation in their analysis. Referenced articles of relevance within these studies were also extracted and included.

There is no universal definition of patient safety. For this review, we conceptualized patient safety to incorporate issues specific to procedures and general hospital care. For procedural complications, we focused on many of the Agency for Healthcare Research and Quality pediatric-specific quality indicator events, including accidental lacerations or punctures, decubitus ulcers, retained foreign body, iatrogenic pneumothoraces, hospital-acquired infections, and perioperative hemorrhage, respiratory failure, sepsis, and wound dehiscence. Under general hospital care, we included patient issues related to blood products, environment, equipment or medical devices, falls, laboratory errors, medications, and radiology.

Terms used for the literature search were pediatric obesity in combination with one of the following terms: safety, acute care, trauma, hospitalization, admission, iatrogenic, falls, thrombosis, infection, screening, pneumothorax, transfusion, foreign body, and errors. Study titles and abstracts were initially reviewed for inclusion criteria, specifically pediatric obesity, any element of patient safety identified above, and patients within the hospital, emergency department, or operating room settings. Studies were excluded if they were not available in English, included only adult patients, were conducted outside of an acute care setting, did not compare an overweight/obese population with a normal-weight population, or were not specific to a patient safety issue identified above. Data extracted from each study included the study design, number of patients studied, definition and prevalence of obesity, the relevant acute care setting, the specific question or association with obesity addressed, and the results. The primary investigator (EEH) independently screened all titles and abstracts identified in the search, and obtained full texts for articles meeting inclusion criteria or if abstracts lacked sufficient information to determine inclusion. Full-text articles were then reviewed to determine inclusion and were classified based on patient safety topic into one of 2 broad categories: procedural complications and general hospital care. Articles were classified based on the type of study and were grouped based on patient safety classification and study design for analysis.

Results

A total of 402 studies met the initial search criteria and were reviewed for inclusion. Applying the criteria noted above narrowed this group to 34 studies, which were included in the final analysis. The search results are displayed in Figure 1. Studies identified possible safety issues associated with obesity across many topics. Articles were reviewed and grouped by general patient safety areas as defined above: procedural complications (n = 22) and general hospital care (n = 12). Overall, most studies (n = 22) were retrospective.

Table 1 lists studies that focused on complications from procedures, specifically accidental punctures, decubitus ulcers, retained foreign bodies, thrombosis, iatrogenic pneumothoraces, hospital-acquired infections, and perioperative complications (both airway related and non–airway related). Most studies focused on perioperative complications; several demonstrated increased risk of airway obstruction and oxygen desaturation during sedation. No other perioperative complications were consistently associated with obesity. A few studies suggested increased risk of decubitus ulcers and thrombosis in obese patients.

Table 2 lists studies related to safety issues affecting general hospital care. Several articles were relevant to the safety of equipment and medical devices when used in obese children. For example, the Broselow tape (used to estimate weight in emergency settings) frequently underestimated weight in obese children. Furthermore, a retrospective chart review by Miller et al demonstrated a statistically significant increase in dosing errors for overweight patients. Studies focused on anticoagulation reported difficulties in attaining therapeutic drug levels in obese patients. Additional studies addressed radiologic issues and the predictive value of C-reactive protein in obtaining a diagnosis of appendicitis in obese patients. No studies specifically addressed blood product safety or falls.
Few studies assessed clinical outcome following the adverse safety event, and none addressed subsequent mortality or hospital charges. Only 7 of the studies assessed length of stay. A recent review suggests that obese children tend to have longer hospital stays than normal-weight children.9 Some studies support this finding, specifically a report of children undergoing adenotonsillectomy for sleep-disordered breathing,22 in which obese children had a higher rate of perioperative complications. Nafiu et al13 also found that body mass index had a positive correlation with length of stay in patients undergoing adenotonsillectomy. However, no difference in hospital length of stay or rate of perioperative complications was seen between normal-weight, overweight, and obese children in patients undergoing ultrasound for diagnosis of appendicitis50 or laparoscopic cholecystectomy.40

**Discussion**

We performed a systematic literature review to assess the incidence of adverse patient-care events and overall safety in obese children in the acute care setting. Our goals were to determine if patient safety was compromised for obese children compared with normal-weight children; if patient safety issues contribute to the documented increases in mortality, length of stay, and hospital charges incurred by obese patients; and if specific issues could be identified for inclusion in institutional patient safety protocols. To our knowledge, this is the first literature review targeting the topic of pediatric obesity and patient safety.

We found clear evidence that obesity influences patient safety in 4 major fields: medication safety, venous thromboembolism, surgery, and airway management. Several studies addressed issues of medication dosing,47-49 although none assessed the effects of medication over- or underdosing. Since medications are typically dosed based on weight or body surface area, appropriate dosing may be difficult to determine for obese patients. Furthermore, medications may be distributed throughout the body differently based on body composition, thus affecting medication efficacy. Drug pharmacokinetics are frequently altered in obese patients, which may be especially problematic in medications with a narrow therapeutic window.17 Studies
<table>
<thead>
<tr>
<th>Patient Safety Issue</th>
<th>Citation/Site</th>
<th>Population Analyzed</th>
<th>Obesity/Overweight Definition</th>
<th>Study Question</th>
<th>Study Design</th>
<th>Findings</th>
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<tbody>
<tr>
<td>Accidental lacerations/punctures</td>
<td>Rana et al., single center, United States</td>
<td>1314 pediatric trauma patients</td>
<td>BMI &gt;95%; 294 obese, 1020 nonobese</td>
<td>Severity of traumatic injury</td>
<td>Retrospective</td>
<td>Increased rate of decubitus ulcer complicating injuries to obese patients</td>
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</table>

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<tr>
<th>Patient Safety Issue</th>
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</thead>
<tbody>
<tr>
<td>Decubitus ulcer</td>
<td>Thrombosis</td>
<td>Heller et al., database, Germany</td>
<td>149 patients with cerebral venous thrombosis, ages 0-18 years</td>
<td>No definition, 2 cases described as obese</td>
<td>Risk of cerebral venous thrombosis</td>
<td>Prospective</td>
</tr>
<tr>
<td></td>
<td>Tavil et al., single center, Turkey</td>
<td>16 cases of patients diagnosed with pulmonary embolus</td>
<td>No definition, 1 case described as obese</td>
<td>Risk of pulmonary embolus</td>
<td>Retrospective</td>
<td>One patient with pulmonary embolism had obesity associated with operated craniopharyngioma</td>
</tr>
<tr>
<td></td>
<td>Vu et al., database, United States</td>
<td>1 651 196 hospital admissions included in database</td>
<td>ICD-9 code for obesity as discharge diagnosis</td>
<td>Risk factors for DVT</td>
<td>Retrospective</td>
<td>Obese patients at higher risk of DVT than nonobese</td>
</tr>
<tr>
<td></td>
<td>Hanevold et al., database, United States</td>
<td>6658 pediatric patients following renal transplant</td>
<td>BMI &gt;95%; 649 obese, 6009 nonobese</td>
<td>Outcomes after renal transplant</td>
<td>Retrospective</td>
<td>Obese patients younger, shorter, and had been on dialysis longer before transplant. Obese children 6-12 years more likely to die than nonobese counterparts. More likely to lose graft due to thrombosis if obese</td>
</tr>
<tr>
<td></td>
<td>Rana et al., single center, United States</td>
<td>1314 pediatric trauma patients</td>
<td>BMI &gt;95%; 294 obese, 1020 nonobese</td>
<td>Severity of traumatic injury</td>
<td>Retrospective</td>
<td>Increased rate of venous thromboembolism complicating injuries to obese patients</td>
</tr>
<tr>
<td>Iatrogenic pneumothorax</td>
<td>Harwood et al., single center, United States</td>
<td>107 children &gt;5 years old undergoing blind percutaneous liver biopsy</td>
<td>Obese BMI &gt;95% (n = 30); nonobese BMI &lt;95% (n = 77)</td>
<td>Perioperative complications, including pneumothorax, following blind percutaneous liver biopsy</td>
<td>Retrospective</td>
<td>No significant difference in biopsy success or complication rate between obese and nonobese patients</td>
</tr>
<tr>
<td>Hospital-acquired infection</td>
<td>Petnehazy et al., single center, Austria</td>
<td>94 patients undergoing appendectomy</td>
<td>BMI &gt;95%; 29 obese, 65 nonobese</td>
<td>Perioperative complications from single-port appendectomy</td>
<td>Retrospective</td>
<td>No significant difference in operative time between obese and nonobese patients. One wound healing complication in obese group; one postoperative bleeding and one wound infection in nonobese group</td>
</tr>
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<td>Patient Safety Issue</td>
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<td></td>
<td>Kraft et al,32 single center, United States</td>
<td>592 patients with &gt;30% body surface area burn</td>
<td>Morbidly obese BMI &gt;95% (n = 144); obese BMI 90% to 95% (n = 83); overweight BMI 85% to 90% (n = 50); normal BMI &lt;85% (n = 315)</td>
<td>Incidence of sepsis</td>
<td>Retrospective</td>
<td>No significant differences in sepsis, multiple organ failure, or mortality</td>
</tr>
<tr>
<td></td>
<td>Brown et al,33 single center, United States</td>
<td>316 trauma patients</td>
<td>Obese BMI &gt;95% (n = 54); lean BMI &lt;95% (n = 262)</td>
<td>Incidence of sepsis and wound infection</td>
<td>Retrospective</td>
<td>Increased incidence of sepsis and wound infection in obese patients, but no difference in incidence of pneumonia. Longer ICU length of stay for obese patients</td>
</tr>
<tr>
<td></td>
<td>Davies et al,34 single center, Canada</td>
<td>282 patients undergoing appendectomy</td>
<td>Very obese weight &gt;2 SD over mean (n = 31); moderately obese weight &gt;1.5 SD over mean (n = 25); normal weight (n = 226)</td>
<td>Length of stay, incidence of wound infection</td>
<td>Retrospective</td>
<td>Trend toward increased incidence of wound infection in very obese patients with perforated appendicitis, but not statistically significant. Longer length of stay in very obese patients</td>
</tr>
<tr>
<td></td>
<td>Linam et al,35 single center, United States</td>
<td>176 patients undergoing spinal fusion</td>
<td>44 case patients who developed surgical site infection each matched to 3 controls who did not</td>
<td>Rate of obesity with BMI &gt;95% in cases versus controls</td>
<td>Retrospective</td>
<td>Obesity with BMI &gt;95% was significant risk factor associated with surgical site infection</td>
</tr>
<tr>
<td>Operative complications—Airway Aspiration</td>
<td>Cook-Sather et al,36 single center, United States</td>
<td>1000 day surgery patients</td>
<td>Lean BMI 25% to 75% (n = 424); overweight BMI 85% to 95% (n = 140); obese BMI &gt;95% (n = 133)</td>
<td>Risk of aspiration during anesthesia</td>
<td>Prospective</td>
<td>No effect of BMI on gastric fluid volumes before anesthesia (indirect measure of aspiration risk). Emesis on induction occurred in 8 patients (50% obese, 75% with obstructive sleep apnea), but no aspiration events</td>
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<td></td>
<td>Fung et al,22 single center, Canada</td>
<td>49 obese patients + matched controls undergoing adenotonsillectomy for sleep-disordered breathing</td>
<td>Overweight BMI 90% to 95% or obese BMI &gt;95%; 49 obese, 49 matched nonobese</td>
<td>Incidence of postoperative respiratory complications</td>
<td>Retrospective</td>
<td>Obesity significantly increases risk of postoperative complications, including major events. Obese children had significantly more upper airway obstruction and longer hospital length of stay</td>
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<td>Morbidly obese BMI &gt;95%</td>
<td>Incidence of postoperative respiratory complications</td>
<td>Retrospective</td>
<td>Most patients had uncomplicated recovery. Some required supplemental oxygen or repositioning, very few required positive-pressure ventilation, none required reintubation</td>
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<td>26 morbidly obese patients undergoing adenotonsillectomy</td>
<td>Morbidly obese BMI &gt;95%</td>
<td>Incidence of postoperative respiratory complications</td>
<td>Retrospective</td>
<td>Most patients had uncomplicated recovery. Some required supplemental oxygen or repositioning, very few required positive-pressure ventilation, none required reintubation</td>
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<td>510 patients undergoing sedation for dental procedure</td>
<td>Weight and BMI percentiles</td>
<td>Incidence of adverse events</td>
<td>Retrospective</td>
<td>Weight percentiles higher in children with one or more adverse events, but not statistically significant</td>
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<td>6094 pediatric surgical patients</td>
<td>Overweight BMI 85% to 95% (n = 875); obese BMI &gt;95% (n = 1048); normal weight BMI &lt;85% (n = 4171)</td>
<td>Incidence of perioperative complications</td>
<td>Retrospective</td>
<td>Overweight and obese patients more likely to have difficult airway, upper airway obstruction in the PACU, PACU stay longer than 3 hours, and need for 2 or more antiemetics. No significant difference in rate of unplanned hospital admission</td>
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<td>1133 patients undergoing inhalation induction anesthesia, ages &lt;12 years</td>
<td>Definition based on “international normative data”; 100 obese, 1033 nonobese</td>
<td>Incidence of perioperative complications</td>
<td>Retrospective</td>
<td>Higher incidence of intraoperative oxygen desaturation and unexpected overnight hospitalization for obese patients</td>
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<td>2025 patients undergoing noncardiac elective procedures, ages 2-18 years</td>
<td>Definition based on “international normative data”; 351 overweight, 294 obese, 1380 normal-weight</td>
<td>Incidence of perioperative complications</td>
<td>Prospective</td>
<td>Obese children had higher prevalence of comorbid conditions, including asthma, diabetes, hypertension, and sleep apnea. Higher incidence of oxygen desaturation, difficult mask ventilation, and airway obstruction</td>
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<tr>
<td>Operative complications—Other</td>
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<td>Kraft et al, 32 single center, United States</td>
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<td>592 patients with &gt;30% body surface area burn</td>
<td>Overweight BMI &gt;85%, 47% overweight</td>
<td>Incidence of sepsis, multiple organ failure, and death</td>
<td>Retrospective</td>
<td>No significant difference in sepsis, multiple organ failure, or mortality</td>
</tr>
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<td>Fung et al, 32 single center, Canada</td>
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<td>49 obese patients plus matched controls undergoing adenotonsillectomy for sleep-disordered breathing</td>
<td>Overweight BMI 90% to 95% or obese BMI &gt;95%; 49 obese, 49 matched nonobese</td>
<td>Incidence of postoperative respiratory complications</td>
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<td>Obesity significantly increases risk of postoperative complications, including major events. Obese children had significantly more upper airway obstruction and longer hospital length of stay</td>
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| Garey et al,
(40) single center, United States | 312 patients undergoing laparoscopic cholecystectomy                                  | Normal weight BMI <85% (n = 150); overweight BMI 85% to 95% (n = 65); obese BMI >95% (n = 97) | Incidence of perioperative complications                  | Retrospective | No difference seen in indication for surgery, operative time, hospital length of stay, or postoperative complications between groups                                                                 |
| Mantadakis et al,
(41) single center, Greece       | 1 morbidly obese patient with Prader-Willi syndrome undergoing orchidopexy           | BMI 22.7 kg/m² (upper limit normal for age 20)                                               | Development of pulmonary edema                           | Case report   | Patient developed pulmonary edema following induction. Subsequent complications included sepsis, pneumonia, ARDS, and prolonged ICU stay                                                              |
| Petnehazy et al,
(31) single center, Austria     | 94 patients undergoing single-port appendectomy                                      | Obese BMI >95%; 31% patients obese                                                          | Incidence of perioperative complications                  | Retrospective | No significant difference in operative time between obese and nonobese patients. One wound healing complication in obese group; one postoperative bleeding and one wound infection in nonobese group |
| Tweedie et al,
(42) single center, United Kingdom | 1735 patients undergoing tonsillectomy and/or adenoidectomy                          | Morbid obesity (n = 20)                                                                       | Need for postoperative PICU admission                     | Retrospective | 4/20 morbidly obese patients required PICU admission; most also had other comorbidities                                                                                                            |
| Kutasy et al,
(43) single center, Ireland       | 1383 obese children who underwent appendectomy                                       | Extremely obese BMI >2 SD over mean; 238 extremely obese, 1145 nonobese                      | Efficacy of open vs laparoscopic approach                 | Retrospective | Laparoscopic surgery in obese children associated with significantly shorter operating time, lower complication rate, and lesser postoperative analgesia                                          |

Abbreviations: BMI, body mass index; ICD-9; International Classification of Diseases, Ninth Revision; DVT, deep venous thrombosis; ICU, intensive care unit; SD, standard deviation; PACU, pediatric acute care unit; ARDS, acute respiratory distress syndrome.
Table 2. Patient Safety Events Related to General Hospital Care.

<table>
<thead>
<tr>
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<td><strong>Behavior</strong></td>
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<td><strong>Blood product</strong></td>
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<tr>
<td>Young et al.</td>
<td>18</td>
<td>survey, United States</td>
<td>Obesity BMI &gt;95%</td>
<td>Do children’s hospitals have specific policies in place for obese inpatients?</td>
<td>Survey sent to 47 NACHRI member hospitals</td>
<td>37% of hospitals have policy to identify and treat overweight/obese patients, 84% promote healthy lifestyle within the hospital. Most noted financial and space issues as barriers to increasing physical activity and improving nutrition</td>
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<td><strong>Environmental safety</strong></td>
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<td><strong>Equipment/medical device safety</strong></td>
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<tr>
<td>Porter et al.</td>
<td>19</td>
<td>survey, United States</td>
<td>Overweight BMI 85% to 95%; obese BMI &gt;95%; severely obese BMI &gt;95% or BMI &gt;40 or weight &gt;260 lb</td>
<td>Are hospitals prepared to address airway management, drug dosing, and equipment needs of obese patients?</td>
<td>Survey sent to 45 freestanding children’s hospitals to assess degree of preparation</td>
<td>Hospitals with a bariatric surgery program seem better-prepared for severely obese patients; &lt;20% of hospitals have adequate training and equipment</td>
</tr>
<tr>
<td>Nafiu et al.</td>
<td>53</td>
<td>single center, United States</td>
<td>Obese BMI &gt;95%; 47 obese, 56 nonobese</td>
<td>Ease of peripheral IV access in obese patients</td>
<td>Prospective</td>
<td>Obese children more likely to have failed first attempt at cannulation and to require 2 or more attempts</td>
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<td>Sinha et al.</td>
<td>44</td>
<td>single center, United States</td>
<td>No definition</td>
<td>Accuracy of weight estimation using Broselow tape</td>
<td>Prospective</td>
<td>Length-based weight estimation underestimates weight with worst underestimation for largest children</td>
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<td>Milne et al.</td>
<td>45</td>
<td>one urban and one rural health center, Canada</td>
<td>BMI z scores calculated using CDC guidelines</td>
<td>Accuracy of weight estimation using Broselow tape</td>
<td>Prospective</td>
<td>Weight estimate correlates with actual weight but underestimates it</td>
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<td>Rosenberg et al.</td>
<td>46</td>
<td>single center, United States</td>
<td>Overweight BMI 85% to 95% (n = 38); obese BMI &gt;95% (n = 39)</td>
<td>Accuracy of weight estimation using Broselow tape</td>
<td>Prospective</td>
<td>Broselow tape more accurate than physician estimation for normal-weight but not obese children</td>
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<td><strong>Falls</strong></td>
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<td>Laboratory</td>
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<tr>
<td>Kutasy et al.</td>
<td>52</td>
<td>single center, Ireland</td>
<td>Extremely obese BMI &gt;2 SD over mean; 164 extremely obese, 783 nonobese</td>
<td>Predictive value of C-reactive protein in diagnosis of appendicitis</td>
<td>Retrospective</td>
<td>Obese patients significantly more likely to have negative appendectomy. C-reactive protein more elevated in obese patients with negative appendectomy than nonobese patients with negative appendectomy. Specificity and positive predictive value significantly lower</td>
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Table 2. (continued)

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</thead>
<tbody>
<tr>
<td><strong>Medication issues</strong></td>
<td></td>
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<tr>
<td>Miller et al.47</td>
<td>single center, United States</td>
<td>839 admissions for 699 patients admitted to the hospital</td>
<td>Overweight BMI &gt;85%, 33% of all admissions</td>
<td>Incidence of medication over- or underdosing in overweight patients</td>
<td>Retrospective</td>
<td>Statistically significant increase in dosing errors for overweight patients, with underdosing occurring more frequently than overdosing</td>
</tr>
<tr>
<td>Moffett et al.48</td>
<td>single center, United States</td>
<td>298 admissions for 184 patients on warfarin</td>
<td>Obese BMI &gt;95%, 22.5% obese</td>
<td>Risk factors for elevated international normalized ratio on warfarin therapy</td>
<td>Retrospective</td>
<td>Obesity was an independent variable associated with nonelevated international normalized ratio</td>
</tr>
<tr>
<td>Lewis et al.49</td>
<td>single center, United States</td>
<td>3 cases of obese patients</td>
<td>BMI 105.9, 85.7, and 29.9 kg/m², all &gt;95%</td>
<td>Concern for underdosing enoxaparin for DVT prophylaxis in obese patients</td>
<td>Case report</td>
<td>Three cases of obese pediatric inpatients all required greater than adult maximum doses of enoxaparin to reach therapeutic anti–factor Xa levels</td>
</tr>
<tr>
<td><strong>Radiology</strong></td>
<td></td>
<td></td>
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<tr>
<td>Sulowski et al.50</td>
<td>single center, Canada</td>
<td>263 patients undergoing screening ultrasound for suspected appendicitis</td>
<td>Obese BMI &gt;85%; 76 obese, 187 nonobese</td>
<td>Does ultrasound for diagnosis of appendicitis in obese children lead to favorable outcome: (1) nonperforated appendicitis or other diagnosis undergoing appropriate surgical procedure within 24 hours without CT scan or (2) no appendicitis and discharged from ED within 24 hours without CT scan</td>
<td>Prospective</td>
<td>Similar rate of favorable outcomes, rate of hospitalization, median hospital length of stay, rate of return ED visit, and time to surgery. Obese patients more likely to undergo CT scan within 30 days of initial presentation</td>
</tr>
<tr>
<td>Kutasy et al.51</td>
<td>single center, Ireland</td>
<td>1228 patients undergoing appendectomy</td>
<td>Extremely obese BMI &gt;2 SD over mean, 207 extremely obese, 1021 nonobese</td>
<td>Incidence of negative appendectomy in obese patients</td>
<td>Retrospective</td>
<td>Incidence of negative appendectomy significantly higher in obese than nonobese patients. Sensitivity, specificity, and predictive value of ultrasound significantly lower in obese patients</td>
</tr>
</tbody>
</table>

Abbreviations: NACHRI, National Association of Children's Hospitals and Related Institutions; BMI, body mass index; IV, intravenous; CDC, Centers for Disease Control and Prevention; ED, emergency department; SD, standard deviation; DVT, deep venous thrombosis; CT, computed tomography.
defining appropriate dosing for specific medications have demonstrated these difficulties. Olutoye et al. prospectively determined the effective dose of propofol for induction of anesthesia in obese children and found it to be lower (in weight-based dosing) than that for normal-weight children. Since obese children may be receiving inappropriate doses of medications, it will be important to determine the incidence of adverse drug events in this population.

Similarly, several studies, mostly retrospective database reviews, suggested that obesity may contribute to an increased incidence of thrombosis; however, they also noted that patients who experienced venous thromboembolism typically had other risk factors, such as presence of a central venous catheter, limited mobility, use of oral contraceptives, or coexisting malignancy or fracture. In adults, obesity is a clear risk factor for venous thromboembolism and is frequently included in guidelines for prophylaxis. There is increasing interest in the potential need for prophylaxis in children, so definitive determination of the risk conferred by obesity will be crucial as these pediatric guidelines are developed.

Most studies reviewed here focused on surgery and anesthesia. Two separate studies by Kutasy et al demonstrated an increased incidence of unnecessary appendectomy in obese children, attributed to the decreased specificity and positive predictive value of C-reactive protein and ultrasound for diagnosis. Researchers also found that certain operative techniques may be more appropriate for obese pediatric patients. An example is the use of laparoscopic appendectomy, which resulted in shorter operating time, lower complication rate, and less need for postoperative analgesia in pediatric obese patients.

Multiple studies raised concerns about obese patients undergoing sedation or general anesthesia. Many demonstrated increased incidence of upper airway obstruction and oxygen desaturation. In the study by Shine et al., however, most obese children had an uneventful recovery following anesthesia for adenotonsillectomy. Data on the incidence of wound infections and sepsis are mixed; several studies reported trends toward increased incidence in obese patients compared with nonobese, while other studies found no difference between the populations. The incidence of other perioperative complications, such as wound dehiscence or postoperative bleeding, was not higher among obese pediatric patients compared with nonobese. However, small sample sizes and retrospective study design limit the interpretation of these reports.

For many other types of patient safety events, no studies have been done to assess obesity as a potential contributing factor. Although one study indicated that the first attempt at peripheral intravenous cannulation was more likely to fail in obese children, no studies specifically assessed the number of accidental punctures or lacerations in such patients. Additionally, no studies examined the risk of falls in obese inpatients. There is evidence that obese children sustain increased extremity fractures and rib and pelvic injuries following trauma compared with nonobese patients, so falls in this population could lead to a worse outcome. Use of hospital equipment not optimized for obese patients could also contribute to increased risk of falls in this population.

Several studies assessed the need for enhanced hospital preparation when treating obese pediatric patients. In 2 survey-based studies, only 37% of children’s hospitals have a policy in place to identify and treat overweight or obese patients, and <20% of freestanding children’s hospitals have adequate training and equipment for severely obese patients. Furthermore, in one report, body mass index was calculated in only 35% of pediatric inpatients, while obesity is documented as a diagnosis for 5.5% of hospital days for obese inpatients. Without adequate recognition of these patients, interventions to improve the safety of obese pediatric patients cannot succeed.

Further research is needed to clearly define interventions to improve the safety of obese pediatric inpatients. Initial efforts could focus on the need for modification of medication dosing or preventive strategies for venous thromboembolism. Studies are needed to assess optimal methods of vascular access and specialized equipment needs in this population. Finally, further research is needed to delineate the risks of decubitus ulcers, falls, and hospital-acquired infections in obese children.

This review is limited by the heterogeneity of patient conditions, inconsistent or unclear definitions of obesity, variable study outcomes, and different research designs across the studies included. Most studies defined obesity as body mass index >95%, a measure which fails to account for actual body composition. Many articles were single-center reports, which may limit the generalizability of the results to broader and more diverse populations. Furthermore, most studies were retrospective and therefore could not address causative effects of obesity relative to patient safety events.

Some studies did identify areas in which pediatric obesity affects issues of patient safety. These areas are disparate and often very specific, such as the use of Broselow tape for estimating weights in acute situations or the efficacy of different diagnostic measures for appendicitis. However, in many areas there is only preliminary or theoretical evidence that obesity
Acknowledgments

The development of institutional policies and protocols to improve the safety of obese pediatric inpatients. Further studies may help influence the development of institutional policies and protocols to improve the safety of obese pediatric inpatients.

Declaration of Conflicting Interests

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References


Dramatic Increase in Venous Thromboembolism in Children's Hospitals in the United States From 2001 to 2007

Leslie Raffini, Yuan-Shung Huang, Char Witmer and Chris Feudtner

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http://pediatrics.aappublications.org/content/124/4/1001.full.html
Dramatic Increase in Venous Thromboembolism in Children’s Hospitals in the United States From 2001 to 2007

OBJECTIVES: The goals were to determine whether there has been an increase in the rate of venous thromboembolism (VTE) in pediatric tertiary care hospitals and to evaluate the use of anticoagulants in the treatment of hospitalized pediatric patients with VTE.

METHODS: A retrospective cohort study of patients <18 years of age who were discharged from 35 to 40 children’s hospitals (depending on the year) across the United States in 2001–2007 was performed. By using the Pediatric Health Information System administrative database, cases were assessed for discharge diagnosis codes for VTE; the use of anticoagulants was assessed by using patient-specific pharmacy files.

RESULTS: During the 7-year study period, in which 11,337 hospitalized patients were diagnosed with VTE, the annual rate of VTE increased by 70%, from 34 to 58 cases per 10,000 hospital admissions (P < .001). This increase was observed in neonates, infants, children, and adolescents. The majority (63%) of children with VTE had ≥1 coexisting chronic complex medical condition. Pediatric malignancy was the medical comorbid condition associated most strongly with recurrent VTE (P < .001). The proportion of children with VTE who were treated with enoxaparin increased from 29% to 49% during this time period (P < .001); the use of warfarin decreased slightly from 11.4% to 9.6% (P = .02). Increasing age was associated with increased likelihood of patients with VTE being treated with either enoxaparin or warfarin.

CONCLUSION: This multicenter study demonstrates a dramatic increase in the diagnosis of VTE at children’s hospitals from 2001 to 2007.
Many authors have suggested that there has been an increase in the rate of venous thromboembolism (VTE) in children; some have even called this a new epidemic in pediatric tertiary care hospitals.\(^1\)\(^-\)\(^7\) Most speculate, on the basis of known risk factors for VTE in children, that this increase is related to advancements in the treatment and supportive care of critically ill children who previously would not have survived.\(^1\)\(^-\)\(^3\)\(^,\)\(^5\)\(^,\)\(^7\) Interestingly, there are no published studies that confirm this perceived increase over time.

Epidemiological studies of the incidence of VTE in children are sparse. The most frequently cited incidence among children 1 month to 18 years of age is 0.07 case per 10,000 children, increasing to 5.3 cases per 10,000 pediatric hospital admissions.\(^1\)\(^,\)\(^2\) These estimates are based on a report from the Canadian Registry on 137 patients with VTE identified in 1990–1992.\(^2\) The report described the first large observational cohort of pediatric patients with thrombosis and greatly enhanced the understanding of risk factors associated with pediatric VTE. A 2-year study of VTE in the Netherlands in 1997–1998 estimated an incidence of 0.14 case per 10,000 children, although that study included neonates.\(^8\) To define more clearly the rate of VTE among hospitalized children in the United States and to evaluate how the rate has changed over time, we performed a retrospective cohort study of pediatric patients diagnosed as having VTE in children’s hospitals throughout the United States in 2001–2007, by using the Pediatric Health Information System (PHIS) database.

**METHODS**

**Institutional Review Board Evaluation**

This study was submitted to the institutional review board of the Children’s Hospital of Philadelphia and was determined to be exempt from review.

**Data Source**

The PHIS is an administrative database that contains comprehensive inpatient data from not-for-profit, tertiary care hospitals throughout the United States. These noncompeting hospitals belong to the Child Health Corporation of America (Shawnee Mission, KS), a business alliance of freestanding children’s hospitals. The database is managed by Solucient (Evanston, IL). Participating hospitals provide discharge data including patient demographic data, diagnoses, and procedure codes. Many of the hospitals also submit resource utilization data, including data on medication use. Data are deidentified and undergo a number of reliability and validity checks before being included.

Forty-one hospitals contributed to the PHIS database between January 1, 2001, and December 31, 2007, although all hospitals did not contribute each year; 2001 was the initial time point because this was the first year with complete robust data. Year-specific hospital records were excluded if a hospital did not provide resource utilization data, if individual patients could not be identified throughout the 7-year study period by using a unique medical identification number, or if there were problems regarding data quality. In our final dataset, 35 hospitals were included in 2001 and 2002, 37 in 2003, 39 in 2004, 40 in 2005 and 2006, and 39 in 2007.

**Subjects**

The source population included pediatric patients (through 18 years of age) who were admitted to PHIS hospitals between January 1, 2001, and December 31, 2007. Subjects with VTE were identified if they had a discharge diagnosis of nonsuperficial venous thrombosis, on the basis of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). The ICD-9-CM codes used were 415.1, 415.11, 415.12, 415.19, 451.1, 451.11, 451.19, 451.2, 451.8, 451.81, 451.83, 451.84, 451.89, 451.9, 452, 453.0, 453.1, 453.2, 453.3, 453.41, 453.42, 453.8, 453.9, 557.0, and 572.1. Unique patient identifiers were used, so that it was possible to determine whether a patient had >1 admission with the diagnosis of VTE; such patients were classified as having recurrent VTE.

**Demographic Characteristics**

Age at admission, gender, race, and ethnicity were recorded for all admissions. We classified age into the following categories: birth to 1 month, 1 month to <1 year, 1 to <6 years, 6 to <13 years, and 13 to 18 years. These categories were chosen so that the rates of VTE in clinically relevant groups (neonates, infants, children, and adolescents) could be compared. Information on length of stay and disposition also was recorded.

**Complex Chronic Conditions**

To determine whether admitted patients had ≥1 coexisting complex chronic condition (CCC), we used a previously published classification scheme that uses ICD-9-CM codes to classify pediatric chronic conditions into the following categories: neuromuscular, cardiovascular, respiratory, renal, gastrointestinal, hematologic and immunodeficiency, metabolic, other congenital or genetic defect, and malignancy.\(^9\)

**Anticoagulant Use**

Anticoagulant use was determined by using pharmacy billing data. The specific anticoagulants evaluated included unfractionated heparin, low-molecular weight heparins (enoxaparin, tinzaparin, and dalteparin), warfarin, and alternative anticoagulants (argatroban, lepirudin, bivalirudin, danaparoid, and fondaparinux).
TABLE 1  Distribution of ICD-9-CM Codes According to VTE Location (N = 14 917)

<table>
<thead>
<tr>
<th>Location of VTE</th>
<th>n</th>
<th>ICD-9-CM Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal vein</td>
<td>338</td>
<td>453.3</td>
</tr>
<tr>
<td>Portal vein</td>
<td>980</td>
<td>452, 572.1</td>
</tr>
<tr>
<td>Intracranial venous sinus</td>
<td>1206</td>
<td>325</td>
</tr>
<tr>
<td>Upper extremities</td>
<td>1377</td>
<td>451.83, 451.84, 451.89</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>1434</td>
<td>415.11, 415.19, 415.12</td>
</tr>
<tr>
<td>Vena cava</td>
<td>1608</td>
<td>451.3</td>
</tr>
<tr>
<td>Unspecified or other</td>
<td>6153</td>
<td>451.8, 451.9, 453.0, 453.1, 453.8, 453.9, 557</td>
</tr>
</tbody>
</table>

Statistical Analyses

Descriptive statistics were used to compare characteristics between patients with 1 VTE episode and those with recurrent VTE. The χ² test was used for dichotomous and categorical variables (age, gender, race, ethnicity, disposition, and CCC). Student’s t test was used compare the mean lengths of stay, and the Mann-Whitney test was used to compare the median lengths of stay. The rate of VTE was calculated by dividing the number of VTE admissions by the total number of hospital admissions. Poisson regression was used to model the rate of VTE in each age group and the use of anticoagulants over time. Linear regression was used to evaluate the effect of age on the use of enoxaparin and warfarin and to model the relationship between the rate of VTE and hospital size, with adjustment for year and hospital clustering. Stata 10.0 (Stata, College Station, TX) was used for all statistical analyses.

RESULTS

VTE Admissions

During the 7-year study period, there were a total of 13 449 hospital admissions among 11 337 pediatric patients with the diagnosis of VTE. Among the 13 449 admissions, there were a total of 14 917 ICD-9-CM codes for VTE; some patients received >1 VTE discharge code. These codes are grouped according to anatomic location in Table 1. Forty-one percent of VTE codes (6153 of 14 917 codes) were nonspecific ICD-9-CM codes. A diagnosis of pulmonary embolism occurred in 11% of VTE admissions (1434 of 13 449 admissions).

The demographic data for all hospital admissions and VTE admissions from 2001 to 2007 are listed in Table 2.

TABLE 2  Characteristics of Study Population

<table>
<thead>
<tr>
<th></th>
<th>All Admissions (N = 2 921 383)</th>
<th>Admissions With VTE (N = 13 449)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at admission, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;28 d</td>
<td>346 127 (12)</td>
<td>2070 (15)</td>
<td></td>
</tr>
<tr>
<td>29 d to &lt;1 y</td>
<td>561 183 (19)</td>
<td>2037 (15)</td>
<td></td>
</tr>
<tr>
<td>1 to &lt;6 y</td>
<td>845 142 (29)</td>
<td>2745 (20)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6 to &lt;13 y</td>
<td>689 411 (23)</td>
<td>2594 (19)</td>
<td></td>
</tr>
<tr>
<td>13–18 y</td>
<td>501 820 (17)</td>
<td>4003 (30)</td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>1 608 381 (55)</td>
<td>7358 (55)</td>
<td>.40</td>
</tr>
<tr>
<td>Race/ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1 884 205 (65)</td>
<td>8970 (67)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>619 006 (21)</td>
<td>2631 (20)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>408 172 (14)</td>
<td>1848 (13)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>488 495 (17)</td>
<td>2099 (15)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Length of stay, d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>6</td>
<td>28</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Median (interquartile range)</td>
<td>3 (2–5)</td>
<td>13 (5–33)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Disposition, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>2 758 392 (94)</td>
<td>10 406 (77)</td>
<td></td>
</tr>
<tr>
<td>Died</td>
<td>29 929 (1)</td>
<td>1030 (8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Other</td>
<td>135 082 (5)</td>
<td>2013 (15)</td>
<td></td>
</tr>
<tr>
<td>CCC, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuromuscular</td>
<td>272 386 (9)</td>
<td>1429 (11)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>249 475 (9)</td>
<td>3465 (26)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Respiratory</td>
<td>91 384 (3)</td>
<td>890 (7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Malignancy</td>
<td>258 103 (9)</td>
<td>2121 (16)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>All other</td>
<td>390 517 (13)</td>
<td>3637 (27)</td>
<td></td>
</tr>
<tr>
<td>No CCC, n (%)</td>
<td>1 855 168 (64)</td>
<td>5029 (37)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

a Some patients had >1 admission.
b Each patient, even those with multiple admissions, was counted once.
c The age, length of stay, and CCC from the first admission were used.
Consistent with previously published studies, infants <1 year of age and teenagers accounted for the majority of VTE admissions.\textsuperscript{5,8,10} Fifty-five percent of the patients admitted with VTE were male, which was identical to the gender distribution for all admissions. Patients admitted with VTE had longer hospitalizations, had a higher mortality rate, and were more likely to have a CCC than were patients without VTE (Table 2). The mean length of stay for all VTE admissions was 28 days, compared with only 6 days for all admissions. The mortality rate for patients for whom VTE was diagnosed was 8% (1030 of 13,449 patients), which was much higher than the 1% rate observed for hospital admissions during the time period. The majority (63%) of patients with VTE had \( \geq 1 \) CCC, compared with 36% of all patients admitted. Among patients with VTE, a cardiovascular condition was the most common CCC (28%), followed by malignancy (14%) and neurovascular condition (11%) (Table 2).

**Patients With VTE**

Twelve percent of patients (1401 of 11,337 patients) had \( \geq 1 \) admission with a diagnosis of VTE and were categorized as having recurrent VTE (Table 2). In comparison with those with only 1 admission for VTE, the proportion of patients with recurrent VTE was significantly lower among children <1 year of age (21% vs 36%; \( P < .001 \)) and was significantly higher among teenagers (37% vs 27%; \( P < .001 \)). Patients with recurrent VTE were more likely to have a CCC; most notably, the prevalence of malignancy among patients with recurrence was twice as high as that among patients without recurrence (24% vs 12%; \( P < .001 \)).

**VTE Admissions Over Time**

The annual rate of VTE admissions increased 70% from 2001 to 2007 (from 34 to 58 cases per 10,000 hospital admissions; \( P < .001 \)). This increase was observed in all age groups and is shown graphically in Fig 1. The rate increased 70% (from 44 to 75 cases per 10,000 admissions) among infants <28 days of age, 100% (from 25 to 50 cases per 10,000 admissions) among infants between 28 days and <1 year of age, 64% (from 25 to 41 cases per 10,000 admissions) among children 1 to <6 years of age, 52% (from 31 to 47 cases per 10,000 admissions) among children 6 to 12 years of age, and 49% (from 63 to 94 cases per 10,000 admissions) among teenagers 13 to 18 years of age.

**Hospital Size and Rate of VTE**

There was significant interhospital variability in the rate of VTE admissions (Fig 2). After accounting for clustering (all hospitals were not included for the same number of years), there was a positive correlation between the annual number of admissions per hospital and the rate of VTE (\( P < .001 \)) (Fig 2).

**Anticoagulant Use**

Enoxaparin was by far the most frequently prescribed low-molecular

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**FIGURE 1**

Rates of VTE diagnosis according to age group, from 2001 to 2007. CI indicates confidence interval.
weight heparin in pediatric hospitals during this time period. The proportion of VTE admissions in which enoxaparin was used increased from 29% in 2001 to 49% in 2007 ($P < .001$), whereas the use of warfarin decreased slightly from 11% to 10% ($P < .001$) (Fig 3). The use of both anticoagulants increased with increasing age (Fig 4).

It was not possible to distinguish between unfractionated heparin administered through continuous infusion for therapeutic anticoagulation and unfractionated heparin dispensed to flush or to maintain the patency of venous or arterial catheters. Therefore, we were unable to assess the proportion of patients who received unfractionated heparin as treatment for their VTE, and we were unable to determine the proportion of patients with VTE who underwent anticoagulation.

The use of anticoagulants other than unfractionated heparin, warfarin, or enoxaparin was quite rare, occurring in only 48 of 13,449 admissions. The usage frequency of these anticoagulants was as follows: lepirudin, $n = 8$; argatroban, $n = 16$; fondaparinux, $n = 2$; tinzaparin, $n = 1$; dalteparin, $n = 21$; danaparoid, $n = 1$; bivalirudin, $n = 1$.

**Additional Analyses**

To confirm that the increase in VTE rate was not simply related to a temporal increase in diagnostic coding for VTE, we also searched for admissions in which enoxaparin was prescribed after 48 hours of admission. We added this exclusion to prevent the inclusion of patients who were being treated for a previous VTE episode. With the use of these criteria, there were an additional 6,227 admissions, and the rate of enoxaparin use (for patients without an ICD-9-CM code for VTE) increased 114% from 2001 to 2007 (data not shown). Because some of those patients might have received enoxaparin for prophylaxis and not necessarily for the treatment of deep VTE, those admissions were not used to determine the rate of VTE.

**DISCUSSION**

This study demonstrates a significant steady increase in the diagnosis of VTE across all age groups in US children’s hospitals from 2001 to 2007. The overall rate increase of 70% is substantial and confirms the observations of pediatric hematologists at single institutions.1–7 Neonates and adolescents had the highest rates of VTE, and the majority of patients had a CCC. The characteristics of patients with VTE in this study are similar to those reported for numerous smaller, prospective, pediatric VTE cohorts, adding confirmatory evidence to the findings of this study.
evidence regarding the validity of our findings.\textsuperscript{5,8,10} The only other study to examine the frequency of VTE over time among children in the United States used data from the National Hospital Discharge Survey (NHDS).\textsuperscript{11} That study estimated that the rate of VTE was 4.9 VTE cases per 100,000 children per year, and the rate did not change from the triennial periods of 1979–1982 to 1999–2001. The NHDS is designed to provide estimates of national hospitalization trends and overall disease burdens, but these estimates are generated from a relatively small proportion (\textless 1\%) of all hospital discharges, and the hospitals that are sampled for the NHDS are short-stay, nonfederal hospitals and therefore are less likely to care for the pediatric patients with complex conditions in whom thrombosis most often occurs. We propose that, because the vast majority of children with VTE are likely to be treated in tertiary care hospitals and many regions in the United States are served by a limited number of such hospitals, this possibility is extremely unlikely.

Whether there has been a true increase in the occurrence of pediatric VTE, an increase in detection of previously undiagnosed VTE, or both cannot be determined from this study and clearly warrants further investigation. The complexity of the medical conditions of pediatric patients in tertiary care hospitals continues to increase, paralleling advances in therapeutics, technology, and supportive care. The presence of a central venous catheter is the single most common risk factor for VTE in children.\textsuperscript{5,8,10} We were unable to assess whether the VTE episodes in this study were related to catheters and whether an increase in the use of catheters during the study period could have explained the increase. Alternatively, perhaps an increase in the frequency and/or sensitivity of diagnostic imaging studies has resulted in the detection of previously undiagnosed VTE cases. It is also possible that heightened awareness of VTE in pediatric children’s hospitals has contributed, particularly in larger centers with pediatric hematologists with expertise in thrombosis.

The use of enoxaparin for the treatment of VTE increased significantly throughout the 7-year period, whereas the use of warfarin decreased slightly. The use of either drug increased with age. The increase in enoxaparin use was not unexpected, because this is now often the drug of choice for the treatment of acute VTE in children.\textsuperscript{12} In contrast to unfractionated heparin, enoxaparin is administered subcutaneously (compared with continuous intravenous infusion) and usually is easier to titrate, with less monitoring. Despite this increase, enoxaparin was not used in more than one half (53\%) of VTE admissions in 2007. Unfortunately, it was not possible to determine whether patients in those admissions received unfractionated heparin for treatment of their VTE or received no anticoagulant. As expected, the use of anticoagulants other than unfractionated heparin, warfarin, or enoxaparin, occurring in <1\% of VTE admissions, is extremely rare in pediatrics.

Interestingly, there was a correlation between hospital size and VTE rates, such that larger hospitals tended to have higher rates of VTE. We hypothesize that larger hospitals may have larger proportions of critically ill children at higher risk of VTE or may be more likely to have a dedicated pediatric thrombosis specialist, which may
lead to a higher index of suspicion and increased screening for VTE in those hospitals, for reasons similar to those described above.

A relatively significant proportion (13%) of patients had >1 admission with a diagnosis of VTE during the study period. Those patients tended to be older and were more likely to have a malignancy than were patients with only 1 VTE admission. These results should be interpreted with caution, because we were unable to verify that these were all recurrent events; it is possible that the previous VTE episode was included in the discharge codes for readmission. Furthermore, it is possible that patients went to other hospitals with recurrent VTE. However, the characteristics (proportion, older age, and association with malignancy) of this group are strikingly similar to those reported for pediatric patients with recurrent VTE in other cohorts, which supports this conclusion.\footnote{10,13}

The primary limitation of our study is that we relied on ICD-9-CM codes for the diagnosis of VTE. In this administrative database, there is potential for misclassifying patients who have VTE but receive codes for alternative diagnoses, or vice versa. It is most likely, however, that we have underestimated the absolute rates of VTE among children in these hospitals, for 3 reasons. First, ICD-9-CM codes have been shown to be more specific than sensitive, underestimating the true frequency of conditions.\footnote{14} Second, as we demonstrated, children with VTE often have complex medical conditions and prolonged hospitalizations, which can result in an extensive array of discharge diagnoses. Each patient in the PHIS database is limited to 21 ICD-9-CM discharge codes, and the diagnosis of VTE might not have been included in some cases. Third, there were an additional 6227 admissions in which enoxaparin was used for patients without an ICD-9-CM code for VTE, which was used as a surrogate indicator for cases of VTE. Although we did not include these patients in our analysis, it is likely that many were being treated for VTE, which suggests that we underestimated the true rate.

It is possible that the sensitivity of the abstractionists to identify and to code VTE accurately changed during the study period, such that patients with VTE were more likely to receive VTE codes in 2007 than in 2001. However, this would have needed to occur in nearly every hospital in the study, and there is no reason to suspect such systematic bias. In addition, by using pharmacy billing data, we were able to demonstrate that the use of enoxaparin increased to an even greater degree that ICD-9-CM–coded VTE, which supports our findings.

**CONCLUSIONS**

In pediatric tertiary care hospitals across the United States, VTE has become a rapidly growing problem. Pediatric hematologists faced with the challenge of caring for children with VTE must contend with the fact that most current treatment recommendations are extrapolated from adult studies.\footnote{12} Studies directed at understanding the cause of this increase and determining optimal treatment strategies are essential for addressing this rapidly increasing condition.

**REFERENCES**


Dramatic Increase in Venous Thromboembolism in Children's Hospitals in the United States From 2001 to 2007

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