



ORIGINAL ARTICLE

# Risk Factors for Intracardiac Thrombosis in the Right Atrium and Superior Vena Cava in Critically Ill Neonates who Required the Installation of a Central Venous Catheter



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## Key Words

coagulation;  
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risk factors

**Background:** Central venous catheter (CVC) installation is essential for the treatment of critically ill neonates; however, it is associated with the development of neonatal intracardiac thrombosis, which is a complication that is associated with a poor prognosis. We aimed to identify specific risk factors for the development of intracardiac thrombosis in the right atrium (RA) and superior vena cava (SVC) related to the use of CVC in critically ill neonates.

**Methods:** A case–control study was conducted at the tertiary referral neonatal intensive care unit of the Pediatric Hospital Siglo XXI in Mexico City, Mexico from 2008 to 2013. The included cases ( $n = 43$ ) were *de novo* patients with intracardiac thrombosis in the RA and SVC diagnosed by echocardiography. The controls ( $n = 43$ ) were neonates without intracardiac thrombosis or thrombosis at other sites. A logistic regression analysis was conducted, and odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated.

**Results:** The independent risk factors for intracardiac thrombosis in the RA and SVC were the surgical cut-down insertion technique (OR = 2.98; 95% CI: 1.18–9.10), a maternal history of gestational diabetes/diabetes mellitus (OR = 10.64; 95% CI: 1.13–121.41), *Staphylococcus*

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*epidermidis* infection (OR = 7.09; 95% CI: 1.09–45.92), and CVC placement in the SVC (OR = 5.77; 95% CI: 1.10–30.18).

**Conclusion:** This study allowed us to identify several contributing factors to the development of intracardiac thrombosis in the RA and SVC related to the installation of a CVC in a subgroup of critically ill neonates. Multicenter and well-designed studies with a larger number of patients could help validate our findings and/or identify other risk factors that were not identified in the present study.

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## 1. Introduction

The neonatal hemostatic system is well-balanced despite its differences from the hemostatic systems of older children and adults. However, it is not as well-balanced in critically ill neonates, a subpopulation of neonates with an increased risk of thrombosis due to certain conditions such as prematurity, asphyxia, sepsis, dehydration, congenital heart diseases, and other conditions.<sup>1–4</sup> In particular, intracardiac thrombosis in the right atrium (RA) and superior vena cava (SVC) has been associated with a high endocarditis risk, sepsis persistence, pulmonary artery obstruction, ventricular dysfunction, acute hemodynamic compromise, and death.<sup>5–7</sup> The use of a central venous catheter (CVC) is an important risk factor for the development of thrombosis at these sites, possibly due to direct damage to the endocardium or endothelium caused by the CVC.<sup>7,8</sup> Neonatologists caring for critically ill neonates with thrombosis at these sites are faced with two major challenges. Firstly, it is difficult to suspect the presence of thrombosis in the RA and SVC because the signs include new onset murmur, persistent sepsis, persistent thrombocytopenia, and cardiac failure, which are all nonspecific.<sup>8</sup> Secondly, the installation of a CVC is mandatory in these patients in order to secure vascular access for the administration of specific medications, transfusions, and total parenteral nutrition, which are important for the treatment of these patients.<sup>5</sup>

To the best of our knowledge, specific risk factors for CVC-related intracardiac thrombosis in the RA and SVC in critically ill neonates have not been reported to date, and most information on this topic has been obtained from case report studies.<sup>6,7,9–11</sup>

## 2. Methods

A case–control study was conducted between January 1, 2008 and December 31, 2013 using information from a database at the Mexican Institute of Social Security that contains all diagnoses of patients cared for at the Neonatal Intensive Care Unit (NICU), Pediatric Hospital “Dr. Silvestre Frenk Freund” of the Medical Unit of High Specialty, Siglo XXI National Medical Center, Mexico City, Mexico to identify patients diagnosed with intracardiac thrombosis during the study period. The cases ( $n = 43$ ) were patients who developed intracardiac thrombosis in the RA and/or SVC after CVC placement. For the control group, we randomly selected 43

neonates from the NICU database who required the installation of a CVC during their stay, who had undergone at least one echocardiogram a week from the date of CVC installation to hospital discharge, and who lacked evidence of intracardiac thrombosis. Echocardiography was performed by the pediatric cardiologist assigned to the NICU.

### 2.1. Data collection

Information on study variables and clinical data were retrospectively collected from the clinical charts and included the following: (1) sex; (2) corrected gestational age (weeks of gestation); (3) birth weight (g); (4) reason for admission to the NICU; (5) maternal history [pre-eclampsia, diabetes (gestational or mellitus), placenta previa, threatened abortion, preterm labor, and oligohydramnios]; (5) perinatal history (prematurity, low birth weight, and perinatal asphyxia); (6) CVC-related factors (catheter type, catheter material, catheter size, lumen number, insertion site, catheter tip location, placement method, and CVC placement duration in days); (7) variables related to total parenteral nutrition (TPN) (number of days and osmolality); (8) documented infection by blood culture; (9) the presence and type of congenital heart disease; (10) cardiac surgery (yes/no); (11) thrombocytopenia ( $< 150,000/\text{mm}^3$ ); (12) the location and size of the intracardiac thrombosis; and (13) transfusions through the CVC (yes/no). For the cases, patients were considered positive for a risk factor only if it was documented prior to the diagnosis of intracardiac thrombosis in the RA or SVC.

### 2.2. Statistical analysis

Dichotomous and categorical variables were compared between the cases and controls using the Chi-square test and/or Fisher’s exact test, as appropriate. Continuous variables were compared between groups using Student *t* test. The variables in the bivariate analysis that were clinically and statistically significant ( $p < 0.1$ ) were introduced into the final unconditional logistic regression model. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated.

## 3. Results

The annual incidence of intracardiac thrombosis in the RA and/or SVC in the NICU of the Pediatric Hospital “Dr.

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