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ORIGINAL ARTICLE

Broad- Versus Narrow-Spectrum Perioperative Antibiotics and Outcomes in Pediatric Congenital Heart Disease Surgery: Analysis of the Vizient Clinical Data Base

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Background: Despite guidelines recommending narrow-spectrum perioperative antibiotics (NSPA) as prophylaxis for most children undergoing congenital heart disease (CHD) surgery, broad-spectrum perioperative antibiotics (BSPA) are variably used, and their impact on postoperative outcomes is poorly understood.

Methods: We used administrative data from U.S. hospitals participating in the Vizient Clinical Data Base. Admissions from 2011 to 2018 containing a qualifying CHD surgery in children 0–17 years old were evaluated for exposure to BSPA versus NSPA. Propensity score-adjusted models were used to compare postoperative length of hospital stay (PLOS) by exposure group, while adjusting for confounders. Secondary outcomes included subsequent antimicrobial treatment and in-hospital mortality.

Results: Among 18 088 eligible encounters from 24 U.S. hospitals, BSPA were given in 21.4% of CHD surgeries, with mean BSPA use varying from 1.7% to 96.1% between centers. PLOS was longer for BSPA-exposed cases (adjusted hazard ratio 0.79; 95% confidence interval [CI]: 0.71–0.89, $P < .0001$). BSPA was associated with higher adjusted odds of subsequent antimicrobial treatment (odds ratio [OR] 1.24; 95% CI: 1.06–1.48), and there was no significant difference in adjusted mortality between exposure groups (OR 2.06; 95% CI: 1.0–4.31; $P = .05$). Analyses of subgroups with the most BSPA exposure, including high-complexity procedures and delayed sternal closure, also did not find (but could not exclude) a measurable benefit from BSPA on PLOS.

Conclusions: BSPA use was common in high-risk populations, and varied substantially between centers. Standardizing perioperative antibiotic practices between centers may reduce unnecessary broad-spectrum antibiotic exposure and improve clinical outcomes.

Key words. anti-bacterial agents; surgical wound infection; antibiotic prophylaxis; cardiac surgical procedures; patient discharge.

INTRODUCTION

Surgical site infections (SSI) contribute to morbidity and mortality in children undergoing congenital heart disease (CHD) surgery [1–3]. National surgical prophylaxis guidelines recommend that most children receive narrow-spectrum perioperative antibiotics (NSPA) at time of CHD surgery, targeted to the pathogens predominantly implicated in SSI [4, 5]. Guideline indications for broad-spectrum perioperative antibiotics (BSPA) are limited to the use of vancomycin for patients allergic to first-line antibiotics, or those colonized with methicillin-resistant *Staphylococcus aureus* (MRSA). Supporting evidence comes from case series or extrapolation from other populations [6–8]; there are no trials comparing perioperative antibiotic regimens in pediatric cardiothoracic surgery.

Nonetheless, BSPA is employed differently within and between centers that perform CHD surgery, with variable use prompted by factors such as patient age, surgical complexity, or postoperative open sternum followed by delayed sternal closure (DSC, a risk factor for SSI not addressed in pediatric or adult surgical antibiotic prophylaxis guidelines) [1, 6, 9–11]. Given the cumulative harms of unnecessary broad-spectrum antibiotic exposure, broad-spectrum regimens carry the burden of proof to demonstrate improved postoperative outcomes. Any desired benefits from BSPA must be balanced against increased antimicrobial resistance, medication toxicities (eg, vancomycin nephrotoxicity), and microbiome disruption (predisposing to secondary infections) [12–15]. Yet substantial practice variation suggests ongoing provider uncertainty about the role of BSPA in pediatric CHD surgery.

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This study was conducted to describe the extent and variation in BSPA use in pediatric CHD surgery within a cohort of U.S. academic hospitals from 2011 to 2018, and investigate whether BSPA versus NSPA use was associated with differences in outcomes, including postoperative length of hospital stay (PLOS).

METHODS

Setting and Participants

This was a multicenter, observational cohort study utilizing the Vizient Clinical Data Base (Vizient CDB/RM, previously University HealthSystem Consortium, Irving, TX) from 2011 to 2018. CDB/RM members (comprising over 100 academic medical centers from all regions of the United States) contribute inpatient billing and medication use data (previously validated against hospital medication administration records) [16–18]. All patient and hospital identifiers are removed. The study was designated exempt from review as "not human subjects' research" by the University of California San Francisco Institutional Review Board.

Participants Selection

We included hospital admissions of participants 0–17 years old containing a CHD surgery categorizable with a Risk Adjustment for Congenital Heart Surgery ("RACHS-1") score, an established metric of CHD procedure mortality approximating surgical complexity [19]. Qualifying CHD surgeries and associated risk scores were derived from diagnosis and procedure codes, based on previously published methods for International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), and adapted for ICD-10-CM (see Supplementary Methods Part 1 for included procedures) [20].

Exclusion criteria included cases with missing procedure or medication dates, no perioperative antibiotics or only penicillin or ampicillin (as these agents lack staphylococcal activity recommended for surgical prophylaxis), heart transplantation, concurrent major noncardiac surgery, suspected preexisting bacterial infection indicated by preoperative antibiotic exposure, cases from centers contributing ≤5 eligible cases per year, and cases with death, hospital discharge, or interfacility transfer on the day of surgery.

Exposure, Outcome, and Covariates

Perioperative antibiotics were any IV antibiotics given on the calendar day of surgery. Unexposed patients received NSPA only (a first- or second-generation cephalosporin, eg, cefazolin or cefuroxime). Exposed patients received BSPA, which was descriptively categorized into vancomycin; extended gram-negative agents; antipseudomonal agents; vancomycin combination regimens; and others (see Supplementary Methods Part 2 for further details on study design and statistical analysis). Cases were analyzed according to their initial exposure, regardless of subsequent changes to their exposure after the day of surgery, or duration of perioperative antibiotics.

The effect of BSPA versus NSPA on PLOS was compared using postoperative hospital discharge rates. PLOS has been used as a proxy for CHD postoperative morbidity [21, 22]. Strengths of PLOS as a primary outcome include objective and unequivocal measurement using administrative data, with complete follow-up, and robustness to competing outcomes such as hospital transfer or mortality [23].

Secondary outcomes included subsequent antimicrobial treatment, defined as ≥7 consecutive days of additional antimicrobial exposure prior to discharge, after ≥1 antimicrobial-free day. Subsequent antimicrobial treatment is sensitive for SSI, while also capturing clinically important postoperative illness that may not be reported as SSI [24]. We also reported postoperative hospital mortality (henceforth "mortality"), and a composite of mortality and participating hospital readmission. Outcomes occurring after 30 days postoperatively were censored.

STATISTICAL ANALYSIS

Propensity Score Analysis

Perioperative antibiotic selection is at risk for confounding by indication, in which clinicians or protocols preferentially select BSPA for patients perceived at higher risk for complications. To mitigate bias in this observational study, including confounding by indication, we employed propensity score adjustment with inverse probability of treatment weighting (henceforth, propensity score weighting). A logistic regression predictive of BSPA exposure was used to calculate a propensity score for each case. This propensity score model was regressed on baseline covariates (Table 1) and year, with center incorporated as a random intercept [25, 26]. Each case received a weight inversely proportional to its propensity score, and the resulting weighted cohort was assessed to assure balance and distribution of key covariates [27]. These included age, presence of a genetic syndrome or major noncardiac congenital anomaly, prematurity, DSC, tiers of surgical risk (ie, RACHS-1 scores), need for perioperative extracorporeal membrane oxygenation (ECMO), and the number of vasopressor medications received the day of surgery ("vasopressor score") (Figure 1). Interactions in the original propensity score regression were iteratively adjusted until these key covariates were balanced between exposure groups, assessed using standardized mean differences and variance ratios [27].

Outcome Models

We compared PLOS between exposure groups, using Cox proportional hazards models (wherein a hazard ratio [HR] <1 indicates a lower rate of postoperative hospital discharge for

Table 1. Unweighted and Weighted Case Characteristics by Narrow- Versus Broad-Spectrum Perioperative Antibiotic Exposure Groups

	Full cohort (unweighted) *N* = 18 088				Propensity score Weighted cohort *N* = 17 672[a]		
	Overall *n* (%)	NSPA *n* (%)	BSPA *n* (%)	Stand. dif %	NSPA *n* (%)	BSPA *n* (%)	Stand. dif %
Total	18 088	14 221 (78.6)	3867 (21.4)	—	13 879 (78.5)	3793 (21.5)	—
Male	9931 (54.9)	7798 (54.8)	2133 (55.2)	0.7	7586 (54.7)	2019 (53.2)	−2.8
Age							
0–30 days	3494 (19.3)	2350 (16.5)	1144 (29.6)	31.4	2602 (18.8)	725 (19.1)	0.9
1–12 months	6819 (37.7)	5631 (39.6)	1187 (30.7)	−18.7	5161 (37.2)	1386 (36.5)	−1.3
1–17 years	7776 (43.0)	6240 (43.9)	1536 (39.7)	−8.4	6115 (44.1)	1681 (44.3)	0.6
Race/ethnicity							
White	9576 (52.9)	7727 (54.3)	1849 (47.8)	−13.1	7423 (53.5)	2,144 (56.5)	6.1
Black	2640 (14.6)	2068 (14.5)	572 (14.8)	0.7	2013 (14.5)	586 (15.5)	2.7
Hispanic	2255 (12.5)	1444 (10.2)	811 (21.0)	30.2	1727 (12.5)	434 (11.5)	−3.1
Asian	726 (4.0)	593 (4.2)	133 (3.4)	−3.8	549 (4.0)	112 (3.0)	−5.5
Other	2891 (16.0)	2589 (16.8)	502 (13.0)	−10.7	2166 (15.6)	516 (13.6)	−5.7
Premature <37 weeks	977 (5.4)	707 (5.0)	270 (7.0)	8.5	791 (5.7)	228 (6.0)	1.3
RACHS-1 score							
1	2327 (12.9)	1990 (14.0)	337 (8.7)	−16.7	1756 (12.6)	485 (12.8)	0.4
2	7070 (39.1)	5825 (41.0)	1245 (32.2)	−18.3	5381 (38.8)	1482 (39.1)	0.6
3	6586 (36.4)	5116 (36.0)	1470 (38.0)	4.2	5147 (37.1)	1378 (36.3)	−1.5
4	1591 (8.8)	1074 (7.6)	517 (13.4)	19.1	1222 (8.8)	348 (9.2)	1.3
5/6	514 (2.9)	216 (1.5)	298 (7.7)	29.8	373 (2.7)	100 (2.6)	−0.4
Syndrome/anomaly	3895 (21.5)	2991 (21.0)	2,991 (23.4)	5.6	3056 (22.0)	881 (23.2)	2.9
Delayed sternal closure	1061 (5.9)	353 (2.5)	708 (18.3)	53.7	782 (5.6)	211 (5.6)	−0.3
Periop ECMO	404 (2.2)	179 (1.3)	225 (5.8)	24.9	310 (2.2)	79 (2.1)	−1.0
Vasoactive score							
0	3916 (21.6)	3559 (25.0)	357 (9.2)	−42.9	3029 (21.8)	779 (20.5)	−3.1
1	5195 (28.7)	4409 (31.0)	786 (20.3)	−24.6	4120 (29.7)	1115 (29.4)	−0.6
2	4749 (26.3)	3652 (25.7)	1097 (28.4)	6.1	3643 (26.2)	1066 (28.1)	4.2
3+	4228 (23.4)	2601 (18.3)	1627 (42.1)	53.6	3087 (22.2)	832 (21.9)	−0.7

Abbreviations: BSPA, broad-spectrum perioperative antibiotics; ECMO, extracorporeal membrane oxygenation; NSPA, narrow-spectrum perioperative antibiotics; RACHS-1, Risk Adjustment for Congenital Heart Surgery; Stand. dif, standardized mean difference.

[a]Differences in sample sizes between weighted and unweighted populations reflect trimming of encounters with propensity scores outside the range of common support shared by both exposure groups, as well as influence of weights.

BSPA- compared with NSPA-exposed cases), and graphically using adjusted survival curves [23, 28–30]. Secondary outcomes were calculated as odds ratios (OR) using logistic regressions.

Sensitivity and Subgroup Analyses

The "*E*-value" for the primary outcome was calculated as a measure of robustness to unmeasured confounding, indicating the strength of an unmeasured confounder that would be needed to explain the identified association [31]. Sensitivity analyses compared PLOS using two alternative statistical methods of adjustment: traditional multivariate-adjusted regression models and a propensity score matched cohort [32].

A "limited duration perioperative antibiotics" sensitivity analysis addressed a possible source of confounding: that some BSPA exposure would represent antibiotics broadened on the day of surgery prompted by clinical markers of illness not captured by covariates in our model. This analysis was restricted to non-DSC cases where all antibiotics were discontinued within two days following CHD surgery, in order to select for antibiotic coverage likely intended as surgical prophylaxis, rather than empirical treatment of infection.

Subgroup Analyses

We compared PLOS in weighted subgroup analyses stratified by RACHS-1 score, restricted to cases with DSC, and among the quartile of centers with the highest annual volume.

Statistical analysis was performed with Stata version 16.1 (StataCorp LLC, College Station, TX). All statistical tests were two-sided and used .05 significance levels.

RESULTS

After applying exclusion criteria (Figure 2), 18 088 cases from 24 centers met eligibility. Baseline characteristics and standardized mean differences before and after weighting are presented

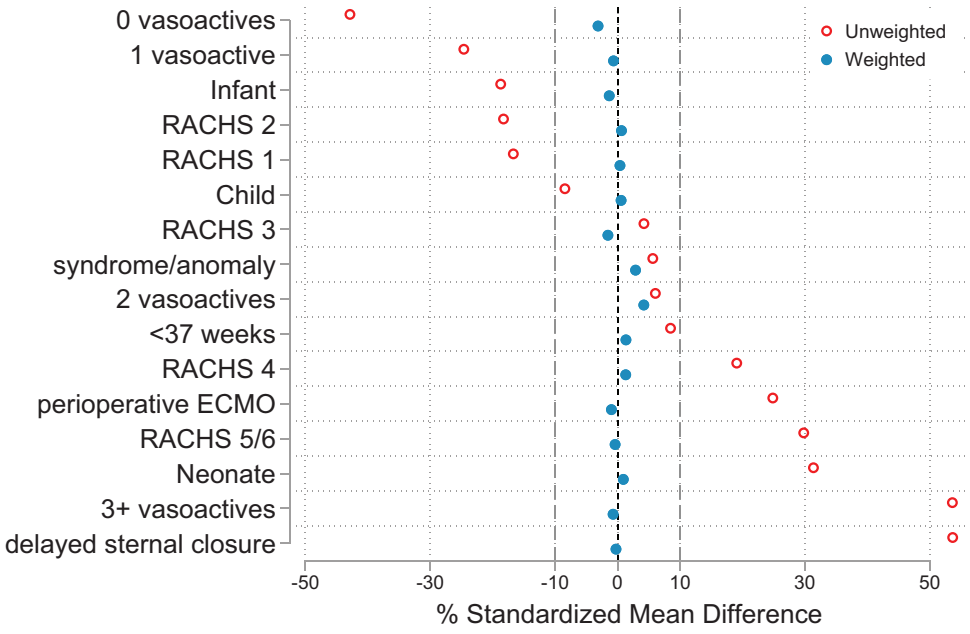

Figure 1. Standardized mean differences before and after weighting. Standardized mean differences as percentages compare how covariates considered probable confounders are distributed between exposure groups in the unweighted cohort (n = 18 088) and propensity score weighted cohort (n = 17 672). Standardized mean differences with negative values indicate covariates with greater prevalence among cases with narrow-spectrum perioperative antibiotic exposure, whereas positive values indicate greater prevalence in cases with broad-spectrum perioperative antibiotic exposure. After weighting, all covariate standardized mean differences were within 10% between exposure groups. Data from the Vizient Clinical Data Base used with permission of Vizient, Inc. All rights reserved.

in Table 1. BSPA was given in 21.4% (3867) of cases, including 32.7% of neonatal cases and 66.7% of cases undergoing DSC. While only 5.9% of cases had DSC (n = 1061), these admissions comprised 18.3% of overall BSPA use. Center surgical volume ranged from 11 to 464 cases per year (median 128); the six centers comprising the highest quartile of surgical volume had 198–464 annual cases. Overall BSPA use across all centers ranged from 1.7% to 96.1%; the range in BSPA use was narrower (10.2%–21.9%) among centers in the highest quartile of surgical volume. Vancomycin was the most utilized broad-spectrum agent, alone or in combination in 85.9% of BSPA regimens (n = 3321). Additional gram-negative coverage was given in 68.2% of cases receiving BSPA (n = 2636). Figure 3 depicts trends in classes and combinations of BSPA by year, with overall annual use varying from 18.6% to 26.1%.

Among eligible cases, 17 672 cases were included in the propensity score weighted cohort for further analysis.

Primary Outcome

Before adjustment, BSPA was associated with longer PLOS (HR of hospital discharge 0.65; 95% confidence interval [CI]: 0.51–0.83; P = .001; Table 2), which remained significant after propensity score adjustment (HR 0.79; 95% CI: 0.71–0.89; P < .0001). The E-value (representing the magnitude of unmeasured confounding that could explain the adjusted HR) was 1.85. Adjusted survival curves graphically depict a significant association between BSPA exposure and a lower cumulative incidence of postoperative hospital discharge (Figure 4).

Secondary Outcomes

BSPA-exposed cases had greater odds of receiving subsequent antimicrobial treatment (OR 1.25; 95% CI: 1.06–1.48; P = .008). Unadjusted in-hospital mortality within 30 days of surgery was 1.28% (n = 231) among the entire cohort: 3.3% (n = 127) for BSPA-, versus 0.73% (n = 104) for NSPA-exposed cases, for an unadjusted OR of 4.61 (95% CI: 2.75–7.73; P < .0001). After adjustment with propensity score weighting, the 95% CI included the null (OR 2.06; 95% CI: 1.0–4.31; P = .05), meaning no significant association was found between BSPA and in-hospital mortality. BSPA-exposed cases had greater odds of the composite outcome of readmission or in-hospital mortality (OR 1.33; 95% CI: 1.01–1.76; P = .045).

Sensitivity Analyses

Findings of the multivariate-adjusted regression analysis were consistent with the primary analysis. The propensity score-matched cohort comprised 4478 cases; differences in PLOS did not meet significance. The sensitivity analysis restricted to cases with limited duration of perioperative antibiotics comprised 13 327 cases after weighting: HRs were calculated over two time periods to satisfy proportionality. Cases exposed to BSPA vs. NSPA remained

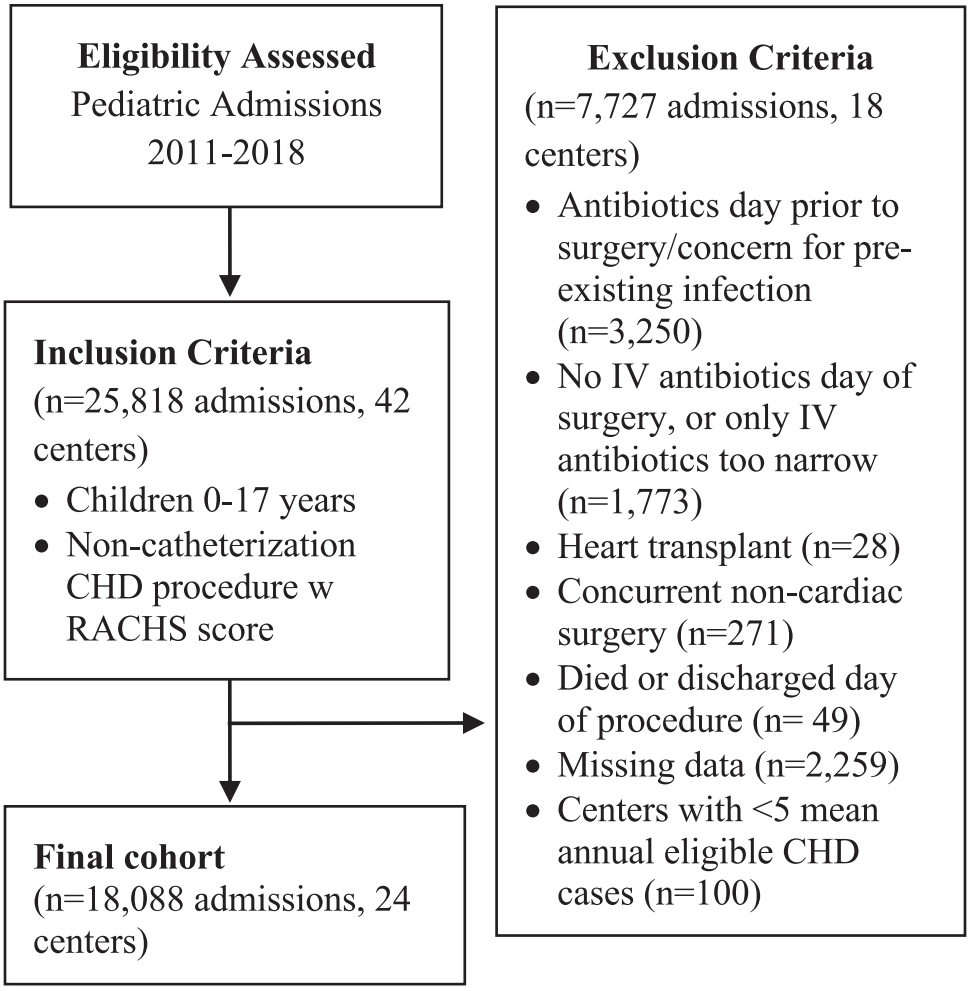

Figure 2. Flow diagram for final cohort inclusion and exclusion. Flow diagram demonstrating number of admissions with eligible case in final cohort after applying inclusion and exclusion criteria. Data from the Vizient Clinical Data Base used with permission of Vizient, Inc. All rights reserved.

with longer PLOS (adjusted HR of hospital discharge: 0.83; 95% CI: 0.75–0.91; $P < .0001$) during days 1–22 while not differing significantly from days 23 to 30. An adjusted survival curve demonstrated similar findings (Supplementary Figure 1a).

Subgroup Analyses

Among low- and mid-surgical complexity subgroups (RACHS-1 scores of 1, 2, and 3), after adjustment with propensity weighting, BSPA use was associated with longer PLOS. There was no significant difference among those with a score of 4, and no subgroup analysis could be performed among cases with scores of 5 or 6, as the propensity score model could not be balanced. The weighted subgroup restricted to higher-volume centers comprised 9234 cases; findings were consistent with the primary analysis. The weighted subgroup with DSC comprised 885 cases; in contrast to other cohorts, the HR trended toward improved PLOS in BSPA-exposed patients; however, 95% CIs were wide and differences were not significant (HR 1.26; 95% CI: 0.91–1.74, $P = .16$) (Supplementary Figures 1b and 1c).

DISCUSSION

This multicenter, observational study did not find evidence to challenge the preferential use of NSPA for most pediatric patients undergoing CHD surgery, while describing notable practice variability between centers.

As postoperative mortality declines, CHD surgery has sought alternative outcomes to compare postoperative morbidity [22, 33, 34]. Use of SSI as an outcome is limited by variable definitions, challenging ascertainment (even prospectively), and underreporting [24, 35–37]. Discharge diagnosis codes have particularly poor sensitivity and specificity for SSI [36]. We chose PLOS as an objective and completely-measured primary outcome. It reflects the impact of SSI, as well as the cumulative impact of any postoperative infectious complications, while balancing potential antimicrobial-related complications like nephrotoxicity [2, 38]. As a secondary outcome, we also report subsequent antimicrobial exposure, a sensitive screen for postoperative infectious complications, including SSI [24].

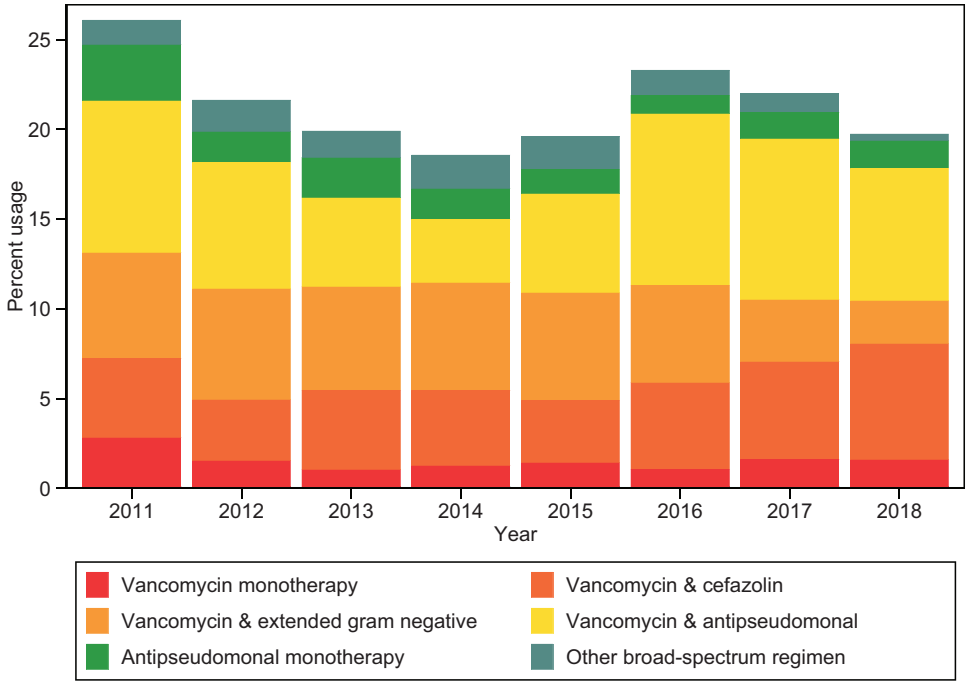

Figure 3. Rates and types of broad-spectrum perioperative antibiotic use from 2011 to 2018. Rates and types of broad-spectrum perioperative antibiotic use by year among 24 U.S. hospitals performing pediatric congenital heart disease surgery, with overall annual use ranging from 18.6% to 26.1%. Extended gram-negative coverage is defined as exposure to a cefotaxime, ceftriaxone, or ampicillin/sulbactam. Antipseudomonal coverage includes piperacillin/tazobactam, cefepime, aminoglycosides, fluoroquinolones, and carbapenems. Data from the Vizient Clinical Data Base used with permission of Vizient, Inc. All rights reserved.

Our study found no significant benefits from BSPA, consistent with multiple randomized trials in adult cardiothoracic surgery examining SSI prevention [7, 39]. This included no significant difference between PLOS among children who underwent DSC, although the 95% CI (0.91–1.74) did not exclude the possibility of clinically meaningful benefits with BSPA. Existing literature addressing the role of BSPA in pediatric DSC remains scant. DSC has been found to be a risk factor for SSI with gram-negative organisms [40], and a single-center observational study of 63 children undergoing DSC found BSPA use (meropenem and vancomycin) was associated with significantly improved combined rates of SSI and clinical sepsis compared to NSPA alone (cefazolin) [8]. However, that study's generalizability is limited by high compound rates of postoperative infection (46%, 29/63), with limited adjustment for confounding.

In our primary analysis, and multiple subanalyses, BSPA exposure remained associated with longer PLOS, even after adjustment for confounding. We are unable to report what specific factors might have mediated these differences. Established cumulative harms of BSPA, such as antimicrobial resistance and microbiome disruption, are unlikely to be captured by short-term postoperative outcomes. While increased PLOS may reflect antibiotic-related postoperative complications, residual confounding must be also considered. We report an "*E*-value" of 1.85 for the adjusted HR of PLOS, a metric of the magnitude of association necessary from unmeasured confounders to fully explain away this difference. Compared to HRs obtained from the multivariate-adjusted Cox regression, such a degree of unmeasured confounding would be substantial, for example, comparable to the association with major perioperative hemodynamic instability (ie, vasopressor score of 3 vs 0, HR: 1.47; 95% CI: 1.16–1.86), or age (0–30 days compared to age 1–17 years, HR: 2.0; 95% CI: 1.88–2.12). A sensitivity analysis restricted to cases with limited duration perioperative antibiotics offered further reassurance against meaningful bias from a hypothesized confounder: cases wherein BSPA was likely intended as empiric treatment for postoperative instability, rather than prophylaxis.

While not well-established in this study population, evidence linking BSPA with acute morbidity has been described elsewhere. In adult noncardiac clean surgical procedures, receipt of BSPA (primarily vancomycin, due to allergy) is associated with higher risk for SSI compared to NSPA [41]. Vancomycin requires a prolonged infusion time, making it challenging to administer in time for adequate tissue levels at the time of incision. While vancomycin alone may be inferior to NSPA at SSI prevention, vancomycin monotherapy comprised only 10% of BPSA exposure in this study. Antibiotic-related adverse events may also be more common with BSPA. Nephrotoxicity from vancomycin- or aminoglycoside-containing regimens, and *Clostridioides*

Table 2. Impact of Broad- Versus Narrow-Spectrum Perioperative Antibiotics on Time to Hospital Discharge Within 30 Days of CHD Surgery

	Hazard ratio (95% CI) of hospital discharge	*P* value
Primary analysis		
Unadjusted cohort (*n* = 18 088)	0.65 (0.51–0.83)	.001
Propensity score-weighted cohort (*n* = 17 672)	0.79 (0.71–0.89)	<.0001
Sensitivity analyses		
Multivariate-adjusted cohort (*n* = 18 088)	0.82 (0.71–0.95)	.008
Propensity score-matched cohort (*n* = 4478)	0.85 (0.72–1.01)	.06
Limited perioperative antibiotics duration (propensity score weighted, *n* = 13 327)		
Days 1–22	0.83 (0.75–0.91)	<.0001
Days 23–30	1.27 (0.97–1.68)	.085
Subgroup analyses		
Delayed sternal closure (propensity score weighted, *n* = 885)	1.26 (0.91–1.74)	.16
Highest volume centers (propensity score weighted, *n* = 9234)	0.77 (0.64–0.95)	.015
RACHS-1 score: 1 (propensity score weighted, *n* = 2148)	0.73 (0.63–0.84)	<.0001
RACHS-1 score: 2 (propensity score weighted, *n* = 5720)	0.76 (0.65–0.89)	.001
RACHS-1 score: 3 (propensity score weighted, *n* = 6535)	0.79 (0.69–0.92)	.002
RACHS-1 score: 4 (propensity score weighted, *n* = 1476)		
Days 1–15	0.78 (0.55–1.09)	.15
Days 16–30	1.19 (0.89–1.60)	.24
RACHS-1 score: 5/6 (*n* = 514)	Unable to balance	

Abbreviations: CI, confidence interval; HR, hazard ratio; OR, odds ratio; RACHS-1, Risk Adjustment for Congenital Heart Surgery.

95% CI via robust variance.

difficile infection from extended gram-negative coverage are well-described in adult patients [13, 14, 38]. Research from extremely preterm neonates implicates even brief broad-spectrum antibiotic exposure with greater infectious complications and mortality [42]. While these support the plausibility of our study findings, further research is needed.

Mortality and readmissions are intended as balancing metrics to the primary outcome, as they represent complications PLOS may miss. Of note, since mortality and subsequent antimicrobial treatment occurrence are only measured in-hospital, these secondary outcomes are limited by the risk of bias from overrepresentation in cases with longer hospitalizations.

Regarding generalizability, the 24 centers in our cohort represent a subset of the 125 centers in the United States and Canada that perform CHD surgeries, with predominantly smaller- to medium-volume programs [43]. We found variability in BSPA use was narrower in larger volume programs, which may be a marker for more protocolized perioperative and postoperative management. Vizient does not include many of the largest-volume centers, and the practices and outcomes we describe may not translate to all centers performing CHD surgery. However, other studies have also described striking variability in antibiotic prophylaxis practices across large-volume pediatric hospitals, including high rates of vancomycin use in CHD surgery [9, 11]. To account for variability in program size, we included center as a random intercept in propensity score models [25, 26], and report consistent findings in a subgroup analysis restricted to high-volume centers.

Limitations of the study include an observational design relying on administrative claims data. Observational studies are at risk for confounding by indication, while administrative data may be incomplete or inaccurate. Additionally, while PLOS is sensitive to postoperative complications, it is not specific. Patient-level risk factors, surgical outcomes, and institutional practices all impact PLOS, and observed variation in PLOS grows markedly with increasing surgical complexity [2, 34].

To mitigate the influence of these confounding variables, we perform comprehensive adjustment for risk factors for CHD morbidity and mortality identified in the literature [1, 3, 44]. Among these covariates, some have high face validity from claims data (ie, age), or have been validated in other settings, such as medication administration (ie, vasopressor score) [16]. While billing data may perform poorly in identifying specific CHD procedures [45], the methodology we adapted to extract procedure risk via RACHS-1 scores has been validated to accurately predict postoperative mortality [19]. In other instances where covariates are derived from procedure or diagnosis codes (such as the need for ECMO, or the presence of prematurity), the completeness or accuracy of coding could not be ascertained, however, the prevalence of these covariates was comparable to other published CHD cohorts [2, 3, 44, 46].

A few established SSI risk factors, such as the need for prolonged preoperative mechanical ventilation, remain unmeasured in this analysis [1, 3]. Administrative claims data does not capture granular indications for BSPA, and we were

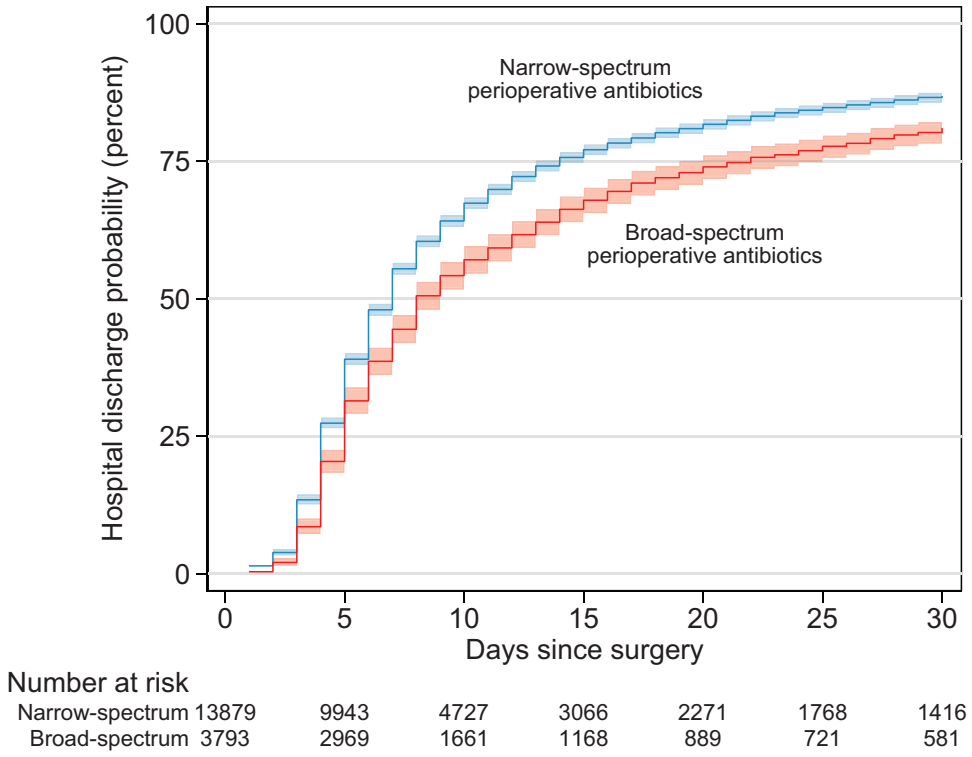

Figure 4. Weighted failure curve for time to hospital discharge. Propensity score-weighted failure curves showing the adjusted cumulative incidence of hospital discharge within a 30-day follow-up period from congenital heart disease surgery, with 95% confidence intervals (CIs) indicated by shading. After adjustment, broad-spectrum perioperative antibiotic exposure is associated with significantly lower rates of hospital discharge during this period (hazard ratio: 0.79; 95% CI: 0.71–0.89, $P < .0001$). The adjusted cumulative incidence of hospital discharge at 30 days was lower in exposed (0.81; 95% CI: 0.79–0.83) versus unexposed cases (0.87; 95% CI: 0.86–0.88). Data from the Vizient Clinical Data Base used with permission of Vizient, Inc. All rights reserved.

also unable to measure and adjust for MRSA colonization or labeled allergies to first-line antibiotics, situations in which practice guidelines recommend the addition of vancomycin. Nonetheless, we did not find evidence suggesting that these indications were major drivers of observed BSPA use. Neonates had the highest rates of BSPA exposure, (26.0%) compared to infants (15.2%) and children (17.7%), while the probability of acquiring an allergy label cumulatively increases with age. Additionally, 68% of BSPA use included extended gram-negative or antipseudomonal coverage, which cannot be attributed to MRSA or allergy indications.

No significant benefit from BSPA was found in any subgroup or sensitivity analysis. Nonetheless, our findings do not exclude the possibility of benefits from BSPA in specific scenarios. Further investigation is warranted for children at higher risk for resistant pathogens, such as those colonized with MRSA, as well as in higher-risk surgical procedures (and cases with DSC). We also did not compare outcomes between different regimens of BSPA, and potential harms and benefits will differ between patients and agents. However, considering the well-established cumulative harm of unnecessary broad-spectrum antibiotic exposure, the burden of proof should be upon broad-spectrum regimens to demonstrate substantial benefit in optimizing postoperative outcomes.

CONCLUSIONS

In an observational study of children undergoing CHD surgery at smaller-volume centers, BSPA was not associated with measurable benefit in any cohort. Wide inter-hospital variability and a potential association with longer PLOS are causes to avoid routine BSPA use for most patients.

Supplementary Data

Supplementary materials are available at the *Journal of The Pediatric Infectious Diseases Society online* (http://jpids.oxfordjournals.org).

Notes

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