Published in final edited form as:
Am J Cardiol. 2011 December 1; 108(11): 1620–1624. doi:10.1016/j.amjcard.2011.07.023.

Relation of Milrinone Following Surgery for Congenital Heart Disease to Significant Postoperative Tachyarrhythmias

Andrew H. Smith, MD[a,b], **Jill Owen, RN, BSN**[b], **Kristie Y. Borgman, MD**[b], **Frank A. Fish, MD**[b], and **Prince J. Kannankeril, MD**[b]
Department of Pediatrics, Monroe Carell Jr. Children's Hospital at Vanderbilt and Vanderbilt University School of Medicine, Nashville, Tennessee, USA

Abstract

Milrinone reduces the risk of low cardiac output syndrome for some pediatric patients following congenital heart surgery. Data from adults undergoing cardiac surgery suggest an association between milrinone and increased risk for postoperative arrhythmias. We tested the hypothesis that milrinone is an independent risk factor for tachyarrhythmias following congenital heart surgery. Subjects undergoing congenital heart surgery at our institution were consecutively enrolled for 38 months, through September 2010. Data was prospectively collected, including review of full-disclosure telemetry and the medical record. Over 38 months, 603 enrolled subjects underwent 724 operative procedures. The median age was 5.5 months (0.0–426), weight was 6.0 kg (0.7–108), and the cohort was 45% female. Overall arrhythmia incidence was 50%, most commonly monomorphic ventricular tachycardia (n=85, 12%), junctional ectopic tachycardia (n=69, 10%), accelerated junctional rhythm (n=58, 8%), and atrial tachyarrhythmias (including atrial fibrillation, atrial flutter, and ectopic or chaotic atrial tachycardia, n=58, 8%). Multivariate logistic regression analysis demonstrated that independent of age less than 1 month, use of cardiopulmonary bypass, duration of cardiopulmonary bypass, RACHS-1 score greater than 3, and the use of epinephrine or dopamine, milrinone use on admission to the cardiac intensive care unit remained independently associated with an increase in the odds of postoperative tachyarrhythmia resulting in an intervention (OR 2.8 [95%CI 1.3–6.0], p=0.007). In conclusion, milrinone use is an independent risk factor for clinically significant tachyarrhythmias in the early postoperative period following congenital heart surgery.

Introduction

Off-label use of the phosphodiesterase inhibitor milrinone is common following congenital heart surgery in children.[1] Prophylactic use of milrinone in some children has been shown to reduce the risk of low cardiac output syndrome following congenital heart surgery.[2] While there exists little reported data in pediatric congenital heart surgery literature to suggest an association between milrinone use and postoperative arrhythmias, data has emerged supporting such an association in adults undergoing elective cardiac surgery.[3] We

Correspondence and Reprints: Andrew H. Smith, MD Monroe Carell Jr. Children's Hospital at Vanderbilt Divisions of Pediatric Critical Care Medicine and Pediatric Cardiology Doctor's Office Tower, Suite 5121 2200 Children's Way Nashville, TN 37232 andrew.h.smith.1@vanderbilt.edu (615) 936 3968 (o) (615) 400 6790 (c).
[a]Division of Pediatric Critical Care Medicine
[b]Thomas P. Graham Jr. Division of Pediatric Cardiology

hypothesized that milrinone was also an independent risk factor for clinically significant tachyarrhythmias following congenital heart surgery.

Methods

Subjects included in this analysis were enrolled in the ongoing prospective, observational Postoperative Arrhythmia in Congenital Heart Surgery (PACS) study. All patients undergoing congenital heart surgery at Monroe Carell Jr. Children's Hospital at Vanderbilt and subsequently admitted to the pediatric cardiac intensive care unit (CICU) from July 2007 through September of 2010 were prospectively approached for enrollment. The Vanderbilt University Institutional Review Board for Research on Human Subjects approved this study. Each patient's parents or legal guardians provided written informed consent, and patient assent was obtained where age-appropriate.

Perioperative data collection included patient demographic characteristics, anatomic diagnoses, prior non-cardiac medical history, preoperative medications, any prior history of arrhythmias, and any family history of arrhythmias. Any history of preoperative arrhythmia was ascertained both through chart review and enrollment history. Operative details noted included the primary procedure as well as any associated secondary procedures, in addition to aortic cross clamp and cardiopulmonary bypass times. Operative procedures were also categorized according to the Risk Adjusted classification for Congenital Heart Surgery, Version 1 (RACHS-1) method.[4] Patients received general endotracheal anesthesia, traditionally consisting of induction with a combination of fentanyl or etomidate and pancuronium, and maintenance with fentanyl, isoflurane, and pancuronium. Vasopressors and inotropes were used with separation from cardiopulmonary bypass at the surgeon and anesthesiologist's discretion. Milrinone therapy specifically was also initiated at the discretion of the anesthesiologist and surgeon. Administration often consisted of a loading dose of 50 μg/kg during the termination of cardiopulmonary bypass, followed by a continuous infusion at rates of 0.25 to 1.0 μg/kg/min. Milrinone was also often utilized for patients who did not receive cardiopulmonary bypass, and again, this practice was instituted at the discretion of the anesthesiologist and surgeon.

Early postoperative data recorded included admission pH, serum lactate, hematocrit, serum electrolytes, as well as continuous infusions administered on admission to the cardiac intensive care unit. Patients underwent continuous monitoring with a full-disclosure telemetry system (Phillips Medical Systems, Bothell WA) for the duration of their hospitalization. Study personnel reviewed telemetry recordings daily at a central station, and all arrhythmias were confirmed and coded by a board certified pediatric cardiologist. Each postoperative arrhythmia was coded with respect to location of onset, type, and any associated therapy. Serum electrolytes were assessed and replaced either parenterally or enterally at the discretion of the provider, traditionally with goals of maintaining potassium 3.5–5.0 mEq/L, ionized Ca 4.5–5.5 mg/dL, and serum magnesium 1.8–2.2 mEq/L. Sedation, analgesia, and neuromuscular blockade were all managed at the discretion of the anesthesia and CICU teams.

This study was designed to include capture all arrhythmias, including those clearly resulting from discrete events such as myocardial ischemia or hypoxia. If a subject underwent more than one operative procedure during an admission, an arrhythmia following the second procedure was classified as an arrhythmia only if the arrhythmia was distinctly different in morphology and character relative to prior arrhythmias. Furthermore, numerous subjects experienced more than one class of arrhythmia following a single operative procedure. These events were also classified as two separate arrhythmias if the arrhythmia was distinctly different in morphology and character relative to prior rhythm disturbances.

Arrhythmias originating in the operating room were captured only if sustained on admission to the CICU. An arrhythmia was considered clinically significant for the purposes of this investigation if it directly led to a provider intervention, including pharmacotherapy, vagal maneuvers, surface cooling, temporary or permanent pacing, pace termination of a reentrant tachycardia, direct current cardioversion or defibrillation, or cardiopulmonary resuscitation. Monomorphic ventricular tachycardia was defined as a uniform, wide-complex rhythm consistent with a ventricular origin, greater than 2 beats in duration (nonsustained) or 30 seconds in duration (sustained). Ventricular tachycardia and junctional ectopic tachycardia were each differentiated from accelerated ventricular and junctional rhythm respectively, by an increase in rate of greater than 10% above the baseline rate, noted prior to the onset of tachycardia.

Normally distributed continuous data are reported as mean ± SD, or median (range) in the case of non-normally distributed variables. Categorical variables are reported as frequencies with percentages. Demographic and clinical data were compared using the Mann-Whitney U test for continuous variables and the X^2 or Fisher's Exact test where appropriate for categorical variables. The odds of tachyarrhythmia were assessed through both univariate and multivariate logistic regression. Variables with a univariate significance threshold (determined *a priori*) of $p<0.1$ were considered for inclusion within the multivariate logistic regression model after assessing for multicollinearity. Patient weight and admission lactate, while significant in univariate analyses, were each excluded from further multivariate analysis due to multicollinearity with patient age ($R^2=0.85$, $p<0.001$) and cardiopulmonary bypass time ($R^2=0.24$, $p<0.001$), respectively. RACHS-1 category also demonstrated weak multicollinearity with cardiopulmonary bypass time ($r^2=0.12$, $p<0.001$), but remained within multivariate analysis as a recognized index of surgical complexity. The number of covariates included within the model was limited to 1 covariate for every 10 events.[5] All multivariate models underwent assessment of fit with the Hosmer and Lemeshow goodness-of-fit test. Data from logistic regression analyses are reported as the estimated odds ratios (ORs) and 95% confidence intervals (CIs). Data were analyzed with SPSS (v.18, SPSS Inc, Chicago, Ill). The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

From July of 2007 through September of 2010, there were 603 subjects enrolled in the study, undergoing a total of 724 operative procedures. Baseline demographic data is summarized in Table 1. Nearly one-fourth of all operative procedures were undertaken in children less than 30 days of age, and over one-third had at least one documented arrhythmia preoperatively. As demonstrated in the operative characteristics detailed in Table 2, there was a broad distribution of operative procedures represented in this cohort. Of the 724 operative procedures, 116 (16%) were performed without cardiopulmonary bypass.

The incidence of at least one documented arrhythmia occurring following an operative procedure was 50% (n=365), and of these, 65% (n=237) were deemed clinically significant to warrant at least one type of therapeutic intervention. Specific arrhythmias noted in the early postoperative period are detailed in Table 3. While monomorphic ventricular tachycardia was the most commonly reported arrhythmia, junctional and atrial tachycardias more frequently prompted therapeutic intervention. Among all recorded tachyarrhythmias (n=392), 53% (n=208) prompted at least one intervention. This included surface cooling in 28% (n=111), atrial overdrive pacing in 21% (n=82), amiodarone administration in 18% (consisting of either a loading dose or continuous infusion, n=70), pace termination in 7% (n=27), adenosine administration in 6% (n=25), and synchronized cardioversion in 3% (n=10).

On admission to the cardiac ICU, milrinone, dopamine, and epinephrine were the most commonly administered continuous infusions, with milrinone administered in over 70% of the operative procedures in this cohort. Milrinone was used in combination with other inotropes including dopamine (n=182, 25%) and epinephrine (n=83, 12%) most commonly. Vasoconstrictor agents vasopressin (n=16, 2%) and norepinephrine (n=4, 0.5%) were also accounted for, however rarely used in our cohort.

Univariate analysis was performed using the incidence of postoperative tachyarrhythmia as a dichotomous endpoint, with results demonstrated in Table 4. There were 267 operative procedures resulting in at least one instance of a documented tachyarrhythmia, and 392 total events classified as distinct tachyarrhythmias. Of all tachyarrhythmias recorded among the 724 operative cases, 8% (n=30) were classified as first noted in the operating room, 81% (n=318) in the CICU, and 11% (n=44) following floor transfer. The majority of these tachyarrhythmias occurred on postoperative day #0 (n=278, 71%), with an additional 12% (n=48) occurring by the conclusion of postoperative day #1.

There was a significant increase in the odds of experiencing a postoperative tachyarrhythmia with respect to age less than 1 month ($p<0.001$), male gender ($p=0.03$), use of cardiopulmonary bypass ($p<0.001$), longer cardiopulmonary bypass time ($p<0.001$), and greater CICU admission lactate ($p<0.001$). On admission to the CICU, administration of dopamine ($p=0.006$), epinephrine ($p<0.001$), and milrinone ($p<0.001$) were all associated with an increase in odds of postoperative tachyarrhythmia.

Given that many tachyarrhythmias did not result in a therapeutic intervention (41%), univariate analysis was then performed assessing incidence of at least one postoperative tachyarrhythmia felt to be clinically significant and prompting intervention prior to CICU discharge (n=148). As demonstrated in Table 5, factors including subject age less than one month ($p<0.001$), patient weight ($p=0.04$), use of cardiopulmonary bypass ($p<0.001$), longer cardiopulmonary bypass time ($p<0.001$), greater admission lactate ($p<0.001$) were all associated with a significant increase in odds of postoperative tachyarrhythmia prompting intervention. RACHS-1 scores were significantly higher among those with a postoperative tachyarrhythmia; the frequency of RACHS-1 scores of greater than 3 was significantly higher among those procedures resulting in at least one tachyarrhythmia requiring therapy (OR 3.1 [95%CI 1.9–5.0], $p<0.001$). The administration of dopamine (OR 1.7 [95% CI 1.2–2.4], $p=0.009$), epinephrine (OR 2.7 [95% CI 1.7–4.3], $p<0.001$), and milrinone (OR 7.1 [95% CI 3.7–13.9], $p<0.001$) were all associated with an increase in odds of postoperative tachyarrhythmia prompting intervention.

Analysis was performed to assess for the presence of independent risk factors for development of clinically significant postoperative tachyarrhythmias resulting in an intervention. As demonstrated in Table 6, multivariate logistic regression analysis demonstrates that subject age less than one month ($p<0.001$), use of cardiopulmonary bypass ($p=0.02$), longer cardiopulmonary bypass time ($p=0.003$), and milrinone infusion on admission to the CICU (OR 2.8 [95% CI 1.3–6.0], $p=0.007$) were all independent risk factors for the development of a tachyarrhythmia prompting intervention.

Discussion

We assessed risk factors for the incidence of clinically relevant postoperative tachyarrhythmias in a single-center, prospectively assembled cohort of patients undergoing congenital heart surgery. We have demonstrated that while univariate analyses confirm the association of previously-described risk factors such as younger patient age, cardiopulmonary bypass time, and the administration of adrenergic agents, multivariate

logistic regression analysis demonstrates that the phosphodiesterase inhibitor milrinone is independently associated with a nearly three-fold increase in the odds of a postoperative tachyarrhythmia prompting intervention.

The PRIMACORP (PRophylactic Intravenous use of Milrinone After Cardiac OpeRation in Pediatrics) trial was one of the first randomized, double-blinded, placebo-controlled trials related to care of children with congenital heart disease. After demonstrating a significant, dose-dependent reduction in the incidence of low cardiac output syndrome in a select population of children undergoing congenital heart surgery, the use of milrinone at many institutions has become routine, particularly following cardiopulmonary bypass.[1,2] Similar to low cardiac output syndrome, the postoperative arrhythmia is also associated with increases in both early postoperative morbidity and mortality following congenital heart surgery.[6] In a preliminary analysis of our cohort alone, the incidence of a postoperative arrhythmia has been shown to significantly and independently increase ICU length of stay (HR 2.0 [95% CI 1.3–3.0], p=0.001).

The PRIMACORP study reported only a single instance of ventricular and supraventricular tachycardia among those randomized to receive milrinone (n=239), an incidence of 0.8%, which is appreciably less frequent than our overall incidence of tachyarrhythmia (37%) and those reported elsewhere.[7–9] The PRIMACORP study cohort differed from ours in several important ways, including an older subject age and the exclusion of single ventricle repairs, which may in part explain the lower arrhythmia incidence. Indeed, while differences in study criteria and detection methods may have led to a relative increase in apparent incidence in our cohort, there is emerging literature to support a causative role of milrinone in the arrhythmia, both in the setting of chronic heart failure and in the perioperative period.[3,10,11]

Milrinone inhibits phosphodiesterase III (PDEIII) and attenuates the degradation of cyclic AMP (cAMP), resulting in increased intracellular calcium currents and improvements in myocardial performance independent of β-adrenoreceptor stimulation.[12] Both β-adrenoreceptor-mediated increases in cAMP production, as well as phosphodiesterase-mediated cAMP degradation, result in alterations in intracellular calcium homeostasis through protein kinase A (PKA) and calmodulin-dependent protein kinase II (CaMKII) phosphorylation of regions including L-type Ca^{2+} channel subunits ($I_{Ca,L}$) and ryanodine receptor (RyR2) sites.[13–15] Disruptions in cAMP-dependent phosphorylation and resultant intracellular calcium handling derangements have already been described in association with tachyarrhythmias in both murine models and humans alike.[16,17] Furthermore, one may also postulate that β-adrenergic stimulation, through such commonly utilized agents as epinephrine and dopamine, may play an additive or even synergistic role in the evolution of postoperative tachyarrhythmias in the setting of phosphodiesterase inhibition with agents such as milrinone.

There were several limitations to this study. First, and perhaps most challenging, is that milrinone use among our patient population has traditionally served as the rule and not the exception. As such, this makes a controlled comparison of milrinone use and any association with tachyarrhythmias among patients following specific operative procedures particularly difficult. Second, our dataset was not designed to demonstrate any potential dose-dependent effect of milrinone on postoperative tachyarrhythmias. While dosing was routinely within a traditional range, doses were not recorded and varied among practitioners. As a result of this variability in dosing and titration practices among providers, the decision was made *a priori* to utilize milrinone on admission to the CICU as our exposure variable of interest. While most postoperative tachyarrhythmias did indeed occur within the first postoperative 48 hours, it is important to note that not all patients were receiving milrinone at the onset of

their respective tachyarrhythmia. Third, as is the case with many CICUs, there exists some degree of variation among practitioners with respect to both diagnosis and treatment of postoperative arrhythmias, as well as occasional differences in opinion regarding the definition of a “clinically significant” arrhythmia. However, the authors contend that despite these differences in thresholds for therapy, the endpoint of a therapeutic intervention provides a relevant, albeit imperfect, outcome of clinical significance. Finally, the association described here between milrinone exposure following congenital heart surgery and postoperative tachyarrhythmias does not necessarily establish a causal relationship; further prospective, randomized, controlled investigation is warranted to confirm an independent contributory association between an agent commonly used following congenital heart surgery and this clinically relevant postoperative morbidity.

Acknowledgments

Financial Support:

1. NIH HL076265 and 5T32HD 44328
2. National Center for Research Resources/NIH 1 UL1 RR024975
3. Turner-Hazinski Research Fund

References

1. Pasquali SK, Hall M, Slonim AD, Jenkins KJ, Marino BS, Cohen MS, Shah SS. Off-label use of cardiovascular medications in children hospitalized with congenital and acquired heart disease. Circ Cardiovasc Qual Outcomes. 2008; 1(2):74–83. [PubMed: 20031793]
2. Hoffman TM, Wernovsky G, Atz AM, Kulik TJ, Nelson DP, Chang AC, Bailey JM, Akbary A, Kocsis JF, Kaczmarek R, Spray TL, Wessel DL. Efficacy and safety of milrinone in preventing low cardiac output syndrome in infants and children after corrective surgery for congenital heart disease. Circulation. 2003; 107(7):996–1002. [PubMed: 12600913]
3. Fleming GA, Murray KT, Yu C, Byrne JG, Greelish JP, Petracek MR, Hoff SJ, Ball SK, Brown NJ, Pretorius M. Milrinone use is associated with postoperative atrial fibrillation after cardiac surgery. Circulation. 2008; 118(16):1619–1625. [PubMed: 18824641]
4. Jenkins K, Gauvreau K, Newburger J, Spray T, Moller J, Iezzoni L. Consensus-based method for risk adjustment for surgery for congenital heart disease. J Thorac Cardiovasc Sur. 2002; 123(1): 110–118.
5. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol. 1996; 49(12):1373–1379. [PubMed: 8970487]
6. Pfammatter JP, Wagner B, Berdat P, Bachmann DC, Pavlovic M, Pfenninger J, Carrel T. Procedural factors associated with early postoperative arrhythmias after repair of congenital heart defects. J Thorac Cardiovasc Surg. 2002; 123(2):258–262. [PubMed: 11828284]
7. Delaney JW, Moltedo JM, Dziura JD, Kopf GS, Snyder CS. Early postoperative arrhythmias after pediatric cardiac surgery. J Thorac Cardiovasc Surg. 2006; 131(6):1296–1300. [PubMed: 16733160]
8. Hoffman TM, Wernovsky G, Wieand TS, Cohen MI, Jennings AC, Vetter VL, Godinez RI, Gaynor JW, Spray TL, Rhodes LA. The incidence of arrhythmias in a pediatric cardiac intensive care unit. Pediatr Cardiol. 2002; 23(6):598–604. [PubMed: 12530491]
9. Valsangiacomo E, Schmid ER, Schupbach RW, Schmidlin D, Molinari L, Waldvogel K, Bauersfeld U. Early postoperative arrhythmias after cardiac operation in children. Ann Thorac Surg. 2002; 74(3):792–796. [PubMed: 12238841]
10. Feneck RO, Sherry KM, Withington PS, Oduro-Dominah A, Group EMMT. Comparison of the hemodynamic effects of milrinone with dobutamine in patients after cardiac surgery. J Cardiothorac Vasc Anesth. 2001; 15(3):306–315. [PubMed: 11426360]

11. Cuffe MS, Califf RM, Adams KF, Benza R, Bourge R, Colucci WS, Massie BM, O'Connor CM, Pina I, Quigg R, Silver MA, Gheorghiade M. Short-term intravenous milrinone for acute exacerbation of chronic heart failure: a randomized controlled trial. JAMA. 2002; 287(12):1541–1547. [PubMed: 11911756]
12. Alousi AA, Johnson DC. Pharmacology of the bipyridines: amrinone and milrinone. Circulation. 1986; 73(3 Pt 2):III10–24. [PubMed: 2417744]
13. Zaugg M, Schaub MC. Cellular mechanisms in sympatho-modulation of the heart. Br J Anaesth. 2004; 93(1):34–52. [PubMed: 15145820]
14. Bers DM. Cardiac excitation-contraction coupling. Nature. 2002; 415(6868):198–205. [PubMed: 11805843]
15. Wehrens XH, Lehnart SE, Reiken SR, Marks AR. Ca2+/calmodulin-dependent protein kinase II phosphorylation regulates the cardiac ryanodine receptor. Circ Res. 2004; 94(6):e61–70. [PubMed: 15016728]
16. Chelu MG, Sarma S, Sood S, Wang S, van Oort RJ, Skapura DG, Li N, Santonastasi M, Müller FU, Schmitz W, Schotten U, Anderson ME, Valderrábano M, Dobrev D, Wehrens XH. Calmodulin kinase II-mediated sarcoplasmic reticulum Ca2+ leak promotes atrial fibrillation in mice. J Clin Invest. 2009; 119(7):1940–1951. [PubMed: 19603549]
17. El-Armouche A, Boknik P, Eschenhagen T, Carrier L, Knaut M, Ravens U, Dobrev D. Molecular determinants of altered Ca2+ handling in human chronic atrial fibrillation. Circulation. 2006; 114(7):670–680. [PubMed: 16894034]

Table 1

Baseline preoperative characteristics (n=724)

Age (months)	5.5 (0.0–426.2)
Age less than 1 month	175 (24%)
Weight (kg)	6.0 (0.7–108.3)
Female	327 (45%)
Primary lesion*	
Hypoplastic left heart syndrome	90 (12%)
Atrioventricular canal defect	84 (12%)
Tetralogy of Fallot	69 (9.5%)
Ventricular septal defect	65 (9.0%)
Coarctation of the aorta	48 (6.6%)
Secundum atrial septal defect	43 (5.9%)
Double outlet right ventricle	40 (5.5%)
Preoperative arrhythmia (% Yes)	268 (37%)

* Incidence within cohort of > 5%

Table 2

Baseline operative characteristics (n=724)

Primary procedure*	
Ventricular septal defect closure	64 (9%)
Tetralogy of Fallot	53 (7%)
Bidirectional Glenn	51 (7%)
Coarctectomy	47 (7%)
Fontan	43 (6%)
Stage 1 (Norwood) palliation	43 (6%)
Systemic to pulmonary artery shunt	41 (6%)
Atrioventricular canal repair	40 (6%)
Secundum atrial septal defect closure	29 (4%)
Arterial switch	26 (4%)
Primum atrial septal defect closure	25 (4%)
Truncus arteriosus repair	8 (1%)
Total anomalous pulmonary venous return repair	7 (1%)
Risk Adjusted classification for Congenital Heart Surgery (RACHS-1) classification	
1	66 (9%)
2	287 (39%)
3	242 (33%)
4	33 (5%)
6	48 (7%)
Unable to classify	48 (7%)
Cardiopulmonary bypass time (min)	102 (0–731)
Cross clamp (min)	36 (0–217)

*Includes all primary operative procedure frequencies ≥ 5%.

Table 3

Early postoperative arrhythmias. (n=724)

	Overall	Treated
Arrhythmia incidence	365 (50%)	239 (66%)
Tachyarrhythmia incidence	267 (37%)	158 (59%)
Tachyarrhythmia		
Monomorphic ventricular tachycardia	85 (12%)	23 (27%)
Junctional ectopic tachycardia	69 (10%)	61 (88%)
Accelerated junctional rhythm	58 (8%)	32 (55%)
Atrial tachyarrhythmia	58 (8%)	33 (57%)
Accelerated ventricular rhythm	41 (6%)	8 (20%)

Table 4

Univariate analysis of overall tachyarrhythmia incidence.

Variable	No (n=457)	Yes (n=267)	OR (95%CI)	*P*
Age (months)	5.9(0.0–275)	4.6(0–276)	1.0 (0.99–1.001)	0.33
Age less than 1 month	89 (19%)	86 (32%)	2.0 (1.4–2.8)	<0.001
Weight (kg)	6.3 (0.7–108)	5.4(1.6–97)	1.0 (0.98–1.006)	0.52
Male	236 (52%)	161 (60%)	1.4 (1.1–1.9)	0.03
History of preoperative arrhythmia	166 (36%)	102 (38%)	1.1 (0.8–1.5)	0.61
Use of cardiopulmonary bypass	359 (79%)	259 (97%)	10.0 (4.8–20.8)	<0.001
Cardiopulmonary bypass time (min)	88(0–499)	130(0–731)	1.011(1.008–1.013)	<0.001
RACHS-1 classification over 3	35 (8%)	44 (17%)	2.5 (1.5–3.9)	<0.001
On cardiac intensive care unit admission				
Initial pH	7.35±0.1	7.34±0.1	0.27 (0.05–1.4)	0.13
Initial lactate (mmol/L)	2.6±2.5	4.1±3.0	1.2 (1.1–1.3)	<0.001
Dopamine	122 (27%)	99 (37%)	1.6 (1.2–2.2)	0.006
Epinephrine	36 (8%)	55 (21%)	3.0 (1.9–4.7)	<0.001
Milrinone	**280 (62%)**	**235 (88%)**	**4.5 (3.0–6.9)**	**<0.001**

Table 5

Univariate analysis of tachyarrhythmia incidence requiring intervention prior to cardiac intensive care unit discharge.

Variable	No (n=576)	Yes (n=148)	OR (95%CI)	*P*
Age (months)	5.7(0.0–425)	3.6(0.0–276)	0.996 (0.992–1.00)	0.04
Age less than 1 month	122 (21%)	53 (36%)	2.1 (1.4–3.1)	<0.001
Weight (kg)	6.4 (0.7–108)	4.6 (1.6–90)	0.99 (0.97–1.00)	0.04
Male	305 (54%)	92 (57%)	1.1 (0.8–1.6)	0.52
History of preoperative arrhythmia	210 (36%)	58 (39%)	1.1 (0.8–1.6)	0.57
Use of cardiopulmonary bypass	463 (80%)	145 (98%)	11.7 (3.7–37.0)	<0.001
Cardiopulmonary bypass time (min)	92 (0–499)	138 (0–422)	1.009 (1.007–1.012)	<0.001
RACHS-1 classification over 3	48 (9%)	31 (22%)	3.1 (1.9–5.0)	<0.001
On cardiac intensive care unit admission				
Initial pH	7.35±0.09	7.34±0.1	0.28 (0.04–2.0)	0.20
Initial lactate (mmol/L)	1.9±2.6	3.5±3.2	1.2 (1.1–1.3)	<0.001
Dopamine	162 (28%)	62 (40%)	1.7 (1.2–2.4)	0.009
Epinephrine	57 (10%)	34 (23%)	2.7 (1.7–4.3)	<0.001
Milrinone	**377 (65%)**	**138 (93%)**	**7.1 (3.7–13.9)**	**<0.001**

Table 6

Multivariate analysis of tachyarrhythmia incidence requiring intervention prior to cardiac intensive care unit discharge.

Variable	OR (95%CI)	*P*
Age less than 1 month	2.9 (1.7–5.1)	<0.001
Use of cardiopulmonary bypass	11.9 (1.5–100)	0.02
Cardiopulmonary bypass time	1.005 (1.002–1.009)	0.003
RACHS-1 over 3	0.9 (0.4–1.7)	0.65
On cardiac intensive care unit admission		
Dopamine	1.1 (0.7–1.7)	0.74
Epinephrine	1.0 (0.6–1.9)	0.94
Milrinone	**2.8 (1.3–6.0)**	**0.007**