УДК 616.12-008.1-07-059.31 МРНТИ 76.29.30,76.29.47

NON-INVASIVE METHODS FOR CARDIAC OUTPUT MEASUREMENT IN NEWBORNS: AN APPRAISAL OF THE LITERATURE

GIOVANNI FARELLO

Pediatric Unit University of L'Aquila, L'Aquila, Italy

Giovanni Farello – https://orcid.org/0000-0002-3230-7555

For citing/ библиографиялық сілтеме/ библиографическая ссылка:

Farello G. Non-invasive methods for cardiac output measurement in newborns: an appraisal of the literature. West Kazakhstan Medical Journal 2019;61(4):212–218.

Farello G. Жаңа туған нәрестелерде Неинвазивные методы измерения сердечного выброса у новорожденных: оценка литературы. West Kazakhstan Medical Journal 2019;61(4):212–218.

Farello G. Неинвазивные методы измерения сердечного выброса у новорожденных: оценка литературы. West Kazakhstan Medical Journal 2019;61(4):212–218.

Non-invasive methods for cardiac output measurement in newborns: an appraisal of the literature

Giovanni Farello Pediatric Unit, University of L'Aquila, L'Aquila, Italy

Hemodynamic disorders accompany any severe pathology in patients of all age groups, including newborns, significantly affect the further quality of life of patients who have undergone critical conditions. The clinical manifestations of hemodynamic disturbances in young children are not specific, they are significantly delayed and, accordingly, are not always recognized in time. Great progress has been made recently in cardiac output assessment in newborn infants. Back in the 1970's cardiac output assessment in neonates was obtained using the Fick method and the dilution or thermodilution methods, these invasive methods are risky and disadvantageous.

An ideal cardiac output monitoring system should be non-invasive, easy to use and reliable. Non-invasive monitoring of cardiac output is a subject of great interest in the treatment of emergency and critical conditions in newborns. Monitoring of hemodynamic parameters allows you to detect minimal changes in the vital functions of the body in the early stages. To ensure the timely start of intensive care, its high-quality conduct and not only increases survival, but also leads to a decrease in disability in newborns due to hypoxic lesions of the central nervous system.

In this literature review we present and compare various noninvasive methods currently used to measure cardiac output in newborn infants and highlight their advantages and disadvantages.

Keywords: newborn, hemodynamic, cardiac output measurement, monitoring, USCOM.

Жаңа туған нәрестелерде жүрек шығуын өлшеудің инвазивті емес әдістері: әдебиетті бағалау

Giovanni Farello

Л'Аквила университеті, Л'Аквила, Италия

Accepted/

. 19.12.2019

Басылымға қабылданды/

Принята к публикации:

Гемодинамикалық бұзылыстар барлық жастағы пациенттерде кез келген ауыр патологиямен бірлесіп келеді, сонымен бірге критикалық жағдайға ұшырған жаңа туған нәрестелердің өмір сапасына айтарлықтай әсер етеді. Ерте жастағы балаларда гемодинамикалық бұзылыстарының кеш диагностикасы клиникалық өзгерістерінің айқын болу-болмауына байланысты. Жақында жаңа туған нәрестелердегі жүрек жұмысын бағалауда үлкен жетістіктерге қол жеткізілді. 1970 жылдары жаңа туған нәрестелердегі жүрек-қан айдау көрсеткіштері Фик эдісімен сұйылту немесе термодиляция әдістерін қолдану арқылы алынды, бұл инвазивті әдістер қауіпті және қолайсыз болып табылады. Жүректің қан айдау қызметінің бақылау әдісі инвазивті емес, қолдануға оңай және сенімді болуы керек. Шұғыл және жедел жағдайға ұшыраған жаңа туған нәрестелердің емінде жүректің қан айдау қызметінің инвазивті емес әдістері үлкен қызығушылық тудырады. Гемодинамикалық параметрлердің мониторингі ерте кезеңдерде ағзаның өмірлік маңызды функцияларындағы ең аз өзгерістерді анықтауға мүмкіндік береді. Интенсивті терапияның уақтылы басталуын қамтамасыз ету үшін, оны сапалы түрде жүргізу өмір сүруді арттырып қана қоймайды, сонымен қатар орталық жүйке жүйесінің гипоксиялық зақымдануы салдарынан нәрестелерде мүгедектіктің төмендеуіне әкеледі.

Осы әдебиетке шолуда қазіргі кезеңде нәрестелерде жүрек қан айдау қызметін



Giovanni Farello e-mail: giovanni.farello@ cc.univaq.it Received/

Келіп түсті/

Поступила:

, 04.12.2019.

West Kazakhstan Medical Journal 61 (4) 2019

ISSN 1814-5620 (Print)

Published by West Kazakhstan Marat Ospanov

© 2019 The Authors

Medical University

анықтау үшін қолданытлатын әртүрлі инвазивті емес әдістерді ұсынып салыстырамыз, олардың артықшылықтары мен кемшіліктерін атап көрсетеміз. *Негізгі сөздер:* жаңа туған нәресте, гемодинамика, жүректің қан айдау қызметін өлшеу, мониторинг, USCOM.

Неинвазивные методы измерения сердечного выброса у новорожденных: оценка литературы

Giovanni Farello

Университет Л'Аквила, Аквила, Италия

Гемодинамические нарушения сопровождают любую тяжелую патологию у пациентов всех возрастных групп, в том числе и новорожденных, существенно влияют на дальнейшее качество жизни пациентов, перенесших критические состояния. Клинические проявления нарушений гемодинамики у детей раннего возраста не являются специфичными, значительно запаздывают и, соответственно, не всегда вовремя распознаются. В последнее время достигнут большой прогресс в оценке сердечного выброса у новорожденных. Еще в 1970-х годах оценка сердечного выброса у новорожденных была получена с использованием метода Фика и методов разведения или термодилюции, эти инвазивные методы являются рискованными и невыгодными. Идеальная система мониторинга сердечного выброса должна быть неинвазивной, простой в использовании и надежной. Неинвазивный мониторинг сердечного выброса является предметом большого интереса в терапии неотложных и критических состояний у новорожденных. Мониторный контроль показателей гемодинамики позволяет обнаружить минимальные изменения витальных функции организма на ранних стадиях. Обеспечение своевременного начала интенсивной терапии и ее качественное проведение не только способствует увеличению показателей выживаемости, но и приводит к снижению показателей инвалидности у новорожденных, связанных с гипоксическими поражениями центральной нервной системы.

В этом обзоре литературы мы представляем и сравниваем различные неинвазивные методы, используемые в настоящее время для измерения сердечного выброса у новорожденных детей, и выделяем их преимущества и недостатки.

Ключевые слова: новорожденный, гемодинамика, измерение сердечного выброса, мониторинг, USCOM.

Introduction

The aim of this literature review is to present and compare various noninvasive methods currently used to measure cardiac output in newborn infants and highlight their advantages and disadvantages.

Great progress has been made recently in cardiac output assessment in newborn infants. Back in the 1970's cardiac output assessment in neonates was obtained using the Fick method and the dilution or thermodilution methods [1].

These invasive methods are risky and disadvantageous [2].

The Fick method measures blood flow to an organ based on the principle that it is possible to calculate the blood flow if the amount of the liquid taken by that organ is known over time, and the quantity of the liquid can be calculated both proximal to and distal to that organ. The main disadvantage of this technique is the necessity for arterial and venous lines and precise calculation of breathby-breath oxygen consumption which could prove challenging in term and in particular, preterm neonates [3].

The indicator-dilution method consists in injecting a known quantity of a dye in the pulmonary artery and measuring the dye concentration through a peripheral arterial line. The main problem with this method is due to the rapid pulmonary circulation time in newborn infants and the recurring presence of a left-to-right shunts resulting in unreliable outcomes [1].

Thermodilution method consists in placing a specific catheter within the pulmonary artery provided with a temperature probe on the distal extremity, like the Swan-Ganz catheter. Even though this technique has shown good correlation with both Fick method and dye-dilution its use is limited by technical restraints [3].

Cardiac output and physiologic changes in the circulation occurring from fetal to neonatal life transition

Cardiac output, expressed in litres/minutes, is the amount of blood the heart pumps in 1 minute. Cardiac output is the product of the stroke volume and the number of beats per minute (heart rate), and it determined by: heart rate, contractility, preload and afterload [4].

Accurate measurement of cardiac output is very important in newborn infants. There are several important differences between fetal and neonatal circulations: the presence of a low-resistance high-flow placental circulation in the fetus; less than 10% of total cardiac output enters the lungs. There are also important shunts present in the fetal life to consider: the ductus venosus and the foramen ovale channel oxygenated blood from the placenta into the left side of the heart to reach coronary and cere-

bral circulation; the ductus arteriosus directs the majority of right ventricular output to the systemic circulation in a right-to-left flow pattern because of high pulmonary vascular resistance. At birth, arterial oxygen tension starts rising and pulmonary vascular resistance begin to fall facilitating an increase in pulmonary blood flow. Increased oxygen tension leads to the ductus arteriosus constriction; This process is usually completed within 60 hours in 93% of term infants. At the same time, increased lung blood flow causes increased pulmonary venous return to the left atrium, and as a result the pressure rises and closes the foramen ovale. The diminished flow through the ductus venosus is caused by the loss of the umbilical venous return and its passive closure usually occurs within 3-7 days after birth [5].

The transition from fetal to neonatal life is associated with a significant increase in systemic vascular resistance (SVR) which leads to an increase in left ventricular (LV) afterload. This occurs following the loss of the low resistance placental circulation and the increase in vasoconstrictor substances as vasopressin and thromboxane A2 [6]. Pulmonary arterial vasodilatation results in decreased pulmonary vascular resistance (PVR). This is facilitated by the increase in the partial pressure of oxygen accompanying lung aeration and the increased production of vasodilators such as prostaglandins, bradykinins and histamine [7]. "The increase in SVR and decrease in PVR allows right ventricular output to shunt towards the pulmonary vascular bed instead of the ductus arteriosus ensuring that LV preload is maintained by adequate pulmonary venous return. An adequate LV preload is essential for an adequate LV output (LVO) in the face of rising LV afterload. Consequently, right ventricular preload becomes dependent on systemic venous return, and right ventricular afterload remains low owing to decreasing PVR" [8].

In addition to heart rate, stroke volume is an important determinant of cardiac output. Van Vonderen et al. suggested that the increase of LVO occurring after birth is a result of an increasing stroke volume rather than hearth rate. In fact, we may observe significant increase in left ventricular dimension and LVO in the first 5 min after birth which usually stabilizes at 10 min, whereas blood pressure (BP) remains stable. LVO and left ventricular dimension increase is a result of the increase in left ventricular preload resulting from pulmonary blood flow [9].

Special considerations for preterm infants

The risk for hemodynamic compromise in preterm infants is high because of the additional challenges they face during the transition period. Firstly, the myocardium of a preterm infant lacks an efficient contractile mechanism which may lead to impaired systolic performance; secondly, they show a preponderance of noncontractile, less compliant collagen which results in impaired diastolic performance [10]. Furthermore, preterm infants usually spend less time in diastole because of a relatively faster heart rate [11]. Consequently, they show difficulty in tolerating increased afterload and lack the necessary reserve to cope with reduced preload. In addition, the presence of left-to-right shunting across a patent ductus arteriosus (PDA) and a patent foramen ovale (PFO) reduce systemic blood flow due to the shunting of blood to the lungs instead of the systemic circulation [8]. Another important factor which could compromise cardiac output is positive end-expiratory pressure, which is necessary for maintaining an adequate functional residual capacity in the lung [12].

Noninvasive cardiac output monitoring in newborns. Neonatal Echocardiography

In the 1980's, there was a drive to employ less invasive methods for cardiac output assessment. This has led to studies focusing on the use of pulsed Doppler ultrasonography for measuring cardiac output. Alverson DC et al. measured mean velocity of ascending aorta blood flow and derived cardiac output in 8 preterm and 14 term healthy infants under one week of age using a 5MHz pulsed Doppler velocimeter, demonstrating that cardiac output values obtained with this noninvasive technique were comparable to the ones achieved with invasive methods such as cardiac catheterization and thermodilution. They also pointed out that this noninvasive and nontraumatic method is portable and it can be used at the bedside. Therefore, is a safe technique and its methodology can be easily learned by the medical operator [13].

In recent years, neonatologists have become more interested in echocardiography because of its ability to assess and monitor hemodynamic status in infants in an intensive care setting [14].

Echocardiography can provide information about the ductus arteriosus and cardiac functional information, and this could be useful to estimate a wide range of hemodynamic measures [15].

Different terms are used to indicate this method such as functional echocardiography, point of care ultrasound, targeted neonatal echocardiography and neonatologist-performed echocardiography (NPE). Those terms describe the use of echocardiography for assessing circulatory status in preterm and term infants. As recently pointed out by Dempsey EM et al. "one of the main uses of NPE is the assessment of cardiac output and end-organ perfusion. Left and right ventricular outputs (LVO and RVO) are often measured as an attempt to determine systemic and pulmonary blood flow states" [16].

Point of care echocardiography could be performed in different ways: two-dimensional grey scale echocardiography which is commonly used to analyze the structural anatomy of the heart, pulsed and continuous wave Doppler which allows the measurement of blood flow and m-mode methods which allows to focus on chamber size, wall thickness, valvular motion and evaluate myocardial function [17].

"Left and right ventricular output can be estimated by measuring the annulus of the aortic or pulmonary valve and the velocity/time integral of the Doppler waveform of the flow through those valves (averaged over three cycles). Stroke volume is calculated and multiplied by the heart rate to derive the output (mL/ min). This is often divided by the patient's weight to derive an index (mL/kg/min)" [15].

However, the presence of a left-to-right shunt could alter measurement of LVO, this is usually the result of a patent ductus arteriosus (PDA) which, through the left to right shunting, causes an increased pulmonary venous and an increase in LVO without an improvement in systemic blood flow. RVO could be used to represent systemic venous return but it can be confounded by the presence of an inter-atrial communication which increases RVO [16]. With echocardiography it is also possible to assess superior vena cava (SVC) flow which is used as a surrogate marker for systemic blood flow because it is a direct reflection of venous return from the brain and upper body and is not affected by shunts [17]. In addition to evaluation of cardiac output, functional echocardiography is a very useful method for the assessment of PDA significance, determining potential benefit of treatment, evaluating if treatment resulted in PDA closure and assessing presence or severity of pulmonary hypertension [18].

Concerning echocardiography reliability, Ficial B. et al. used compared echocardiography to PC MRI (Phase-contrast magnetic resonance imaging) to assess the accuracy of LVO measurement in newborn infants. They enrolled 49 infants with a median gestational age of 32 weeks and a median weight at birth of 1,750 g and they performed paired PC MRI and echocardiography examinations. LVO measured using echocardiography demonstrated good correlation with PC MRI with a small mean bias of -9.6 mL/Kg/min between PC-MRI and echocardiography. This study, therefore, supports the use of echocardiography for LVO assessment due to the high degree of accuracy showed when compared with PC MRI [19].

In conclusion, even though neonatal echocardiography is an invaluable method of hemodynamic assessment, its limits are represented by the need for expensive equipment and extensive training to perform cardiac output evaluations [17]. The main problems with echo are the following: firstly, it requires well trained and accredited echographers; secondly, the assessment takes some time due to multiple measurements needed and may lead to clinical instability and inter-rater variability; and thirdly, unfortunately it cannot be used as a continuous monitoring tool [16].

NICOM (Noninvasive Cardiac Output Monitor)

The necessity of a noninvasive continuous method for cardiac output monitoring in neonatal unit has led to the development of a new technique called bio-impedance which is a measure of how well the body hinders electric current flow, also defined as the expanded theory of the electrical conductance through body tissues. Two different methods were derived from this theory such as Electrical Velocimetry (EV) and trans-thoracic bioreactance (TBR) [16].

The noninvasive continuous cardiac output monitor (NICOM) exploits trans-thoracic bioreactance which is "based on an analysis of relative phase shifts of oscillating currents that occur when an injected current traverses the thoracic cavity". To achieve this, four emitting and receiving electrodes must be placed so that they can "box" the heart [20].

One of the studies assessing the feasibility of the use of NICOM in neonates was published in 2012: Weisz DE et al. measured left ventricular output (LVO) in 10 infants with a median birth weight of 2.72 kg and a median gestational age of 37 weeks using Echo and NICOM simultaneously over a 2- to 4-hour period, obtaining 97 paired NICOM and Echo assessments of LVO. The median NICOM-derived LVO measurements were lower than Echo ones by 153±56 ml/kg showing that NICOM consistently under-read LVO by 31%. Even though this study has demonstrated the feasibility of NICOM in newborns, it has also showed that NICOM cannot provide accurate measure of LVO because a systematic bias of 31% [20]. Later in 2014, Weisz et al. tried to evaluate utility of NICOM in preterm infants under 30 weeks' gestation undergoing patent ductus arteriosus (PDA) ligation for LVO assessment compared with Echo. Twenty-six preterm infants underwent 78 paired Echo and NICOM assessments and once again an overall NICOM-Echo systematic bias of 39% in LVO measurements was found showing that NICOM tend to underestimate echocardiography values. This study also demonstrated an increasing in bias between NICOM and echocardiography with increasing time of monitoring [21].

More recently, Forman et al. used NICOM to measure CO in infants with neonatal encephalopathy (NE) undergoing therapeutic hypothermia (TH) and compared the results with Echo-derived CO.

They enrolled 20 infants older than 35 weeks gestation with a median birth weight of 3.6 kg and a diagnosis of NE requiring TH. NICOM measurements of CO were started within 10 hours of TH initiation and once again, after NICOM-derived CO were compared with Echo-derived ones a strong positive correlation between the two was found but NICOM-CO were lower than Echo-CO showing a bias of 27% [22].

Although all previously mentioned studies demonstrated the feasibility and the reliability of NICOM compared with Echo, they also showed that NICOM tend to under-read Echo with a systematic bias of 27-30%.

One of the possible reasons for this bias is that NICOM algorithm used to calculate aortic diameter size in neonates is derived from adults resulting in lower CO values with NICOM [23]. On the other hand, echocardiography could be responsible for overestimating CO because it uses blood flow velocity in the central portion of aortic root to assess CO [20]. Even though further studies are required, NICOM could be an efficient non-invasive continuous method for cardiac output assessment in both healthy term, late-preterm and preterm infants after PDA ligation but its use should be confined to monitoring trends in cardiac output after always a preliminary Echo evaluation.

EV (Electrical Velocimetry)

Electrical Velocimetry is a noninvasive method for continuous monitoring of cardiac output which has showed a good correlation with many of the invasive methods in adults, children and recently in newborn infants. It differs from NICOM as it is based on impedance cardiography technology and consists of four electrocardiographic electrodes which are placed over the skin of the forehead, left side of the neck, left midaxillary line at the level of the xiphoid process and left thigh. A small alternating electrical current flows through the infant from the outer electrocardiographic electrodes and the obtained voltage is measured by the inner electrodes. Blood flow in the ascending aorta is the major factor contributing to conductance (1/impedance) and the impedance of the flow of the current is related to the alignment of red blood cells in the ascending aorta; precisely, when aortic valve opens during systole, red blood cells align allowing the forward flow of blood in the ascending aorta and causing a sudden decrease of impedance. On the contrary, during diastole blood cells misalign and the blood flow in the ascending aorta stops resulting in an increase of impedance. Therefore, the difference between the measured voltage during systole and diastole serves as the basis for CO assessment.

In 2012 Noori et al. tried to validate the use of EV in neonates by investigating the agreement between EV and echocardiography for cardiac output measurement.

They enrolled 20 healthy term neonates during the first two postnatal days and at three time points within a 30 minutes period they measured LVO both with EV and echocardiography on the first day and second day after birth. After a total of 115 pairs of LVO measurements they found out similar values of LVO with EV and echocardiography (534±105 vs 538±105 ml/min) with a bias and a precision of EV of -4 and 234 ml/min. They also tried to calculate the true precision of EV and comparing it with the precision of echocardiography they resulted similar (31,6% vs 30% respectively). This study pointed out how EV accuracy and precision in assessing cardiac output are highly comparable with echocardiography in healthy term infants but additional studies in both preterm and term neonates with hemodynamical instabilities are essential to evaluate its validity for detecting cardiac output changes [24].

In 2015 Ma et al. tried to evaluate cardiac output changes in response to short-term prone positioning in neonates using EV to monitor CO. They enrolled 30 hemodynamically stable neonates with a mean gestational age of 35 weeks and they were studied initially while lying supine, then in prone position and finally back-to-supine position. They noticed that heart rate (HR) remained stable during the change in position while 26 neonates showed a decreasing in stroke volume (SV) and CO when placed in prone position with CO decreasing from 206±44 to 180±41 ml/kg/min. They however highlighted the limitations of using EV such as the possibility of measurement errors or the unknown effect of prone positioning on thoracic bioimpedance. Despite these limitations they could demonstrate significant changes in cardiac and vascular function in response to prone positioning [25].

Later in 2017, Wu et al. tried to investigate changes

in cardiac output and cerebral oxygenation between supine and prone position in healthy neonates. They enrolled 34 healthy term infants with a mean age of 4 days and a mean birth weight of 3.2 kg who underwent 66 sets of CO measurements, 34 with EV and 32 with echocardiography while they were placed in supine, prone and backto-supine position for 15 minutes during the sleep. They detected a decrease in CO in prone position with mean EV-derived CO values decreasing from 182±57 to 170±50 ml/kg/min and echo-derived CO values decreasing from 193±48 to 174±40 ml/kg/min. They identified the intrinsic imprecision of both EV and echocardiography as a limitation but both methods showed a decreasing in CO during prone position suggesting that these findings cannot be considered errors related to device limitations [26].

Recently, Wu et al. tried to define systemic and cerebral hemodynamic changes in response to the increase in core temperature during the rewarming phase of therapeutic hypothermia in infants with hypoxic-ischemic encephalopathy (HIE) using EV to assess CO from 4 hours before the start of rewarming to 1 hour after its completion [26]. They also used echocardiography and transcranial Doppler 3 hours and 1 hours before starting rewarming and then at 2, 4 and 7 hours after the start of it to assess CO and others hemodynamic parameters [27].

Previous studies have already detected hemodynamic changes during the rewarming phase of TH such as an increase in cardiac output and systolic blood pressure and a decrease in systemic vascular resistance (SVR) and diastolic blood pressure [28]. However, these studies used just a single monitoring tool instead of comparing results obtained by different methods.

Therefore, Wu et al. enrolled 20 infants with HIE with a mean gestational age of 38 weeks and a mean birth weight of 3.5 kg and they demonstrated that there were no significant changes in HR, systolic and diastolic blood pressure, echo- and EV-derived CO and others hemodynamic parameters between 4 to 1 hour before rewarming started while during rewarming there were an increase in HR and in echo- and EV-derived CO. EV-CO was increased from 153 ± 43 to 197 ± 42 ml/Kg/min after completion of rewarming (overall CO increase of 29%) while echo-CO was increased from 149 ± 35 to 179 ± 34 ml/Kg/min (overall CO increase of 20%) [27].

In conclusion, all previously mentioned studies have used EV for noninvasive assessment of CO and comparing these results with echocardiography CO assessments they showed good agreement even though further studies are required to confirm electrical velocimetry reliability for use in the NICU.

USCOM

USCOM (Ultrasonic Cardiac Output Monitor) is a non-invasive transcutaneous method for measuring cardiac output (CO) based on continuous wave Doppler ultrasound. Its clinical use started in 2001 but since then it was successfully used only in adults while its feasibility in neonates has recently started to be assessed [29].

This method uses transaortic or transpulmonary Dop-

pler ultrasound flow tracing to measure cardiac output in a method similar to that of echocardiography [30].

In 2010 Patel at al. tried to assess the agreement between USCOM-derived cardiac output measurements and Echo-derived measurements in newborn infants. They enrolled 56 infants with a median gestational age of 39 weeks, a median weight of 3.4 kg with no evidence of hemodynamic shunts or structural or functional cardiovascular problems. To assess the agreement between Echo and USCOM paired measurements of both LVO and RVO were conducted using each method and they found out that mean Echo-derived RVO value was lower than USCOM-derived one (279 vs 338 ml/kg/min) while there wasn't significant difference in mean LVO between the two methods (251 vs 233 ml/kg/min). This study highlighted that RVO measurement with USCOM were higher than Echo ones leading to errors while LVO values showed better agreement. As a result, RVO measurement with USCOM cannot be considered reliable for clinical use. One of the possible reasons of measurement error could be represented by erroneous positioning of the Doppler sample, difficulty in minimizing angles of insonation of the Doppler beam or miscalculation of the accurate position of the Doppler beam due to the lack of two-dimensional imaging [31].

Later in 2013 Zheng et al. tried to investigate the reliability and clinical utility of USCOM in term and preterm healthy neonates comparing cardiac output measurements obtained by USCOM and Echo. They enrolled 20 term infants with a mean gestational age of (38.1 ± 0.56) weeks, a mean weight of (3.2 ± 0.29) kg and a mean Apgar score of 10 and 29 preterm infants with a mean gestational age of (32.6 ± 2.8) weeks, and a mean weight of (1.88 ± 0.57) kg. They measured RVO and LVO using USCOM and Echo in term infants finding a bias between USCOM and Echo of (30.6 ± 51.1) ml/(kg·min) for LVO and (-21.8 ± 105) ml/(kg·min) for RVO with a mean % error of 21% for LVO and 33.2% for RVO. In preterm infants the agreement between Echo and USCOM was (24.1 \pm 71.2) ml/ (kg·min) for LVO measurements and (-29.5 \pm 192.9) ml/ (kg·min) for RVO values with a mean % error of 27.4% for LVO and 51.8% for RVO. This study demonstrated a very poor agreement between USCOM and echocardiography for RVO measurement and RVO values assessed by USCOM cannot be recommended for clinical use [32].

More recently Beltramo et al. tried to assess validity of cardiac output measurements performed by USCOM comparing them with CO values obtained with pulmonary arterial catheter (PAC). They enrolled 31 children under 18 years with normal cardiac anatomy showing a bias between the two methods for CO assessment of 0.2 L/min and a mean % error of 11%. They consequently demonstrated that USCOM-derived CO measurements could reliably represent PAC-derived CO values in healthy children [33]. Although these results cannot be extended to neonates because the use of PAC is not feasible, USCOM has previously shown a good intra- and inter-observer reliability in newborns [34]. USCOM, as above mentioned, has been recommended for clinical use for LVO measurement but it is not interchangeable with Echo for RVO assessment. Even though USCOM is a fast and convenient noninvasive hemodynamic monitoring method for newborns some limitations can be underlined: firstly, this method uses continuous wave Doppler and turbulence or acceleration due to abnormal valves or arteries can interfere with the signal [35]; secondly, USCOM doesn't use a 2D Echo as guide for placing the beam, leading to a larger than usual Doppler velocity time integrals (VTI); thirdly, it is difficult to determine the proper angle of insonation with USCOM method because, even if the dominant signal is obtained from the aortic valve, wrong vessel or wrong region could be insonated due to lack of experience [33].

In conclusion, further studies are required to assess the reliability of USCOM in detecting clinically significant changes in cardiac output in both healthy and unhealthy neonates.

Conclusions

Monitoring hemodynamic status in term and preterm newborn infants can be challenging. That is the reason why most of the noninvasive methods which resulted successful in adult patient are starting to be adopted in newborns showing promising results. The most reliable of them has remains to be echocardiography but one of its main limitation is to be a non-continuous hemodynamical assessment method while other noninvasive monitoring methods such as NICOM or EV could be used continuously and without any risk for neonates. Further studies are needed to detect the reliability of this noninvasive encouraging monitoring methods in newborn infants as they could represent an important turning point in the management of both healthy and unhealthy neonates.

References:

24:1057-1078.

- 3. McGovern M, Miletin J. Cardiac output monitoring in preterm infants.
- Vincent JL, Understanding Cardiac Output. Critical Care. 2008;12(4):174.
- Archer N, Cardiovascular disease. Textbook of Neonatology, Third Edition, Janet M. Rennie, N.R.C. Roberton, 1999.
- Liedel JL, Meadow W, Nachman J, et al. Use of vasopressin in a refractory hypotension in children with vasodilatory shock; five cases and a review of the literature. Pediatr Crit Care Med.

Emmanouilides GC, Moss AJ, Michelle Monset-Couchard, Marcano BA et al. Cardiac Output in newborn infants. Biol Neonate. 1970;15:186–197.

Mertens L, Seri I, Marek J, Arlettaz R, Barker P, McNamara P, Moon-Grady AJ et al. Practice Guidelines and Recommendations for Training Writing group of the American Society of Echocardiography (ASE) in collaboration with the European Association of Echocardiography (EAE) and the Association for European Pediatric Cardiologists (AEPC). J Am Soc Echocardiogr. 2011;

2002;3(1):15-8.

- Lang JA, Pearson JT, te Pas AB, et al. Ventilation/perfusion mismatch during lung aeration at birth. J Appl Physiol. (1985). 2014;117(5):535–43.
- El-Khuffash AF, McNamara PJ. Heamodynamic Assessment and Monitoring of Premature Infants. Clin Perinatol. 2017;44(2):377– 393.
- Van Vonderen JJ, Roest AA, Siew ML, et al. Noninvasive measurement of heamodynamic transition directly afterbirth. Pediatr Res 2014;75(3):448–52.
- Rowland DG, Gutgesel HP. Noninvasive assessment of myocardial contractility, preload, and afterload in healthy newborn infants. Am J Cardiol. 1995;75(12):818–21.
- 11. Ali I, Ryan CA. Transient renal failure in twins with maternal Cox-1/Cox-2 use in pregnancy. Ir Med J. 2005;98(10):249–50.
- Fajardo MF, Claure N, Swaminathan S, et al. Effect of positive end-expiratory pressure on ductal shunting and systemic blood flow in preterm infants with patent ductus arteriosus. Neonatology. 2014;105(1):9–13.
- Alverson DC, Eldridge MW, Johnson JD et al. Noninvasive measurement of cardiac output in healthy preterm and term newborn infants. American J Perinatology. 1984;1(2):148–151.
- 14. Skinner J, Alverson D, Hunter S, editors. Echocardiography for the neonatologist. Edinburgh: Churchill Livingstone; 2000.
- Wyllie J, Neonatal echocardiography, Seminars in Fetal & Neonatal Medicine. 2015;1–8.
- Dempsey EM, El-Khuffash AF. Objective cardiovascular assessment in the neonatal intensive unit care. Arch Dis Fetal Neonatal .2017;0:1–6.
- El-Khuffash AF, McNamara PJ. Neonatologist-performed functional echocardiography in the neonatal intensive care unit. Seminars in Fetal & Neonatal Medicine. 2011:50–60.
- El-Khuffash AF, Weisz DE, McNamara PJ. Reflection on the changes in patent ductus arteriosus management during the last 10 years. Arch Dis Fetal Neonatal. 2016;101(5):F474–8.
- Ficial B, Finnemore AE, Cox DJ, Broadhouse KM, Price AN, Durighel G, Ekitzidou G, Hajnal JW, Edwards AD, Groves AM. Validation study of the accuracy of echocardiographic measurements of systemic blood flow volume in newborn infants. J Am Society Echocardiography. 2013;26(12):1365–1371.
- Weisz DE, Jain A, McNamara P, El-Khuffash AF. Non-invasive cardiac output monitoring in neonates using Bioreactance: A comparison with Echocardiography. Neonatology 2012;102:61–67.
- Weisz DE, Jain A, Ting J, McNamara , El-Khuffash AF. Non-invasive cardiac output monitoring in preterm infants undergoing patent ductus arteriosus ligation: A comparison with Echocardiography. Neonatology. 2014;106:330–336.
- 22. Forman E, Breatnach CA, Ryan S, Semberova J, Miletin J, Foran A, El-Khuffash AF. Noninvasive continuous cardiac output and cerebral perfusion monitoring in term infants with neonatal encephalopathy: assessment of feasibility and reliability. Pediatric Research. 2017;0:1–7.

- Keren H, Burkhoff D, Squara P. Evaluation of a noninvasive continuous cardiac output monitoring system based on thoracic bioreactance. Am J Physiol Heart Circ Physiol. 2007;293:H583–9.
- Noori S, Drabu B, Soleymani S, Seri I. Continuous non-invasive cardiac output measurements in the neonate by electrical velocimetry: a comparison with echocardiography. Arch Dis Child Fetal Neonatal .2012;97:F340–343.
- Ma M, Noori S, Maarek J-M, Holschneider DP, Rubinstein EH, Seri I. Prone positioning decreases cardiac output and increases systemic vascular resistance in neonates. Journal of Perinatology. 2015;35:424–427.
- Wu T-W, Lien R-I, Seri I, Noori S. Changes in cardiac output and cerebral oxygenation during prone and supine sleep positioning in healthy term infants. Arch Dis Child Fetal Neonatal. 2017;0:1–7.
- Wu T-W, Tamrazi B, Soleymani S, Seri I, Noori S. Hemodynamic Changes During Rewarming Phase of Whole-Body Hypothermia-Therapy in Neonates with Hypoxic-Ischemic Encephalopathy. J Pediatr. 2018.
- Giesinger RE, Bailey LJ, Deshpande P, McNamara PJ. Hypoxic-ischemic encephalopathy and therapeutic hypothermia; the hemodynamic perspective. J Pediatr. 2017;180:22–30.
- Meyer S, Todd D, Wright I, Gortner L, Reynolds G. Non-invasive assessment of cardiac output with portable continuous wave Doppler ultrasound (USCOM). Emerg. Med. Australas. 2008;20:201– 8.
- Nguyen HB, Banta DP, Stewart G, Kim T, Bansal R, Anholm J et al. Cardiac index measurements by transcutaneous Doppler ultrasound and transthoracic echocardiography in adult and pediatric emergency patients. J Clin Monit Comput 2010;24:237–47.
- Patel N, Dodsworth M, Mills JF. Cardiac output measurement in newborn infants using the ultrasonic cardiac output monitor: an assessment of agreement with conventional echocardiography, repeatability and a new user experience. Arch Dis Child Fetal Neonatal. 2011;96:F202–211.
- Zheng ML1, Sun X, Zhong J, He SR, Pan W, Pang CC, Sun YX, Liu YM. [Clinical study of neonatal cardiac output measurement methods]. Zhonghua Er Ke Za Zhi. 2013 Jan;51(1):58–63.
- Beltramo F, Menteer J, Razavil A, Khemanil RG, Szmuszkovicz J, Newth CJL, Ross PA. Validation of an Ultrasound Cardiac Output Monitor as a Bedside Tool for Pediatric Patients. Pediatr Cardiol .2016;37(1):177–183.
- Meyer S, Todd D, Shadboldt B. Assessment of portable continuous wave Doppler ultrasound (ultrasonic cardiac output monitor) for cardiac output measurements in neonates. J Paediatr Child Health. 2009;45(7-8):464–468.
- 35. Knirsch W, Kretschmar O, Tomaske M, Stutz K, Nagdyman N, Balmer C, Schmitz A, Bettex D, Berger F, Bauersfeld U, Weiss M. Cardiac output measurement in children: comparison of the ultrasound cardiac output monitor with thermodilution cardiac output measurement. Intensive Care Med. 2008;34(6):1060–1064.