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Review

Neonatal myocardial infarction: A retrospective study and literature review

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ABSTRACT

Neonatal myocardial infarction (MI), in the absence of congenital heart disease or cardiac surgery involving the coronaries, is a rare condition with associated high mortality. A cluster of neonatal myocardial infarction cases was observed, leading to an investigation of causes and contributors. We performed a single-center review of neonates >37 weeks between 2011 and 2017 to identify neonates with myocardial infarction. Neonates with prior cardiac surgery, congenital anomalies of the coronaries, or sepsis were excluded. Diagnosis of MI was based on ECG changes, elevated troponin, decreased function or regional wall abnormality, and abnormal coronary angiography. There were 4,583 admissions to the NICU without interval changes in referrals or the incidence of neonatal asphyxia. There were six cases of neonatal myocardial infarction. Of 2,155 admissions in the first three years, there were no cases. The incidence in the next three years was 1.3/1,000, 2.7/1,000, and 3.3/1,000. There was a significant difference (0.03, Fishers exact) between the first and second halves of the study period. All cases underwent catheterization, revealing coronary artery thrombosis requiring thrombolytic therapy. Additionally, obstetric providers were surveyed to determine changes in umbilical cord handling practices. Of 48 obstetric providers, 57% changed their practice of cord clamping since 2014: 13% reported cord milking then clamping; 47% delayed cord clamping for a few minutes; 28% delayed cord clamping until the cord stopped pulsating; and 13% immediate clamping. Only 40% reported routine documentation of cord clamping. In conclusion, there was an increased incidence of neonatal myocardial infarction due to coronary thrombosis. Early diagnosis and initiation of therapy of neonates with myocardial infarction can improve outcomes. A larger study cohort could lead to better understanding of risk factors and outcomes of myocardial infraction in neonates.

1. Introduction

Neonatal myocardial infarction (MI) in structurally normal heart and coronary anatomy is a rare condition with high mortality [1]. There have been sporadic reports since the first description in 1947, with mortality due to severe MI of 90% [2]. Neonatal MI can be classified into three types: (1) neonatal MI associated with congenital heart disease (CHD); (2) neonatal MI after cardiac surgery; and (3) neonatal MI without associated structural/congenital heart disease [3].

Most of the reported cases of perinatal MI in structurally normal hearts are associated with thromboembolism and/or birth asphyxia [1]. In near-term pregnancies, thrombosis of umbilical vessels is not uncommon [1,4]. These thrombi have the potential to embolize to the fetus, can compromise fetal circulation, and cause fetal death [4].

In late 2012, the American College of Obstetricians and Gynecologists (ACOG) released a committee opinion recommending delayed cord clamping (DCC) when feasible for preterm births (<32 weeks) and commenting on potential benefits [5]. The American Academy of Pediatrics (AAP) endorsed ACOG's recommendations in 2012, and along with the American Heart Association (AHA) changed

Abbreviations: MI, myocardial infarction; DCC, delayed cord clamping; CHD, congenital heart disease; ACOG, American College of Obstetricians and Gynecologists; AAP, American Academy of Pediatrics; AHA, American Heart Association; NRP, Neonatal Resuscitation Program; DOL, day of life; echo, echocardiogram; cath, catheterization

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the Neonatal Resuscitation Program (NRP) guidelines in 2015 to recommend DCC in "most vigorous term and preterm newborns for at least 30-60 seconds". The World Health Organization recommends a similar practice. DCC has been associated with increased hemoglobin levels at birth and improved iron store for several months after birth in term infants. For preterm infants, DCC may improve transitional circulation and increase red blood cell volume, reducing the need for blood transfusions, and the incidence of both necrotizing enterocolitis and intraventricular hemorrhage. This practice may increase the risk of jaundice, and appropriate monitoring and access to treatment are recommended [6]. Prior to the formal recommendations made by ACOG and the AAP, there was variable umbilical cord care between obstetric providers and institutions. The practices include immediate cord clamping and variation of milking or stripping of the umbilical cord. Umbilical cord milking has been considered as a means of achieving increased placental to newborn transfusion in a rapid time frame of 10–15 s. It has particular appeal for circumstances in which the recommended 30–60 s delay in umbilical cord clamping may be deemed too long, such as when immediate infant resuscitation is needed or maternal hemodynamic instability occurs. Currently, ACOG and the AAP have stated there is insufficient evidence to either support or refute umbilical cord milking in term or preterm infants [7].

In 2017, Molkara et al. reported three cases of neonatal MI and proposed a treatment algorithm using tissue plasminogen activator (tPA) at our institution [8]. Since that report, there have been three additional cases, prompting a retrospective review study to assess both the incidence of neonatal MI and potential contributing factors (from 2011 to 2017). We hypothesized that the incidence of neonatal MI had increased in recent years. The study included an online survey of regional obstetric providers to assess changes in umbilical cord handling practices.

2. Material and methods

2.1. Study design and population

The Institutional Review Board of Rady Children's Hospital of San Diego (RCHSD) approved the retrospective chart review study and questionnaire. RCHSD is a tertiary referral center serving San Diego, Imperial, and southern Riverside counties, and is the only center in the region providing subspecialty neonatal cardiac and cardiac surgical services. All charts of neonates with the diagnosis of coronary artery thrombosis, coronary ischemia, and myocardial infarction admitted to the neonatal intensive care unit (NICU) at our institution from August 2011 to July 2017 were reviewed. Potential cases of MI were ascertained from our electronic medical record system and reviewed for diagnostic criteria used, as well as for demographics, identified potential causes, treatments, and outcomes. Assessments of changes in referral population and any changes in recommendations for obstetric and neonatal care were made.

Term neonates ($\geq$37 weeks) admitted to the NICU between 0 and 14 days of life with neonatal MI formed the study population. Preterm neonates (gestational age < 37 weeks), neonates older than two weeks of age at the time of presentation, patients post-cardiac surgery, and patients with clinical sepsis confirmed by positive blood cultures were excluded.

Neonatal MI was diagnosed based on the presence of ischemic ECG changes, elevated troponin levels, abnormal echocardiogram (echo) findings compatible with ischemia and infarction, and abnormal coronary artery angiography during cardiac catheterization.

Data on pregnancy, delivery, family history of CHD, clotting disorders, or sudden death were collected. Laboratory data collected were results of CBC, chemistry panel, troponin T, troponin I, brain natriuretic peptide (BNP), coagulation panel, fibrinogen, protein C, protein S, factor V Leiden mutation, prothrombin G20210A mutation, antithrombin III, antiphospholipid antibody panel, cardiolipin antibody panel, beta-2 glycoprotein 1 (B2GP1) antibody assay, DRVVT screen (Lupus anticoagulant), and homocysteine level.

An assessment of changes in umbilical cord handling practices was performed by an online survey of regional obstetric providers. The survey was voluntary, and responses were kept anonymous and confidential.

2.2. Statistical analysis

Categorical variables were summarized as frequencies and percentages while continuous variables were summarized as medians with ranges (minimum-maximum). Fisher's exact test was used to compare the incidence between the first three years (August 2011–July 2014) vs. the last three years (August 2014–July 2017). Statistical significance was defined as $P < 0.05$.

3. Results

During the study period, there were 4,583 admissions to the NICU. There were no changes in the referral region, incidence of neonatal asphyxia among admissions, or changes in the diagnostic criteria for neonatal MI. Demographics and clinical data are summarized in Tables 1 and 2. Out of 2,155 admissions in the first three years between Aug 2011 and Jul 2014, no cases were identified. The incidence increased in the following three years: 1.3 cases per 1,000 (1 case in 743 admissions); 2.7 cases per 1,000 (2 cases in 784 admissions); and 3.3 cases per 1,000 (3 cases in 901 admissions). There was a statistically significant difference between the first and second halves of the study period (P-value of 0.03 using Fisher's exact test (0/2,155 admissions vs. 6/2,428 admissions). Two patients had identifiable risk factors; one patient had a history of birth asphyxia requiring cooling, and the other patient had complex CHD [infradiaphragmatic total anomalous pulmonary venous connection (TAPVC)]. All six cases underwent cardiac catheterization and were found to have coronary thrombosis requiring thrombolytic therapy. Out of five patients who presented with respiratory distress, four had abnormal troponin levels and ECGs, and all had abnormal echocardiograms.

The online survey was sent to obstetric care providers who were members of a regional perinatal CME group with 48 respondents. 57% of those responding reported changing their practice related to the timing of cord clamping since 2014 (Table 3). For infants >37 weeks, 13% reported cord milking then clamping, 47% reported DCC for a few minutes, 28% reported cord clamping after the cord stops pulsating, and 13% reported immediate cord clamping. 40% reported routine documentation of cord clamping.

3.1. ECG analysis

Only two of the six patients (4 and 6) had classic ECG infarction patterns with QS morphologies corresponding to the presumed location by imaging and catheterization. One of these patients had high troponin

Table 1
Patient demographics and clinical data.

N = 6	
Birth weight (kg)[a]	3.37 (2.78–4.16)
Age of presentation	0 h–10 days
Gestational age (weeks)[a]	39.5 (37.5–40.5)
Female gender, n (%)	4 (66.6%)
C-section	2 (33.3%)
Hemoglobin (g/dL)/hematocrit (%)[a]	15.2 (13.4–17.5)/45 (41–47)
Platelet count[a] (10^3/UL)	217 (124–233)
Structural heart disease	1 (16.6%)
Mortality	1 (16.6%)

[a] Values are presented as median, range.

Table 2
Summary of clinical data.

Case#	Age/symptoms at presentation	ECG findings	CXR	Peak troponin[a]	Initial echo					Cath	Umbilical cord practice
					EF	MR	Regional wall abnormalities	LAE	Other	Affected coronaries	
1	5 hrs/respiratory distress	T wave inversion in the lateral leads	Bilateral interstitial opacities	0.11	41%	Mild-moderate	Posterior & lateral LV walls	Yes		RCA, LAD, LCx	Not documented
2	15 hrs/respiratory distress	Possible RVH	Bilateral small pleural effusions & pulmonary edema	0.1	70%	Severe	Posterior & lateral LV walls	Yes	Moderate TR, severe RV HTN	LMCA, LAD, LCX, RCA	Not documented
3	10 days/cardiogenic shock	Decreased voltages in the lateral leads	Cardiomegaly	12.7	39%	Moderate	Posterior LV wall & basal septum	Yes		LAD, LCx	Not documented
4	At birth/respiratory distress	Lateral infarction	Trace pleural effusion	8.4	39%	Mild	Anterolateral & inferolateral walls	Yes		LAD, LCx	Not documented
5	At birth/respiratory distress	RAD, RVH, Nonspecific ST changes	Cardiomegaly	0.44	62%	Moderate	Posterior & lateral walls	Yes	Severe RV HTN,	LMCA, LAD, LCx	DCC
6	1 day/respiratory distress & cyanosis	ST-segment depression in septal leads & inferolateral infarct pattern	Diffuse pulmonary opacification, small right pleural effusion, borderline cardiomegaly	None	39%	Mild - moderate	Global decreased function	No	TAPVC, PDA with bidirectional flow	LAD	DCC + milking

Abbreviations: hrs: hours; HTN: hypertension; IVS: interventricular septum; LAD: left anterior descending artery; LCX: left circumflex; LMCA: left main coronary artery; LV: left ventricle; PDA: patent ductus arteriosus; RCA: right coronary artery; RAD: right axis deviation; RVH: right ventricular hypertrophy; RV: right ventricle; TR: tricuspid regurgitation.

[a] Normal troponin level < 0.05 ng/mL.

Table 3
Umbilical cord handling practices survey results.

Have you changed your practice on the interval to cord clamping in the last 2 years? (n = 44 respondents)	
Yes	25 (57%)
No	19 (43%)
How do you handle the cord now in < 34 weeks gestation? (n = 40 respondents)	
Immediate cord clamping	2 (5%)
Delayed cord clamping for a few minutes	11 (27.5%)
Delayed cord clamping until the cord stop pulsating	6 (15%)
Milking and then clamping	21 (52.5%)
How do you usually handle the cord in > 36 weeks gestation? (n = 47 respondents)	
Immediate cord clamping	6 (12.8%)
Delayed cord clamping for a few minutes	22 (46.8%)
Delayed cord clamping until the cord stop pulsating	13 (27.6%)
Milk and then clamp	6 (12.8%)
Do you routinely document cord handling? (n = 48 respondents)	
Yes	19 (39.6%)
No	16 (33.3%)
Sometimes	13 (27.1%)

(patient #4) and the other had coexisting complex CHD and died (patient #6). Otherwise, ECG findings in the other four were not diagnostic of myocardial ischemia and/or infarction: four patients had flat/biphasic inferolateral T waves and two of the four had poor R wave progression, the latter finding being indistinguishable in newborns from RVH or normal evolution of surface ECG RV forces. ECGs showed resolution of abnormalities in all five survivors between the first week of life and six months of age.

3.2. Patient profiles

3.2.1. Case #1–3

The details of the first three cases including the treatment algorithm were previously published and therefore will only be mentioned briefly in this report (Tables 1, 2, and 4) [8].

3.2.2. Case #4

A 3.24 kg male was born at 38 weeks gestation and delivered by C-section due to a non-reassuring fetal heart rate. Pregnancy was otherwise uncomplicated. Apgar scores were 2, 6 and 7 at 1, 5 and 10 min, respectively. Cord handling was not documented. The patient required positive pressure ventilation and intubation due to apnea, severe acidosis on arterial blood gas (pH 7.06, base deficit 21), and elevated lactate of 13 mmol/L (normal 0.5–2.0). Brain US was normal. Due to these findings, cooling protocol was initiated. ECG was consistent with lateral myocardial infarction (Fig. 1). On day of life (DOL) #1, echo demonstrated severely diminished left ventricular (LV) function with ejection fraction (EF) of 34%, pulmonary hypertension with right ventricular (RV) dysfunction, and mild mitral regurgitation (MR). Troponin peaked at 8.42 on DOL#1 (normal < 0.05 ng/mL). BNP was >5000 (normal < 100 pg/mL). Cardiac catheterization on DOL#2 revealed filling defect with sluggish flow in the left anterior descending (LAD) coronary artery compatible with mid LAD thrombus (Fig. 2). Intracoronary nitroglycerin and tPA were administered into the left main coronary artery resulting in an improved flow. On DOL#7, cardiac magnetic resonance imaging (MRI) revealed evidence of sub-endocardial enhancement, mostly in the left circumflex territory with some segments of LAD and RCA territories (Fig. 3). He was extubated on DOL#8 and milrinone was stopped on DOL#15. He remained on furosemide, spironolactone, captopril, and clopidogrel. Echo at latest follow-up at six months of age revealed low normal LV systolic function (LVEF of 55% by bullet method), normal right ventricular size and function, and resolution of MR. ECG normalized for age.

Table 4
Hypercoagulable workup results.

Case #	Protein C activity (70–180%)	Protein S activity	Fibrinogen (160–425 mg/dL)	PT/INR 11.4–14 s/ ≤ 2	PTT (24–38 s)	Factor V Leiden mutation	G20210A mutation	Antithrombin III	Antiphospholipid antibodies panel	Cardiolipin antibodies	Lupus anticoagulant
1	26	57 (60–140%)	220	15.9/1.3	130	Neg.	Neg.	109 (39–87%)	Neg.	Neg.	Neg.
2	80	74 (57–171%)	217	18.1/1.5	40	Neg.	Neg.	80 (80–120%)	Not done	Neg.	Neg.
3	34	59 (60–140%)	485	1/12.8	36	Neg.	Neg.	85 (80–140%)	Neg.	Not done	Not done
4	33	60 (57–171%)	200	18.7/1.6	46	Neg.	Not done	53 (80–120%)	Not done	Neg.	Neg.
5	16	43 (50–147%)	330	15.2/1.3	44	Neg.	Not done	88 (80–120%)	Not done	Neg.	Neg.
6	Not done	Not done	113	20.7/1.8	>130	Not done	Not done	43 (80–140%)	Not done	Not done	Not done

3.2.3. Case #5

A 4.16 kg female was born at 39 weeks gestation via spontaneous vaginal delivery. Pregnancy and delivery were uncomplicated. DCC was documented. Apgar scores were 8 and 8 at 1 min and 5 min, respectively. A murmur was noted. Chest x-ray revealed cardiomegaly with normal lung vascularity. ECG demonstrated nonspecific ST segment changes. An echo revealed moderate MR and LV dysfunction with hypokinetic posterior and lateral walls. Troponin was 0.44 ng/mL. Brain US was normal. She underwent cardiac catheterization on DOL#2, which revealed evidence of thrombosis in the left main coronary artery, LAD, and left circumflex (LCx) (Fig. 4). The patient received intracoronary eptifibatide (Integrilin), nitroglycerin, and tPA. Post-intervention selective left coronary arteriography revealed significant improvement in the opacification of the left coronary arterial vasculature, including the distal branches. Post catheterization, she was treated with aspirin and clopidogrel. Repeat echo on DOL#7 revealed mild MR, moderately dilated left atrium (LA), and normal ventricular function with no regional wall motion abnormalities. At three months of age, follow-up ECG and echo were normal.

3.2.4. Case #6

A 2.92 kg male was born at 37 4/7 weeks of gestation via C-section due to transverse lie. DCC and milking were performed. Apgar scores were 6 and 8 at 1 and 5 min, respectively. The patient was intubated due to cyanosis. He was placed on high-frequency oscillator and iNO with improvement in saturations from the high 60s to mid-80s. He was started on dopamine and low-dose epinephrine due to hypotension. Chest x-ray demonstrated diffuse pulmonary opacification with mild cardiomegaly. Brain US was normal. Initial ECG showed ST-segment depression in inferior, anterior and lateral leads. Echo demonstrated obstructed infradiaphragmatic TAPVC, bidirectional PDA, LA hypertension and severely diminished LV function. Due to severely depressed LV function, he was placed on venoarterial extracorporeal membrane oxygenation (VA ECMO). He was then taken to the catheterization lab and selective left coronary arteriography demonstrated thrombus in the LAD artery with a paucity of vascularization to the LV apex. Nitroglycerin and tPA were administered in the left main coronary artery. Palliation was done with stenting of the ductus venosus and the vertical vein. The patient developed significant brain hemorrhage; therefore ECMO support was withdrawn on DOL#2.

4. Discussion

In 1947, Ravich et al. reported two full-term neonates with MI; the first neonate had a “slight difficulty” with delivery and died suddenly at 6 h of life, and the second neonate had a difficult labor and died around 10 h of life. Both cases were diagnosed with coronary arterial thrombosis at autopsy [9]. In 1959, Richard et al. reported two cases of neonatal MI; delivery of both was complicated by birth asphyxia (cord around the neck) and both died (at 16 h and 4 days of life). The diagnosis was made in both cases at autopsy [10]. In 1960, Gault et al. reported a case of neonatal coronary artery thrombosis with ECG changes and postmortem findings [11]. de Vetten et al. reported a 29 week-gestation who developed cardiogenic shock in the second week of life with a workup suggesting myocardial infarction vs. myocarditis. The authors reviewed most of the reported cases of neonatal MI between 1960 and 1999 and reported 20 proven cases of neonatal MI in which only two survived. In their review, the most common causes of neonatal MI were coronary thrombosis (13 out 20) and birth asphyxia (7 out of 20) [12].

Papneja et al. reviewed all cases of neonatal MI reported between 2000 and 2014. The review included neonatal MI associated with CHD and/or post cardiac surgery. In neonates who had no history of CHD or cardiac surgery, neonatal MI was reported in association with perinatal asphyxia, idiopathic infantile arterial calcification, congenital diaphragmatic hernia, eosinophilic endomyocarditis, and genetic

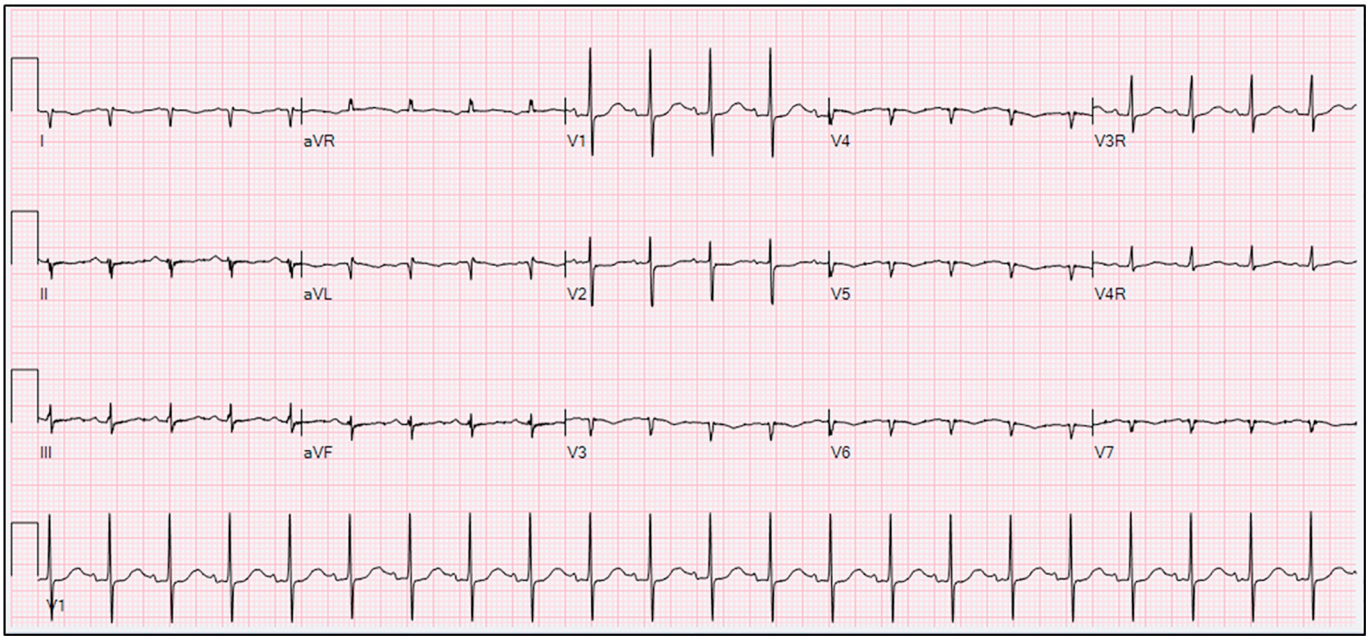

Fig. 1. ECG of case #1 showing NSR, RAD, lateral infarction (Q waves in leads I and aVL), and poor R wave progression.

mutations [1]. Other reported cases of neonatal MI are in association with neonatal asphyxia and severe anemia [13], myocarditis [12,14], severe septal hypertrophy in an infant of diabetic mother [15], Kawasaki disease [16,17], hypercholesterolemia [3], thromboembolism secondary to umbilical cord hematoma [18], and umbilical venous catheterization [19,20]. Caruso et al. described two cases of neonatal MI due to polycythemia and birth asphyxia [21]. Perrier et al. described a neonate with MI secondary to aortic root thrombus who was treated with surgical thrombectomy followed by ECMO support. A left ventricular assist device (EXCOR Berlin®) was inserted on DOL#12. The patient received a heart transplant at around 5.5 months of age [22]. Giralt et al. described a neonate with MI due to left coronary artery thrombosis of unknown etiology. The patient had a prolonged hospital course and was discharged on heart failure therapies and eventually received a heart transplant at 17 months of age [23]. Haubner et al. published a neonate with MI who had a full recovery of ventricular function after stabilizing with ECMO and receiving thrombolytic therapy [24].

In the present study, we observed an increased incidence of neonatal MI since 2014, which coincides with a change in the practice of umbilical cord handling practice. This temporal relationship may imply an association between the two. It is not clear whether the incidence of neonatal MI has truly increased or if this is due to improved disease diagnosis due to a higher index of suspicion. The potential impacts of DCC have been an active area of investigation for nearly a decade, and there have been numerous case series involving both preterm and term infants [6]. Neonatal MI was not reported in association in any of the reports of DCC but may have been missed by study design. The findings of a shift in cord blood handling demonstrated by our survey are consistent with both our observations and recent publications. In 2014, the American College of Nurse-Midwives unequivocally endorsed DCC, when feasible, for both term and preterm infants [25]. The ACOG,

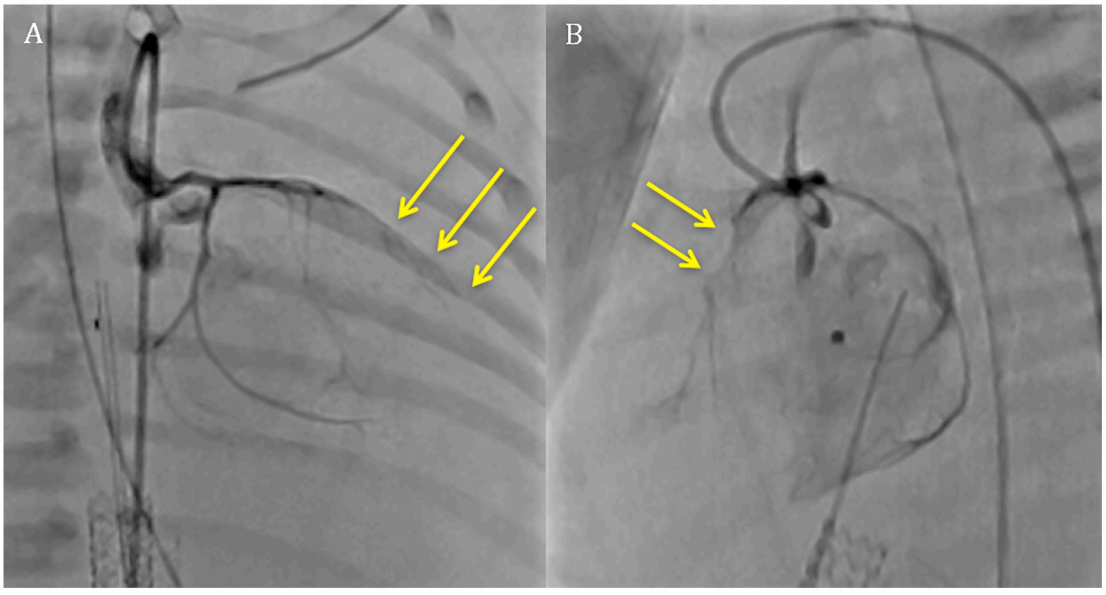

Fig. 2. Selective left coronary angiogram showing termination of the LAD with a thrombus.

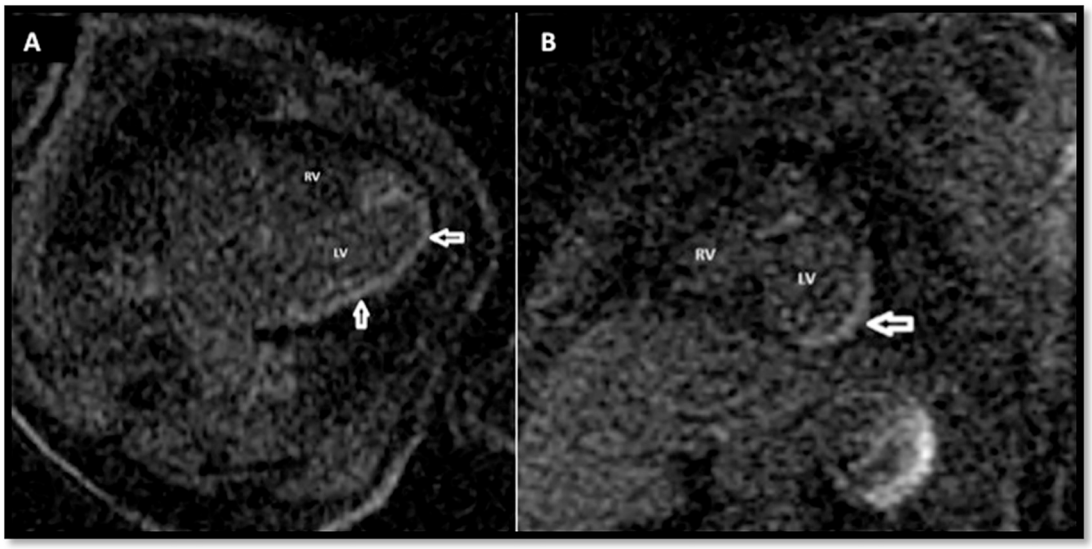

Fig. 3. Cardiac MRI with delayed enhancement utilizing an SSFP coronary artery sequence following the administration of 0.5 ml of gadolinium-based contrast demonstrating an area of sub-endocardial enhancement (white arrow) along the inferolateral and inferior segments of LV basal region, anterior, anterolateral, inferolateral, inferior and inferoseptal segments of LV mid-cavity. The myocardial enhancement appears to be mostly in the left circumflex territory with some segments of LAD and RCA territories. (A) 4-chamber view. (B) Short-axis view.

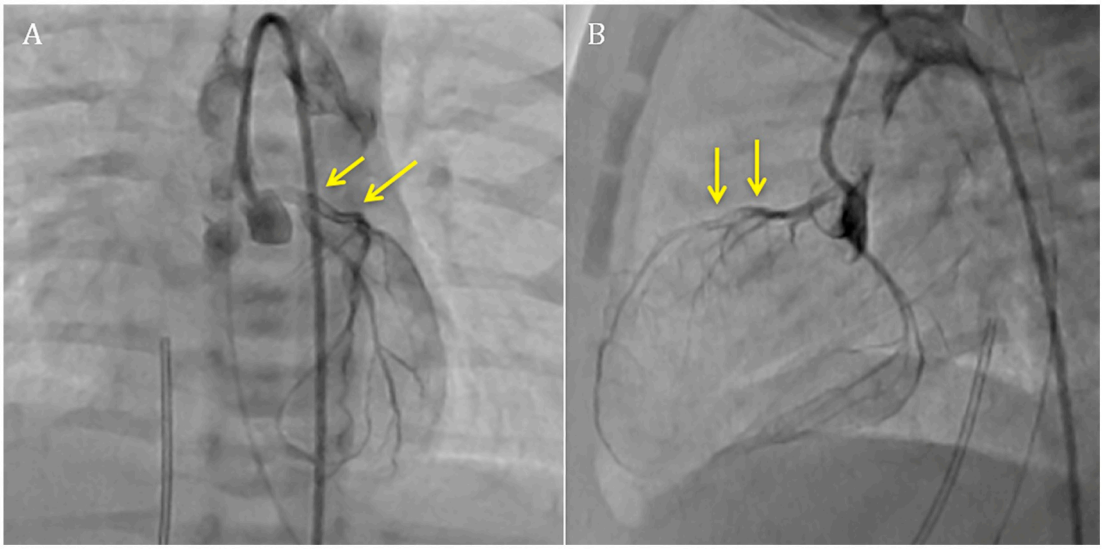

Fig. 4. Selective left coronary angiogram showing a subtle linear strand-like thrombus in the LAD.

which had issued an equivocal analysis in 2012, published a similar endorsement in 2017 [26]. Jelin et al., in an article published in 2014, surveyed ACOG members and found that the great majority indicated that their institution had no policy regarding cord blood handling, and concluded that "obstetricians' beliefs about the appropriate timing for umbilical cord clamping are not consistent with the evidence that demonstrates its beneficial impact on neonatal outcomes" [27]. In contrast, in a more recent survey by Leslie and colleagues, published in 2018, found that 73% and 79% of obstetricians practiced DCC for preterm and term infants, respectively [28].

Increased rate of jaundice is the only adverse outcome reported in association with DCC or cord milking, as demonstrated in some studies [26]. However, the rate of neonatal MI is extremely low; at our institution, with a catchment area of over 50,000 deliveries per year, a maximum of three cases per year were observed. The outcomes analyzed by most studies of DCC have been neonatal death and morbidities such as intraventricular hemorrhage, brain injury, and sepsis [29]. The number of cases of DCC in the most recent Cochrane meta-analysis of studies of outcomes in term infants included 15 studies including $<4{,}000$ cases; the largest studies to date included $<2{,}000$ patients [6,29]. Thus, even if neonatal MI had been specifically sought, it is unlikely that cases would have been detected.

Theoretically, stasis of umbilical blood flow could lead to thrombus formation, which can embolize to the coronaries, brain or kidneys. However, none of the patients in this report had renal or brain involvement, and we are unaware of an increased incidence of renal artery thrombosis or thromboembolic stroke at our institution. ECG, echo and troponin were obtained in patients presenting in cardiogenic shock, and/or respiratory distress requiring intubation who had evidence of myocardial injury suggested by echo (regional wall abnormalities, mitral regurgitation, LA hypertension, or decrease LV function), ECG and elevated troponin. Only patients with regional wall abnormalities, mitral regurgitation, evidence of LA hypertension, or decrease LV function underwent cardiac catheterization, as ECG findings could be

nonspecific. However, if a patient is hemodynamically stable, we would start therapeutic heparin and aspirin, and repeat the echo, ECG and troponin. If there is no clinical improvement, then we would perform a cardiac catheterization.

Early interventional catheterization to reestablish coronary blood flow is a key factor for myocardial recovery in neonates with MI. Umbilical cord access should be used whenever possible. Catheterization procedures Identification of coronary thrombus can be seen in case of complete termination of the vessel (Fig. 2), but sometimes it is subtle with a strand of thrombus seen in the vessel (Fig. 4). If the facility has no access to cardiac catheterization and/or an interventional team familiar with intracoronary tPA administration, anticoagulation therapy with heparin infusion should be considered. Cranial ultrasound should be performed prior to initiation of anticoagulation therapy to rule out bleeding. The patient should be considered for transfer to a healthcare facility with access to a cardiac catheterization where advanced care can be provided. While coronary CT angiography has an excellent resolution to visualize the origin of coronary arteries and proximal course, the distal course can be difficult to visualize. Additionally, the quality of coronary CT angiography can be limited secondary to blurring artifact caused by fast heart rate, especially in newborns [30]. Due to these limitations, none of the patients reported in the present study had coronary CT angiography. If coronary artery thrombosis is suspected, we would perform a diagnostic cardiac catheterization and intervene if indicated. Troponin in neonates should be interpreted with caution, as there can be variations between labs and even between healthy newborns. Additionally, guidelines are lacking in the pediatric population when compared to adults [1,31].

4.1. Limitations

This study has several limitations. First, it is a retrospective chart review study performed at a single center. However, it is important to keep in consideration that neonatal MI is very rare. Second, the patient with infra-diaphragmatic TAPVC is different from the other patient population as he had a complex primary cardiac anomaly. Third, there was no consistency in hypercoagulable workup performed (Table 4). Most of these patients had a low protein C activity level. Karpatkin et al. reported low protein C in the neonatal period based on electroimmunoassay in 47 neonates. The mean protein C level was 27% (10–67% of the normal adult mean) [32]. The effect of DCC on protein C is unknown, but neonatal hypoxia was reported to be associated with low protein C, protein S, and antithrombin III [33]. Most of the reported cases were not tested for G20210A mutation, antithrombin III, and antiphospholipid antibodies, which are essential tests to rule out hemophilias. Fourth, none of the subjects in the present study had a unifying hypercoagulable diagnosis. Pregnancy was complicated in one case with maternal lupus. There was no documentation of the umbilical cord handling practice in four out of the six reported patients. As demonstrated from the survey results, umbilical cord handling method is not routinely documented. The survey results highlight the heterogeneity in umbilical cord handling practices among obstetric care providers and the recent changes in umbilical cord handling practice. It is important to note that the survey results are not generalizable to obstetric care providers working at other institutions. Additionally, there is a potential for non-response bias as the number of survey nonresponders is unknown.

5. Conclusion

There was an increased incidence of neonatal MI at our institution due to coronary thrombosis, which may reflect the improved disease diagnosis due to a higher index of suspicion. Early diagnosis and initiation of therapy can improve outcomes of neonatal MI. Further prospective studies and improved documentation of cord handling practices are needed to assess risk factors and outcomes of neonatal MI.

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Declaration of competing interest

No authors have any conflict of interests, financial or otherwise, related to the content of this manuscript.

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