# The Effect of Noncardiac and Genetic Abnormalities on Outcomes Following Neonatal Congenital Heart Surgery

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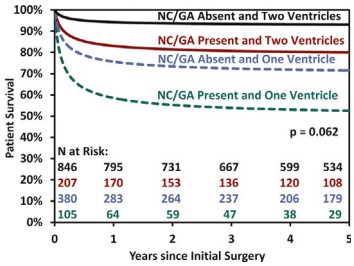
Significant noncardiac and genetic abnormalities (NC and GA) are common in neonates with congenital heart defects. We sought to examine current-era effect of those abnormalities on early and late outcomes following cardiac surgery. The method from 2002-2012, 1538 neonates underwent repair ($n = 860$, 56%) or palliation ($n = 678$, 44%) of congenital heart defects. Regression models examined the effect of NC and GA on operative results, resource utilization, and late outcomes. Neonates with NC and GA ($n = 312$, 20%) had higher incidence of prematurity (21% vs 13%; $P < 0.001$) and weight $\leq$2.5 kg (24% vs 12%; $P < 0.001$) than neonates without NC and GA ($n = 1226$, 80%). Although the incidence of single ventricle was comparable (34% vs 31%; $P = 0.37$), neonates with NC and GA underwent more palliation (52% vs 42%; $P = 0.001$) and subsequently had higher percentage of STAT mortality categories (Society of Thoracic Surgeons (STS) and the European Association for Cardio-thoracic Surgery (EACTS) Congenital Heart Surgery Mortality Categories) 4 and 5 procedures (78% vs 66%; $P < 0.001$). Adjusted logistic regression models that included disparate patient and operative variables showed that the presence of NC and GA was associated with increased unplanned reoperation (odds ratio = 1.7; 95% CI: 1.1-2.7; $P = 0.03$) and hospital mortality (odds ratio = 2.2; 95% CI: 1.3-3.6; $P = 0.002$). Adjusted linear regression models showed significant association between NC and GA and increased postoperative mechanical ventilation duration, intensive care unit, and hospital stays ($P < 0.001$ each). Adjusted hazard analysis showed that the presence of NC and GA was associated with diminished late survival (hazard ratio = 2.4; 95% CI: 1.9-3.1; $P < 0.001$) and that was evident in all subgroups of patients ($P < 0.001$ each). Conclusion is neonates with NC and GA commonly have associated risk factors for morbidity and mortality such as prematurity and low weight. After adjusting for those factors, the presence of NC and GA continues to have significant association with increased unplanned reoperation, hospital mortality, and resource utilization after palliative and corrective cardiac surgery. Importantly, the hazard of death in those patients continues beyond the perioperative period for at least 1 year. Our findings show that the presence of NC and GA should be emphasized during parent counseling and decision making; and underscore the need to explore strategies to improve outcomes for this high-risk population that must address perioperative care, outpatient surveillance, and management.




Parametric hazard model for survival following surgery showing the interaction between NC and GA (present vs absent) and underlying cardiac anomaly (single ventricle vs 2 ventricles).

**Central Message**

Noncardiac and genetic anomalies in neonates with congenital heart disease are associated with worse early and late outcomes.

**Perspective**

The presence of NC and GA is an independent risk factor that is associated with increased unplanned reoperation, hospital mortality, and resource utilization after palliative and corrective cardiac surgery. Importantly, the hazard of death in those neonates continues beyond the perioperative period for at least 1 year. Those inferior outcomes in neonates with NC and GA are present in all subgroups of patients.

See Editorial Commentary pages 118–119.

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## INTRODUCTION

The incidence of congenital heart disease is estimated to be between 4 and 10 of every 1000 live birth. Many of those children require neonatal cardiac surgery to palliate or repair their congenital heart disease. The incidence of associated major noncardiac and genetic abnormalities (NC and GA) in neonates with congenital heart disease is reported to be approximately 20%-30%.[1-5] Neonates with NC and GA might have associated risk factors such as prematurity, low birth weight, and poor clinical condition secondary to the additional noncardiac malformations. Subsequently, the presence of associated NC and GA might affect timing of surgical intervention and procedure choice, and might complicate perioperative care and home management following neonatal cardiac surgery.

Although the presence of NC and GA have been linked to worse outcomes following surgery for several cardiac malformations such as single ventricle and conotruncal anomalies; limited information is available on the effect of NC and GA on hospital recovery and late survival following neonatal cardiac surgery.[6-12]

We aim in the current series to examine the prevalence of NC and GA in neonates undergoing cardiac surgery at our institution, to report associated risk factors in those patients, and to examine the effect of those anomalies on hospital outcomes, resource utilization, and late survival.

## PATIENTS AND METHODS

### Inclusion Criteria

From 2002-2012, 1538 neonates underwent congenital cardiac surgery at Children's Healthcare of Atlanta, Emory University. Our patient cohort included all neonates who had palliative and corrective congenital cardiac surgeries with the exception of primary ligation of a patent ductus arteriosus and primary pacemaker implantation for congenital heart block. Patients were identified using our institutional surgical database. Demographic, anatomic, clinical, operative, and hospital details were abstracted from medical records for analysis. Approval of this study was obtained from our hospital's Institutional Review Board and requirement for individual consent was waived for this observational study.

### Screening for NC and GA

At our institution, neonates, who are admitted to the cardiac intensive care unit, undergo chromosomal analysis if they have cardiac defects that are commonly associated with genetic anomalies (eg, conotruncal lesions and complete atrioventricular septal defect), if they have extracardiac malformations (eg, imperforate anus and tracheaesophageal fistula), or if they have any dysmorphic features. During the course of this current study, the type of chromosomal analysis has changed. Whereas in the earlier phase, those neonates underwent standard metaphase karyotype chromosomal analysis (450-550 bands), high-resolution banding (600-850 bands), and fluorescent in situ hybridization studies; in the later phase starting in 2010, chromosomal microarray testing became the standard study for chromosomal analysis in our unit.

### Follow-Up

Time-related outcomes were determined from recent office visits documented in Children's Healthcare of Atlanta electronic chart system or from direct correspondence with other pediatric cardiologists outside the system. Follow-up was 90% complete. Median follow-up duration for all patients was 5.6 years (interquartile range [IQR]: 2.5-8.9); concomitantly, those classified as NC and GA had a median follow-up time of 4.1 years (IQR: 1.0-8.1), and those without NC and GA had a median duration of 6.0 years (IQR: 2.8-9.0) ($P < 0.001$).

### Statistical Analysis

Statistical significance was evaluated at the 0.05 level, and data analyses were performed using SAS v9.3 (Cary, NC) and R Project (Vienna, Austria). Patient demographic and clinical characteristics were evaluated overall and by presence of a NC and GA using means and standard deviations for continuous variables and frequencies and percents in discrete cases. In circumstances of nonnormality, means, and standard deviations were replaced with medians and IQR. Differences between the study groups (NC and GA present vs absent) were assessed using *t*-tests for continuous variables and Chi-square tests of independence in discrete cases. In situations of nonnormality, the *t*-test was replaced by a nonparametric equivalent (Mann-Whitney *U* or Kolmogorov-Smirnov test); likewise, an exact form of the Pearson's Chi-square test was implemented when expected frequency counts were low ($<5$). Continuous outcomes of interest included durations of ventilation, intensive care unit, and postoperative hospital stay; concurrently, hospital death, need for extracorporeal membrane oxygenation (ECMO) support, and unplanned reoperation were evaluated as bivariates. General linear regression and binary logistic regression were