INPLASY PROTOCOL

Corresponding author:
Jingyi Wang

metamorphosisara@gmail.com

Author Affiliation:
Hainan Modern Women and Children's Hospital

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Review Stage at time of this submission: Piloting of the study selection process

Conflicts of interest: No.

Incidence and mortality of Neonatal pericardial effusion associated with central venous catheters: A meta-analysis of retrospective cohort studies, case series and case reports

Wang J[1]; Du, J[2]; Usman, M[3].

ABSTRACT

Review question: 1. What is the incidence of pericardial effusion in neonates with central venous catheters worldwide (approximately one pericardial effusion every 200 neonated with central venous catheter)? 2.What factors(e.g. catheter tip position, whether regularly recheck tip positions by ultrasound or not, type of catheter, catheter material, developing or developed countries, year before or after 2004) are relevant to this incidence? 3.Why is it urgent to analyze this incidence? 4.How to lower this incidence? 5.What is the mortality rate of this condition? 6.What (e.g., pericardiocentesis, adrenaline, timely indentification of this condition) can be done to improve prognosis and reduce mortality?

Rationale: Neonatal pericardial effusion(PCE) is mostly induced by perforation or osmotic injury of central venous catheters (peripherally inserted central catheter, umbilical venous catheter, etc.). According to our preliminary evaluation, the incidence of this complication is approximately 0.5% among NICU patients with central venous catheters. Because of its rarity and the fact that only a few cases had undergone autopsies, this complication is under-estimated, possibly poorly-understood.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 March 2020 and was last updated on 29 March 2020 (registration number INPLASY202030014.

INTRODUCTION

Objectives / Review question: 1. What is the incidence of pericardial effusion in neonates with central venous catheters worldwide (approximately one pericardial effusion every 200 neonated with central venous catheter)? 2.What factors(e.g. catheter tip position, whether regularly recheck tip positions by ultrasound or not, type of catheter, catheter material, developing or developed countries, year

before or after 2004) are relevant to this incidence? 3.Why is it urgent to analyze this incidence? 4.How to lower this incidence? 5.What is the mortality rate of this condition? 6.What (e.g., pericardiocentesis, adrenaline, timely indentification of this condition) can be done to improve prognosis and reduce mortality?

Rationale: Neonatal pericardial effusion(PCE) is mostly induced by perforation or osmotic injury of central venous catheters (peripherally inserted central catheter, umbilical venous catheter, etc.). According to our preliminary evaluation, the incidence of this complication is approximately 0.5% among NICU patients with central venous catheters. Because of its rarity and the fact that only a few cases had undergone autopsies, this complication is under-estimated, possibly poorly-understood.

Condition being studied: The neonatal intensive care units which regularly check catheter tip positions have found out that migration is almost inevitable. More than 20% of catheter tips are confirmed to be intracardiac despite correct initial position (outside the cardiac silhouette). Without serial evaluation of catheter placement and timely withdrawal to ensure a safe location, an ignored intracardiac catheter tip puts the newborn at risk of PCE. The majority of PCE cases deteriorate into cardiac tamponade(CT) with an estimated mortality rate of 60%. In this review, we aim to figure out the incidence and mortality rate of this condition as accurately as possible. And by statistical analysis, we will examine the risk factors of PCE/CT and provide references for future practice.

METHODS

Participant or population: Participants inclusion criteria: neonates with a central venous catheter for parenteral nutrition and medication infusion will be included in our review. Participants exclusion criteria: neonates with cancer, congenital heart diseases, cardiovascular deformities, inherited metabolic disorders and neonates who had cardiovascular surgery, ECMO, dialysis will be ruled out.

Intervention: This is a meta-analysis of single rate. Intervention or exposure is not applicable.

Comparator: This is a meta-analysis of single rate. There is no control group or comparator.

Study designs to be included: Studies with explicit sample size (number of neonates with central venous catheters) and disease group size.

Eligibility criteria: Study selection: Two reviewers will independently screen titles and abstracts of the searched results according to the eligibility criteria. The third reviewer will arbitrate the disagreements. Excel worksheets will be used to record study information. Data extraction: Two reviewers will identify data from the included studies with the aid of data extraction forms independently. Following data are to be extracted: author, year of publication, title, country, characteristics of neonates (e.g., weight), catheter type (PICC, UVC or others) , catheter material (polyurethane or silicone), sample size, disease group size, whether NICU units of the study recheck the tip position or not. The third reviewer will check the extracted data and settle the disagreements between individual judgements. If there is critical unreported data, investigators will be contacted for it. Excel worksheets will be used to record data. disease group size.

Information sources: Sources: MEDLINE, Embase, Cochrane Library, Web of Science, CNKI, Wanfang Data, CBM(sinomed) Search dates: not restricted (from when central venous catheter started to apply in neonates 1973 to date).

Main outcome(s): Incidence of neonatal pericardial effusion associated with central venous catheters. Central catheters venous catheters include PICC, UVC, etc. Pericardial effusions are diagnosed by ultrasound.

Search strategy: #1 ((((((central venous catheter[Title/Abstract]) OR PICC[Title/Abstract]) OR Peripherally inserted central catheter[Title/Abstract]) OR umbilical venous catheter[Title/Abstract]) OR central line[Title/Abstract]) OR Umbilical Vein Catheterization[Title/Abstract]) OR Central Venous Catheterization[Title/Abstract] #2 (((pericardial effusion[Title/Abstract]) OR cardiac tamponade[Title/Abstract]) OR hydropericardium[Title/Abstract]) OR PCE/CT[Title/Abstract]#3 ((((((((((neonate[Title/Abstract]) OR neonatal[Title/Abstract]) OR infant[Title/Abstract]) OR newborn[Title/Abstract]) OR NICU[Title/Abstract]) OR Intensive Care Units, Neonatal[Title/Abstract]) OR Intensive Care, Neonatal[Title/Abstract]) OR preterm[Title/Abstract]) OR premature[Title/Abstract]) OR baby[Title/Abstract]) OR babies[Title/Abstract] #4 ((#1) AND #2) AND #3

Data management: Excel worksheets are used to manage records and data.

Quality assessment / Risk of bias analysis: To assess risk of bias, full texts of included retrospective cohort studies will be downloaded. Their selection, comparability and outcome domains will be scrutinized using the Newcastile-Ottawa scale(NOS) . A final score of 6 will be regarded as high quality.

Strategy of data synthesis: To synthesize individual study incidence, we will use STATA version 16.0 to combine data. The estimate of combined incidence will subsequently be computed using random-effects model; and the estimate of heterogeneity will be calculated using Freeman-Tukey double arcsine transformation of proportions. In this way, studies with zero events and rare events will be included. Transformed rates with confidence intervals will be carried out using random-effects meta-analysis, and result will be displayed in forrest plots. Heterogeneity will be evaluated using I^2 statistic.

Sensibility analysis: Influence analysis will be used by the removal of each study respectively.

Subgroup analysis: Subgroup 1: intracardiac catheter tip position. Intracardiac position dramatically increases the risk of pericardial effusion. Most guidelines have specified the safe placement of the catheter tip to be outside the cardiac silhouette.The number of malpositioned tips in studies with or without pericardial effusion patients will be assessed respectively. Subgroup 2: studies without routinely recheck tip positions. Without serial evaluation of catheter placement and timely withdrawal to ensure a safe position, an ignored intracardiac catheter tip puts the newborn at risk of PCE. The incidence rate of studies which routinely recheck tip positions and otherwise will be assessed respectively. Subgroup 3: catheter type (PICC versus UVC). UVC is more prone to migrate, which could result in greater risk for PCE. The number of patients using PICC and the numer of patients using UVC will be assessed respectively. Subgroup 4: catheter material (polyurethane versus silicone). As is the fact that polyurethane is stiffer than silicone, some suggests that polyurethane catheters should not be used in neonates. The number of patients number using polyurethane catheters and the numer of patients using silicone ones will be assessed respectively. We will use meta-regression analysis based on the intracardiac catheter tip position, studies without routinely recheck tip positions, UVC, polyurethane catheters to indentify source of heterogeneity of pericardial effusion incidence.

Language: No limitation.

Countries involved: The United States, the United Kingdom, Germany, Italy, Brazil, China, etc.

Keywords: Neonates pericardial effuision; cardiac tamponade; Central venous catheter.

Dissemination plans: Completion date: 01/06/2020.

Contributions of each author:

Author 1 - The work is a product of the intellectual environment of the whole team; and that all members have contributed in various degrees to the analytical methods used, to the research concept, and to the experiment design.

Author 2 - The work is a product of the intellectual environment of the whole team; and that all members have contributed in various degrees to the analytical methods used, to the research concept, and to the experiment design.

Author 3 - The work is a product of the intellectual environment of the whole team; and that all members have contributed in various degrees to the analytical methods used, to the research concept, and to the experiment design.