12-1-2012

Influence of body mass index and antibiotic dose on the risk of surgical site infections in pediatric clean orthopedic surgery.

Jeffrey J Cies
St. Christopher's Hospital for Children, Philadelphia, PA &Alfred I. DuPont Hospital for Children, Nemours Children's Clinic, Wilmington, DE

Shannon Chan
Alfred I. DuPont Hospital for Children, Nemours Children's Clinic, Wilmington, DE

Jobayer Hossain
Alfred I. DuPont Hospital for Children, Nemours Children's Clinic, Wilmington, DE

B Randall Brenn
Alfred I. DuPont Hospital for Children, Nemours Children's Clinic, Wilmington, DE & Thomas Jefferson University, Philadelphia, PA

M. Cecilia Di Pentima
Vanderbilt University Medical Center, Nashville, TN

SURGICAL INFECTIONS
Volume 13, Number 6, 2012

DOI: 10.1089/sur.2011.096

Influence of Body Mass Index and Antibiotic Dose on the Risk of Surgical Site Infections in Pediatric Clean Orthopedic Surgery

Jeffrey J. Cies,[1,2] Shannon Chan,[2] Jobayer Hossain,[2] B. Randall Brenn,[2,3] and M. Cecilia Di Pentima[4]

Abstract

Objective: To evaluate body mass index (BMI) and antimicrobial dose as risk factors for surgical site infections in pediatric patients.
Patients and Methods: Children between 2 and 19 years of age undergoing clean orthopedic procedures and receiving at least one dose of perioperative antibiotics (cefazolin, vancomycin, or clindamycin) were studied. The retrospective case-controlled study was conducted at the Alfred I. duPont Hospital for Children, a 180-bed tertiary-care academic pediatric hospital in Wilmington, DE. Data were collected from January 1, 2002, to December 31, 2005.
Results: Underweight children had a higher risk for SSIs than overweight and normal-weight children. American Society of Anesthesiologists classes II and greater were associated with a greater risk of SSI. Longer procedures were also associated with a higher risk of SSI, specifically, duration of surgery >2 h. Children weighing ≥ 70 kg who received a standard dose of cefazolin (maximum of 1 g) had a higher risk of SSI caused by methicillin-sensitive *Staphylococcus aureus* (MSSA).
Conclusions: Being underweight and undergoing an operation lasting >2 h created significant risks for SSI. Children weighing ≥ 70 kg receiving a standard 1-g dose of cefazolin had a greater risk of MSSA SSIs than children weighing <70 kg who received an appropriate weight-based dose of this antibiotic.

The U.S. Centers for Disease Control and Prevention (CDC) estimates that surgical site infections (SSIs) are the second most common type of hospital-acquired infection, accounting for 22% of all such infections. Surgical site infections increase the hospital length of stay significantly and entail a total increase in cost ranging from $10,443 to $25,546 [1–3]. Currently, limited information exists regarding risk factors for or causes of SSIs in the pediatric population.

Poor nutritional status is associated with more SSIs in the literature [4–7]. Obesity is a well-known risk factor for SSI in the adult population [4,5,8,9]. Studies suggest that current antibiotic dosing for surgical prophylaxis in obese adult patients may fail to provide adequate perioperative prophylaxis [10–12]. Furthermore, data from adults demonstrate that the volume of distribution and total body clearance of drugs is altered in obese patients. Factors affecting tissue concentrations of drug and the volume of distribution include body composition, regional blood flow, and the affinity of the therapeutic agent for plasma proteins and the selected tissue compartment [11,12]. Blood flow per gram of fat is reduced greatly in morbidly obese patients compared with their moderately overweight or lean counterparts [13]. In addition, pediatric patients have faster metabolism and elimination of drugs than adults; therefore, obese pediatric patients could have a higher risk of SSI, as suggested by a recent case-control study [14]. In the studies by Malone et al. [6] and Pessaux et al. [7], both underweight and malnourishment (defined as >10% weight loss in the six months prior to surgery) were shown to be risk factors for SSIs in the adult population. However, data evaluating body mass index (BMI) as a risk factor for SSI are lacking.

The primary objective of this study was to determine whether BMI is a risk factor for SSIs in pediatric patients undergoing clean orthopedic surgical procedures. A secondary

[1]St. Christopher's Hospital for Children, Philadelphia, Pennsylvania.
[2]Alfred I. duPont Hospital for Children, Nemours Children's Clinic, Wilmington, Delaware.
[3]Thomas Jefferson University, Philadelphia, Pennsylvania.
[4]Vanderbilt University Medical Center, Nashville, Tennessee.

objective was to determine the impact of weight-based dosing of perioperative antibiotics on the risk of SSIs. To the best of our knowledge, this is the first study specifically evaluating the association between BMI and antimicrobial dose and the risk of SSIs in pediatric patients undergoing clean orthopedic procedures.

Patients and Methods

Study design and patient population

This study was approved by the Nemours Institutional Review Board. It was a retrospective case-control study conducted at the Alfred I. duPont Hospital for Children, a 180-bed tertiary-care academic pediatric hospital in Wilmington, DE. Data were collected for January 1, 2002, to December 31, 2005. Patients between 2 and 19 years of age who underwent an elective, clean orthopedic procedure and received at least one dose of a peri-operative antibiotic (cefazolin, vancomycin, or clindamycin) were included. Surgical site infection was defined according to the Infectious Diseases Society of America (IDSA) and Surgical Infection Prevention Project (SIP) definitions [15,16]. Patients who did not have instrumentation placed during their procedure had to have an infection develop within 30 d of the procedure. If patients did have instrumentation placed, the infection had to develop within one year of the date of surgery [15,16]. We attempted to match one case to two controls (i.e., one infected patient to two non-infected patients) based on surgical site and procedure and age. There were 105 cases and 212 controls. Subjects were categorized into three BMI groups based on the CDC definition: Healthy weight (BMI fifth through 84th percentile for age and gender), underweight (BMI less than fifth percentile for age and gender), and overweight (BMI $\geq$85th percentile for age and gender). Obesity was defined according to the CDC guidelines [17]. A repeat dose was defined as an additional perioperative antibiotic administered during the surgical procedure. The American Society of Anesthesiologists (ASA) classification system grade was collected for each patient. The ASA classification is used to stratify the severity of a patient's underlying disease and potential for suffering complications from general anesthesia. The classification is as follows:

- Class I: Normal healthy patient;
- Class II: A patient with mild systemic disease and no functional limitations;
- Class III: A patient with severe systemic disease and definite functional impairment;
- Class IV: A patient with severe systemic disease that is a constant threat to life;
- Class V: An unstable moribund patient not expected to survive 24 h with or without the operation;
- Class VI: A brain-dead patient whose organs are to be removed for donation.

Data collection

Patients who underwent clean orthopedic surgical procedures and developed SSI were retrieved from the A. I. duPont Hospital Infection Control database. A diagnosis of SSI for each patient was performed by the orthopedic surgeon and reported monthly to Infection Control. Medical records were reviewed for each patient. The data collected included height, weight, age, gender, ethnicity, ASA class, duration of surgery ($<$2 or $\geq$2 h), type of surgical procedure, timing of antibiotic dose before the first incision, doses of perioperative antibiotic received, and microbiology findings. Surgical procedures were categorized into the following types: Spine, upper extremity, lower extremity, hip, and multiple sites. The timing of first antibiotic dose was categorized into the following: At the time of incision, 0–30 min, 30–60 min, and $>$60 min after the first incision. Doses of antibiotics were classified as therapeutic or subtherapeutic (defined as 10% below the therapeutic dose) based on the target range of 20–30 mg/kg for cefazolin to a maximum standard dose of 1 g, 7.5–10 mg/kg for clindamycin to a maximum standard dose of 600 mg, or 10–15 mg/kg for vancomycin to a maximum standard dose of 1 g [15,16].

Statistical analyses

The study variables were presented by main predictor BMI status and response variable infection status (case and control). Categorical variables were described using frequency and percentages, whereas continuous variables were summarized using mean, standard deviation, minimum, and maximum. A Pearson χ^2 statistic and two-sample *t*-test for categorical and numerical variables, respectively, were used to examine the balance of distribution of the study characteristics among the BMI groups and infection status. A simple binary logistic regression was used to detect the association of an SSI with BMI and other study variables. The odds ratios (ORs), along with 95% confidence intervals (CIs) and p values, were provided to compare the prevalence of SSI for different groups of predictors. In addition, a multiple logistic regression model was used to adjust simultaneously for the effect of the potential confounding variables on the association between SSI and BMI. To be included in the adjusted model, a variable must have been either clinically or statistically significant at $p<0.1$. Subanalyses were attempted to determine the impact of a weight-based dose of cefazolin on the methicillin-sensitive *Staphylococcus aureus* (MSSA) infection status. A simple logistic regression analysis was performed to compare the SSI rates of individuals who weighed $\geq$70 kg and those who weighed $<$70 kg. Another simple logistic regression was performed to compare the odds of developing an SSI caused by MSSA among any kind of infection between individuals $\geq$70 kg and $<$70 kg. All analyses were two-tailed at the $p<0.05$ significance level. All analyses were performed using the statistical package SPSS version 17.0 (Chicago, IL).

Results

Table 1 displays the study variables stratified according to BMI. The difference in the distribution of gender, age, ASA class, and surgical site among the three BMI groups was significant ($p<0.05$). There was no difference in the distribution of ethnicity or the duration of surgery. The majority of patients with SSI had positive surgical site cultures (93%; 98/105) at the time of diagnosis. Of these, 28.5% (28) had polymicrobial growth. *S. aureus* was recovered in 65% of patients (69/105) with SSI. Table 2 depicts all isolates recovered from surgical site cultures.

Table 3 shows the association between the risk of developing an SSI and BMI and the other study variables. Patients who were classified as underweight had a higher risk of SSI

Table 1. Baseline Characteristics of 317 Pediatric Patients Undergoing Clean Orthopedic Surgical Procedures by Body Mass Index (BMI) Group

	BMI group				
Variable	*Healthy weight (%)*	*Underweight (%)*	*Overweight (%)*	*Total patients*	p[a]
Male/female	87 (51)/111 (76)	43 (25)/15 (10)	41 (24)/20 (14)	171/146	<0.001
Ethnicity					0.646
African American	26 (59.1)	9 (20.5)	9 (20.5)	44	
Caucasian	160 (64.3)	44 (17.7)	45 (18.1)	249	
Other	12 (50)	5 (20.8)	7 (29.2)	24	
Age (years)					0.040
N	198	58	61	317	
Mean (SD)	12.9 (3.65)	13.6 (3.98)	11.9 (3.78)	12.8 (3.78)	
Range	4–19	3–18	3–17	3–19	
ASA class					<0.001
I	53 (76.8)	4 (5.8)	12 (17.4)	69	
II or III	92 (63.9)	20 (13.9)	32 (22.2)	144	
>III	53 (51)	34 (32.7)	17 (16.3)	104	
Duration of surgery (h)					0.881
<2	67 (64.4)	18 (17.3)	19 (18.3)	104	
≥2	131 (61.5)	40 (18.8)	42 (19.7)	213	
Surgical site					0.001
Spine	87 (59.2)	36 (24.5)	24 (16.3)	147	
Upper extremity	13 (56.5)	5 (21.7)	5 (21.7)	23	
Lower extremity	53 (65.4)	3 (3.7)	25 (30.9)	81	
Hip	30 (65.2)	12 (26.1)	4 (8.7)	46	
Multiple sites	15 (75)	2 (10)	3 (15)	20	
Timing of preoperative antibiotic (min)					0.306
<0	30 (71.4)	6 (14.3)	6 (14.3)	42	
0–30	123 (64.1)	30 (15.6)	39 (20.3)	192	
30–60	32 (55.2)	14 (24.1)	12 (20.7)	58	
>60	13 (52)	8 (32)	4 (16)	25	
Repeat dose					0.013
No	178 (60.3)	58 (19.7)	59 (20)	295	
Yes	20 (90.9)	0 (0)	2 (9.1)	22	

[a]P value is from either χ^2 statistic or one-way analysis of variance.
ASA = American Society of Anesthesiologists; SD = standard deviation.

than patients classified as of healthy weight (OR 2; 95% CI 1.1-3.67; p = 0.023). The ASA class was also a risk factor for SSI. Specifically, both ASA class II–III (OR 2.6; 95% CI 1.2-5.5; p = 0.014) and ASA class >III (OR 5.7; 95% CI 2.6-12.3; p < 0.001) were associated with a higher risk of SSIs. The duration of surgery was associated with the risk of SSI, as surgery requiring >2 h increased the risk significantly (OR 2.2; 95% CI 1.3-3.8; p = 0.004). On the other hand, ethnicity and gender were not associated with the risk of SSI.

Table 2. Bacteria Recovered from 98 Pediatric Patients with Surgical Site Infection (SSI)[a]

Microorganism	*Number of isolates (%)*
Staphylococcus aureus	
Methicillin sensitive	47 (33)
Methicillin resistant	22 (16)
Coagulase-negative staphylococci	18 (13)
Pseudomonas aeruginosa	16 (11.3)
Escherichia coli	8 (5.7)
Enterococcus faecalis	11 (7.8)
Proteus mirabilis	8 (5.7)
Acinetobacter baumannii	5 (3.5)
Enterobacter cloacae	6 (4)
Total	141

[a]Of the 105 SSI cases, 98 patients had microbiology data supporting the infection. Of these patients, 28 had polymicrobial infections.

The results of the multivariable logistic regression analysis are shown in Table 4. After adjustment for other variables, the risk of SSI in patients classified as underweight compared with the healthy-weight group did not reach statistical significance (OR 1.695; 95% CI 0.835-3.44; p = 0.144). In our model, an ASA class of II or III (OR 3.6; 95% CI 1.48-8.87; p = 0.006) and an ASA class >III (OR 7.8; 95% CI 2.97-20.57; p < 0.001) both were determined to be risk factors for SSI. Moreover, the association between SSIs and duration of surgery >2 h remained significant (OR 2.4; 95% CI 1.24-4.85; p = 0.01).

To evaluate our secondary objective, a subanalysis was performed to determine the impact of the dose of cefazolin on the rate of SSIs caused by MSSA, stratified according to patient weight. In our cohort, 200 patients received cefazolin for perioperative prophylaxis. Of these patients, 161 (80%) weighed <70 kg. Patients weighing <70 kg received an appropriate weight-based dose of cefazolin to a maximum of 1 g, and patients weighing ≥70 kg received a standard 1-g dose. Of the 200 patients who received cefazolin, 47 (23.5%) developed an SSI caused by MSSA, and 153 (76.5%) did not develop SSI.

Table 3. Baseline Characteristics of 317 Pediatric Patients Undergoing Clean Orthopedic Surgical Procedures by Infection Status

	Infection status (%)				
Variable	*Infected*	*Not infected*	*Total patients*	*Odds ratio (95% CI)*	p[a]
Gender					
Male	61 (35.7)	110 (64.3)	171	Reference	
Female	44 (30.1)	102 (69.9)	146	0.807 (0.514-1.270)	0.297
Ethnicity					
African American	20 (45.5)	24 (54.5)	44	Reference	
Caucasian	78 (31.3)	171 (68.7)	249	0.547 (0.285-1.050)	0.070
Other	7 (29.2)	17 (70.8)	24	0.494 (0.171-1.428)	0.193
Age (years)				0.989 (0.930-1.052)	0.729
N	105	212	317		
Mean (SD)	12.7 (3.86)	12.9 (3.75)	12.8 (3.78)		
Range	3–18	3–19	3–19		
BMI group					
Healthy weight	57 (28.8)	141 (71.2)	198	Reference	
Underweight	26 (44.8)	32 (55.2)	58	2.010 (1.101-3.670)	0.023
Overweight	22 (36.1)	39 (63.9)	61	1.395 (0.761-2.559)	0.282
ASA class					
I	10 (14.5)	59 (85.5)	69	Reference	
II or III	44 (30.6)	100 (69.4)	144	2.596 (1.216-5.541)	0.014
>III	51 (49)	53 (51)	104	5.677 (2.622-12.295)	<0.001
Duration of surgery (h)					
<2	23 (22.1)	81 (77.9)	104	Reference	
≥2 h	82 (38.5)	131 (61.5)	213	2.204 (1.289-3.779)	0.004
Timing of preoperative antibiotic (min)					
<0	12 (28.6)	30 (71.4)	42	Reference	
0–30	66 (34.4)	126 (65.6)	192	1.310 (0.629-2.725)	0.471
30–60	18 (31)	40 (69)	58	1.125 (0.471-2.686)	0.79
>60	9 (36)	16 (64)	25	1.406 (0.489-4.043)	0.527

[a]P value is from either χ^2 statistic or one-way analysis of variance.
BMI = body mass index; SD = standard deviation.

Table 4. Body Mass Index (BMI) Does Not Predict a Higher Risk of Surgical Infection after Clean Orthopedic Surgical Procedures in Pediatric Patients

Variable	*Odds ratio (95% CI)*	p
BMI group		
Healthy weight	Reference (1.0)	–
Underweight	1.695 (0.835-3.440)	0.144
Overweight	1.049 (0.507-2.170)	0.898
ASA class		
I	Reference (1.0)	–
II or III	3.626 (1.483-8.869)	0.006
>III	7.810 (2.966-20.566)	<0.001
Duration of surgery (h)		
<2	Reference (1.0)	–
≥2	2.447 (1.236-4.846)	0.010
Ethnicity		
African American	Reference (1.0)	–
Caucasian	0.506 (0.156-1.634)	0.255
Other	0.725 (0.349-1.508)	0.390

Multivariable logistic regression analysis to determine the effect of BMI after adjustment of the effect of covariates.
CI = confidence interval.

Those patients who weighed ≥70 kg had a statistically significant increase in the risk of MSSA SSI compared with patients who weighed <70 kg, 35.9% (14/39) vs. 20.5% (33/161), respectively (OR 2.17; 95% CI 1.02-4.64; p = 0.045).

Discussion

There are data demonstrating alterations in pharmacokinetics and pharmacodynamics of drugs in obese adults compared with non-obese patients. These alterations are a risk factor for SSIs, as are malnourishment and being underweight [6,7,10–13]. Taking into consideration some additional factors specific to pediatric patients, such as their greater renal elimination, it was hypothesized that in pediatric patients, the incidence of SSIs could differ with BMI status [14]. To the authors' knowledge, there is only a single study evaluating the risk factors for SSI in a pediatric population undergoing clean orthopedic surgical procedures [14].

In our cohort, being overweight was not a risk factor for SSI. Nevertheless, children and adolescents weighing ≥70 kg, regardless of BMI status, did have a higher risk of SSI compared with children and adolescents weighing <70 kg receiving an appropriate weight-adjusted dose of cefazolin to a maximum of 1 g. The organism most often implicated in the SSIs in children and adolescents who weighed ≥70 kg was

MSSA. Guidelines published by the American Society of Health-System Pharmacists recommend 1 g of cefazolin for all adult orthopedic surgical procedures, including those involving implantation of foreign materials [16]. Guidelines for pediatric patients recommend 20–30 mg/kg/dose [16]. At Nemours, surgical prophylaxis guidelines have followed these recommendations, and in most cases, cefazolin is capped at 1 g/dose. A recent advisory statement from the National Surgical Infection Prevention Project recommends a maximum single dose of 2 g of cefazolin for patients weighing at least 80 kg [15]. This recommendation was based on a higher risk of SSI among adult patients weighing >80 kg who underwent gastroplasty and received a 1-g dose of cefazolin in comparison with patients receiving twice that dose. Similarly, our cohort of pediatric patients who weighed ≥70 kg had a higher risk of SSI when receiving a 1-g dose of cefazolin as preoperative surgical prophylaxis for clean orthopedic surgical procedures. Therefore, caution is needed when setting institution-specific maximum doses for perioperative prophylaxis with cefazolin, and the 20–30 mg/kg/dose recommendation should be followed to a maximum of 2 g/dose.

In our cohort, underweight children and adolescents with a BMI less than the fifth percentile had a greater risk of SSI by univariable analysis, which is consistent with published data in adults [6,7]. One hypothesis to explain this finding is that children who are underweight, according to their BMI, often are malnourished. Additionally, underweight children may not have the immunologic reserve to defend against an infection because of their poor nutritional status, as poor nutritional status has been suggested to contribute to decreased lymphocyte function [18,19]. Furthermore, good nutritional status is crucial for wound healing, which could contribute to this association and has been demonstrated in other studies [20,21]. However, in multivariable analysis, this finding was not found to reach statistical significance.

Linam et al., in a retrospective analysis of children undergoing posterior spinal fusion, recently reported that obese children had a higher rate of SSI [14]. We did not find a greater rate of SSI in overweight patients. However, our population was not limited to patients undergoing posterior spinal fusion. In the study by Linam et al., clindamycin was the perioperative antibiotic of choice in 11% of patients, whereas in our study, the rate of clindamycin use was much lower, at approximately 1%. Our findings support a higher risk of MSSA SSIs in patients receiving a standard 1-g dose of cefazolin in patients who weigh ≥70 kg. We did not perform a separate analysis for overweight patients who developed an MSSA SSI. However, one possible explanation for the difference in the rate of SSIs in the overweight patients reviewed in the earlier and our cohort is the choice of perioperative antibiotic. Clindamycin and cefazolin have different mechanisms of action and spectra of activity, and the patients in the study by Linam et al. had a higher rate of gram-negative SSIs than did our cohort.

The ASA classification is used to assess a patient's physical state prior to selecting anesthesia for surgery, of which nutritional status may be a component. By definition, having a BMI ≥85th percentile for age and gender requires, at a minimum, an ASA classification of III. Considering that every overweight patient has an ASA classification of at least III, it was surprising that an ASA classification of ≥III was an independent risk factor for SSI in both univariable and multivariable analysis, yet overweight status according to BMI was not a risk factor in our analysis; only an underweight BMI was a risk factor. The ASA classification system is not based solely on objective criteria, so there is the potential for misclassifying patients and differences in classification status depending on the person conducting the evaluation. In our study, an ASA classification of ≥III was one of the risk factors that maintained statistical significance through univariable and multivariable logistic regression analysis.

Undergoing surgery with a duration of >2 h was a risk factor for SSI in both univariable and multivariable analysis. There are many reasons this could be the case. First, operations that last >2 h usually have a greater degree of complexity. With a higher degree of complexity come a larger number of manipulations and a larger number of areas involved and the potential for injuring/infecting an area involved in the surgery. Second, the amount of blood loss that is likely to occur with longer operations is greater, and with any blood loss, there is the potential for lower serum concentrations of the perioperative antimicrobial agent. Having an appropriate serum concentration of the drug is crucial to ensure an appropriate concentration at the site of the potential infection. Furthermore, in longer operations, the risk of tissue hypoxemia and hypotension increases. Tissue hypoxia can occur as a result of reduced perfusion of the area of interest. One hallmark of successful antimicrobial prophylaxis is delivery of the drug to the area of increased infection susceptibility at an appropriate concentration. With reduced perfusion of the area of concern, there is a reduction in the amount of the antimicrobial agent reaching that area. Specifically, for cefazolin, the primary mechanism of efficacy correlates with the concept of time-dependent killing. With time-dependent killing, there needs to be a serum concentration at the site of the infection or area of increased risk that is above the minimum inhibitory concentration (MIC) for as long as possible to ensure efficacy. With tissue hypoxia and reduced perfusion, there is less blood with an appropriate antimicrobial drug concentration, which could contribute to the higher risk of SSIs when the duration of surgery is >2 h.

Our results support an association between being underweight for age and gender, an ASA status ≥II, and surgery lasting >2 h and a greater risk of SSI. These results are similar to those of a recent retrospective analysis in children undergoing posterior spinal fusion [14]. Furthermore, our study supports using a higher dose of cefazolin in children and adolescents weighing ≥70 kg, regardless of BMI status, which is similar to the recent recommendation in adults to use 2 g of cefazolin for patients ≥80 kg [15].

Conclusions

Our study highlights the importance of optimizing antimicrobial dosing in children and adolescents ≥70 kg, especially when using cefazolin, the drug of choice for clean orthopedic surgical procedures. Additionally, our cohort suggests being underweight, surgery duration ≥2 h, and higher ASA class are risk factors for SSI after clean orthopedic surgery.

Data presented here were collected as part of a single-center, retrospective study and have all the attendant limitations: Causation cannot be demonstrated, and the influence of factors not reviewed cannot be excluded. Furthermore, our results could be explained by sampling bias. However, this

study represents the first evaluation specifically of BMI status and antimicrobial dose in pediatric patients undergoing clean orthopedic surgery.

Author Disclosure Statement

No financial support was received for this study. The authors have no conflicts of interest to report.

References

1. Centers for Disease Control and Prevention, Division of Healthcare Quality Promotion. Estimates of healthcare-associated infections. May 30, 2007. Available at www.cdc.gov/ncidod/dhqp/hai.html. Accessed July 2009.
2. Klevens RM, Edwards JR, Richards CL Jr, et al. Estimating healthcare-associated infections in U.S. hospitals, 2002. Public Health Rep 2007;122:160–166.
3. Stone PW, Braccia D, Larson E. Systematic review of economic analyses of health care-associated infections. Am J Infect Control 2005;33:501–509.
4. Olsen MA, Nepple JJ, Riew KD, et al. Risk factors for surgical site infection following orthopedic spinal operations. J Bone Joint Surg Am 2008;90:62–69.
5. Choban PS, Heckler R, Burge JC, Flancbaum L. Increased incidence of nosocomial infections in obese surgical patients. Am Surg 1995;61:1001–1005.
6. Malone DL, Genuit T, Tracy JK, et al. Surgical site infections: Reanalysis of risk factors. J Surg Res 2002;103:89–95.
7. Pessaux P, Msika S, Atalla D, et al., French Association for Surgical Research. Risk factors for postoperative infectious complications in noncolorectal abdominal surgery: A multivariate analysis based on a prospective multicenter study of 4718 patients. Arch Surg 2003;138:314–324.
8. Olsen MA, Mayfield J, Lauryssen C, et al. Risk factors for surgical site infection in spinal surgery. J Neurosurg 2003; 98(2 Suppl):149–155.
9. Canturk Z, Canturk NZ, Cetinarslan B, et al. Nosocomial infections and obesity in surgical patients. Obesity Res 2003; 11:769–775.
10. Edmiston CE, Krepel C, Kelly H, et al. Perioperative antibiotic prophylaxis in the gastric bypass patient: Do we achieve therapeutic levels? Surgery 2004;136:738–747.
11. Cheymol G. Effects of obesity on pharmacokinetics: Implications for drug therapy. Clin Pharmacokinet 2000;39: 215–231.
12. Bauer LA, Black DJ, Lill JS. Vancomycin dosing in morbidly obese patients. Eur J Clin Pharmacol 1998;54:621–625.
13. Lesser GT, Deutsch S. Measurement of adipose tissue blood flow and perfusion in man by uptake of 85Kr. J Appl Physiol 1967;23:621–630.
14. Linam WM, Margolis PA, Staat MA, et al. Risk factors associated with surgical site infection after pediatric posterior spinal fusion procedure. Infect Control Hosp Epidemiol 2009;30:109–116.
15. Bratzler DW, Houck PM, Surgical Infection Prevention Guidelines Writers Workgroup, American Academy of Orthopaedic Surgeons, American Association of Critical Care Nurses, American Association of Anesthesiologists, et al. Antimicrobial prophylaxis for surgery: An advisory statement from the National Surgical Infection Prevention Project. Clin Infect Dis 2004;38:1706–1715.
16. American Society of Health-System Pharmacists. ASHP therapeutic guidelines on antimicrobial prophylaxis in surgery. Am J Health-Sys Pharm 1999;56:1839–1888.
17. U.S. Centers for Disease Control and Prevention. BMI for children and teens. Available at www.cdc.gov/nccdphp/dnpa/bmi/bmi-for-age.htm. Accessed July 2009.
18. Sayarlioglu H, Erkoc R, Demir C, et al. Nutritional status and immune functions in maintenance hemodialysis patients. Mediators Inflamm 2006;2006:20264.
19. Molls RR, Ahluwalia N, Mastro AM, et al. Nutritional status predicts primary subclasses of T cells and the lymphocyte proliferation response in healthy older women. J Nutr 2005; 135:2644–2650.
20. Dickhaut SC, DeLee JC, Page CP. Nutritional status: Importance in predicting wound-healing after amputation. J Bone Joint Surg Am 1984;66:71–75.
21. Dwyer AJ, John B, Mam MK, et al. Nutritional status and wound healing in open fractures of the lower limb. Int Orthop 2005;29:251–254.

Address correspondence to:
Dr. M. Cecilia Di Pentima
Department of Pediatrics
Monroe Carell, Jr. Children's Hospital at Vanderbilt
Vanderbilt University School of Medicine
1161 21st Ave. South, D-7235 MCN
Nashville, TN 37232-2581

E-mail: cecilia.dipentima@vanderbilit.edu