Umbilical catheter placement and pericardial effusion in neonates: The US national database

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Abstract

We aimed to assess the association of umbilical catheters placement with pericardial effusion (PCE) in newborn infants after controlling for confounding variables. We analyzed three subpopulations: infants with birth weight (BW) > 2500g, infants with BW < 1500g, and infants with congenital heart diseases (CHD). We utilized the US-National Inpatient Sample dataset (1997–2012). First analysis included a 22,822,931 infants with BW > 2500g with no hydrops fetalis. Of them, 2583 neonates (0.01%) had PCE. PCE was found in 0.33% of infants with UAC only, 0.22% of infants with UVC only and 0.37% of infants with both catheters (aOR = 2.7, CI:2.4–3.2, $p < 0.001$), aOR = 2.8, CI: 2.3–3.5, $p < 0.001$), and aOR = 2.8, CI: 2.4–3.2, $p < 0.001$), respectively. The second analysis included a 200,288 infants with CHD and BW > 2500g. Of them, 1130 (0.56%) had PCE. PCE was found in 1.46% of infants with UAC, 0.78% of infants with UVC and 0.98% of infants with both catheters (aOR = 2.1, CI:1.8–2.6, $p < 0.001$), aOR = 1.4, CI:1.1–1.9, $p = 0.036$) and a OR = 1.6, CI:1.3–1.9, $p < 0.001$), respectively. While, a total of 1,187,727 infants with BW < 1500g were included in the third analysis. Of them, 1667 (0.14%) had PCE. PCE was found in 0.15% of infants with UAC, 0.19% of infants with UVC and 0.26% of infants with both catheters. (aOR = 1.1, CI: 0.9–1.3, $p < 0.90$), aOR = 1.4, CI: 1.2–1.7, $p < 0.001$) and aOR = 1.6, CI:1.4–1.8, $p < 0.001$), respectively. *Conclusion*: Central umbilical catheters are associated with increased risk for pericardial effusion and they may be independently associated with the occurrence of pericardial effusion in infants with congenital heart disease.

Introduction

Umbilical artery catheters (UAC) and umbilical venous catheters (UVC) have been used in very low birth weight (VLBW) infants and sick neonates to provide secured central access for fluid and nutrition support, blood sampling and blood pressure monitoring [1]. Both umbilical vascular catheters are routinely placed as an initial step in the management of critically ill infants with congenital heart disease [2]. Although, Umbilical catheters placement have been a routine practice in neonatal intensive care units for several decades, their placement was associated with several complications including arterial or venous thrombosis, vascular injury or perforation and organ injury [3, 4].

Pericardial effusion (PCE) is an uncommon disease in neonatal period [5]. It presents as an isolated finding or as apart of systemic anasarca or hydrops fetalis in newborn [6]. Several case reports associated iatrogenic pericardial effusion in neonates with insertion of central venous or arterial catheters [7–9]. Other causes of PE include thyroid dysfunction, cardiac and pericardial tumors, multiple congenital anomalies, congenital or acquired viral infections, postoperative and idiopathic [10, 11]. Pericardial effusion may occur in infants with trisomy 21 suffering from transient myeloproliferative disorder [12].

Pericardial effusion is a life-threatening condition if associated with cardiac tamponade which causes neonatal hemodynamic instability, low cardiac output, severe hypotension and increased mortality [13]. Sudden cardiovascular collapse such as bradycardia, hypotension, desaturation or in extreme cases

cardiac arrest are keys to suspect cardiac tamponade especially following umbilical catheter insertions [14]. Etiology is unclear but anticipated causes include a direct puncture of a vessel or myocardium by the tip of the catheter during insertion or delayed perforation secondary to erosion of the cardiac or vascular wall [5–17].

The prevalence of line-related pericardial effusion is unknown. Systematic studies on the association of central umbilical catheters with pericardial effusion in neonates and its outcomes are lacking. Most of available publications are case reports. This study aims to examine the relationship between umbilical catheters placement and pericardial effusion in newborn infants. The analyses involve three different populations: infants with birth weight (BW) > 2500g, infants with BW < 1500g and infants with congenital heart diseases.

Methods

Data source

We utilized the National Inpatient Sample (NIS) and its pediatric version (KID) datasets. This is the largest publicly available inpatient database produced by the Agency for Healthcare Research and Quality (AHRQ). The datasets collect data from millions of in-hospitals stays every year from all States participating in the HealthCare Utilization Project, covering > 95% of the US population. These datasets are an all-payer database that includes patients covered by Medicare, Medicaid, private insurance, or uninsured. The datasets contain all information about hospitalization including demographic and clinical factors such as primary and secondary diagnoses and procedures (using ICD-9 codes), patient demographics, hospital characteristics, and payment source. The large sample size and its broad coverage provides a unique opportunity to study rare clinical conditions and uncommon treatments and capture populations missed by other databases. The datasets use a stratified, single-stage cluster sampling design, with region, urban/rural location, teaching status, ownership, and bed size to identify strata. After stratification, NIS dataset is sampled using 20% random samples of all ages, while in KID dataset normal newborns (with little variance) are sampled at a rate of 10% and complicated newborns are sampled at a rate of 80% [18].

Patient selection

We used KID dataset for the years 1997, 2000, 2003, 2006, 2009 and 2012 for this study. We examined hospital records of all included infants. We excluded infants with congenital hydrops fetalis using ICD9 code 7780 for non-immune hydrops fetalis that may be associated with chromosomal or genetic disorders, cardiac arrhythmia, congenital infection or idiopathic disorders. We also excluded infants with iso-immune hydrops fetalis using ICD9 code 7733. We used the ICD-9 code 4239 to identify cases with pericardial effusion using general equivalence mapping method [19]. Cases of pericardial effusion were verified against the presence or absence pericardiocentesis using the ICD-9 procedure codes 370. We used the ICD-9 procedure codes 3891 and 3892 to identify umbilical artery catheter placement (UAC) and umbilical venous catheters placement (UVC), respectively. Demographic, clinical and outcome

characteristics were identified using respective ICD9 codes. HCUP datasets are publicly available and deidentified and no IRB is required.

Study design and analysis

As the indications for UAC and/or UVC placement varies by the neonatal population, we examined the association of umbilical lines placements with pericardial effusion in three distinct subsets: infants > 34 weeks and more than 2500g at birth, very low birth weight infants (VLBW) < 1500g, and infants > 34 weeks and more than 2500g diagnosed with congenital heart disease. To enhance the sample size, we used a combination of NIS and KID datasets for years 1993–2014 in the analysis of infants < 1500g. Continuous variables were described using median and interquartile range. Categorical variables were described using frequencies and percentages. Statistical significance was set at $p < 0.05$. The association of UAC and/or UVC placement with pericardial effusion was examined using Chi square and Fisher exact tests. The findings were verified using logistic regression models controlling for maternal hypertension and diabetes and the infants' sex, race/ethnicity and the presence of multiple chromosomal or genetic disorders, complex congenital anomalies, congenital heart disease (CHD), congenital diaphragmatic hernia (CDH), respiratory distress syndrome (RDS), pulmonary hypertension (PPHN) and pulmonary hemorrhage. We also controlled for BW < 1000g in the VLBW infant's analysis. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

Results

The weighted sample of the 6 years of the KID dataset included 24,528,771 unique hospital discharge records. We identified 22,822,931 infants in the subset of infants with GA ≥ 35 weeks and BW > 2500g with no hydrops fetalis. Of them, 48.5% were females, 43.3% were Caucasians, 0.9% had an associated diagnosis of CHD and 0.4% had chromosomal, genetic or multiple congenital anomalies. Pericardial effusion was found in 2583 neonates (0.01%), with UVC placement in 0.24%, UAC placement in 0.31% and both catheters in 0.34%. Pericardial effusion was found in 0.33% of infants with UAC only, 0.22% of infants with UVC only and 0.37% of infants with both catheters compared to 0.01% in infants with no umbilical catheters placed; adjusted odds ratios is 2.7 (2.4–3.2, $p < 0.001$), 2.8 (2.3–3.5, $p < 0.001$), and 2.8 (2.4–3.2, $p < 0.001$), respectively, controlling for demographic and clinical confounders mentioned above, Table 1.

There were 200,288 infants with congenital heart disease among infants with GA ≥ 35 weeks, BW > 2500g with no hydrops fetalis in the weighted sample. Of them, 47.3 were females, 41.6% Caucasians, 43.7 delivered via Cesarean section, 6.4% had chromosomal or genetic disorders and 4.3% had multiple congenital anomalies. Pericardial effusion was found in 1130 (0.56%). Placement of a UVC was found in 3.5%, UAC in 5% and both catheters in 6.8% of the infants. Pericardial effusion was found in 1.46% of infants with UAC, 0.78% of infants with UVC and 0.98% of infants with both UAC and UVC compared to 0.47% in infants with no catheters; adjusted odds ratios is 2.1 (1.8–2.6, $p < 0.001$), 1.4 (1.1–1.9, $p = 0.036$) and 1.6 (1.3–1.9, $p < 0.001$), respectively, controlling for same confounding factors as above, Table 2.

We identified 1,187,727 infants with BW < 1500g in the NIS/KID combined datasets excluding infants with hydrops fetalis. Of them, 52.6% were < 28 weeks, 44% <1000g, 49.1% were females and 59.3% were born via Cesarean section. Pericardial effusion was found in 1667 infants (0.14%). In addition, 7.9% infants had only UVC placed, 10.9% had only UAC placed and 20.5% had both catheters placed. Pericardial effusion was found in 0.15% of infants with only UAC, 0.19% of infants with only UVC and 0.26% of infants with both umbilical catheters placed compared to 0.11% in infants without any umbilical catheters placed; adjusted odds ratios (aOR) is 1.1 (0.9–1.3, $p < 0.90$), 1.4 (1.2–1.7, $p < 0.001$) and 1.6 (1.4–1.8, $p < 0.001$), respectively, controlling for confounding variables mentioned above in addition to BW < 1000g, Table 3.

Discussion

To our knowledge, this is the first and the largest population study to assess the association of umbilical catheters placement with pericardial effusion in newborn infants. This study showed that central umbilical catheters were associated with increased risk for pericardial effusion in newborn infants whether they were VLBW infants, near term or term infants, or those diagnosed with congenital heart disease. This association was consistent after controlling for several potential contributing factors such as infant's sex, race/ ethnicity and several maternal and infant concurrent diagnosis. In addition, central umbilical catheters were independently associated with the occurrence of pericardial effusion in infants with congenital heart disease.

UVC is commonly used as a secure central catheter to provide parenteral nutrition (TPN) and medications for VLBW infants and sick full-term infants. Infusion of TPN with hyperosmolar fluids might play a role in the pathogenesis of pericardial effusion as it causes osmotic damage of the pericardium endothelium, then the fluids diffuse into the pericardial space forming an effusion. Another speculation for the association between UVC placement and occurrence of PE in VLBW infants is the in accurate position of the tip of UVC in the heart [20]. The recommended position for the tip of an UVC is the junction of inferior vena cava (IVC) and right atrium [21]. The tip of UVC is routinely determined by radiography to ensure that the tip has not migrated and in optimal position. Endothelial cell damage will be initiated with repeated contact of the catheter's tip with the cardiac wall during cardiac contraction causing transmural necrosis with subsequent pericardial effusion [22].

Long duration of UVC insertion in VLBW infants besides, immaturity of the myocardium in preterm infants might precipitate in PCE compared to full term infants. UAC is routinely used in the care of critically ill newborns and neonates with congenital heart diseases. The mechanism of UAC induced PCE in neonates is unclear. It might be direct perforation at the time of UAC insertion or potential hemostatic and aortic wall vascular complications [23]. The resulting thrombus fosters attachment of the catheter tip to the heart, causing irritation of the endothelial cell lining and osmotic injury. Through the damaged lining, fluid then diffuses into the pericardial space forming an effusion [24].

This study has the strength of being inclusive that truly represents the nation. It is the largest to describe prevalence of pericardial effusion in association with umbilical central catheters in VLBW infants, full term neonates and all neonates diagnosed with congenital heart disease. However, the study inherited some limitations. It is not possible to determine the median time from catheter insertion to PCE detection in HCUP dataset. However, the routine practice in most NICUs is to insert UAC and/or UVC within the first couple hours of life.

Conclusion

Pericardial effusion is a potential complication of umbilical central catheters in neonates. Further studies are needed to explain pathogenesis of this association. Central umbilical catheters may be independently associated with the occurrence of pericardial effusion in infants with congenital heart disease.

Declarations

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Informed consent for participant: not applicable

Authors Contributions:

Dr. Elgendy conceptualized and designed the study, interpreted the statistical analyses, drafted the initial manuscript, reviewed and revised the manuscript and critically reviewed the manuscript for important intellectual content.

Dr. Aly conceptualized and designed the study, interpreted the statistical analyses, reviewed and revised the manuscript and critically reviewed the manuscript for important intellectual content.

Dr. Mohamed conceptualized and designed the study, conducted the statistical analyses, edited and revised the initial manuscript, reviewed and revised the manuscript and critically reviewed the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Tables

Table.1 Association of umbilical catheters placement with pericardial effusion in infants ≥ 35 weeks GA and > 2500g BW

	Pericardial effusion n = 2583	No Pericardial effusion n =	Adjusted OR (CI), *p* value
male Sex	44.4	48.5	0.99 (0.89-1.1), 0.83
ce			
Caucasian	35.2	43.3	<0.001
African American	19.6	10.3	
Hispanic/Latino	20.2	17.0	
Asian/Pacific Islander	3.09	3.47	
Native	0.74	0.51	
ıternal hypertension	0.56	0.08	2.8 (1.6-4.8), <0.001
ıternal diabetes mellitus	2.90	0.93	0.8 (0.6-1.1), 0.10
romosomal disorders	6.36	0.15	2.2 (1.8-2.6), <0.001
ıltiple Congenital omalies	8.34	0.26	2.0 (1.7-2.4), <0.001
ngenital heart diseases	43.7	0.87	34 (31-38), <0.001
ngenital diaphragmatic rnia	2.91	0.04	1.1 (0.8-1.5), 0.59
spiratory distress	10.5	0.80	1.6 (1.4-1.8), <0.001
lmonary hypertension	13.9	0.16	3.8 (3.4-4.4), <0.001
lmonary hemorrhage	2.06	0.02	2.9 (2.1-3.9), <0.001
echanical ventilation	26.6	0.31	8.8 (7.8-9.9), <0.001
ortality	10.6	0.12	2.6 (2.3-3.1), <0.001
ngth of stay among rvivors	10 (3-23)	2 (2-3)	<0.001
AC only	0.33	0.01	2.7 (2.4-3.2), <0.001
VC only	0.22	0.01	2.8 (2.3-3.5), <0.001
th lines placed	0.37	0.01	2.8 (2.4-3.2), <0.001

UAC: umbilical artery catheter, UVC: umbilical venous catheter
Logistic regression models controlled for maternal hypertension and diabetes mellitus, infant's sex, race and the presence of chromosomal disorders, multiple congenital anomalies, congenital heart disease, congenital diaphragmatic hernia, respiratory distress syndrome, pulmonary hypertension, pulmonary hemorrhage and mechanical ventilation

Table.2 Association of umbilical catheters placement with pericardial effusion in preterm infants <1500g BW

	Pericardial effusion n =	No Pericardial effusion n =	Adjusted OR (CI), *p* value
W < 1000g	53.6	43.5	1.3 (1.2-1.4), <0.001
male Sex	55.3	49.2	0.77 (0.7-0.8), <0.001
ce			
Caucasian	35.5	35.3	<0.001
African American	25.5	23.2	
Hispanic/Latino	16.1	13.7	
Asian/Pacific Islander	2.62	2.45	
Native	0.82	0.67	
aternal hypertension	1.70	2.12	0.9 (0.6-1.3), 0.52
aternal diabetes mellitus	1.79	1.62	0.9 (0.7-1.3), 0.70
romosomal disorders	3.2	0.6	3.1 (2.4-4.1), <0.001
ultiple congenital omalies	9.1	3.3	2.2 (1.8-2.5), <0.001
ngenital heart diseases	38.4	10.9	3.9 (3.5-4.3), <0.001
ngenital diaphragmatic rnia	0.41	0.14	0.8 (0.4-1.7), 0.56
spiratory distress	66.6	54.3	1.2 (1.1-1.4), <0.001
lmonary hypertension	7.28	1.22	2.5 (2.1-3.0), <0.001
lmonary hemorrhage	3.12	2.00	1.1 (0.8-1.4), 0.56
echanical ventilation	47.5	25.6	1.8 (1.6-2.0), <0.001
ortality	20.1	16.7	1.4 (1.2-1.5), <0.001
ngth of stay among rvivors	60 (32-84)	40 (19-65)	<0.001
AC only	0.15	0.11	1.1 (0.9-1.3), 0.90
VC only	0.19	0.11	1.4 (1.2-1.7), <0.001
th lines placed	0.26	0.11	1.6 (1.4-1.8), <0.001

UAC: umbilical artery catheter, UVC: umbilical venous catheter

Logistic regression models controlled for maternal hypertension and diabetes mellitus, infant's birth weight <1000g, sex, race and the presence of chromosomal disorders, multiple congenital anomalies, congenital heart disease, congenital diaphragmatic hernia, respiratory distress syndrome, pulmonary hypertension, pulmonary hemorrhage and mechanical ventilation

Table.3 Association of umbilical catheters placement with pericardial effusion in infants with congenital heart disease

	Pericardial effusion n = 199158	No Pericardial effusion n = 1130	Adjusted OR (CI), *p* value
male Sex	45.6	47.4	1.0 (0.91-1.2), 0.57
ce			
Caucasian	36.3	41.7	<0.001
African American	13.6	10.7	
Hispanic/Latino	24.3	20.4	
Asian/Pacific Islander	3.48	2.58	
Native	0.88	0.63	
aternal hypertension	0.40	0.25	1.6 (0.63-4.1), 0.32
aternal diabetes mellitus	3.11	5.34	0.54 (0.39-0.76), <0.001
romosomal disorders	9.57	6.42	1.4 (1.2-1.7), <0.001
ultiple congenital omalies	7.50	4.27	1.1 (0.8-1.4), 0.58
ngenital diaphragmatic rnia	2.50	0.85	1.1 (0.7-1.7), 0.69
spiratory distress	6.36	6.00	0.6 (0.5-0.8), <0.001
lmonary hypertension	13.46	4.56	2.2 (1.8-2.6), <0.001
lmonary hemorrhage	1.95	0.35	2.4 (1.5-3.6), <0.001
echanical ventilation	30.26	8.23	4.4 (3.8-5.0), <0.001
ortality	11.3	3.40	1.9 (1.5-2.3), <0.001
edian length of stay	16 (7-30)	3 (2-10)	<0.001
AC only	1.46	0.47	2.1 (1.8-2.6), <0.001
VC only	0.78	0.47	1.4 (1.1-1.9), 0.036
th UAC and UVC	0.98	0.47	1.6 (1.3-1.9), <0.001

UAC: umbilical artery catheter, UVC: umbilical venous catheter

Logistic regression models controlled for maternal hypertension and diabetes mellitus, infant's sex, race and the presence of chromosomal disorders, multiple congenital anomalies, congenital heart disease, congenital diaphragmatic hernia, respiratory distress syndrome, pulmonary hypertension, pulmonary hemorrhage and mechanical ventilation