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"The best that a person can leave behind after his death are three things: a righteous child who makes du'a [prays] for them, an ongoing sadagah [charity] whose rewards continue to reach them, and a knowledge that continues to benefit and be implemented after them."

Prophet Mohammed

THIS WORK CONTAINS CONTRIBUTIONS FROM THE FOLLOWING INTERNATIONAL EXPERT FACULTY

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https://www.nature.com/collections/pjlqbgkmwk

PREAMBLE

The use of Neonatologist-Performed Echocardiography (NPE) for the evaluation of the cardiovascular wellbeing is gaining interest. The purpose of NPE is to provide physiological information in real time, in order to support clinical decision making [2]. This approach is designed to enhance clinical judgment, provide a better understanding of active physiological processes and monitor the response to treatment. Combination of clinical examination and bedside echocardiography can improve clinical diagnosis and patient management [3] in the adult population. There is some evidence that routine use of NPE in the neonatal unit may lead to identification of cardiovascular compromise, guide changes in management [4], and potentially improve short-term outcomes [5]. There is little evidence supporting the role of cardiovascular support in premature and term infants. This largely stems from the lack of clearly defined thresholds for therapeutic interventions and the poor reliability of clinical evaluation. Capillary refill and time and blood pressure monitoring do not reflect systemic blood flow, nor do they correlate with outcome [6, 7].

The use of targeted neonatal echo (NPE) has gained momentum over the last five years [8]. This modality is being increasingly used by neonatologists to identify the haemodynamic significance of a patent ductus arteriosus [9], assessing myocardial function and systemic blood flow [2], in addition to the assessment of pulmonary hemodynamics. The use of NPE has enabled more targeted management of the haemodynamic state of the infant, determining the type of inotropic agent most likely to be of benefit, and monitoring treatment response. The provision of real-time information on cardiovascular performance and systemic haemodynamics, non-invasive nature of the technique, rapidity of data acquisition and report generation, and ability to perform longitudinal functional assessments have all contributed to in the increased utilisation of functional echocardiography by neonatologists.

Over the last decade, there has been an increasing use of echocardiography performed by neonatologists around the world [10]. NPE is currently used in many NICUs as a standard of care. There are an increasing number of prospective studies which highlight the potential merits of NPE in identification of cardiovascular compromise and guiding neonatal cardiovascular care [3, 5, 11, 12]. There is a need to ensure standardization of training and clinical practice guidelines, with quality assurance systems in place to ensure safe dissemination of this practice. The published guidelines by an ESPR expert group outline a framework for standardization of training neonatologists and regulating clinical practice in the NICU. The guidelines are representative of a collaborative initiative between neonatologists and paediatric cardiologists and set out the core and advanced skills required for competency in conducting a complete NPE examination.

This teaching manual will focus mostly on neonatologist performed functional echocardiography. This manual is not intended to teach structural assessment of the heart. A cardiology consultation confirming normal structural anatomy should always be sought prior to using NPE to guide management.

SECTION 1: NPE TRAINING CONSENSUS STATEMENT 2016

Recommendations for neonatologist performed echocardiography in Europe: Consensus Statement endorsed by European Society for Paediatric Research (ESPR) and European Society for Neonatology (ESN)

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Abstract

Echocardiography is increasingly used for hemodynamic assessment to support clinical decision-making in neonatal intensive care. Implementation of the current published guidelines regarding neonatal echocardiography with recommendations for training and accreditation is rather difficult for many European countries. Under the auspices of the European Society for Paediatric Research (ESPR) and the European Society for Neonatology (ESN) [now known as the European Board of Neonatology – EBN] a consensus statement was composed by a working group with recommendations for Neonatologist Performed Echocardiography (NPE) considering the heterogeneous nature of training facilities, personnel and infrastructure across Europe. The aim of this consensus statement is to ensure standardization of training and clinical practice guidelines in order to maintain patient safety and promote the optimal use of echocardiography in neonatal intensive care. A minimum requirement for NPE is defined, that can serve as a foundation upon which each nation can base their national guideline given their specific logistic characteristics.

Introduction

The use of echocardiography for the evaluation of the cardiovascular wellbeing of term and preterm infants is gaining significant interest, aiming to provide haemodynamic information in real time, in order to support bedside clinical decision-making [2, 10, 13]. This approach is perceived to enhance clinical judgment, provide a better understanding of active physiological processes and monitor the response to treatment. Combination of clinical examination and bedside echocardiography has been shown to facilitate clinical decision making [3]. There is some evidence that routine use of echocardiography on the neonatal unit might lead to early identification of cardiovascular compromise that could facilitate clinical management [4], potentially improving short-term outcomes [5, 8].

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There is growing literature highlighting the potential merits of echocardiography in the identification of cardiovascular compromise and guiding neonatal cardiovascular care [3, 5, 11, 12]. Therefore, there is a need to ensure standardization of training and clinical practice guidelines, with quality assurance systems in place to maintain safe dissemination of this practice. There are currently two published guidelines in neonatal echocardiography with recommendations for training and an accredited structured training program with accreditation in neonatal cardiac ultrasound. The practice guidelines and recommendations for the use of echocardiography (Targeted Neonatal Echocardiography, TNE) and Expert consensus statement on Neonatologist performed echocardiography in UK (NoPE) were published in the last 5 years [14, 15]. However, some aspects of these two guidelines are difficult to implement in a pan European setting. The Australian Society of Ultrasound in medicine (ASUM) has developed and implemented a basic training and accreditation process in Australia encompassing cardiac, brain and abdominal ultrasound that is difficult to adopt in Europe (http://www.asum.com.au).

As a result, a working group under the auspices of the European Society for Paediatric Research (ESPR) and the European Society for Neonatology (ESN) was convened to devise a consensus statement for neonatologist performed echocardiography training taking into account the heterogeneous nature of training facilities, personnel and infrastructure across Europe. In this statement, we aim to 1) Highlight the difficulties in implementing the current TNE and UK NoPE guidelines in a European setting; 2) Define the training facilities and infrastructure necessary for optimal training conditions; 3) Identify training standards applicable across Europe and; 4) Discuss some practical aspects including a suggested governance structure for oversight of training and continued quality assurance. We have elected to use the term neonatologist performed echocardiography (NPE) as used in the UK guideline because it identifies the person performing the assessment and the target organ assessed. This consensus statement deals with NPE for assessment of hemodynamic function in infants with a structurally normal heart (patent ductus arteriosus and patent foramen ovale included). Although confirmation of normal structural anatomy is within the remit of this practice, diagnosis and management of congenital heart disease (CHD) is beyond the scope of this guideline. This practice should always remain under the remit of paediatric cardiology services. Preterm and term infants with clinical or echocardiographic suspicion of CHD should be immediately referred to a paediatric cardiologist.

The Current Guidelines in a European Context

Neonatology services in Europe are very heterogeneous in nature and include Level 1 and 2 units, stand-alone Level 3 maternity units, those co-located with adult services, and quaternary maternity units located either physically with, or in the vicinity of, a children's hospital. More importantly, the proximity between paediatric cardiology services and neonatal intensive care units are very variable across Europe. In general, paediatric cardiology services in Europe are under pressure and might not be adequately resourced to take in an additional influx of echocardiography trainees outside a dedicated cardiology fellowship program. As a result, a "one size fits all" approach for NPE training and accreditation in Europe may not be feasible.

The ASE/EAE/AEPC guideline for targeted neonatal echocardiography training is an ideal example of a structured approach to standardise training and maintenance of competence [15, 16]. Our consensus group fully endorses large sections of those guidelines including the background and indications, practical aspects, the suggested approach to the various clinical indications (Sections 1 and 2) and we suggest the reader to refer to the sections for a comprehensive overview of those topics. However, certain aspects of the proposals for training are currently not achievable in a European context. The guideline proposes a two-phase process of a core training period followed by an advanced period of training, both lasting 4 to 6 months. During the core period, the candidates should carry out >150 scans and review a further 150 scans, 80% of which should be structurally abnormal. This training is mandated to be carried out in an echocardiography laboratory under the direction of the paediatric cardiology service. Following an unspecified assessment process, the candidate moves on to the advanced stage for another period of 4 – 6 months and an additional 150 scans and 150 study reviews. The suggested place of training is the NICU for the advanced phase. However, direct or indirect supervision and co-ordination by the paediatric cardiology service is mandated during this phase of training as well.

This approach to training has faced difficulties in lead North American centres and is not feasible in Europe where paediatric cardiology services cannot accommodate a significant influx of neonatal trainees into their already saturated echocardiography laboratories. We suggest that NPE training would define the standards to be met while delivered through a close collaboration between neonatologists and paediatric cardiologists. Training in an echocardiography laboratory for the neonatal trainee may be an alternative option where training cannot feasibly be conducted in an NICU setting. Eventually Neonatology fellowship programs in Europe should incorporate echocardiography training but in the interim an intermediate model for acquiring competencies will be suggested. Similarly, consultant neonatologists planning to undertake NPE may not be able to take a six-month period away from clinical practice but will be required to meet the standards and demonstrate engagement so alternate solutions need to be determined.

The Expert Consensus Statement for NoPE training and accreditation in the United Kingdom (UK) (three of whom are also authors in this statement: Y.S, S.G, and A.G.) is endorsed by Neonatologists in UK with interest in Cardiology & Haemodynamics (NICHe) and the British Congenital Cardiac Association (BCCA), have tailored training to meet the requirements without compromising on the quality. The guidelines mandate a 6-month period of training to be carried out in a paediatric cardiology department during core registrar or higher specialist training in neonatology [14] and another minimum of 6 months in a neonatal centre with expertise in echocardiography for haemodynamic assessment. It provides guidance for new trainees, those who are already practicing and for maintaining competencies. While this approach is appropriate in a UK setting, for reasons outlined above, this might be difficult to be implemented in some parts of Europe where paediatric cardiology placements might not be available.

Other European countries have established their own training guidelines. In Switzerland, a working group with representatives of the Swiss Society of Neonatology and the Swiss Society of Paediatric Cardiology has adapted the European recommendations on TNE, with two levels of training: core and advanced (http://www.neonet.ch/en/education/postgraduate-training-neonatology and http://www.neonet.ch/files/2914/3141/1324/).

In Australia, a Neonatal Certificate in Clinician Performed Ultrasound (CCPU) provides the only accredited training pathway currently in existence for cardiac, brain and abdominal ultrasound. The Australian Society of Ultrasound in Medicine (ASUM) should be commended for developing and instituting this program. This program operates on the premise that CHD has been excluded by a paediatric cardiologist or an equivalently trained person, which is generally done by review of the initial scan by the nominated expert. After a two-day basic course, the trainees must be signed off by a supervisor after doing 50 cardiac and 25 head scans. After approval of the log book and passing a physics course the trainee qualifies for basic CCPU and is eligible to attend the advanced course. After completion of a two-day advanced course an additional 50 cardiac scans, 20 cranial scans and 10 abdominal scans should be performed. As this program does not require establishing structural normality of heart and includes other organ scans, it cannot be adopted as it is. It requires modification to allow integrating in clinical practice and develop a system, which is fit for practice across Europe where emphasis is on confirming structural normality.

Training Facilities and Infrastructure

We advocate that training in NPE in Europe could be carried out in a neonatal intensive care setting with appropriate supervision by paediatric cardiologists or accredited neonatologists with expertise in echocardiography. In cases where this is not feasible, initial training can occur through a paediatric cardiology program with emphasis on neonatal pathology. We advocate that training should be co-ordinated, directed and conducted by a qualified neonatologist with the necessary skillset. However, we also suggest that endorsement by, and close collaboration with, local paediatric cardiology services is an absolute necessity for a successful training program. In the section below, we will outline the necessary infrastructure and personnel requirements needed to run a successful training program in a European Setting.

Training in a tertiary/quaternary neonatal intensive care unit or Paediatric cardiology centre

The tertiary neonatal unit(s) or paediatric cardiology units undertaking NPE training should provide ample opportunities to meet the training requirements as set out by the NPE program and fulfil certain criteria which are intended to ensure that an adequate number of infants with diverse pathology (including congenital heart disease) are available to the NPE trainee. Emphasis should be placed on infants with normal structural anatomy but with neonatal haemodynamic pathophysiology. Close collaboration with paediatric cardiology services is essential. Further exposure to infants with CHD could be catered for in facilities where local paediatric cardiology services can accommodate an influx of neonatal trainees for specific periods of time. This exposure to CHD can be catered for in NICUs with a fetal medicine program and a throughput of infants with CHD.

The above criteria will ensure that NPE trainees will be exposed to a wide variety of gestational ages and pathologies including exposure to CHD during the early neonatal period. We do not recommend training to take place in level 1 or 2 NICUs as the infant case mix is inadequate to facilitate training.

Credentials of NPE Trainers

As stated above, directing, coordinating and conducting training should be done by neonatologists with an extensive expertise in NPE. Currently, no formal certification in NPE for trainer or trainees exists. Therefore, NPE trainers should possess a skill set that is sufficient for independent scanning and facilitates training: Trainers should be able to obtain all the required echocardiography views (in B-mode (2D), M-Mode and colour Doppler), be competent in confirming normal structural anatomy, identifying pathology, and be fully competent in performing all the functional modalities outlined in the TNE/ NoPE guideline [15, 16].

Other key elements should include the following:

- NPE trainers should have a designated and established link with a consultant paediatric cardiologist who endorses the echocardiography skills of the trainer and should maintain a logbook of scans and report on a standard template.
- NPE trainers should carry out a minimum of 50 echocardiograms per annum to demonstrate maintenance of competency. Half of those scans should demonstrate a functional or a structural abnormality (including a PDA). They should have a detailed review of >10 scans each year with a paediatric cardiologist. We understand that some neonatologists across Europe do perform echocardiography to rule out CHD but this practice is beyond the scope of this consensus statement.

Echocardiography Equipment and Archiving

Echocardiography equipment used for training purposes should have B-mode (2D), Mmode, pulsed wave, continuous wave and colour Doppler facilities. Tissue Doppler imaging capability is not a prerequisite for training. ECG tracing capability is also an essential component that should be used on all scans. A range of probes should be available to cater for a wide range of infant sizes. A dedicated work station with an archiving system for image storage and offline review in the vicinity of the NICU is to facilitate study storage, review, and reporting. Reporting of echocardiography examinations should be formalised and standardised. Studies undertaken for teaching purposes should be reported as such.

Governance Structure

Currently an overarching governance structure for NPE across Europe does not exist. However, the ultimate aim is to form a pan European Neonatal Echocardiography Certification Program with close collaboration with the Association for European Paediatric Cardiology (AEPC). This program will be run by neonatologists with advanced echocardiography skills in collaboration with paediatric cardiologists and will serve to assess local training structures and provide accreditation, training oversight and direct continuing assessment. This program should be endorsed by ESPR/ESN. In the interim we propose that units, which fulfil the requirements for training outlined above, should nominate an advanced NPE trainer to act as a director for the local training program and identify a paediatric cardiologist who will act as training support. The units considering training should adhere to the training requirements set out below.

Training Requirements

Introduction to echocardiography concepts (Pre-training Phase)

Candidates undertaking a NPE training program should partake in a pre-training phase aimed to prepare the candidate for carrying out echocardiograms. A thorough and comprehensive understanding of cardiovascular anatomy, physiology and hemodynamics, as it applies to neonatal health and disease, is essential as NPE should always be taken in the clinical context and used to guide clinical management. In addition, the candidate should demonstrate an understanding of the physics and principles of ultrasound, pulsed wave, continuous wave and colour Doppler. In order to aid in image acquisition during the practical training phase, the candidate should become familiar with all the necessary echocardiography views required to perform a standard NPE study including M-mode imaging and its use in functional echocardiography. There are a variety of print and online multimedia resources available to facilitate this pre-training phase (**Table 1.1**). Attendance at an echocardiography course is also encouraged. The use of echocardiography simulators when available may also be a valuable aid to learning.

Table 1.1: Supportive material for NPE training

Resources available for NPE pre-training Echocardiography for the Neonatologist, 1st Edition by Jonathan Skinner MBChB DCH MRCP(UK) FRCPCH MD (Editor), Dale Alverson MD (Editor), Susan M Hunter BA Hons PGDips. ISBN-13: 978-0443054808

- www.tnecho.com
- www.neonatalechoskills.com
- http://www.slhd.nsw.gov.au/rpa/neonatal/cardiac.html
- https://itunes.apple.com/ie/app/tnecho

Basic Echocardiography Training

By the end of the basic NPE training phase, the candidate should be able to demonstrate competent operation of the echocardiography machine, and can use appropriate probes, optimise images and adequately store and archive completed studies. In addition, the candidate should be capable of adequately acquiring all the basic echocardiographic views, perform pulsed wave, continuous wave and colour Doppler interrogation as appropriate, use M-mode echocardiography to measure basic function and wall dimensions, and be capable of demonstrating normal structural anatomy of the heart. The candidate should be able to communicate those findings to a NPE trainer and compose a written report of the findings. *The candidate should not independently utilize NPE to guide clinical decisions during the basic training phase*. Following completion of the basic training, the echocardiograms performed by the candidate can be used to guide clinical management once reviewed by a NPE trainer. We emphasise on strengthening clinical governance by reviewing these studies in departmental echocardiography meetings, which should be led by an advanced NPE trainer. We propose the following key elements that are required to complete the basic echocardiography training phase:

- Complete, log, archive and report > 100 complete NPE studies over a 6-month period. Up to 50 of these scans may be performed on a neonatal echocardiography simulator.
- Studies performed during the initial training period while becoming acquainted with the machine and probe positioning do not form part of those 100 studies.
- At least 70% of those studies should be in infants with normal structural anatomy (including PDA/PFO). Infants with a functional pathology are included in this 70% group.
- At least 10 of those studies should be in infants with CHD during the early neonatal period (other than a PDA/PFO). Those scans should all be reviewed with a paediatric cardiologist or NPE trainer.

During the basic training phase, the candidate should perform at least 5 NPE studies observed by the NPE trainer and/or the paediatric cardiologist to demonstrate competencies. The candidate can then progress to the advanced training phase.

Advanced Echocardiography Training

Following the advanced NPE training phase, the candidate should be able to competently acquire fully optimised images, confidently demonstrate normal structural anatomy, perform complete functional assessment on infants with a wide range of gestations and pathologies including the measurement of dimensions, be able to interpret findings in the clinical content, and devise a management and follow up plan that is appropriate to the patient. An understanding of the physiology of different haemodynamic conditions is essential.

In addition, the candidate should demonstrate an understanding of the limitation of all the echocardiography techniques used. Following the completion of this training the candidate should be able to independently perform NPE scans and use the newly acquired skill in clinical practise. We propose the following key elements that are required to complete the advanced echocardiography training phase:

- Complete, log, archive and report > 100 complete NPE studies including a functional assessment over a 6 to 12-month period (equating to a minimum frequency of 2 scans per week) in the NICU. Up to 50 of these scans may be performed on a neonatal echocardiography simulator, provided that also structural abnormalities and/or functional measurements can be trained.
- Interpret all the scans in a clinical context and devise a management plan with the NPE trainer.
- Continued exposure to infants with CHD should occur aiming for an additional 10 to 20 scans in infants with known structural abnormalities. All of those scans should be reviewed with a paediatric cardiologist or NPE trainer.

Following completion of the advanced training phase, the candidate should demonstrate a study with functional assessment in at least one infant with the following conditions: Patent Ductus Arteriosus; Persistent Pulmonary Hypertension of the Newborn; infant undergoing therapeutic hypothermia; infant with hypotension; infant with a central line. In addition, the NPE trainer and the designated paediatric cardiologist should assess the candidate's ability to confirm normal structural anatomy of the heart.

To maintain ongoing competency, the successful candidate should continue to perform 50 NPE studies per annum and establish a formal link with a designated paediatric cardiologist as outlined in the trainer requirements above. If the candidate wishes to become a NPE trainer, a time based progression over a 3 to 5 year period demonstrating engagement with paediatric cardiology services, and skill maintenance is required. A further six months training in a cardiac centre is encouraged.

Practical Aspects

Considerations for scanning preterm infants

Preterm infants are particularly vulnerable to prolonged handling and external stimuli. Therefore, extreme care should be taken when performing NPE in very low birth weight (VLBW) infants. A specific approach to those infants should be considered. We recommend the use of warm sterile ultrasound gel for all imaging to reduce insensible heat loss. The duration of first examination should not be greater than 30 minutes, and subsequent scans not more than 15 minutes' duration. A clear ECG signal should be obtained on the imaging screen and time should be taken to ensure the optimal environment for imaging.

Measurement of dimensions and function should ideally be done offline following the completion of image acquisition to minimize discomfort. The use of sucrose cannot be recommended routinely but on an ad hoc basis as a recent randomized controlled trial demonstrated no additional benefit and non-pharmacological methods should be attempted first to limit discomfort [17].

The "First Scan" and normal structural anatomy

One of the principal concepts of healthcare provision is "first do no harm". The use of NPE to guide clinical care should only be carried out once normal structural anatomy is confirmed. Significant potential harm can occur if treatment is instigated in the presence of undiagnosed CHD. Obvious examples include PDA treatment in an undiagnosed ductal dependent lesion, commencing inhaled nitric oxide in infants with total anomalous pulmonary venous drainage, using diuretics in infants with left ventricular outflow tract obstruction, and excessive use of oxygen in infants with undiagnosed left to right shunts. (ventricular septal defects). An assumption of the absence of CHD is in our view an unacceptable approach. As a result, the first echocardiogram should be comprehensive enough to reliably confirm normal structural anatomy. We propose an approach to confirming normal structural anatomy in **Table 1.2**. Follow up studies should also examine certain anatomical components to ensure that interventions used did not have any unanticipated effects (e.g. PDA closure and arch constriction).

We propose that a designated NPE trainer can reliably confirm structural anatomy in infants where the clinical suspicion of CHD is low and the recommended approach outlined in **Table 1.2** is followed. A clear distinction should be made between performing a NPE for functional assessment in infants where the level of clinical suspicion of CHD is low, and performing an echocardiogram to rule out CHD when there is a clinical suspicion of abnormal structural anatomy. The scope of practice of a neonatologist should always be the former. If there is a clinical or echocardiography suspicion of CHD then the infant should be referred to a paediatric cardiologist. We recognise that many neonatologists across Europe (including several authors of this statement) undertake additional clinical roles in diagnosis and follow up of congenital heart disease. This however should only be done in collaboration with local paediatric cardiology services and is beyond the scope of this consensus statement.

The use of newer functional assessment techniques

There has been a recent interest in the use of tissue Doppler velocities and deformation imaging using tissue Doppler and speckle tracking techniques for the assessment of myocardial performance in term and preterm infants [18-24]. Those techniques have proven to be valuable diagnostic tools in adults and children with some studies in neonates demonstrating some usefulness in the clinical setting [18, 25]. In addition, the objective assessment of RV function with quantitative parameters is becoming well established [21, 26-30]. Although we cannot recommend routine clinical use of those functional techniques, we encourage further exploration of those measurements in the research setting.

Conclusion

Neonatologist performed echocardiography (NPE) is an evolving practice in Europe. The pace of its evolution and uptake by neonatologists is increasing rapidly. However, in order to maintain patient safety and ensure the optimal use of this skill, adherence to training guidelines along with continued collaboration with our paediatric cardiology colleagues is of paramount importance. Given the heterogeneity in training and accreditation throughout Europe, a minimum requirement for NPE is defined, that can serve as a foundation upon which each country can base their national guideline given their specific logistic characteristics.

Table 1.2: Approach to confirming normal structural anatomy

Echocardiography View	First Study	Subsequent Scans
Situs and position of the heart in the thorax	\checkmark	
Systemic venous return to the RA (IVC/SVC)	\checkmark	
Left and right atrial size and shape	\checkmark	\checkmark
Intra-atrial septum, PFO, ASD, direction of shunting	\checkmark	\checkmark
AV valve morphology	\checkmark	
Atrio-ventricular concordance	\checkmark	
Presence of AV regurgitation/flow acceleration	\checkmark	\checkmark
Ventricular chamber size and shape	\checkmark	\checkmark
Presence or absence of VSDs (Sweeps required)	\checkmark	\checkmark
Left and right ventricular outflow tract obstruction	\checkmark	\checkmark
Ventricular-arterial concordance	\checkmark	
Aortic and Pulmonary valve morphology	\checkmark	
Presence of aortic and pulmonary valve regurgitation	\checkmark	\checkmark
Aortic valve leaflets and coronary origins	\checkmark	
Branch pulmonary artery size and flow	\checkmark	\checkmark
Presence/Absence of PDA and shunt	\checkmark	\checkmark
Arch patency	\checkmark	\checkmark
Pulmonary Venous Drainage into left atrium	\checkmark	

IVC: inferior vena cava; SVC: superior vena cava; RA: right atrium; PFO: patent foramen ovale; ASD: atrial septal defect; AV: atrio-ventricular; VSD: ventricular septal defect; PDA: patent ductus arteriosus.

SECTION 2: ULTRASOUND CONCEPTS AND TECHNIQUES

In our experience novice scanners are often intimidated by the need to understand the principles of physics when learning ultrasound. However, it is vital that the user of the ultrasound machine understands the basics of how images are obtained and reconstructed to appreciate the limitations of the technology and understand common artefacts. In this section we provide an overview of imaging physics and refer the reader to more comprehensive texts for additional detail [1, 31-33].

Characteristics of ultrasound waves

Sound waves are described in terms of their *wavelength* (λ), the distance between two points of the same phase; *frequency* (*f*) - the number of cycles per second, measured in hertz (Hz); *amplitude* (*A*) - maximum particle displacement, measured in decibels (dB); and velocity (c) - the speed of propagation through a given medium, measured in meters/second (**Figure 2.1**). Velocity in turn depends on the physical characteristics of the medium and can be calculated by applying the following formula:

$$c = \sqrt{\frac{\beta}{\rho}}$$

where β denotes *stiffness* and ρ denotes *density*. The average speed of ultrasound in soft tissues is around 1500 m/s, with slight differences between tissue types. The wave equation dictates that velocity of sound is proportional to the wavelength (λ) and the frequency (f) ($c \propto f \times \lambda$). Given that the velocity of ultrasound in soft tissues is relatively constant then frequency can be assumed to be inversely related to wavelength ($f \propto c/\lambda$).

Generation of ultrasound

In the imaging setting, ultrasound waves are generated by transducers equipped with piezoelectric crystals. These crystals change shape when electric currents are applied through them and similarly, they generate electric signals upon mechanical compression. Individual crystals are located adjacent to each other in an 'array' and are connected electrically. Applying rapid alternating current to the crystals generates vibration and ultrasound emission. This 'transmission phase' is very brief (0.5 - 3 microseconds) and is followed by a 'receiver phase' in which returning sound waves compress the piezoelectric crystals and generate electric signals. This phase is much longer (up to 1 millisecond) than the transmission phase since echoes from a range of depths must be detected. The combined durations of the transmission and receiver phases is the pulse repetition period; a shallower depth allows for a shortened receiver phase and therefore a shorter pulse repetition period and a higher frame rate (**Figure 2.2**).

pulse repetition period (transmission + receiver phase)

Types of probes

Ultrasound probes are available in a variety of types of array. In echocardiography, a phased array transducer is generally used because of its small footprint, allowing imaging through small intercostal windows. Phased array probes can be steered and focused to further optimize imaging. Some vascular applications favor a linear array for maximal spatial resolution.

Interaction of ultrasound with tissues

Interactions between emitted ultrasound waves and tissues are what produce the images. These interactions may be of different types, an awareness of which is key to understanding common image artefacts (**Figure 2.3**).

Figure 2.3. Ultrasound and tissue interactions

- 1. **Reflection**: When an ultrasound beam hits a boundary/interface between two different tissues, part of the ultrasound is reflected back to the probe. The amount of reflection depends on the difference in the acoustic properties of the two tissues, specifically the acoustic impedance, which is mainly a product of tissue density. It is the significant difference between density of soft tissue and air that prevents ultrasound being able to image through overlying lung or pneumothorax. The magnitude of returning reflection is also influenced by the angle between the tissue border and the ultrasound beam. Maximal reflection is obtained when tissue border is orthogonal to the ultrasound beam. A clear demonstration of this property is in imaging the membranous intraventricular septum from the four-chamber view (see below) when the false impression of a septal defect can be made since there is so little reflection from a structure that is almost in line with the ultrasound beam. Hence the ventricular septum should be interrogated from a subcostal or parasternal view, where the septum is orthogonal to the beam.
- 2. Scattering: When an ultrasound beam meets a boundary consisting of small structures (smaller than the wavelength of the sound) the ultrasound beam is scattered. This results in reflection of the beam to all directions and a disorganized returning signal. Most of the signal is lost due to the scattering in multiple directions. Nonetheless, backscattering plays an important role in generating the eventual 2D image and most organs have a characteristic scatter signature owing to their specific structures. Hyperechoic (bright) regions within an organ usually represent increased scattering.

- 3. **Refraction**: Refraction refers to the bending of the ultrasound beam when it enters a medium where its propagation speed is different (as is seen when looking at an object below the surface of water). The degree of bending depends on the angle between the beam and the surface (angle of insonation), and the degree of difference in propagation speeds between tissues. Refraction artefact may cause objects to appear in altered locations.
- 4. **Attenuation**: As ultrasound travels within tissues, part of the energy is lost to absorption and scattering. This results in weaker signal intensity from structures that are farther from the probe. The higher the frequency the greater the attenuation, and therefore the lower the penetration. Modern scanners use automatic 'time gain compensation' to ameliorate this problem.
- 5. Absorption and Cavitation: Absorption of ultrasound by human tissues is the process of energy loss by conversion to heat. Cavitation occurs when microbubbles are formed due to high-energy ultrasound interaction. All clinical ultrasound systems work within carefully controlled energy settings, such as those set by the US Food and Drugs Administration [34], and ultrasound imaging is not considered to have any biologic ill effects. Since all imaging introduces energy into the body, imaging power and duration of scans should be kept to a minimum.

Image production

Returning ultrasound waves lead to compression of the piezoelectric crystals and is converted to an electric signal and processed to produce an image on the screen. In **B-mode** (Brightness mode) a two-dimensional image is produced which is a representation of an anatomic slice of tissue. Two-dimensional imaging is the most common modality and is typically used to illustrate the structural anatomy of the heart. The ultrasound probe sends a sweeping beam from side to side along a particular plane of the heart to generate the two-dimensional image. The frame rate of the probe is the number of sweeps per second. In order to generate seamless images of the moving myocardium, the frame rate needs to be faster than the heart rate of the infant. The most commonly used probe in echocardiography is the curvilinear probe. This provides a wide field of vision both close to the probe and at depth. The frequency of the ultrasound waves dictates image quality and resolution. High frequencies provide good image resolution. However, the limited power admissible in infants limits the depth of the image. Conversely, lower frequencies can reach deeper into tissue, but with poorer resolution. In term and preterm infants, a probe frequency range of 7 to 12 MHz provides excellent resolution with adequate tissue penetration.

In **M-mode** (Motion mode), one dedicated scan line is used to detect rapidly moving structures. This form of imaging provides the highest temporal and spatial resolution. M-mode scanning interrogates moving tissue along a single line with respect to time. The time base is displayed in a sideways fashion perpendicular to the line of interrogation. The display screen represents each reflected echo along a line.

Stationary echoes are represented as a straight flat line along the screen and moving echoes are represented as curvy lines reflecting movement in relation to time. The clinical applications of M-mode echocardiography include the evaluation of chamber size, wall thickness, valvular motion and quantification of myocardial function [See figure 4.4 later for an example].

Harmonic imaging is applied in echocardiography to resolve the potential influence of tissue resonance on image quality. An ultrasound wave that penetrates the body will lead to resonance of tissue. The frequency of this resonance is characteristically a multiple of the initial transmitted frequency. Since these harmonic frequencies are also being reflected in tissue, they contribute to the creation of the two-dimensional picture. In **harmonic imaging**, all harmonic frequencies are filtered, except for the second harmonic component of the original signal, resulting in a higher resolution and fewer artefacts. Harmonic imaging is widely used in adult echocardiography, as it results in better signal-to-noise ratio. As it has poorer axial resolution, it is not widely applied in newborns.

Resolution

Resolution of ultrasound imaging includes both spatial and temporal resolution. Spatial resolution is further divided into axial, lateral and elevational resolution. Axial resolution is the ability to differentiate structures that are aligned along the imaging beam (Figure 2.4). Axial resolution is determined by spatial pulse length (SPL), which is the product of wavelength and the number of cycles in one pulse. The lower the SPL, the higher the resolution. Increasing the frequency decreases the wavelength, therefore yielding better resolution. Typical axial resolution is 0.5 mm at a transmitting frequency of 5 MHz and 0.25 mm at 10 MHz. Lateral resolution is the ability to discriminate objects located in an axis perpendicular to the ultrasound beam (Figure 2.4). The major determinant of lateral resolution is beam width. Focusing the transmitted beam by applying the electric current to the individual piezoelectric crystals with time delay decreases the width at beam the focal point thereby improving lateral resolution. The focus position can be set by the operator and is one of the key steps in image optimization. Multiple focal points yield more homogenously distributed lateral resolution in the 2D image but comes at the expense of a decrease in frame rate. Lateral resolution is best at shallow depths and narrow beams and worse with deeper imaging and wide beams.

Figure 2.4. Axial and lateral resolution. Reproduced with permission from Rovner [1] Temporal resolution is the ability to detect that an object has moved over time; it is described in terms of frame rate, in Hz or frames/second. Frame rate depends on the time taken to create a single image line, and the number of lines that form each image. Frame rate can therefore be improved by decreasing the imaging depth, narrowing the image sector width, zooming into an area of interest, reducing the number of focus points or decreasing the line density of the sector.

Artefacts

In pursuit of an accurate representation of anatomy, the ultrasound machine makes a number of assumptions about sound propagation in tissue. Artefacts are errors in image production and are normally caused by physical processes that affect the ultrasound beam. Recognizing imaging artefacts is of great importance to prevent misinterpretation of echocardiograms. A key principle of all imaging is a constant awareness of the possibility of image artefacts. Artefacts can often be recognized by altering the image plane, depth or frequency. Any unusual object should be viewed from multiple directions to ensure that it is anatomic rather than artefactual.

- Reverberation artefacts are generated by strong reflectors, such as the ribs or pericardium, when waves do not travel directly to and from a tissue but have additional reflections within the tissue (Figure 2.5) before returning to the echo probe. Since the echo transducer assumes that waves have taken a direct path to the tissue and back reverberation artefacts appear as multiple images behind reflectors or "comet tails".
- 2. Side lobe artefacts scanners display a 2D representation of tissue on the ultrasound screen assuming the ultrasound beam is infinitely thin. However, this is not the case and objects in front or behind the 2D plane being imaged can also appear in the main image if a very strong reflector is encountered. Since ultrasound energy is focused at the center of the image field the reflections from objects in front of or behind the imaging plane often appear faint (Figure 2.5).

Figure 2.5. Arch view in a newborn showing reverberation and sidelobe artefacts

- 3. **Shadowing** occurs when a strong reflector has already transmitted most of the emitted sound waves back to the transducer, leaving minimal residual waves to reflect on deeper objects (**Figure 2.6**).
- 4. Mirror imaging appears as a display of two images, one real and one artifact, due to the sound beam interacting with a strong reflector. The surface acts as mirror and reflects the pulse to another tissue interface and the ultrasound system believes the second interface is beyond the first surface, and this is where it appears on the scan. The artifact is always deeper than the true anatomy and the distance between the mirror and the real anatomy on the proximal side and the artifact on the distal side are equal (Figure 2.6).

Figure 2.6. A subcostal situs view demonstrating an echogenic focus in the liver and shadow artefact (left panel) and a subcostal parasagittal view of the liver and inferior vena cava (IVC) demonstrating a mirror image against the diaphragm (right panel).

5. **Beam width artefacts** occur when a poorly focused ultrasound beam is wider than the reflector being imaged. As the echogenicity of the reflector will be averaged with the adjacent normal tissue, subtle solid lesions might disappear from the image or cystic lesion may appear to be solid (**Figure 2.7**).

Figure 2.7: An example of beam width artefact in the parasternal short axis view at the level of the papillary muscle.

Optimizing images in neonatal echocardiography

The small size of the neonatal heart and its rapid heart rate make high spatial and temporal resolutions essential. Fortunately, the lack of need for deep tissue penetration allows use of high frequency probes and high frame rates. Spatial and temporal resolutions are competing entities: obtaining high resolution images takes longer, therefore decreasing temporal resolution. Key steps of image optimization in neonates include:

- Use the highest transducer frequency available that provides adequate penetration, generally 8 12 MHz.
- Increase temporal resolution by narrowing the sector width, decreasing the image depth, using zoom and using a single focus point.
- Optimize focus point and image depth for each view and region of interest
- Use fundamental imaging rather than harmonic imaging, as the latter provides poorer axial resolution.
- Adjust image gain to improve image contrast but remember that this does not change signal-to-noise ratio.

Principles of Doppler ultrasound

The change in pitch of sound when a vehicle with a siren passes us in the street is a familiar example of the Doppler phenomenon. When travelling towards us the pitch of the sound is artificially increased as the vehicle has travelled closer to us with each sound emission, so the sound appears to have a higher frequency. Conversely when traveling away from us the frequency appears lower. In ultrasound, the concepts are similar as the same shift in frequency occurs as sound is reflected off a moving object. The extent of this **Doppler shift** (the difference between the emitted and the received ultrasound frequencies) depends primarily on the velocity of the moving tissue and the angle of insonation between the ultrasound beam and the direction of movement (**Figure 2.8**). Doppler applications can be used to quantify velocity of blood flow and myocardial tissue motion.

The angle of insonation of the ultrasound beam has a great impact on the extent of Doppler shift, such that minimization of the angle of insonation is a key step in all approaches to Doppler measurement. In practice, an angle of insonation of <20° is considered acceptable, since this produces only a 6% reduction in velocity estimation (**Figure 2.8**). If necessary, correction can be made for remaining angle of insonation, but at high angles this process becomes more inaccurate. If the direction of movement is orthogonal to the imaging plane no Doppler shift is produced. While higher frequency probes provide optimal spatial resolution, lower frequencies may be required to provide adequate Doppler information, especially at higher flow velocities.

Figure 2.8. Doppler shift and angle of insonation. Reproduced with permission from Rovner [1]

Continuous-wave (CW) Doppler and pulsed-wave (PW) Doppler

In Continuous Wave (CW) Doppler, two separate crystals simultaneously emit and receive signal. Continuous signal transmission can detect a wide range of velocities anywhere in the line of the ultrasound beam. Unlike PW Doppler (below), CW Doppler has no upper limit for velocity detection. Continuous wave (CW) Doppler is the older and more basic of the two techniques. The transducer generates continuous waves with simultaneous wave reception. The main advantage of this modality is the ability to accurately measure blood flow at high velocities. This is of particular importance in assessing infants with a restrictive ductus arteriosus, pulmonary hypertension and tricuspid regurgitation, valvular abnormalities or septal wall defects. These lesions usually have velocities in excess of 2 m/sec, and therefore CW is ideal for the examination of the full abnormal flow pattern. Knowing the peak velocity of blood flow between two chambers facilitates the assessment of the pressure gradient (i.e. between the right ventricle and the right atrium). The Bernoulli equation relates the pressure difference between two chambers to the velocity of fluid passing between them. The peak velocity of the regurgitant jet is measured using continuous way Doppler. This can be converted to a pressure drop by applying the modified Bernoulli equation: pressure (mmHg) = 4 x velocity² [35]. CW is limited however as it lacks selectivity or depth recognition. Due to its continuous nature, there is no provision for gating or selective interrogation of a particular sample. The output of CW contains information on the movement of every blood cell along its beam.

Modern echo machines possess the ability of alternating 2-D imaging with CW Doppler function, thus enabling the operator to objective assess a particular valve or flow pattern. This switching is done at extremely high speeds giving the operator the impression that both studies are done simultaneously. During the Doppler period, the image display is generated from previously stored data from preceding cycles.

Pulsed wave Doppler alternates transmission and reception of the ultrasound beam. The location of this sample volume is operator controlled. One main advantage of pulsed Doppler is its ability to provide Doppler shift data selectively from a small segment along the ultrasound beam, referred to as the "sample volume". The location of the sample volume is operator controlled. Only ultrasound beams reflected back from the chosen sample volume are displayed. All other beams reflected from different depths are ignored. A wider range of interest ('sample gate') increases signal but reduces spatial resolution. To measure a frequency shift, the sampling rate must be twice as high as the given frequency shift (**Figure 2.9**). Therefore, at any given sampling rate there is a highest resolvable frequency (i.e. maximal velocity which can be detected), which is called the **Nyquist limit**. Above this Nyquist limit signal 'aliases' to show an apparent opposite direction of motion (**Figure 2.9**). By selecting a timeframe for receiving the data, one can measure exclusively velocities from a spatial range of interest. Decreasing the imaging depth to increase the sampling frequency or decreasing the frequency of the ultrasound beam can be useful to overcome aliasing. A 'wall thump filter' is applied to PW imaging to remove low-velocity, high-amplitude noises arising from the myocardium, but this setting must be adjusted when low velocity flow is being sought (e.g. when looking for diastolic flow reversal in the descending aorta [36] or venous flow).

Figure 2.9. Continuous-wave (CW) and pulsed-wave (PW) Doppler. Signal sampling and aliasing. Reproduced with permission from Rovner [1]

Color Flow Imaging

Color Doppler is a technique for visualizing the velocity of blood within an image plane, such that local blood flow velocities are superimposed onto the corresponding B mode image. Velocities moving towards and away from the transducer are color-coded as red or blue, respectively. High variance of velocity (turbulent flow) is encoded by adding yellow or green to the pixels, whereas aliasing at the Nyquist limit is represented by color reversal. For computing a color flow map PW Doppler technique is employed. Given the complexity of the calculation and the high sampling requirement, the temporal resolution of color flow imaging is typically poor. But the technique remains extremely useful for detecting shunts and blood flow in regions of interest. Using the narrowest possible sector and minimal depth helps increase frame rate. Choice of gain settings is key - accepted best practice being to increase the gain until background noise appears outside the vessels, then reducing it back until the noise is suppressed. However, this approach still leaves significant variability in gain settings which may produce clinically important variability in measurements, e.g. in assessment of PDA diameter [37]. For low-velocity signals it is important to reduce the velocity scale to enable proper visualization.

Flow volumes are calculated by defining the cross-sectional area (CSA) of the vessel of interest and measuring the velocity of flow by Doppler method. In the case of pulsatile flow pattern, the velocity time integral (VTI) of the corresponding PW Doppler waveform is the area under a velocity time curve and is equivalent to the stroke distance. Multiplying this by the cross-sectional area of the vessel gives an estimate of stroke volume (SV). In neonates estimates of flow volume are subject to significant variability, particularly from estimation of vessel diameters, which are then squared to estimate area (and any associated errors are also squared). Cardiac output is then the product of stroke volume and heart rate. Accuracy of these measurements is dependent on the quality of the 2D imaging, angle of insonation and beat to beat variability. Errors are minimized by optimization of image quality and averaging multiple measurements.

Tissue Doppler Imaging

Tissue Doppler Imaging (TDI) is a relatively new ultrasound modality that derives measurement of displacement velocities directly from the myocardium. This offers a quantitative assessment of both systolic and diastolic function by assessing the displacement of the mitral and tricuspid annuli during the cardiac cycle. [38] Longitudinal myocardial motion velocity (from base to apex in systole and the reverse in diastole) can be measured from the mitral and tricuspid valve annuli. Systolic function of the left and right ventricular free walls as well as the intraventricular septum can be assessed by measuring the peak systolic velocity of the myocardial muscle in that region (termed s` wave). [38, 39] Tissue Doppler imaging derived indices of LV diastolic function have included the following: [40] the peak early diastolic mitral valve annular velocity (e`), reflecting the active ventricular relaxation phase in diastole; the ratio of peak blood flow velocity across the mitral valve to mitral valve annular velocity during early diastole (E/e` ratio), which correlates well with LV filling pressures; and the peak late (or atrial phase) diastolic mitral valve velocity (a`). This modality offers the ability to assess systolic and diastolic function of both ventricles. [39, 41] TDI velocities can detect both systolic and diastolic dysfunction in various disease states with known impact on myocardial performance. These qualities can be potentially implemented in the preterm setting where both systolic and diastolic dysfunction is thought to exist.

Myocardial Strain (ϵ) and Strain Rate (SR) Imaging

Myocardial strain (ε) and strain rate (SR) imaging are measures of ventricular deformation (change in shape in multiple planes while maintaining volume). Strain is a measure of absolute tissue deformation (shortening, and lengthening) assessed by using two reference points along the ventricular wall during the cardiac cycle. Strain is a dimensionless measurement of tissue deformation (expressed as a percentage) relating the change in the shape of an object to its original shape, and strain rate represents the rate of change of this measurement over time (expressed as per second). Strain is an analogue of regional ejection fraction, and therefore is influenced by preload (which increases wall strain) and afterload (which reduces wall strain). Strain *rate* measure the time course of deformation (velocity of shortening/time unit). [42] Strain rate correlates with the rate of change of pressure and reflects intrinsic contractility, thereby being less influenced by loading conditions [43].

PATIENT SAFETY DURING ECHOCARDIOGRAPHY

Minimal handling is one of the central tenets of neonatal care [44]. While some studies have demonstrated clinicians' ability to perform echocardiography without producing significant cardiorespiratory or thermal instability [45, 46], lack of attention to infant status may have clinical consequences. Examinations should be targeted to key clinical questions where possible, while ensuring normal structural anatomy has been effectively confirmed.

- 1. **Keep the baby warm** by using warm gel. Single sachets can be placed in the isolette to warm and minimize infection control risks. Only one door on the incubator should be opened to avoid drafts. The sonographer should avoid getting gel on the infants' temperature sensor, as the servo-controlled temperature mode will be disrupted. It is important to keep the baby swaddled if possible. This may also keep the baby more settled, allowing you to obtain images more quickly and thereby finish the scan sooner.
- 2. **Keep the baby stable** by using minimal pressure on the skin try to 'float' the ultrasound probe above the skin. It is important for the sonographer to be especially sensitive in the subcostal views where too much pressure may cause the infant to vomit. One should ask the bedside nurse to monitor the child's stability and provide timely feedback if the scan is impacting oxygenation it can be hard to monitor this effectively while also performing the scan. Pause or discontinue scanning if the baby is unstable. The bedside nurse can also assist with repositioning the baby to aid image acquisition if necessary.
- 3. Keep the baby safe from infection by wiping down all usable surfaces of the ultrasound machine before and after every scan. Appropriate antimicrobial agents will vary with individual hospital policies and ultrasound vendors; specific agents are generally required for the ultrasound probe to avoid damaging the delicate head. We recommend auditing a regular clean of all surfaces on the ultrasound machine with a signed sheet attached to the machine. Single use gel sachets prevent avoidable infection control risks from an often-handled and frequently crusty ultrasound gel bottle.
- 4. **Protect the baby's skin** by using the child's existing ECG leads rather than applying a new set to provide an ECG trace for the scan. Most ultrasound vendors will provide you with a 'slave' cable to allow the ultrasound machine to display the ECG trace from the infant's cot-side monitor or an adapter to connect the child's existing ECG leads to the ultrasound machine.

SECTION 3: BASIC NEONATAL ECHOCARDIOGRAPHIC WINDOWS

This section will focus on image acquisition and obtaining the echocardiographic views. The different echocardiographic windows, probe positions, and corresponding heart images will be discussed. An accompanying freely available website (www.tnecho.com) can serve as an adjunct to the text.

Echocardiographic Windows and Newborn Imaging

Echocardiography evaluation of the newborn is complicated by issues related to patient size and trans-thoracic acoustic windows. The interpretation of hemodynamic data is totally dependent on the quality of the images hence the competence of the operator is important. Serial scans of the same patient should ideally be performed by one examiner to limit interobserver variability and maximise patient benefit. As explained in the previous chapter, NPE includes evaluation of the heart using two-dimensional (2D), pulse wave Doppler (PWD), continuous wave Doppler (CWD) and m-mode methods. There are many challenges facing the ultrasonographer, particularly in the setting of preterm infants. In preterm infants, image quality may be compromised in the presence of hyperinflated lungs. Imaging neonates with bronchopulmonary dysplasia often poses a challenge as the hyperinflated lung fields or areas of air trapping may obstruct the heart limiting adequate image acquisition. In addition, preterm infants may decompensate with excessive handling or chest compression from overzealous probe positioning to acquire images. All efforts should be directed to limiting the duration of these studies aiming to gather all the information needed to assess clinical judgment while keeping in mind patient stability.

Probe frequency between 5-7 MHz for term and to 10-12 MHz for preterm infants are ideal for imaging newborn with the 12 MHz probe being most suitable for preterm infants of extremely low birth weight. The thorax of the newborn has relatively less ossified cartilage and therefore, the size of the echocardiographic windows is larger than adults. those of This allows for more manoeuvrability with the probe thereby facilitating better image acquisition. The windows used for obtaining echocardiographic images are the same as those used in older children and include: apical, low and high parasternal, suprasternal, and subcostal.

Figure 3.1: Ultrasound Windows

The apical view is obtained by placing the probe on the area just below the left nipple (the 4th or 5th intercostals space, midclavicular line). The parasternal view is on the lower third of the sternum to the left, and the higher parasternal view is obtained by placing the probe below the clavicle alone the sternal edge on the left. The suprasternal view is obtained from the suprasternal notch and the subcostal view is from the area below the xipoid process. Figure 3.1 illustrates the different echocardiographic windows.

The Subcostal View

This view may be left towards the end of the examination **if normal structural anatomy has already been established** as it causes discomfort to the infant. It is used to determine the situs of the structures; assess the atria more closely; determine superior vena cava (SVC) Doppler flow, assess the abdominal aorta along with the celiac trunk and mesenteric arteries, and assess the inferior vena cava (IVC). To assess the atria, the probe is positioned below the xiphoid process in an axial fashion with the marker pointing to the left. The beam is then angled towards the anterior chest wall until the atria come into view [Figure 3.2]. Further anterior angulation of the beam will reveal the outflow tract of the left (LVOT), and then the right (RVOT) ventricle [Figure 3.2].

Figure 3.2: Subcostal view of Atria (A), LVOT(B) and RVOT (C).

Bringing the probe into the axial position will display the liver and the aorta/IVC in cross section **[Figure 3.3A]**. To view the abdominal aorta, the probe is placed perpendicular to the chest in a sagittal fashion with the marker pointing towards the head **[Figure 3.3C]**. Angling the beam to the right will show the IVC **[Figure 3.3B]**.

Figure 3.3: Subcostal views of the aorta, IVC and liver.

The Apical View

This view is the conventional starting point for some neonatologists. However, it is not recommended as the starting point where normal structural anatomy has not been established as important outflow tract abnormalities (such as transposition, double outlet ventricles and truncus arteriosus can be missed on first instance. The image acquired illustrates the 4 well recognised cardiac chambers. The images are used to assess mitral and tricuspid valve inflow Doppler and assess left and right outflow tracts. The interventricular and interatrial septa are visualised here, this view however is not ideal for assessing the presence of defects in these walls as there may be artificial "drop off" in the signal retuning to the ultrasound probe.

Modifications of this view enables the examiner to assess the left and right ventricular outflow tracts for the presence of stenosis and obtain Doppler signals that may be used in the calculation of the left and right ventricular

Figure 3.5: Apical view showing the four chambers (A) the aorta (5 chamber view, B), and the pulmonary artery (C). These views maybe used to assess aortic and pulmonary stenosis, acquire Doppler signals to measure VTI and calculate outputs (see later text), and assess the membranous part of the IVS. Occasionally the left to tight flow from the PDA may be visualised when the shunt is significant.

outputs **Figure 3.5]**. To obtain the 4-chamber view, the probe is placed on the apex, at an angle pointing towards the right shoulder. The positioning marker of the probe faces the left shoulder. The operator may need on occasion to move the probe in a more lateral position to obtain this view. This particularly applies to infants a few weeks of age with evolving chronic lung disease. To bring the left ventricular outflow tract and aortic valve into view, the probe is rotated in a clockwise motion and angled slightly anterior. Further anterior angulation will bring the right ventricular outflow tract and the pulmonary valve into view.

Long Axis Parasternal View

The long axis parasternal view [Figure 3.6] is one of the most widely used in neonatal intensive care. А lot of useful information may be derived This from it. includes shortening fraction (as a guide for left ventricular function), left atrial to aortic root ratio (to assess PDA related volume loading), ventricular filling, the diameter of the aortic and pulmonary roots (used to calculate outputs), the presence of mitral valve regurgitation, the tricuspid valve regurgitant jet if present (used to calculate RV systolic pressure), in addition to visual inspection of the thickness of the ventricular walls including the septum. This view is ideal for the examination of the interventricular septum for defects, and the origins of the great arteries. Ventricular septal defects may also be visualised here using colour Doppler.

Figure 3.6: Long axis parasternal view. Refer to text for explanation.

The starting point is illustrated in **Figure 3.6A**. The probe is placed perpendicular to the chest, left of the lower third of the sternum, with the probe marker pointing towards the right shoulder. The corresponding image of the heart will illustrate the left heart structures. Directing the beam towards the left shoulder (by angling the probe *away* from the left shoulder) will reveal the pulmonary artery **[Figure 3.6B]**. This view is ideal for assessment of the pulmonary valve as it lies directly parallel to the direction of the ultrasound beam. The tricuspid valve long axis view is obtained by angling the beam towards the right flank (by angling the probe *towards* the left shoulder – **Figure 3.6C**). To understand the probe manipulation necessary to obtain the right sided heart structures, one must realise that the right ventricle and atrium wrap around the left ventricular structures. This may become more evident when examining the short axis view of the heart next.

The short Axis View

Using the same probe position used to obtain the long axis parasternal view, the probe is rotated clockwise with the marker facing the left shoulder. This brings into view the aorta and its cusps centrally, with the right heart structures wrapping around it **[Figure 3.7A].** This view is used to assess the tri-leaflet aortic valve, high peri membranous VSDs, the coronary arteries, and the right ventricular inflow and outflow tract. Continuous angling of the ultrasound beam towards the left flank (by angling the probe toward the right shoulder) will display the structures of the left ventricle in short axis including the mitral valve (with its typical 'fish mouth' appearance', **Figure 3.7B**), the papillary muscles (usually situated at 3 and 7 o'clock, **Figure 3.7C**), and eventually the apex. This sweep is used to further assess the presence of VSDs in short axis, assess the function of the left and right ventricles, and examine septal wall motion.

Figure 3.7: Short axis parasternal view.

High Parasternal view

The probe position is shifted towards the upper third of the left edge of the sternum. The probe marker is directed to the left of the patient in a transverse position (side to side). The pulmonary artery and its two branches become visible. The ascending aorta is noted to be to the right of the PA followed by the SVC to the extreme right, all in short axis [Figure 3.8]. This view is used to assess the size of the branch pulmonary arteries and the presence of pulmonary branch stenosis often present in preterm infant and may clinically present mimicking a PDA. In the presence of PDA, a red Doppler jet is often seen in this view depicting left to right shunting.

Figure 3.8: High parasternal view of the pulmonary artery and its branches.

Ductal View

The probe is positioned in a complete sagittal fashion along the left border of the sternum, with the marker pointing towards the head. The probe is angled side to side to bring the duct (if present) into view. Angling the beam too much towards the right (by angling the probe towards the left) will bring the ascending aorta and part of the aortic arch into display. In the absent of the PDA, the pulmonary artery is seen above the descending aorta **[Figure 3.9]**. PDA assessment is further explained in the following chapters.

Figure 3.9: Ductal View.

Version Date 2019

Aortic arch view

The arch is visualised by maintaining the ductal view described above, moving the probe slightly to the right of the sternum, and rotating the probe in slight clockwise fashion. Angling the ultrasound beam to the left (by right sided probe angulation) is necessary. Compare the probe position in **figure 3.10** below to the one in **figure 3.9**.

Figure 3.10: Aortic arch view.

Suprasternal View

This view is used to assess the pulmonary veins draining into the left atrium. It is to be stressed that this view is very difficult to obtain. <u>The paediatric cardiology service must be</u> <u>contacted if any suspicion exists regarding any structural defects.</u> In addition, this position may cause considerable discomfort and potentially some cardio-respiratory compromise in untrained hands. The probe is positioned in the suprasternal notch perpendicular to the chest with the marker pointing towards the left. The ultrasound beam is then angled towards the anterior chest wall [Figure 3.11].

Figure 3.11: Suprasternal view.

SECTION 4: ASSESSMENT OF MYOCARDIAL FUNCTION – CONVENTIONAL MEASUREMENTS

Haemodynamic compromise in the early neonatal period is common and may contribute to poor neurodevelopmental outcome later in life. A thorough understanding of the physiology of the cardiovascular system in the preterm infants, influence of antenatal factors, and post natal adaptation is essential for the management of these infants during the early critical phase. The influence of the various ventilator modes, the presence of a patent ductus arteriosus (PDA), and sepsis all influence the cardiovascular system. The poor clinical indicators of systemic perfusion [6], and the relative insensitivity of conventional echocardiographic techniques in assessing myocardial contractility [47] mean that monitoring of the cardiovascular status of the preterm infant remains a challenge.

Evaluation of Left Ventricular Output

Assessment of LVO involves measuring the mean velocity of blood flow across the ascending aorta from an apical five chamber view using pulsed wave Doppler and determining the diameter of the aortic root from a parasternal long-axis view using M-mode **[Figure 4.1]** methods. The maximum ascending and descending aortic velocity in preterm infants is usually below 2.0 m/s in the absence of valvular disease and therefore pulsed wave Doppler is better suited for analysis. Mean aortic velocity can be measured with the Doppler probe. The area under the wave of the aortic systolic beat can be used to calculate the velocity time integral, which is a measure of the distance travelled by blood during a given beat. Multiplying that by the aortic cross-sectional area derived from: $\pi \times aortic diameter^2/4$ (AoCSA) gives the stroke volume. LVO can be derived from multiplying stroke volume by heart rate:

$LVO = \frac{AoCSA \times VTI \times Heart Rate}{Weight}$

LVO expressed in ml/kg/min. Normal values range from 170 to 320 ml/kg/min[48]. LVO must be used with caution as it may give a falsely reassuring picture of acceptable systemic blood flow in the presence of a PDA; specifically, as a high volume left to right shunt will lead to increased pulmonary venous return left heart preload and stroke volume, but at the expense of systemic blood flow. Early measurement of LVO following PDA ligation has been shown to predict late onset impairment in LV contractility, low systolic arterial pressure and need for cardiotropic medication [49-51].


Figure 4.1: Probe position (A) and apical long axis view of the heart (B). A pulsed wave Doppler measures blood flow across the aortic valve (white lines). The area under the curve is then traced to obtain the VTI (C) (yellow line). RV: right ventricle; LV: left ventricle; Ao: aorta; LA: left atrium.

Evaluation of Right Ventricular Output

Measurement of RVO is done using a similar approach described above. The pulmonary artery diameter is best assessed from an oblique long axis parasternal view **[Figure 4.2].** The RV velocity time integral is obtained from Doppler interrogation of the same view. RVO reflects blood return from the systemic circulation and, in the absence of a large left-to-right transatrial shunt, is reflective systemic blood flow in infants. However, RVO measurements are confounded by the presence of atrial shunt and if the PDA is present. Typically, the atrial shunts, are much smaller than ductal shunts, therefore RVO may be used as an estimation of systemic blood flow [48, 52].



Figure 4.2:

Measurement of RVO. The probe position (A) and the corresponding view (B) are shown. The pulmonary artery (PA) Doppler is traced (C) and the same formula used for LVO is applied to calculate RVO. RV: right ventricle; PA: pulmonary artery; Ao: aorta; LA: left atrium.

Evaluation of Superior Vena Cava Flow

Superior Vena Cava (SVC) flow has been proposed as a better measure of systemic blood flow as it reflects exclusive venous return from the brain and upper body and is untainted by shunts. SVC flow can be assessed using echocardiography [53]. A subcostal approach is used to assess SVC Doppler signals and a high supra-sternal view is used to measure SVC diameter. As four-fifths of flow in the superior caval vein represents venous return from the head and neck, such



measurements may provide novel insights into any association between regional cerebral blood flow and cerebral injury. SVC return reflects blood supply to the brain and upper body and therefore no information regarding blood supply to the liver, kidney and gut can be derived. Secondly, cerebral blood flow is subjected to intrinsic auto-regulatory mechanisms and may not truly reflect cardiac performance [54]. Measurement of SVC diameter beyond 48 hours of life is difficult and the diameter of the vessel varies widely within the cardiac cycle.

Evaluation of Shortening Fraction and Mean Velocity of Circumferential Fractional Shortening

Left ventricular systolic function can be assessed by shortening fraction (SF), ejection fraction (EF, see below) or the rate corrected mean velocity of circumferential fibre shortening (mVCFc). Shortening fraction can assess LV function using m-mode methods from either a long parasternal axis or short axis view of the left ventricle. It is calculated by measuring left ventricular end diastolic diameter (LVEDD) and left ventricular end systolic diameter (LVESD) using Mmode echo and applying the following formula:

$$FS(\%) = \frac{LVEDD - LVESD}{LVEDD}$$



Figure 4.4: Calculation of SF

Normal neonatal values for FS% are = 28 to 40%. Shortening fraction is an unreliable measure of systolic left ventricular function in the first few days of life as high right ventricular pressures impair ventricular septal wall movement [55].

Left Ventricular Mean Velocity of Circumferential Fractional Shortening (mVCFc) is a preload independent afterload adjusted measure of LV function. It is determined by the following method [56]:

$$mVCFc = \frac{LVEDC - LVESC}{LVEDC \times ETc}$$

where LVEDC = LV end-diastolic circumference; LVESC = LV end-systolic circumference, and ETc = left ventricular ejection time corrected for heart rate (ET/VRR interval). The stressvelocity relationship is a load-independent measure of myocardial contractility [47] where the relationship between mVCFc and end-systolic wall stress analysis is examined by linear regression methods. The clinical applicability of these markers is not well studied in neonates. However, there is some evidence that mVCFc correlates with cardiac troponin levels in the early neonatal period [57].

Measuring Simpson's Biplane ejection fraction

Ejection fraction may provide a better quantitative assessment of left ventricular function in the presence of paradoxical septal motion. Of the many mathematical methods, Simpsons Biplane rule has been shown to be the most accurate. This method involves manual tracing of the LV cavity endocardium from the 4chamber view and а modified 2-chamber view (see below) at end-systole and end-diastole. The machine's software then divides the cavity into many parallel discs, calculate the volume of each disc and automatically combines the volume to provide the user with estimated LV cavity volume in end diastole (LVEDV) and end systole (LVESV).



Figure 4.5: The LV viewed in 4 and 2 chamber images

Simpson's rule always assumes the LV cavity to be ellipsoidal. Normal value of EF in newborn infants is between 55-65%. It should also be recognized that both SF and EF are affected by changes in loading conditions. [15]

$$EF(\%) = \frac{LVEDV - LVESV}{LVEDV}$$

The apical 4 chamber view is used as a starting point. Most modern machines have an option to measure ejection fraction using Simpson's biplane method. The LV cavity in the 4-chamber view is traced at the end of diastole (maximal area) and then at the end of systole (minimal area). The probe is then angled *anticlockwise* until the RV chamber is no longer visible to obtain the 2-chamber view. The LV cavity is traced again in systole and diastole. The machine's software then should calculate the ejection fraction [**Figure 4.5**].

Diastolic Performance

Diastolic performance of the heart can be assessed indirectly by examining the biphasic pattern of flow across the mitral valve known as trans-mitral flow. Characteristic flow pattern is observed during diastole. First phase is the early wave (E wave) and it is a result of blood flow across the atrio-ventricular valves in early diastole. The second phase is the atrial contraction wave (A wave) and is a result of atrial contraction at the end of diastole. Maximum E and A wave velocities are compared as ratios. In the normal setting, the majority of blood flow occurs during the active ventricular relaxation phase (E wave) and therefore, the E wave is usually of a higher velocity than the A wave. When expressed as a ratio, in the normal setting, E wave to A wave ratio (E:A) is greater than 1 [58]. When ventricular relaxation is compromised, ventricular filling is driven mainly by atrial contraction in late diastole thereby reversing the E:A ratio. An E:A ratio less than one indicates diastolic dysfunction (indicating a noncompliant ventricle). Both E and A wave velocities and E:A ratio are indirect measures of ventricular systolic and diastolic function and give very little information on muscle contraction and relaxation velocities. In addition, they are dependent on loading conditions and therefore the volume status of the infant and the use of inotropes [Figure 4.6] [15]. The measurements can be obtained as detailed below.



Figure 4.6: Assessment of diastolic function. The position of the probe (A) with the corresponding 4-chamber apical view (B) are shown. Doppler traces of transmitral (C) and tricuspid valves (D) can be obtained. The early wave (E-wave, early diastolic blood flow) and atrial wave (A-wave, flow due to atrial contraction) are measured. The area under the curve (VTI) can also be traced.

Myocardial Performance Index

On the tissue Doppler traces obtained at the lateral mitral annulus one can further assess the isovolumic contraction (IVC) and relaxation (IVR) times. The sweep of the Doppler image should be increased and the isovolumic contraction and relaxation times can be measured. The IVC time is measured in milliseconds (ms) from the end of the a` wave to the beginning of the s` wave [Figure 4.7]. The IVR time is measured in ms from the end of the s` wave to the beginning of the e` wave. The myocardial performance index (MPI) has been found to be a valuable quantitative echocardiography index of ventricular function by incorporating both systolic and diastolic performance of the right and left ventricles. It is defined as the sum of iso-volumetric contraction and relaxation times divided by the systolic time, which requires measurement of the time interval between the end and onset of mitral or tricuspid inflow (the "a" interval) and the ejection time of the LV or RV outflow (the "b" interval) [59]. The MPI index is then calculated by the formula (a - b)/b. The MPI is reproducible, and independent of heart rate and blood pressure. Normal values in healthy neonates range from 0.25 to 0.38 [60]. It is relatively independent of age and also has a low degree of inter-observer and intra-observer variability [61].



 $MPI = \frac{(IVRT + IVCT)}{Systolic Time}$

Figure 4.7: The phases of the cardiac cycle identified by TDI. Note that there are waves during the isovolumic phases. Do not confuse them with the systolic and diastolic waves. Use the ECG tracing as a guide.

Tricuspid Annular Plane Systolic Excursion

Tricuspid annular plane systolic excursion (TASPE) is a measure of movement of the tricuspid annulus from base to apex during systole and reflects global RV function. The distance travelled by the TV annulus from diastole to systole is measured in millimeters. The 4 chamber is used to obtain a focussed image of the RV [Figure 4.8] and the cursor is placed in a place traversing the tricuspid valve annulus. M-Mode is then used to measure the distance travelled by the annulus towards the apex during systole [Figure 4.9].



Figure 4.8: Measurement of TAPSE. This is obtained from a focussed RV 4-Chamber view and is measured using M-mode echocardiography with the line of interrogation passing through the free wall of tricuspid annulus while maintaining vertical alignment with the apex.

Values achieved in neonate range from 4 to 5 mm in ELBW infants to 9-11 mm in healthy term infants[29]. This method is also dependent on loading conditions.



Figure 4.9 Tricuspid Annular Plane Systolic Excursion (TAPSE) measurement. Assessment of the movement of the annular plane towards the apex can be carried out in Tissue Doppler and 2D M-mode.

Fractional area change of the Right Ventricle

Fractional Area Change (FAC) is a measure of the change in RV cavity area from diastole to systole in the 4-chamber view. It is analogous to LV shortening fraction and is therefore also potentially influenced by loading conditions. The values achieved in neonates range between 25 to 40%. This measurement is not commonly used in the neonatal population, but it may prove useful in the assessment of RV function in the setting of pulmonary hypertension.

The RV areas at end-diastole (EDA) and end-systole (ESA) are calculated by the software from manual tracings of the endocardial borders **[Figure 4.10]**. The echocardiography machine measurement software should be able to provide an area of the trace in cm². FAC (%) is then calculated by using the formula:

$$FAC(\%) = \frac{EDA - ESA}{EDA}$$



Figure 4.10: Calculation FAC. Trabeculations should be considered part of the cavity when performing the traces. To ensure that the endocardial borders were reliably delineated the 2D clips should be frozen and reviewed by the sonographer during acquisition and settings including probe position, sector width and 2D gain were optimized as required.

SECTION 5: TISSUE DOPPLER VELOCITY IMAGING

Introduction

More recently, the use of the Doppler Effect has expanded to the assessment of heart muscle (tissue) characteristics. This was first demonstrated by Isaaz *et al* in their assessment of the left ventricular wall in 1989 using a pulse wave frequency signal. Tissue Doppler imaging (TDI) captures information using high frame rates (typically greater than 200 frames per second). The high temporal resolution achieved using this technique facilitates the measurements of a wide array of myocardial muscle characteristics including the velocity of muscle movement during systole and diastole, deformation measurements (also known as strain and strain rate measurements), in addition to the measurements of the timing of events within the cardiac cycle (systolic and diastolic times / isovolumic contraction and relaxation times). Those measurements can now be derived by pulsed wave tissue Doppler imaging (pwTDI) and colour Tissue Doppler Imaging (cTDI) [**FIGURE 5.1**].



Figure 5.1: Pulsed Wave Tissue Doppler Imaging (TDI) and Colour TDI. Pulsed wave TDI can be used to derive myocardial velocity during systole (s`) and diastole (e` and a`), in addition to event timings (see text for further details) including isovolumic relaxation time (IVRT) and isovolumic contraction time (IVCT). Movement towards the probe is depicted as positive, and movement away from the probe is depicted as negative. Colour TDI can be used to derive velocity and deformation values. Conventionally in colour TDI, the muscle is coloured red when travelling towards the probe and blue when travelling away from the probe.

Unlike conventional methods of functional assessment which mainly assess changes in cavity dimension and blood flow velocity, namely shortening fraction, ejection fraction and blood pool analysis, this modality directly assesses muscle wall characteristics such as velocity and deformation. In addition, it has shown improved sensitivity over older methods as an intensive care monitoring tool for myocardial dysfunction in critically ill term and preterm infants in conditions such as congenital diaphragmatic hernia and neonatal sepsis [18, 49, 62].

This provides the physician with valuable data on myocardial performance and can assist in outcome prediction [63, 64]. TDI is influenced by loading conditions and is therefore not a true surrogate for intrinsic myocardial function (see below) [65].

Pulsed Wave Tissue Doppler Velocity Measurements

Tissue Doppler velocities can be acquired by spectral analysis using a pulsed wave Doppler technique. Muscle tissue wall moves at a significantly slower velocity and a higher decibel amplitude range than blood thus facilitating a high temporal resolution, with minimal artefact from blood. Recent advances have enabled the distinction between the faster moving blood (>50cm/s) and the slower moving muscle tissue (<25cm/s). PwTDI assesses longitudinal velocity of a ventricular wall segment from base to apex, providing a measure of systolic function which is recorded as the peak systolic velocity of the myocardial muscle (s` wave) [66]. The systolic wave is usually preceded by a short upstroke during isovolumic contraction.

In addition, a measure of diastolic performance can be obtained as the ventricular wall moves away from the apex in the opposite direction. The diastolic wave is biphasic and is recorded as the peak early diastolic velocity (e` wave) and the late diastolic peak velocity (a` wave) which reflects the active ventricular relaxation and atrial contraction phases of diastole respectively. The diastolic waves are usually preceded by another short upstroke during isovolumic relaxation time. The duration of the isovolumic relation and contraction phases, in addition to the systolic and diastolic times, can also be accurately obtained using this modality [**FIGURE 5.1**].

Colour tissue Doppler velocity

Colour Doppler tissue imaging (cTDI) uses phase shift analysis to capture atrioventricular annular excursions. Compared with pwTDI, cTDI provides the ability to visualize multiple segments of the heart from one single view. It measures mean rather than peak systolic and diastolic velocities. As a result, velocities obtained using this technique are generally 20% lower in systole and diastole compared to pulse wave tissue Doppler imaging. The two methods are therefore not interchangeable [66]. CDTI does have the advantage of combining the high temporal resolution seen with pwTDI, with a high spatial resolution. In addition to this, myocardial velocities recorded at the left and right ventricular base, and septal wall, can be obtained from a single image for later offline analysis. A comparison between left and right ventricular function can therefore be performed. Muscle tissue at the base moves at a higher velocity than that closer to the apex. cTDI can be used to assess this velocity gradient across the wall of interest [FIGURE 5.2]. As with other TDI modalities, images are attained in the apical 4 chamber view. Eriksen et al compared cTDI with tricuspid and mitral annular plane systolic excursions in a cohort of preterm infants. They found that the value on cTDI were lower and more dependent on image quality than excursions by grey-scale m-mode. Another potential disadvantage to cTDI is poor reproducibility reported in some studies. Data on cTDI values and clinical applicability in the neonatal setting are limited. This is likely due to the need for offline analysis to obtain those values when compared with pwTDI, where data can be acquired at the bedside. The data presented below relates only to pwTDI.



Figure 5.2: Colour Tissue Doppler Imaging. The top demonstrates an assessment of the velocity gradients of the septal wall in a term infant. Note that the velocities measured at the base (yellow) are higher in systole and diastole than those measured in the mid segment of the wall (green). The bottom panel demonstrated the assessment of the septal wall and the right ventricular free wall in a preterm infant. Right ventricular velocities (green) are higher than septal velocities (yellow). Note the fusion of the e` and a` occurring due to the higher heart rate seen in preterm infants.

Measurement of TDI velocities

Accurate TDI velocity measurements are highly dependent on obtaining good quality images. This may be challenging in the neonatal setting, particularly in premature infants where lung artefact can interfere with obtaining clear images of the walls of interest. Images are usually obtained from an apical four-chamber view. The sector width of the field of view is usually narrowed to only include the wall of interest. This ensures that the temporal resolution is enhanced and a frame rate of over 200 frames per second is obtained. A pulsed wave Doppler sample is placed at the base of the left ventricular free wall, the base of the septum and at the base of the right ventricular free wall. The sample gate is narrowed to only capture the velocity of the area of interest (usually 1 - 2 mm). It is crucial to maintain an angle of insonation of less than 20° to prevent underestimation of velocities. TDI velocity measurement modality will only assess muscle movement parallel to the probe beam [FIGURE 5.3]. This is a limitation of this modality as muscle movement perpendicular to the line of interrogation will not be assessed and as a result, TDI velocity measurements are reserved for longitudinal (base to apex) muscle tissue movement.



Figure 5.3: Measurement of TDI velocities. Narrowing the sector width and reducing the sample gate increases the frame rate and improves the temporal resolution. This enables easier identification of the various events throughout the cardiac cycle. The angle of insonation should be less than 20° to avoid underestimating the velocity values.

As outlined above, TDI velocity assessment measures myocardial function rather than intrinsic contractility and as such, the values are highly influenced by loading conditions (in addition to intrinsic contractility). Increased preload increases systolic tissue Doppler velocities while increased afterload reduces those velocities [18]. Therefore, clinical interpretation of those measurements must be while considering the loading conditions likely to be present in the clinical situation. This has important implications for therapeutic interventions where in some instances it may be more beneficial to improve preload (using volume support) or reducing afterload (using lusitropic medication) rather than targeting an improvement in intrinsic contractility [FIGURE 5.4].



Figure 5.4: Effect of Loading Conditions on TDI Systolic Velocities. Increasing afterload reduces systolic velocities. Increasing preload increases systolic velocities. [Data adapted from a cohort of 141 preterm infants < 29 weeks gestation on Day 1 of age].

In addition, it is important to recognise that tissue Doppler velocity imaging cannot distinguish between active muscle movement, and translational wall motion (a non-deforming segment tethered to a functioning segment). Tissue Doppler velocities may be falsely elevated as they interrogate motion at a single point in the muscle wall with reference to the ultrasound transducer. Therefore this movement can be influenced by translational motion [30]. Deformation imaging (see later) can easily differentiate between the two.

Clinical application of TDI velocity measurements

The use of TDI in the neonatal setting has significantly expanded in recent years. TDI assessment is very feasible in small infants and has been validated in term and premature neonatal populations as well as in fetuses [67, 68]. Reference values for both term and preterm infants are shown below. [**TABLE 5.1**]. Several studies have documented serial changes in those functional measurements over the first day of life and up to 36 weeks post menstrual age. Tissue Doppler velocity imaging is dependent on the gestational age with lower gestations exhibiting lower myocardial velocities in both systole and diastole. Reduced myocardial velocity is also present during the transitional period from the foetal to the neonatal circulation and increases over the first few weeks. This is likely due to the changing loading conditions seen during this period which become more favourable. In premature infants, TDI velocities have been used to predict clinical deterioration following patent ductus arteriosus (PDA) ligation and as a guide to institute targeted therapy [26, 27, 49, 64, 69-71].

In addition, they can be used to assess treatment response in this scenario when conventional measures of function, including shortening and ejection fraction are not sensitive enough. Incorporating TDI for the assessment of myocardial performance in the setting of a PDA during the first few days of age may facilitate a more targeted approach to PDA treatment and facilitate the development of prediction markers for adverse outcomes. There is an emerging association between lower diastolic function measured using TDI and chronic lung disease in premature infants [72]. In term infants, TDI can be used to assess RV function to provide important clinical prognostic information in infants with congenital diaphragmatic hernia and may be used to monitor treatment response in infants with persistent pulmonary hypertension of the newborn (PPHN) [73]. The superior sensitivity of TDI to subtle myocardial dysfunction when compared with shortening an ejection fraction in term infants was recently demonstrated. In infants born to mothers with diabetes mellitus (of any cause), left and right systolic function measured using TDI velocity is lower than control term infants. This occurs without differences in shortening fraction between the two groups [74].

In summary, muscle tissue velocities obtained using TDI are a feasible, reliable and a valid modality for the assessment of myocardial performance in the premature and term neonatal population. Those measurements are highly influenced by loading conditions and therefore do not represent intrinsic function (contractility). Reference ranges across a wide variety of gestations have emerged; and their use in detecting myocardial dysfunction, guiding therapeutic interventions, predicting important clinical outcomes, and monitoring response to treatment is expanding in the neonatal population.

	Distance Cabout		Torm Cohort			
	Preterm Conort		Term	conort		
	Day 1	Day 2	Day 1	Day 2		
Left Ventricle Free Wall						
s`	2.8 (0.9)	3.3 (0.7)	4.9 (0.8)	4.6 (0.6)		
e`	3.6 (1.4)	4.2 (1.3)	6.7 (1.4)	6.5 (1.2)		
a`	4.0 (1.5)	4.8 (1.4)	5.5 (1.3)	5.4 (1.3)		
e`/a`	0.95 (0.36)	0.91 (0.25)	1.3 (0.4)	1.3 (0.4)		
Septum						
s`	2.4 (0.6)	3.0 (0.6)	3.6 (0.6)	3.5 (0.5)		
e`	2.8 (0.8)	3.6 (1.1)	4.7 (1.1)	4.8 (0.9)		
a`	3.9 (1.1)	4.7 (1.4)	4.2 (0.8)	4.4 (0.8)		
e`/a`	0.76 (0.21)	0.91 (0.25)	1.1 (0.23)	1.1 (0.23)		
Right Ventricle Free Wall						
s`	3.6 (0.9)	4.4 (1.0)	6.6 (1.1)	6.5 (1.1)		
e`	3.9 (1.3)	4.5 (1.1)	8.0 (1.6)	7.3 (1.2)		
a`	6.7 (1.8)	8.6 (2.6)	8.3 (1.6)	8.0 (1.3)		
Left Ventricle Event Times						
Heart Rate	154 (14)	160 (12)	119 (15)	125 (18)		
Isovolumic Relaxation time	58 (13)	52 (12)	53 (12)	52 (10)		
Isovolumic Contraction time	56 (13)	46 (11)	65 (14)	65 (12)		
Systolic time	147 (20)	150 (18)	188 (23)	184 (16)		
Diastolic time	131 (22)	126 (22)	199 (43)	195 (44)		

Table 5.1: TDI velocities and event times in preterm and term infants over the transitional period. The preterm cohort comprised 66 infants <29 weeks gestation free of inotropes. The term cohort comprised 50 infants between 37 – 42 weeks gestation, appropriately grown and free of significant maternal illness.

[Adapted from Jain et al. J Pediatr. 2016 ; Jain et al. J Am Soc Echocardiogr. 2014 Dec;27(12):1293-304; and James et al. Early Hum Dev. 2014 Dec;90(12):829-35.]

SECTION 6: DEFORMATION IMAGING AND ROTATIONAL MECHANICS

Introduction

The ability to objectively assess myocardial performance in neonates using echocardiography is an important part of a comprehensive haemodynamic assessment. Visual assessment of myocardial function is highly subjective, variable, and cannot be utilised as an aid to clinical assessment [75]. In addition, many challenges exist for monitoring the cardiovascular status of preterm infants and sick term infants; those stem from the relative insensitivity of clinical markers (such as blood pressure and capillary refill time) in defining haemodynamic compromise [6, 76] and the several limitations of conventional echocardiography methods such as fractional shortening and ejection fraction [18]. Furthermore, the objective assessment of right ventricular (RV) function cannot be performed using conventional means due to the unique nature of its shape and morphology [21]. Tissue Doppler velocity techniques that measure the velocity of movement of myocardial tissue may also have some disadvantages: In addition to their relatively higher dependency on ventricular size and on loading conditions, tissue Doppler velocity imaging interrogates motion at a single point in the myocardial wall and a non-functioning segment can be influenced by adjacent motion of a viable normally functioning segment giving a falsely reassuring picture [77].

Deformation imaging is a recently introduced technique in the field of neonatology. Myocardial strain (ϵ) and strain rate (SR) imaging are promising new techniques that can objectively assess both regional and global function in both ventricles. A thorough understanding of the basic principles of deformation imaging and rotational mechanics and recognition of their applicability and limitations in a neonatal setting are essential for advancing those techniques to routine clinical care. This section will outline the basic concepts of those functional modalities, their characteristics, image acquisition and measurement techniques, clinical applicability and available reference ranges in the term and preterm population.

Basic Concepts of Myocardial Deformation

Deformation refers to the change in the shape of the myocardium throughout the cardiac cycle form diastole to systole. This occurs as a result of sarcomere shortening due to contraction (**Figure 6.1a**). This deformation leads to a reduction in cavity size and an ejection of blood from the ventricle. The left ventricle (LV) wall consists of longitudinal fibres (from base to apex) in the endocardium and epicardium, and circumferential fibres in the mid muscular layer [78]. As a result, due this arrangement of fibres, deformation generally occurs in three planes: Longitudinal (from base to apex) leading to shortening; circumferential (shortening of the circumference in the parasternal short axis views of the LV); and radial (parasternal short axis views) or transverse (apical views) which leads to thickening of the LV muscle wall (**Figure 6.1b**). The thickening is the result of the shortening in the other two planes, due to the incompressibility of the myocardium. Due its unique myofibril architecture, which is composed of superficial oblique and deep longitudinal fibres, the dominant RV deformation is longitudinal shortening [79].



Figure 6.1: Principles of deformation. (a) Longitudinal strain refers to the change in length of a segment from its baseline length in end diastole to its deformed shape in systole. Strain refers to the degree of change in shape relative to the baseline and is expressed in (%). Shortening reflects negative values and lengthening positive values. In this image, shortening of the mid segment of the LV free wall is illustrated. (b) LV deformation occurring in three directions; L: longitudinal; C: circumferential; R: radial.

Myocardial strain (ϵ) is the term used to define the relative deformation (change in shape) occurring in systole. Two different models can be used to calculate deformation. Most software packages assess the strain as the change in length relative to the length at end diastole. Strain calculated as the change in length relative to a baseline length is termed Lagrangian strain. Strain can also be calculated as Eulerian strain, which is the sum of the instantaneous strains between consecutive frames. In calculation of the Eulerian strain, the change in length is divided by the instantaneous length at each frame and not by the length at end-diastole. The denominator in the fraction becomes smaller during contraction for circumferential and longitudinal strain. Therefore, these Eulerian strains will be larger than the corresponding Lagrangian strains. For transverse and radial strains, the instantaneous length increases during contraction and the Eulerian strains will be closer to zero than Lagrangian strains since the denominator in the fraction will be larger for the Eulerian calculations. Both strain indices are expressed as a percentage (%). Because of the differences between Lagrangian and Eulerian calculations, studies should state if the values reported are Lagrangian or Eulerian. Longitudinal and circumferential deformations are assigned a negative strain to indicate shortening and radial deformation a positive strain to indicate thickening. Peak systolic strain is the peak shortening in systole and usually occurs at the end of systole at aortic valve closure before returning to baseline at mitral valve closure (Figure 6.2A). Strain rate (SR) refers to the rate at which myocardial deformation occurs. It is expressed in 1/s and is calculated as Eulerian strain rate by most software packages. Peak systolic SR occurs in mid systole and returns to baseline (zero velocity) at aortic valve closure when no deformation occurs. During diastole, the rate at which the deformed myocardium returns to baseline shape can also be measured and this occurs in two phases: early phase (e) and atrial phase (a) (Figure 6.2B).



Figure 6.2: Strain and strain curves in one cardiac cycle in the ventricle. (A) Strain usually peaks during end systole at aortic valve closure (AVC) and returns to baseline during diastole at mitral valve closure (MVC). (B) Strain rate usually peaks in mid systole and returns to baseline at AVC when no deformation occurs. During diastole, the rate of strain returning to baseline is biphasic. MVO: mitral valve opening; AVO: aortic valve closure; SRe: early diastolic strain rate; SRa: late diastolic strain rate (during atrial contraction).

Deformation has the advantage over tissue Doppler velocities in identifying nonfunctioning segments, at is assess the change in shape regionally. For example, in an infarcted segment of myocardium, that lack of change in shape of that segment in systole translates to zero strain (and SR). As that non-functioning segment is tethered to a functioning component of the myocardium, it would still generate a displacement velocity. Several studies have established the validity of deformation measurements in the adult population obtained using echocardiography against 3-dimensional myocardial strain obtained using tagged magnetic resonance imaging (MRI) techniques [80-83].

As for ejection fraction, strain assessed either regionally (when examining a specific segment) or globally (when assessing the whole ventricle) is dependent on loading conditions. Strain rate on the other hand correlates well with load independent measures of contractility and is a more accurate reflection of myocardial contractile function [84]. Studies in animal models and in preterm infants have demonstrated that preload has a positive impact on strain and that an increasing afterload results in a reduction in strain [84-86]. In addition, following patent ductus arteriosus (PDA) ligation in preterm infants (which results in a sudden increase in LV afterload and a reduction in LV preload), LV strain significantly decreases in the immediate post-operative period [18]. In the early transitional period, there is a significant negative correlation between strain and surrogate measures of afterload and a significant positive correlation between strain and surrogate measures of preload [87]. The administration of antenatal magnesium sulphate to the preterm population results in an improvement in strain, possibly by lowering systemic vascular resistance (SVR) in the early transitional period [88]. However, SR appears to be less influenced by loading conditions (Figure 6.3). This further supports the results of animal studies suggesting the lower SR dependency on loading conditions. Recognising those differing characteristics between strain and SR will ensure that they are used in the right context when loading conditions are accounted for.



Figure 6.3: The relationship between loading conditions and deformation parameters. There is a negative relationship between strain and systemic vascular resistance (a surrogate of afterload) but a positive relationship between strain and left ventricle end diastolic diameter (a surrogate of preload). Note the lack of relationship between systolic strain rate and loading measures (data set from James et al. Neonatology. 2016;109(1):69-75)

There are two methods available for the measurement and calculation of strain and strain rate: tissue Doppler-derived deformation imaging and 2-dimentional grey scale speckle tracking echocardiography (2DSTE). Those two techniques will be considered separately.

Tissue Doppler Deformation Imaging

Principles and Validation in the Neonatal Population

In the longitudinal plane of the ventricle, there is a velocity gradient from the base of the heart towards the apex. In other words, myocardium near the base moves at a higher velocity (towards the apex in systole) than myocardium near the apex (**Figure 6.4**), because of tethering effects and the apex being stationary.



Figure 6.4: Difference in velocity between two points along the long axis of the septum. The curves show tissue velocities by tissue Doppler during the cardiac cycle. The point closer to the base (yellow) has a higher systolic and diastolic velocity when compared with the point closer to the base (green). The difference in velocity is used to calculate strain rate and derive strain of that segment bordered by the two points.

Tissue Doppler (TD) derived (longitudinal) deformation imaging calculates strain rate by assessing the difference in velocity (the velocity gradient) between points along the longitudinal plane. Strain is then assessed by integrating strain rate values by time. Only velocities along (parallel to) the beam of the ultrasound is measured by the TD method and the deformation indices by tissue Doppler are therefore highly dependent on the angle of insonation. Due to the high temporal resolution of this technique TD is well suited for measurement of SR values in neonates (with a higher baseline heart rate) as it employs a calculation method that utilizes the high tissue Doppler frame rates (> 180 frames per second) [87, 89]. The major disadvantage of this approach is the dependence on the angle of insonation (>20° resulting in a significant underestimation of values) [90]. The other disadvantage is the high dependency on the requirement for clear imaging of the myocardial walls. Therefore, artifacts of extra-cardiac structures (that are usually stationary), or image dropouts can lead to over- and underestimation of strain and SR values [90]. In the neonatal population, deformation values derived using TD can be obtained from several regions of the heart. Longitudinal deformation can be measured from most parts of the left and right ventricle, while circumferential and radial deformation can be assessed only in a few LV regions. Most studies in neonates have assessed the longitudinal deformation. Some studies have assessed values from many heart segments while others have obtained values from the basal segment of the LV and RV free walls in addition to the septum as representative of the heart function. The basal segment of the LV free wall is often obscured by artefact arising from the lungs, and it is often difficult to maintain an angle insonation less than 20° between the ultrasound beam and the LV wall bringing into question the reliability of results obtained from that segment.

Several studies have established the feasibility and reproducibility of TD-derived deformation parameters in the term and preterm population. Most studies have assessed longitudinal deformation, although radial deformation has been studied as well. Recent studies have demonstrated that measurements are obtainable in about 90% of infants provided adequate imaging quality is achieved [27]. However, the LV base remains the most difficult segment to assess due to the challenges mentioned above. Nestaas et all conducted the first studies of reproducibility in term infants and revealed moderate reproducibility in obtaining strain and systolic SR with an intraclass correlation coefficients (ICC) ranging between 0.6 – 0.7 for intra- and 0.4 – 0.5 for inter-observer repeated measures [91, 92]. More recently and with further image optimization measures (see below) reproducibility data has improved in term neonates for basal strain with coefficients of variation (COV) values < 15% and ICC values > 0.75 [19, 20, 93]. Reproducibility is better in longer segments. The size of the myocardial wall limits the maximal segment size. In term neonates, a segment including most of the myocardial wall will show better reproducibility than analysis of smaller segments from the same recordings; a segment length of 21 mm vs. 11 mm in term neonates showed ICC values of 0.93-0.97 vs. 0.76-0.89 and COV values 6-12% vs. 22-38% [93]. Reproducibility data for the preterm population are more encouraging. Poon et al. reported COV values of < 5% for LV, septal and RV basal strain in preterm infants with a mean gestation of 27 weeks. Helfer et al illustrated more modest reproducibility results in preterm infants with mean gestation and birthweight of 27 weeks and 980 grams: the septum showed the best COV ranging from 10.44%-34.40% for intra- and 22.46%-27.18% for inter-observer variability, and the left wall, again showing the most maximal values (16.65%-57.21% for intra- & 28.59%-60.22% for inter-observer variability) [94].

More recently, James *et al* examined the reproducibility of LV, septal and RV basal strain and SR measurements (systolic and diastolic) in preterm infants < 29 weeks gestation. Their intra-observer ICC values ranged between 0.43 - 0.93 for LV, 0.92 - 0.97 for septal and 0.87 -0.94 for RV basal strain and SR values. The results for inter-observer reproducibility were similar: 0.69 - 0.85 for LV, 0.89 - 0.98 for septal and 0.91 - 0.96 for RV basal strain and SR values [27]. All those studies consistently show poor reproducibility of LV basal strain values and cite the poor image quality and the difficulty in obtaining an angle on insonation < 20° as the main reason. In summary, the most reproducible measurements are assessed in longer segments and when the LV base free wall is avoided as a site of measurement.

Image Acquisition and Offline Measurement

In order to obtain reliable deformation results using TD imaging, the quality of the images are of utmost importance. A clear electrocardiogram (ECG) signal with a well-defined QRS is necessary for obtaining a complete cardiac cycle for offline processing. Pulsed wave Doppler of the aortic and mitral valves should be used to annotate the timing of events as indicated in Figure 6.2. Timing of the aortic valve closure may also be obtained from the TDI curves [95]. In the neonatal population, TD imaging is used to obtain longitudinal deformation measurement from larger regions of the myocardial walls in term neonates while in preterm infants, deformation in the basal segments of the LV and RV free walls as well as the intraventricular septum has often been used. Therefore, a 4-chamber view is used to obtain a clear image of the walls with minimal artefact. The transducer should be manipulated to align the wall of interest parallel to the ultrasound beam. The sector width and depth should be narrowed to just beyond the borders of the wall to obtain a high frame rate (>180). The velocity scale (PRF) should be adjusted to avoid aliasing. A minimum of three cardiac cycles should be recorded to offline processing **[Table 6.1]**.

	Term infants	Preterm infants
Probe	5s or 7s	10s or 12s
Sector Width	Narrow	Narrow
Sector depth	Shallow	Shallow
Velocity scale (cm/s) (avoid Aliasing)	-16 - 16	-16 - 16
Transducer Frequency (MHz)	2.5 - 3.0	8.0
Pulse Repetition Frequency (kHz)	1.0	2.0
Velocity Scale (cm/s)	16	16
Frame Rate (FPS)	>200	>200
Region of Interest Length (mm)	1	1
Region of Interest Width (mm)	2 or 3	2 or 3
Strain Length (mm)	10-20	6
Linear Drift Compensation	On	On
Gaussian Smoothing	On	On

Table 6.1: Optima	I Setting for	Tissue Doppler	Deformation	Measurement.
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Those settings apply for the General Electric Vivid scanners and Echo Pac Software (GE Medical, Milwaukee, USA). Those recommendations are a guide only and setting may differ depending on new information emerging.

Obtaining Strain and SR values is achieved during offline analysis. The parameters are derived from a sample area (segment). The size of the segment is set by the size of a specific region of interest (ROI) within the myocardial wall, which is set by the operator (length and width) and a strain length (SL). The length of the ROI should be adequate to for optimal calculation while minimising noise and the width should not be larger than the width of the actual wall of interest. The operator is also required to set a strain length (SL, also referred to as a computational distance). The SL is the length along the ultrasound beam against which the velocities for each point within the ROI are compared to derive the velocity gradient. Hence, the segment size will be larger than the ROI, stretching from the ROI ½ strain length parallel to the ultrasound beams towards the apex and the base of the heart (**Figure 6.5**). The SL should not project outside the borders of the wall (into the atrial tissue for example) (**Figure 6.5**). Additional optional settings such as Gaussian smoothing and drift compensation can be utilised to minimise noise although with good image quality those may not be necessary (**Figure 6.6**). Optimal probe choices, ideal ROI width and length and SL lengths have been published for term and preterm infants and are summarised in Table 6.1 [19, 91-94].



Figure 6.5: Offline measurement of SR and Strain using Tissue Doppler. The sector width should be narrowed to increase the frame rate. The basal segment of the wall is usually interrogated to obtain SR and strain values. The ROI dimensions (length and width) are set by the operator. Strain length is also set while ensuring that the borders of the segment are not in contact with artefact or atrial tissue. The ROI can be moved slightly along the wall to obtain a clean and noise free SR and strain curve (See Figure 6.6).



Figure 6.6: An example of clear and artefact-free strain and strain rate curves over three cardiac cycles. Note the timing of events within the cardiac cycle. Strain peaks at end systolic at aortic valve closure (AVC) and systolic strain rate peaks in mid systole between aortic valve opening (AVO) and AVC.

Reference Ranges and Clinical Utility in the Neonatal Population

Several groups have published reference ranges for deformation parameters in the term and preterm population (**Table 6.2**, the summary only includes values from basal segments, the most commonly measured region and the reader is directed to the manuscripts for other segments). In the term population, longitudinal strain values range between -20 to -25 (%), while SRs values range between -1.5 to -2.5 1/s, SRe between 2.8 to 3.2 1/s, and SRa slightly lower between 2.1 – 2.4 1/s. The RV free wall has higher strain values when compared with LV free wall and septum; however, SR values are comparable. This may indicate that differing loading conditions between the RV and LV in the early neonatal period may have an impact on strain but not SR. Age at the time of scanning, heart rate, and the persistence of fetal shunts during the early transitional period appear to have a negligible impact on the measurements.

Deformation parameters have been examined in some disease states in term infants. Nestaas *et al.* have demonstrated that LV and RV deformation parameters are uniformly lower in infants with hypoxic ischaemic encephalopathy (HIE) compared with healthy controls: Overall strain in all walls: -17.8 vs -21.2 %, SRs -1.43 vs -1.61 1/s, SRe 1.72 vs 2.00 1/s and SRa 1.92 vs 2.27 1/s (all p<0.05). Interestingly, this difference occurred despite no difference in shortening fraction highlighting the advantages of deformation imaging in identifying subtle functional differences [93]. The same group have also highlighted that infants with HIE have similarly impaired myocardial function during days 1–3 whether they are cooled or not, indicating that myocardial injury may be a result of the initial asphyxial insult rather than cooling [23]. In term infants with severe persistent pulmonary hypertension of the newborn (PPHN) not responsive to inhaled nitric oxide, RV strain (-17 %) and SRs (-1.5 1/s) significantly improves following the administration of milrinone over a 24 hour period (to -23 % and -2.2 1/s respectively). This further highlights the ability of deformation parameters to identify myocardial dysfunction and monitor treatment response.

In the preterm population, transitional strain and SR values are uniformly lower than those of term infants (**Table 6.2**). Two studies have examined the maturational changes of basal deformation parameters over the first few weeks of age. LV free wall strain and SR values remain stable over the first week of age with LV strain showing an increase by 36 weeks post menstrual age (PMA). Septal and RV free wall on the other hand show a steadier increase over the first week of age [87, 96]. Like term infants, weight, gestation and heart rate have a minimal impact on those parameters. However, in the early transitional period, there is a negative correlation between echo-measured SVR and LV/Septal strain values, and a positive correlation between increasing preload associated with a PDA and LV strain. The relationship between SR values and the loading measures were less marked. This further supports the load dependency of strain but not SR. Finally, infants with chronic lung disease (CLD) have a lower RV strain (- 26.4 vs. -30.7%, p = 0.0.1) and RV SRa [4.2 vs. 5.3 1/s, p = 0.04) independent of gestation. CLD is associated with increased pulmonary arterial pressure which may explain this association.

Study and Equipment	Population	Values						
Pena <i>et al</i> [97]	Gest: 39Wks ±1.2	L		LV		Septum	RV	
	Wt=3.17Kg ±0.37		S -24.5 (3		3.8)	-25.9 (4.8)	-28.3 (4.	9)
General Electric	N=55		SRs -1.8 (0.).4)	-1.9 (0.6)	-1.9 (0.5	5)
	Age= 20 hours	SRe		3.2 (1	.5)	3.2 (1.6)	2.8 (0.8	5)
			SRa 2.1 (1.		.3)	2.4 (0.9)	2.1 (0.9)
Nestaas <i>et al</i> [98]	Gest: 41Wks[37- 42]				Day 1	Day	2 Day	3
	Wt: 3.7Kg±0.7		LV S	_	-21.1	-20.0) -21.	5
General Electric	N=48		LV S	Rs	-1.8	-1.6	-1.9)
	Day 1: 12 Hours		Septum S		-15.8	-17.1	1 -15.3	8
	Day 2: 36 Hours		Sept	tum SRs	-1.4	-1.6	-1.5	
	Day 3: 57 Hours		RV S		-22.7	-25.1	1 -25.	1
			RV S	Rs	-1.7	-2.0	-1.9)
James <i>et al</i> [87]	Gest: 27Wks[26-28]			Day1	D	ay2	Da 5-7	36 wks
	Wt: 965kg[785-1135] N=105 Day 1: 10 Hours	LV				- />		
General Electric		S		-12.2 (2.8)	-12.	8 (2.8)	-12.7 (2.2)	-15.0 (2.2)
		SRs		-1.5 (0.5)	-1.7	(0.6)*	-1.7 (0.5)	-1.8 (0.5)
Day 2: 43 Hours Day 5-7: 143 Hours	Day 2: 43 Hours	SRe		1.6 (0.8)	2.1	(0.6)	2.1 (0.7)	2.1 (0.9)
	SRa		2.6 (0.8)	2.7	(1.0)	2.7 (0.9)	3.2 (1.2)	
	36 Wks PMA (n=47)	Septu	m	/			/	/ >
	50 WK3 HWX (II-47)	S		-15.5 (3.0)	-17.	4 (3.5)	-17.9 (3.1)	-20.6 (3.6)
		SRs		-1.6 (0.3)	-1.9	9 (0.4)	-2.0 (0.4)	-2.1 (0.4)
		SRe		1.7 (0.6)	2.1	(0.6)	2.1 (0.7)	2.0 (0.6)
		SRa		2.3 (0.8)	2.7	(1.0)	2.7 (0.9)	2.7 (1.0)
		RV						
		S		-22.8 (4.8)	-24.	3 (4.7)	-25.1 (4.9)	-28.0 (5.5)
		SRs		-2.1 (0.5)	-2.5	5 (0.7)	-2.9 (0.7)	-3.0 (0.7)
		SRe		2.4 (0.8)	2.6	(0.7)	2.7 (0.9)	2.9 (0.9)
		SRa		3.6 (1.0)	4.4	(1.3)	4.3 (1.3)	4.6 (1.6)
Nestaas <i>et al</i> (ref#25)	Gest: 39Wks ±1.2			LV		Septum	RV	
General Electric	Wt=3.17Kg ±0.37		S	-19.9 (6.2)	-15.9 (4.8) 24.6 (4.8	8)
	N=55 Age= 1-3 days		SRs	-1.6 (0).4)	-1.4 (0.4)	-1.8 (0.5	5)
			SRe 2.2 (1.		.2) 1.4 (0.8)		2.2 (1.0))
			SRa	2.0 (1	.0)	1.6 (0.8)	2.8 (1.0))

Table 6.2: Reference Ranges for Tissue Doppler Deformation Parameters in the Neonatal Population

Values presented as Means and standard deviations if available. All values are obtained from the basal segments in the 4-chamber view. All strain units are %, strain rate 1/s. Gest: gestation; N: number of infants; Wt: birthweight; Wks: weeks; LV: left ventricle; RV: right ventricle; PMA: post menstrual age; S: Strain; SRs: systolic strain rate; SRe: early diastolic strain rate; SRa: late diastolic strain rate (during atrial contraction).

Two-Dimensional Speckle Tracking Echocardiography

Principles and Validation in the Neonatal Population

Two-dimensional speckle tracking echocardiography (2D STE) is an imaging technique that measures deformation by tracking the movement of speckles within the myocardial wall. Speckles are acoustic backscatter generated by the ultrasound beam and form a unique pattern in each wall segment [99]. Those speckles can be tracked frame by frame to derive the following information from segments of the myocardial wall: displacement (the movement of those speckles), velocity (the speed at which this movement occurs), strain (the relative change in distance between those speckles) and strain rate (the speed at which the change in distance occurs). The measuring software divides the walls of interest into segments and provides strain and strain rate values for each segment (**Figure 6.7**). Speckles can be tracked in any direction by the software and therefore 2D STE is angle independent within the ultrasound sector [100]. Both regional and global functional parameters can be derived using this technique. 2D deformation has a major advantage over TD-derived deformation imaging as the alignment of the wall relative to ultrasound beam is not necessary. With this relative freedom, better imaging of the walls can be sought. This is of particular importance to the LV free wall; in preterm infants, the LV can be imaged at an angle to avoid lung artefact.



Figure 6.7: 2D Speckle Tracking Echocardiography. Speckles are acoustic back scatter that form a unique pattern within the myocardial walls. Those can be tracked throughout the cardiac cycle to derive deformation measurements. In this apical 3-chamber view of the LV, the myocardial walls are divided into segments and deformation parameters are presented individually for each segment to determine regional function. In addition, deformation for the whole region of interest is used to determine global function.

2D STE employs relatively lower frame rates than TD-derived deformation (80 – 120 vs >200) and therefore strain rate parameters which rely on high temporal resolution may not be as easy to interpret as strain particularly in preterm infants with high heart rates. Circumferential deformation can be more prone to under sampling due to low frame rates when compared with longitudinal deformation [101], and generally, under sampling is avoided by a frame rate/heart rate ratio above 1 frame per second/beat per minute (in vitro model). 2D STE is carried out from the apical view to derive LV longitudinal and transverse strain (**Figure 6.8**) and in the LV parasternal short axis view to derive circumferential strain, radial strain and rotational mechanics (see later). In addition, RV longitudinal strain can be derived (**Figure 6.9**). Although 2D STE is less influenced by artefact, it remains highly reliant on clear imaging of the walls without drop outs.



Figure 6.8: Segmental strain in the three apical planes of the LV and a summary in a "Bullseye" pattern. Global longitudinal strain (often referred to as GLS) is the peak value in a compound curve made from the region of interest from the three planes.

2D STE imaging is feasible in the neonatal population with over 85% of acquisitions being of adequate quality to analyse [18, 21]. In preterm infants, the reproducibility of LV global longitudinal strain (LV GLS) is high with intra-observer and inter-observer ICC values of 0.92 and 0.93 respectively and Bland-Altman analysis showing no significant bias between observers, with good agreement [18]. Another study also reported high reproducibility for longitudinal LV global SRs with intra-observer COV and ICC of 5.1% and 0.9, and inter-observer COV and ICC of 4.7 and 0.9 respectively. De Waal et al also reported reproducibility data on LV circumferential and radial deformation parameters [79]. Circumferential strain was highly reproducible with intra- and inter-observer ICC >0.85 and COV < 10%. However, radial strain demonstrated very poor reproducibility with COV values between 18 to 50% [79]. With RV-focussed imaging, there is a high intra-observer (bias 3%; COV 2.7%; ICC 0.97) and inter-observer (bias 7%; COV 3.9%; ICC 0.93; P < .05) agreement for RV longitudinal strain [21]. In the term neonatal population, Jain et al have demonstrated that RV longitudinal strain measurements are highly reproducible with ICCs > 0.9 and COVs < 10% [26]. Recently, Nestaas et al demonstrated that the ICC for longitudinal peak systolic strain was 0.94/0.87 inter/intra observer and 0.91/0.94 for peak systolic strain rate in analyses of left and right ventricles combined [102].



Figure 6.9: Strain and Strain Rate Curves from the LV 4 Chamber View and the RV Free Walls. The coloured lines represent the deformation values from each segment and the dotted white line represents the values from the whole region of interest. Notice the relative increased level of noise in the strain rate curves (see text).

Image Acquisition and Offline Measurement

In the adult population, regional and LV longitudinal deformation parameters are obtained from the apical four, two and three chamber views (Figure 6.8). Although the same views can be utilized in neonates, most publications have used the left ventricle 4-chamber view. LV circumferential deformation is obtained from the parasternal short axis view at the level of the mitral valve, papillary muscles, and the apex. RV longitudinal deformation is obtained from a focussed RV 4 chamber view (Figure 6.9, inset). A modified RV 3 chamber view is also used to obtain RV deformation parameters in a different plane [26]. Although in theory, the septum can be regarded as bi-layered and contributing to function to both ventricles it is currently regarded as part of LV function [103].

For optimal results, the same principles of image acquisition described for TD derived deformation apply to 2D STE. Grey scale images need to illustrate walls clearly and without artefact. An ECG signal is also mandatory in addition to event timing annotation as described earlier. Fundamental and harmonic imaging with different probe types have not shown differences in strain and strain rate values in an in-vitro study [101]. The choice of transducer should probably aim at obtaining images with clear speckles. 2D STE is angle independent so the transducer can be manipulated off plane to obtain the ideal image. Recently, Levy et al has demonstrated that in order to obtain optimal reproducibility results for longitudinal strain assessment, a frame rate (FR) to heart rate (HR) ratio of at least 0.7 - 0.9 needs to applied to the acquired images. Manipulations of depth and sector width can be used to achieve this ratio. Generally a FR of 110 - 130 is required for preterm infants and 90 - 110 for term infants [104]. The images should be optimized to demonstrate the speckles and endocardial and epicardial borders clearly.

Measurement of deformation parameters is performed offline using dedicated software. In some software packages, a ROI is defined by tracing the endocardial border of the myocardium at end systole. The width of the ROI is then set to match the width of the wall of interest (**Figure 6.7**). The software then automatically tracks the movement of speckles to derive the deformation parameters. The acceptability of the tracking is automatically suggested by the software and the user can also visually inspect the quality of the tracking before finally accepting or rejecting analysis of the segment. Some adjustment of the borders may be necessary to avoid artefact. Results are then displayed for each segment (**Figure 9**) The deformation indices for the whole ROI as one large, curved segment is usually also shown (**Figure 6.8**).

Reference Ranges and Clinical Utility in the Neonatal Population

Normative data and reference ranges are still emerging for deformation parameters obtained using 2D STE in the preterm and term population. The studies to date have assessed 2D STE deformation parameters in a relatively small number of infant at differing time points and using a variety of vendors and software versions for analysis making standardisation somewhat difficult.

Table 3 summarises some of the literature available. Due to poor reliability of some deformation parameters derived using 2D STE only longitudinal and circumferential strain and systolic strain rate were presented. Radial deformation values and diastolic strain rate parameters measured using 2D STE remain unreliable in the neonatal population (**Table 6.3**).

In general, LV and RV deformation parameters measured using 2D STE appear to remain stable during the transitional period and up to 28 days. RV strain and SRs have higher values than the LV.There are ongoing studies involving a larger number of infants in both the preterm and term population aiming to publish normative and reference values.

2D STE has also been examined in some disease states in the neonatal population. One of the first studies of 2D STE in preterm infants illustrated the negative impact a PDA ligation has on LV GLS in the immediate post-operative period with a recovery 24 hours later [18]. The reduction in LV GLS post-operatively was attributed to the increase in afterload and the decrease in preload associated with the procedure. In the early transitional period, another study demonstrated that the administration of MgSO₄ in the antenatal period is associated with a lower SVR and a higher LV GLS on day 1 of age [88]. Those studies further highlight the load dependency of strain (neither study reported SR). The influence of important disease states in preterm infants (such as PDA and CLD) remains unclear and warrants further study in a large cohort of infants [105].

LV function was also evaluated in term infants of diabetic mothers (gestational and pregestational diabetes). LV GLS is significantly lower in in pre-gestational (-10.4 ± 3.2, n=20) and gestational (-13.1 ± 4.7, n=25) groups when compared with the control group (-19 ± 2, n=45) [p<0.01] [106]. Similarly, LV GLS can identify dysfunction in severely asphyxiated term infants who are undergoing therapeutic hypothermia when compared with healthy controls (-11.01% ±2.48 vs. -21.45% ±2.74, p <0.001). In this study, LV GLS had a significant correlation with troponin levels ($r^2 = 0.64$, p< 0.001) suggesting that LV GLS is also capable of grading disease severity [25].

Table 6.3: Reference Ranges for Speckle Tracking Echocardiography Deformation Parameters in theNeonatal Population

Study and Equipment	Population	Values						
Klitsie et al [107]	Gest: 40Wks ±1.2	LV 4 Chamber view only for Longitudinal Strain						
	Wt=3.5Kg ±0.5	LV parasternal short axis view (papillary muscles) for Circ strain						
General Electric	N=28							
	2 Days			1 – 3 Days	3 Weeks	6 – 7 Weeks		
	23 Days	Longitud	inal Strain	-18.8 ± 3.5	-18.6 ± 2.5	-19.4 ± 2.3		
	48 Days	Circ Strai	n	-19.7 ± 4.3	-20.5 ± 4.5	-19.6 ± 4.9		
Schubert <i>et al</i> [108]	Gest: Term	4 Chamber view only was used.						
	Wt= No SGA							
General Electric	N=30			LV Septum RV				
	170 hours [135-207]	Longitud	inal Strain	-19.5 ±2.1	-19.5 ±2.1	-23.0 ±4.3		
		Systolic S	train Rate*	-2.94 ±1.05	-2.23 ±0.77	-3.61 ±1.59		
		*Basal Val	ues Presented.	Refer to manu	iscript for furth	er details		
Jain <i>et al</i> [26]	Gest: 40Wks ±1.2	RV parame	ters only					
	Wt: 3.49Kg ±0.44	-						
General Electric	N=50			0	Day 1 [Day 2		
	Day 1: 15 Hours	R	V 4-Chamber St	rain -21	.2 ± 5.3 -21	3 ± 5.4		
	Day 2: 35 Hours	R	V 3-Chamber St	t rain -21	.4 ± 4.4 -20	.6 ± 4.2		
		R	V Global Strain	-21	.2 ± 3.9 -21	1.2 ± 4.2		
Nasu <i>et al</i> [103]	Gest: 33 Wks ± 2	4 Chamber	View Used. Sep	otum was divid	ded into LV and	RV sides		
	Wt= 1.9Kg ± 0.21							
QLAB, Philips	N=21		1 Hr	24 Hr	48 Hr	72 Hr		
	Serial Data	LV	-23.8 ± 4.0	-23.4 ± 3.2	-23.8 ± 5.1	-24.9 ± 3.2		
		Sep-LV	-22.7 ± 5.7	-21.0 ± 5.1	-19.8 ± 3.1	-20.9 ± 3.0		
		RV	-22.0 ± 4.7	-24.7 ± 4.7	-20.8 ± 2.6	-22.9 ± 5.1		
		Sep-RV	-17.9 ± 4.5	-17.7 ± 4.6	-17.3 ± 4.5	-14.7 ± 4.6		
		More time	points available	e in the Manus	script.			
Hirose et al [109]	Preterm Group	4 Chamber	view only used	for longitudir	nal Strain			
	Gest: 27Wks ± 1.2	LV base an	d apes planes w	vere used for c	circ strain			
General Electric	Wt: 1.1 Kg ± 0.2			Pre	term	Term		
	N=30	Loi	ngitudinal Strai	n -16.0) ± 3.3 -17	.6 ± 3.7		
	Age: 28 Days	Loi	ngitudinal SRs	-1.63	-1.63 ± 0.26 -1.59 ± 0.26			
		Cir	c Strain (Basal)	-15.5	5 ± 3.2 -15	.3 ± 4.7		
	Control Group	Cir	c SRs (Basal)	-1.75	± 0.39 -1.7	9 ± 0.41		
	Gest >37	Cir	c Strain (Apical)	-24.0	-24.0 ± 3.9 -23.7 ± 5.9			
	Wt: 3.3Kg ± 0.6	Cir	c SRs (Apical)	-2.58	± 0.68 -2.3	5 ± 0.69		
	N=30					1.55		
	Age: 28 Days	16 preterm	i infants had rep	beat scans nea	ar term. There v	was no difference		
	Casta 2714/4. [22, 20]*	In the value	es wnen compa	red with 28 da	ays.			
de waai <i>et di</i> [110]	Gest: 2/WKS [23-29]*	4 Chamber	view only used	Dev 7	Dev 44	Day 20		
TamTaalmasina	vvt: 965 [550−1530]*				Day 14			
Functional Superior	N=54		-22.9 ± 2.5	-23.2 ± 2.6	-23.4 ± 2.5	-23.3 ± 2.4		
System	serial data	LV SKS	-2.04 ± 0.41	-2.70 ± 0.55	-2.05 ± 0.41	-2.00 ± 0.47		
Crossile at al [105]	Cost: 27W/kc [2C 20]*	1 Chamber		(Madice Value				
Czernik et al [105]	Gest: 27 WKS [26-29]*	4 Champer	view only used	(iviedian valu	ies)			
Conoral Electric	VVI: 990 [745-1200]**		Davi 1	Dav: 7	Day 14			
General Electric	Serial data	1//16		15 1	15 ⊑	∪ay ∠o _1⊑ 1		
			-12.2	-12.1	-12.2	-15.1		
	IUK	LV SKS	-1.4	-1.5	-1.0	-1.0		

Schubert et al [111]	Preterm Group 4 Chamber view only was used.								
General Electric	Gest 27 WKS \pm 1.2 Wt 1153 g + 258	3 g ± 258		40 Wks PMA		53 Wks PMA			
	N=25		Prem	Prem	Term	Prem	Term	p*	
	Age 28 Wks corrected	LV LS	-17.9	-18.7	-19.5	-20.0	-22.0†	0.03	
		LV SRs	-2.33	-2.60	-2.40	-3.37†	-3.06†	0.53	
	Control Group	LV SRe	2.78	3.51	3.05	3.33	4.33†	0.28	
	Gest 39.0 Wks ± 1.2	LV SRa	2.28	2.76	2.10	2.52	3.22†	0.28	
	Wt 3456 g ± 437	Sep LS	-19.0	-20.3	-20.1	-21.9	-22.5†	0.44	
		Sep SRs	-2.12	-2.32	-2.08	-2.62	-2.60†	0.75	
		Sep SRe	2.72	2.62	2.32	3.22†	3.44†	0.93	
		Sep SRa	2.45	2.47	1.88	2.56	2.57†	0.23	
		RV LV	-20.5	-23.3	-23.0	-23.9	-24.4	0.69	
		RV SRs	-2.79	-3.81	-2.70	-4.17	-3.79†	0.38	
		RV SRe	3.20	3.59	3.00	4.54†	4.16†	0.82	
		RV SRa	2.64	3.33	2.30	2.90	3.53†	0.38	
		* For the d	ifference be	etween gro	ups at 53 w	eeks PMA	N N		
Louis Q. El. Khuffesh et al		T within gro	oup p<0.05	from 40 to	53 WEEKS F	'MA			
[112]		Day 1		Day 2		Day 5 – 7			
	Entire cohort		Bu	, -	Duy	-	Days	· •	
General Electric	Number of infants		13	2	132	32 98			
	LV GLS (%)		-18.4	+ 3.8	-20.5 ± 3.1*		-21.8 ± 3.3* †		
	LV GLSRs (1/s)		-1.8	± 0.4	-2.1 + (0.4*	-2.4 + ().4* †	
	IVS GLS (%)		-17.7	+ 2.1	-17.9 +	2.1	-18.4 +	2.1*†	
	VS GLS (70)		-1.7 :	± 0.2	-1.8 ±	0.2	-1.9 ±	·1.9 ± 0.2†	
	BV FWI S (%)		-18.8	+ 4.7	-20.1 +	5.1	-21.1	+ 4.7	
	RV FWLSRs (1/s)		-2.0 ± 0.6		-2.3 ±	0.7*	-2.8 ± 0).6* †	
	Healthy uncomplicated cohort								
	Number of infants 65						36		
	LV GLS (%)		-18.4 ± 3.5		-20.3 ± 3.2*		-20.7 ± 3.0 +		
	LV GLSRs (1/s) IVS GLS (%) IVS GLSR (1/s)		-1.8 ± 0.3		$-2.1 \pm 0.3^*$		-2.3 ± 0.4 †		
			-17.7 ± 2.1		-18.0 ± 2.1		-18.4 ± 2.1*†		
			-1.7 ± 0.2		-1.8 ± 0.2		-1.9± 0.2†		
	RV FWLS (%)		-18.1 ± 4.0		-20.3 ± 3.2		-20.5 ± 3.2*		
	RV FWLSRs (1/s)		-1.9 ± 0.5 -2.2 ±		. 0.6 -2.7 ± 0.7†				
	Data are presented as mean ± SD. Uncomplicated, defined as infants without bronchopulmonary dysplasia, echocardiographic signs of pulmonary hypertension at 32 or 36 weeks PMA, and/or a hemodynamically significant patent ductus arteriosus at Day 5-7 or any size PDA at 32 or 36 weeks PMA. RV, right ventricle; LV, left ventricle; IVS, interventricular septum FWLS, free wall longitudinal strain; FWLSRs, free wall longitudinal systolic strain rate GLS, global longitudinal strain; GLSRs, global systolic longitudinal strain rate								
Values presented a	as Means and standard de	viations if a	vailable u	nless state	d otherwis	se. All str	ain units		

Values presented as Means and standard deviations if available unless stated otherwise. All strain units are %, strain rate 1/s. Gest: gestation; N: number of infants; Wt: birthweight; Wks: weeks; LV: left ventricle; RV: right ventricle; Sep: Septum; PMA: post menstrual age; Circ: Circumferential; LS: Longitudinal strain; SRs: Systolic strain rate; SRe: early diastolic strain rate; SRa: late diastolic strain rate.

Left Ventricular Rotational Mechanics

The unique helical arrangement of subendocardial fibers (left handed) and the subepicardial fibers (right handed) enable the LV to have unique rotational properties. During systole (viewed from the apex) the apex (in addition to circumferential shortening and radial thickening) also rotates in an anticlockwise direction [6]. The base on the other hand, rotates in an opposing clockwise direction. Those rotations are expressed in degrees (°) and are assigned a positive sign if *anticlockwise* and a negative sign if *clockwise*. The net effect of this phenomenon is an LV wringing motion (in addition to shortening in the longitudinal plane) termed twist (also expressed in degrees). "Torsion" is the term used to describe LV twist indexed to its length and enables the comparison of LV twist across differing LV sizes. This wringing motion improves the ability of the LV to eject blood during systole. During diastole, the LV untwists to return to its baseline un-deformed and untwisted shape. The act of untwisting also aids in diastolic function and contributes to early diastolic filling. This is highly dependent on the elasticity of the LV [113].

The speed at which twist occurs is termed LV twist rate (LVTR) and is expressed in °/s. Similarly, the speed at which LV untwist occurs is termed LV untwist rate (LVUTR). LV untwist is facilitated by the kinetic energy stored during twisting in systole and therefore, LVUTR is highly dependent on LVTR (an example of systolic-diastolic interdependence) [114]. Like deformation, an increasing afterload appears to decrease LV twist and untwist rate in experimental animal models (mongrel dogs) and human adults [115]. Similarly, in the preterm neonatal population, increased afterload appears to negatively impact those measurements [88]. LVUTR also appears to be negatively influenced by an increasing afterload as it is highly dependent on LV twist [114]. *Ramani et al.* in a study of adult patients demonstrated that pulmonary arterial hypertension significantly reduces basal LV rotation but no effect was seen on LV apical rotation [116].

2D STE is also used to derive rotational parameters. The methodology for image acquisition and offline assessment is similar to deformation. The measurement of rotation and twist is feasible and reliable in neonates [114]. Rotational mechanics was recently studied in preterm infants [mean (SD) gestation of 26.8 weeks (\pm 1.5) and a mean birth weight of 945 grams (\pm 233), n=51]. Apical rotation remains constant over the first week of age [11.8° (\pm 5.0) vs. 12.1° (\pm 6.1) vs. 11.7° (\pm 8.3), on Days 1, 2 and 5-7 p =0.92]. Basal rotation however, changes from counter clockwise on day 1 and 2 to clockwise on day 7 [5.5 [-0.3 – 8.3] vs. 4.0 [-4.7 – 7.2] vs. -4.5 [-5.8 – -2.3], p<0.001] with a resultant net increase in twist and torsion. This translates to an increasing LVUTR over the same time period [114]. However, further studies are required to determine the clinical relevance of rotational mechanics, the effects of various disease states, and to determine reference ranges in preterm and term infants. A challenge in assessing and interpreting indices based on twist and torsion are the lack of good landmarks in the parasternal views.



Figure 6.10: Left Ventricle Rotational Mechanics. (A) Basal rotation occurs in a clockwise direction (negative and (B) Apical rotation occurs in an anti-clockwise direction (positive). (C) The net effect of the opposing rotations is called Twist. (D)The speed at which twist occurs is called twist rate (LVTR) and the speed at which untwist occurs is called untwist rate (LVUTR).

Conclusion

The assessment of deformation parameters and rotational mechanics in neonates continues to gain considerable interest. The emerging literature has clearly demonstrated their feasibility and reproducibility in the neonatal population, and the relative advantages of those techniques when compared to conventional measures. In addition, with reference ranges and normative data continuing to emerge, in addition to studies assessing their diagnostic and prognostic values and their ability to monitor treatment response, their routine clinical use is likely to become more common.

SECTION 7: ASSESSMENT OF A PDA AND CLINICAL RELEVANCE

Early treatment of a patent ductus arteriosus (PDA) in extremely low birth weight preterm infants is a controversial topic. Left to right shunting across the duct can lead to pulmonary over-circulation and compromised systemic perfusion [117]. The presence of a PDA in preterm infants is associated with several morbidities including necrotizing enterocolitis (NEC), intraventricular haemorrhage (IVH), bronchopulmonary dysplasia (BPD), death, and poor neurodevelopmental outcome [118-123]. However, a cause and effect relationship has been difficult to prove to date. Randomized studies of prophylactic and early PDA treatment have failed to demonstrate a reduction in the above-mentioned morbidities or result in an improvement in neurodevelopmental outcome [124-127]. All of these studies failed to specifically study the hemodynamic impact of the PDA prior to treatment. This is an important limitation when studying the effect of treatment on short and long-term morbidity. The presence of a PDA in the preterm infant's early life should be regarded as a continuum from being physiologic, and even potentially beneficial (during periods of elevated pulmonary pressure) to being obviously pathological (when pulmonary vascular resistance drops) leading to systemic hypoperfusion and pulmonary congestion. The hemodynamic impact of a PDA can be difficult to assess clinically. Echocardiography could potentially be used, not only for diagnosis, but also to define when a PDA becomes a harmful entity thus warranting treatment [128].

There is an increasing body of evidence suggesting that infants with a PDA associated with significant pulmonary overflow, left ventricular volume loading and decreased systemic perfusion, benefit from treatment [129]. Recent observational studies have demonstrated that a comprehensive echocardiographic assessment applied at 24 to 48 hours of the infant's life predict infants with a PDA that went on to develop severe IVH or death [123]. In addition, these markers may be able to identify poor neurodevelopmental outcome associated with a PDA [118]. Institutions which adopt a conservative approach to PDA treatment report a 4 to 7 fold increased in mortality [122, 130]. Studies implementing a more targeted approach have demonstrated some benefit in early treatment [5, 11].

Prior to echocardiography, the diagnosis of a PDA was reliant on the evolution of clinical signs including: a murmur, increased precordial activity, widened pulse pressure and bounding peripheral pulses. However, the diagnosis of a significant PDA by echocardiography precedes the development of clinical signs by a mean of 2 days [131]. There is poor correlation between physical signs and the presence of a PDA by echo in the first week of life [6, 132]. Bounding pulses and a murmur may be absent in up to 20% of infants with a PDA [133]. Therefore echocardiography remains the gold standard for PDA diagnosis [6]. This section will describe how to perform a comprehensive echocardiography assessment of the degree of PDA significance.

Assessment of PDA Diameter

The ductus is a dynamic vessel of variable architecture, with an unpredictable response to treatment. It is not possible to directly quantify the magnitude of transductal flow, however the impact on the pulmonary and systemic circulations are measurable. Two-dimensional echocardiography and Doppler methods can be used to perform a comprehensive evaluation of the significance of the ductal shunt. The high parasternal view is used to obtain a 2D image of the PDA. The probe is positioned in a complete sagittal fashion along the left border of the sternum, with the marker pointing towards the head. The probe is angled side to side to bring the duct (if present) into view. Angling the beam too much towards the right (by angling the probe towards the left) will bring the ascending aorta and part of the aortic arch into display. In the absent of the PDA, the pulmonary artery is seen above the descending aorta. The PDA diameter should be obtained in 2D from the pulmonary end **[Figure 7.1]**.



Figure 7.1: High parasternal view for PDA visualisation. The picture demonstrates probe position (A) and the echo image shows the corresponding view (B). The PDA is seen to connect the descending aorta (DAo) to the pulmonary artery (PA).

Colour Doppler should then be used to identify flow across the PDA **[Figure 7.2]**. The scale of the colour should be adjusted upwards to remove aliasing. Use pulsed wave Doppler to obtain the flow wave of the PDA. Record the peak systolic and end diastolic velocity. If the PDA is bidirectional, record the peak positive and peak negative velocity. Obtain a trace of the PDA flow and record the pressure gradient obtained from the PDA. CWD may be required in high velocity restrictive shunts.

The common Doppler patterns of a PDA are demonstrated in **Figure 7.3.** Non-restrictive flow patterns are usually of low velocity with systolic flow much higher than diastolic flow. Restrictive flow patterns are usually of a higher velocity with the systolic and diastolic flows of similar magnitude. Bidirectional flows across the PDA can occur in the early transitional period, elevated pulmonary pressures, ductal dependent lesions and coarctation of the aorta. Predominant right to left shunting is usually always pathological.


Figure 7.2: Colour Doppler of Ductal Flow (A): Imaging of a patent ductus arteriosus in a 26 week gestation neonate. The diameter measured 1.8mm. (B): Colour Doppler of the ductal flow allows visualisation of the left to right shunt across the PDA. Red flow indicates left to right shunting towards the ultrasound probe. RV: right ventricle; PA: pulmonary artery; PDA: patent ductus arteriosus; LA: left atrium; DAo: descending aorta.



Figure 7.3 Doppler patterns of Ductal Flow.

Markers of Pulmonary overcirculation

Measurements Required:

- 1) Left atrial to aortic root ratio (LA:Ao)
- 2) Left ventricular end diastolic diameter (LVEDD)
- 3) Pulmonary vein peak systolic and diastolic velocity
- 4) Mitral valve E and A velocities, E:A ratio, and mitral valve VTI
- 5) Isovolumic Relaxation time
- 6) Left ventricular output (LVO). This is described in Section 4.
- 7) Left Pulmonary artery systolic and diastolic velocity
- 8) The presence of PFO/ASD and the velocity of the shunt.

Technique for LA:Ao and LVEDD

The long axis parasternal view is used to obtain the images necessary to measure LA:Ao and LVEDD. The increase in effective pulmonary blood flow may be estimated by the left atrial to aortic ratio (LA:Ao). The LA:Ao uses the relatively fixed diameter of the aorta to assess the degree of left atrial volume loading **[Figure 7.4 & 7.5]**.

Figure 7.4: LA:Ao can be measured using this view to obtain an M-mode tracing (A). The cursor should be perpendicular to the aortic wall at the level of the aortic valve. Mmode can also be used to measure LVEDD (B). Again, the cursor should be perpendicular to the septum at the level of the mitral valve tips. M-Mode is used to measure the widest diameter of the LV during diastole.





Figure 7.5: LA:Ao ratio (A) Normal aortic to left atrial ratio. (B) Volume loaded left atrial and left ventricle indicating the presence of a significant left to right shunt. LV: Left ventricle; Ao: aorta; LA: left atrium.

Technique for Mitral valve Parameters

In the developing fetus and premature infants, the early phase of filling (E wave) is lower in velocity than the late phase (A wave) resulting in an E/A wave ratio of less than 1.0. This relates to developmental immaturity of the preterm which leads to myocardium, poor myocardial compliance and impaired diastolic performance therein limiting early diastolic flow. This differs from pattern seen in the term neonate, child and young adult where the majority of trans-mitral flow occurs in the early phase such that the E/A ratio is greater than 1.0. In neonates with a hemodynamically significant DA, an increase in trans-mitral flow occurs secondary to increased left atrial pressure, resulting in a pseudonormalization of the E/A ratio which may be greater than 1.0 resembling the pattern seen in more mature patients. To obtain the 4-chamber view, the probe is placed on the apex, at an angle pointing towards the right shoulder. The positioning marker of the probe faces the left shoulder. The operator may need on occasion to move the probe in a more lateral position to obtain this view. This particularly applies to infants a few weeks of age with evolving chronic lung disease [Figure 7.6].

The isovolumic relaxation time is the time between closure of the aortic valve and opening of the mitral valve and is prolonged in the fetus and immature neonate. It decreases in neonates with a significant PDA due to early pressure related valve closure/opening. Other potential effects of volume / pressure loading of the left heart include mitral valve regurgitation and stretching of the inter-atrial septum leading to increase in the size of the atrial septal defect **[Figure 7.7]**.



be obtained. In the Top panel, the E wave is smaller than the A wave. This is the usual pattern seen in preterm infants (see text). In the bottom pane, the E wave is larger than the E wave due to increased left atrial pressure.



Figure 7.7: IVRT Measurement. Refer to TDI section for IVRT measurement using TDI velocities.

Left Pulmonary Artery Technique

Imaging of the pulmonary arteries is obtained from the high parasternal view. In the presence of PDA, a red Doppler jet is often seen in this view depicting left to right shunting. The presence of diastolic blood flow in the left pulmonary artery is also a useful indicator of ductal significance; specifically, a high end diastolic velocity is representative a large left to right shunt and increased pulmonary blood flow. The peak systolic velocity of LPA flow in addition to the end diastolic velocity should be measured [Figure 7.8]. Colour Doppler should be used to identify flow in the left pulmonary artery. PWD should be used to with the gate placed just beyond the level of bifurcation.



Figure 7.8: Pulmonary Artery Flow (A) Normal flow in the left pulmonary artery. In the absence of a significant duct there is usually no flow in the diastolic phase. (B) Turbulent flow with a significant end diastolic velocity, a sign of a large PDA.

Assessment of pulmonary vein Doppler

This view is used to assess the pulmonary veins draining into the left atrium. It is to be stressed that this view is very difficult to obtain from the high parasternal view. In addition, this position may cause considerable discomfort and potentially some cardio-respiratory compromise in untrained hands. Pulmonary vein velocities may also be obtained from the apical 4-chamber view. PWD is used to measure the peak systolic velocity of the left and right lower pulmonary veins. Pulmonary vein VTI should also be measured **[Figure 7.9]**.



Figure 7.9: Use colour Doppler to identify the left and right pulmonary veins (PVs). The scale of the colour should be lowered to about 30 – 40 cm/seconds. Use pulsed wave Doppler to obtain the wave form at the point of entry of the right and left PVs in to the LA. Measure the S wave (systolic velocity). Also note the D wave (diastolic velocity) and A wave (atrial contraction velocity).

Version Date 2019

Assessment of the Intra-Atrial Shunt

The subcostal view is usually left towards the end of the examination as it causes discomfort to the infant. To assess the atria, the probe is positioned below the xiphoid process in an axial fashion with the marker pointing to the left. The beam is then angled towards the anterior chest wall until the atria come into view. Colour Doppler is applied to assess the presence or absence of an intra-atrial shunt. In this view, measurement of the diameter of the of the PFO, in addition to measuring the peak velocity of the shunt is necessary. Pulsed wave Doppler should be used to assess the velocity of the shunt. The gate width of the cursor should be reduced to 1-2mm.



Figure 7.10: (A) Probe position to obtain a subcostal view of the atrial. (B) The anatomy of the various structures. (C) colour Doppler showing presence of flow across the PFO/ASD. (D) shows a high velocity left to right shunt across the PFO/ASD.

Markers of Systemic Hypoperfusion

Markers of systemic hypoperfusion

- 1) Descending aortic peak systolic velocity and diastolic flow direction and velocity.
- 2) Celiac artery peak systolic velocity and diastolic flow direction and velocity.
- 3) Middle cerebral artery peak systolic velocity and diastolic flow direction and velocity.

Imaging of the Aorta

Colour Doppler should be used to demonstrate arch flow. The pulsed wave Doppler should be placed 1 cm below the opening of the PDA if present. Measure peak systolic velocity, end diastolic velocity and systolic VTI of the descending aortic flow.

Figure 7.11: The flow in the descending aorta.

Panel (A) demonstrates forward flow in diastole in the absence of a PDA. Panel (B) demonstrates the presence of absent diastolic flow in the presence of a moderately significant PDA. Panel (C) shows reversed diastolic flow in the presence of a very significant PDA.



Celiac Artery Flow

A sagittal abdominal view of the vessel is obtained in 2D **[Figure 7.12 top panel]** and colour Doppler is used to visualise the celiac trunk and the superior mesenteric artery **[Bottom Panel]**. In Figure 7.13 (A) illustrates normal flow in the absence of a significant PDA. (B) Demonstrates absent diastolic flow and a diminished systolic wave from in the presence of left to right PDA steal. (C) Shows reversed end diastolic flow

in the celiac trunk when the left to right shunting is very significant..



Figure 7.13: Doppler Flow Patterns.



Superior mesenterio

Figure 7.12: 2D and colour Doppler view of the celiac trunk.

Measurement of Middle cerebral artery Doppler

The middle cerebral artery (MCA) can be visualised using colour Doppler in the crosssectional plane from the lateral coronal suture. The transducer then manoeuvred so that as much of the MCA as possible is in view. The pulsed Doppler range gate is then placed in the artery as it runs laterally. Peak systolic velocity, end diastolic velocity and the VTI of the pulsed wave Doppler should be recorded [Figure 7.14].



Figure 7.14: Cross section of the brain at the level of the MCA. The MCA is seen coursing through laterally towards the probe. Panel (A) shows normal systolic and diastolic flow in the absence of a PDA. Panel (B) shows reduced systolic velocity and absent diastolic flow in the presence of a PDA. Panel (C) shows reversed diastolic flow in a highly significant PDA.

Determining Clinical Significance of a PDA

Combining echocardiography markers of pulmonary over-circulation and systemic hypoperfusion in a more comprehensive assessment may provide a more accurate method of grading PDA severity and selecting which PDAs warrant treatment. However, treatment of a PDA should be related to the clinical context of the infant in order to ascertain potential benefit. Below is a guide to help grade the degree of PDA significance for early treatment of a PDA (in the first 72 hours of life). The decision to treat a PDA should ultimately rest with the clinician.

Measurement	Moderate PDA	Large PDA
Ductus Arteriosus		
Diameter (mm)	1.5 – 3.0	>3.0
Ductal Velocity (m/s)	1.5 – 2.0	<1.5
Pulmonary overcirculation		
LA:Ao ratio	1.5 – 1.7	> 1.7
E wave to A wave ratio	1.0	> 1.0
IVRT (ms)	35 – 45	< 35
LVO (ml/kg/min)	200 - 300	> 300
Pulmonary Vein Doppler (m/s)	0.3 – 0.5	≥ 0.5
PA diastolic flow (m/s)	0.3 – 0.5	> 0.5
Systemic Hypoperfusion		
Descending Aorta diastolic flow	Absent	Reversed
Celiac Artery diastolic flow	Absent	Reversed
Middle Cerebral Artery diastolic flow	Absent	Reversed

Assessing the need for PDA ligation

The selection of patients for PDA ligation is challenging. Some commentators advocate that the lack of hard evidence of benefit from PDA closure negates the need to treat unless intractable hypotension or refractory congestive heart failure occurs. Conversely, others argue that a PDA is always pathological and therefore should always be treated [134, 135]. Reconciling these polar opposite viewpoints has led to confusion amongst physicians and has complicated the decision-making process. However, consideration of the ductus arteriosus as a dichotomous entity represents a physiologic oversimplification; rather, it is a physiologic continuum where shunt volume is influenced by ductal diameter and trans-ductal resistance. It is not possible to measure PDA shunt volume; however, the magnitude of the shunt volume may be estimated and classified as small, moderate or large according to surrogate echocardiography markers of pulmonary over-circulation and systemic hypoperfusion.

In response to escalating numbers of requests for PDA ligation at the Hospital for Sick Children (Toronto) and prolonged surgical wait times, a categorization system was established based on strict clinical criterion and echocardiography markers of pulmonary overcirculation and systemic hypoperfusion. [129] The purpose of the categorization system was to streamline the decision-making process and assist with case prioritization and triaging through more objective evaluation of PDA illness severity and hemodynamic significance. In addition, PDA category was linked to surgical wait times. The operationalization of this system was such that admission for surgical consideration occurred within 24 hours for category I cases, within 3 days for category II cases and within 7 days for category III cases. Since its introduction in 2005 the numbers of PDA ligation has reduced by over 50% without an increase in morbidity [128]. The components of the categorization system are summarized below:

Clinical Criteria*				
Category 1	a. Profound pulmonary hemorrhage with significant oxygenation difficulties (OI >			
		15 or MAP > 12 and $FiO_2 > 0.5$)		
	b.	Low cardiac o	output syndrome or rapidly prog	ressive cardio-respiratory failure
		requiring ≥ 2	inotropes	
Category 2	a.	a. Deteriorating respiratory status (OI > 15 or MAP > 12 and $FiO_2 > 0.5$)		
	b.	Preterm < 26	weeks with large HSDA and me	dical treatment is contraindicated
	с.	. Low cardiac output syndrome or cardio-respiratory failure requiring ≥ 1		
		inotropes		
	d.	Neonate with	NEC and large PDA which is felt	t to be a significant contributor to
		clinical instab	biity	
Category 3	a.	Inability to ex	tubate or wean respiratory sup	port
	b.	Cardiac failur	e associated with failure to thriv	/e
Echocardiography [¶]	A. PD	A diameter	B. Pulmonary over-	C. Systemic hypo-perfusion
Criteria			circulation§	
Moderate volume	1.5mm	to 3.0mm	At least two of the following-	Absent diastolic flow in at least
shunt	with un	restrictive	La:Ao ratio 1.5 – 2.0	<u>two</u> of the following-
	pulsatil	e flow (V _{max} <	IVRT 45 – 55 msec	Abdominal aorta
(A + B &/or C)	2m/s)		E:A ratio 1.0	Celiac trunk
			LVO 300 – 400 mls/kg/min	Middle cerebral artery
Large volume shunt	> 3.0 m	m with	At least two of the following-	Reversed diastolic flow in at
	unrestr	ictive	La:Ao ratio > 2.0	least <u>two</u> of the following-
(A + B + C) pulsatile flow (V _{max} <		IVRT < 45 msec	Abdominal aorta	
	2m/s)		E:A ratio > 1.0	Celiac trunk
			LVO > 400 mls/kg/min	Middle cerebral artery

* Clinical criteria must be interpreted in the setting of a PDA, and the absence of sepsis, necrotizing enterocolitis and coagulopathy. [¶] PDA ligation triaging in carried out primarily on the basis of clinical criteria but infant must have echocardiography signs consistent with at least moderate volume shunt. § May not be reliable in the presence of a large ASD (>2.0 mm) which may off-load the left atrium resulting in pseudo-normalisation of echocardiography markers.

SECTION 8: ASSESSMENT OF PULMONARY HEMODYNAMICS

Term infants born with evidence of hypoxaemia in the early neonatal period pose a diagnostic challenge. Persistent hypertension (PN) is a diagnosis usually made following echocardiography confirmation of normal cardiac anatomy. Although this initial scan should ideally be done by a cardiologist, the immediate availability of the test may not be feasible. Critical decisions may need to be made in the meantime in terms of starting appropriate therapy (inhaled nitric oxide vs. prostaglandins), the decision to transfer the infant to an appropriate facility, and parent counselling. In addition, a lengthy detailed anatomical examination at the early critical period may cause clinical instability. A functional echocardiogram performed to rule out *major* anatomical abnormalities, and establish pulmonary pressures would be ideal. Similarly, preterm infants with chronic lung disease and increasing oxygen requirements may have subclinical raised pulmonary vascular resistance. Knowing the pulmonary pressures in this population may be of benefit in instituting treatment strategies.

Demonstration of normal cardiac anatomy is essential to confirm a diagnosis of PN. Sometimes it is challenging to rule out a cyanotic heart lesion in a hypoxemic infant using clinical examination alone. Clinical signs that may indicate congenital heart disease include absence of respiratory distress, presence of a murmur, dampened lower limb pulsations, blood pressure gradient between upper and lower limbs, and failure to respond to vasodilator therapy. A detailed clinical examination may be indicative at best and the hyperoxia test is sometimes equivocal in this setting. A complete structural echocardiographic assessment is the definitive test. This test is mandatory in the setting of a presumptive diagnosis of PH where there is absence of parenchymal lung disease. In some patients with congenital heart disease, PH may coexist at presentation. Failure of early recognition of cyanotic congenital heart defects and appropriate referral has been shown to worsen the prognosis. In addition, therapeutic strategies used to reduce PVR may further compromise some patients with certain forms of heart defects. For instance, lesions associated with excessive pulmonary blood flow (e.g. total anomalous pulmonary venous connection (TAPVD); double outlet right ventricle) and lesions with critical left sided outflow tract obstruction (e.g. hypoplastic left heart syndrome). Occasionally congenital heart disease may be a coincidental finding on NPE; nevertheless, it is imperative that all patients with PH, where the likelihood of cyanotic congenital heart disease is high, have a timely anatomical evaluation by an experienced paediatric cardiologist. It such cases it is safer to maintain a patent ductus arteriosus (PDA) by intravenous infusion of prostaglandins until a duct dependent heart lesion can be ruled out. In addition prostaglandin therapy is sometimes used as an adjunct in management of severe PPHN. A widely open ductus arteriosus can 'offload' the right ventricle by shunting blood from the pulmonary to systemic circulation, thereby reducing the RV afterload and potentially preventing RV failure. The evaluation of the neonate with pulmonary hypertension may be divided into (1) evaluation of the severity of the pulmonary hypertension, (2) evaluation of the impact on right ventricular performance and pulmonary hemodynamics and (3) evaluation of the impact on left ventricular performance and systemic blood flow. A systematic approach will be presented below for the assessment of an infant with PH. For the assessment of LV and RV function, refer to other relevant sections. This section will focus on PPHN-specific findings.

1) SUBCOSTAL VIEW

Inferior Vena Cava View

Inspection of the inferior vena cava in pulmonary hypertension (PH) can demonstrate a dilated vessel due to elevated RA pressures **[Figure 8.1]**. The IVC remains dilated throughout the cardiac cycle due to the increased right atrial pressure during systole and diastole. Colour Doppler can demonstrate low velocity bidirectional flow in both the IVC and the hepatic veins is the RA pressures are high. The low velocity and bidirectional flow shown in figure 8.1 is secondary to elevated right atrial pressures and indicates impaired systemic venous return.



Figure 8.1: Dilated IVC and low velocity bidirectional flow on PWD.

Atrial View

Elevated right atrial pressures can be identified by a bulging inter-atrial septum into the left atrium in 2D imaging. The PFO membrane can move in a bidirectional fashion during the cardiac cycle. Elevated RA pressures may be a reflection of impaired RV diastolic function secondary to elevated pulmonary arterial pressures in the setting of PH. In Figure **8.2,** colour Doppler demonstrates the presence of a right to left component to the shunting across the PFO. The PWD illustrates bidirectional flow.



Figure 8.2: Right to left flow across the PFO and bidirectional shunting on PWD.

2) LONG AXIS PARASTERNAL VIEW

RV Inflow: Tricuspid Valve Regurgitation

The tricuspid valve can be used to assess the presence of tricuspid valve regurgitation. By utilizing Doppler ultrasound, it is possible to estimate right ventricular systolic pressure (RVSP) in the presence of a tricuspid regurgitation (TR). According to this equation the pressure gradient between two chambers is directly related to the peak velocity of flow. The peak velocity of tricuspid regurgitation jet can be measured by CW Doppler interrogation of the tricuspid valve from the apical four chamber and/or parasternal long axis views. Colour Doppler is used to identify the presence of a TR jet as illustrated **[Figure 8.3]**. The blue jet occurring in systole seen across the valve is TR. The modified Bernoulli's equation can then be applied to the velocity of the TR jet obtained by CW Doppler as:

$$RSVP = RAP + (4 \times Vmax^2)$$

Where RVSP is right ventricle systolic pressure, RAP is right atrial pressure (usually taken as 5-7 mmHg) and Vmax is peak velocity of TR jet.

Figure 8.3: TR jet and corresponding CWD image.

The Upper panel demonstrates the presence of TR in systole and the lower panel illustrates that the velocity of the TR jet is about 4m/s giving a pressure gradient of 64 mmHg across the valve. To ensure accuracy the angle between the TR jet and line of interrogation should be minimal. This can be achieved by visualization of flow by simultaneous use of colour flow Doppler. Note that the degree of pulmonary hypertension maybe underestimated in the presence of RV dysfunction.



RV outflow

Visualisation of the pulmonary artery (PA) in this view can be used to determine the presence of PA dilatation, the presence of pulmonary incompetence (PI) and the measurement of PAAT: RVET Ratio (see below). In the 2D image, the pulmonary artery can be dilated due increased PA pressure. Colour Doppler interrogation of the PΑ may also demonstrate the presence of pulmonary valve regurgitation (or incompetence). This occurs due to the elevated diastolic pressures of the pulmonary arteries [Figure 8.4]. The Bernoulli equation can be used to determine PA diastolic pressures from this view.

Under normal circumstances the Doppler envelope of the flow waveform in the main pulmonary artery (MPA) is laminar with gradual acceleration and deceleration, almost acquiring the shape of an "isosceles" triangle. In PH as the right ventricle pumps against a high resistance, the Doppler envelope of the MPA becomes more like a "right angled" triangle with rapid acceleration, notching and gradual deceleration. The ratio between pulmonary artery acceleration time (PAAT), also known as time to peak velocity, and right ventricle ejection time (RVET) can provide a semi-



Figure 8.4: Pulmonary valve incompetence.



Figure 8.6: Low pulmonary artery blood flow in PPHN.

quantitative measure of severity of pulmonary hypertension. The normal value of PAAT: RVETinv is < 4 [Figure 8.5]. In addition to this measurement, reduced pulmonary blood flow may be illustrated by a low velocity flow across the pulmonary artery [Figure 8.6].



Figure 8.5: Measurement of PAAT:RVET.

3) SHORT AXIS PARASTERNAL VIEW

Examination of the septal wall motion during systole can provide a qualitative assessment of the degree of PH. The septal wall normally curves into the RV as the LV pressures exceed the pressures on the right side. When the RV pressures increase (between ½ systemic to systemic levels), the septum becomes flattened in systole as the RV pressures approach the LV pressures. In severe pulmonary hypertension the left ventricle cavity may become crescentic in shape due to the effect of a pressure and volume loaded left ventricle (when RV pressures exceed LV pressures) [Figure 5.7].



Figure 8.7: Varying septal morphology depending on degree PH on the short axis view.

4) APICAL VIEW

Four Chamber View

Significant or prolonged exposure to increased afterload often leads to right ventricular (RV) dysfunction. The coexistence of a high PVR and RV dysfunction may result in critically low pulmonary blood flow. In addition, high PVR may also lead to RV dilatation causing leftward deviation of the interventricular septum, thereby reducing the LV cavity size and compliance. This will further compromise left heart preload, and both systolic and diastolic function. This phenomenon is termed as 'interventricular interaction' and has been demonstrated in animal models as well as adult patients of pulmonary hypertension. If the clinical state remains uncorrected, the LV ultimately decompensates causing critically low cardiac output and systemic hypoperfusion. The right ventricle is crescentic in shape and 'wraps' around the LV which makes guantitative evaluation challenging. Nevertheless, moderate to severe RV dysfunction can usually be diagnosed by subjective assessment in 2D echocardiography [Figure 8.8]. In addition, TAPSE, FAC and TDI can be carried out to assess the degree of RV dysfunction.



Figure 8.8: RV dysfunction with bowing of the septum into the LV cavity (A) and RV dilatation (B).

Mitral Valve & Pulmonary Vein Doppler

The mitral valve can be easily and accurately interrogated from the apical 4chamber view. The pulse wave Doppler gate is placed within the valve annulus and the envelope is traced to measure the area under the curve (velocity time index; VTI). This provides a quantitative assessment of effective left ventricle preload (i.e. pulmonary venous return ± net shunt across foramen ovale). In the setting of increased SVR, MV regurgitation can also be seen as illustrated **Figure 8.9**. In the presence of PH, there is reduced MV inflow in diastole due to reduced pulmonary venous return.

Figure 8.9: MV inflow and Doppler. Mitral valve inflow wave form may be reduced in the presence of reduced pulmonary venous return secondary to high PVR.



5) HIGH PARASTERNAL VIEW

Ductal view

PASP can be calculated if the systemic systolic blood pressure (SSBP) is known by one of the following equation:

$$PASP = SSBP + (4 \times Vmax^2)$$

if right to left shunt is \geq 30% of cardiac cycle use the peak velocity of right to left flow across the PDA. Otherwise if the right to left shunt is < 30% of cardiac cycle use this formula:

$PASP = SSBP - (4 \times Vmax^2)$

Note that the PDA can close or become restrictive and the TR jet can become undetectable especially in the presence of right ventricle dysfunction. This will render those methods useless for PASP estimation.



Figure 8.10: Right to left flow across the PDA

SECTION 9: OTHER POTENTIAL APPLICATIONS OF NPE

The expanded role of point of care ultrasound includes screening for intraventricular haemorrhage, umbilical or percutaneous catheter insertion and monitoring, evaluation of intraabdominal organs e.g. bladder size or screening for ascites or other cavity effusions. The role of point of care ultrasound in facilitating catheter insertion is particularly important. With echocardiography, the inferior vena cava-right atrial junction can be easily visualized using a para-sagittal subcostal view. This may facilitate real time placement of UVCs thereby minimizing the amount of radiographs taken, and infant manipulation. In a study of 53 newborns, echocardiography revealed that 77% of UVCs deemed in good position by chest radiographs were incorrectly positioned [136] **[Figure 9.1].**

The introduction of NPE in the NICU to aid in PICC placement and positioning is feasible and results in a reduction of the number of radiographs taken to confirm line positioning thus minimizing exposure to radiation [51]. Following the initial radiograph which remains necessary in identifying the approximate location of the tip, rule out aberrant line course and rule out intravascular coiling, further assessment may be done using NPE. This modality may also reduce the incidence of complications associated with PICC lines by ensuring correct tip placement. However, the introduction of NPE into NICUs requires a cost-benefit analysis, trained staff to perform the procedure and ongoing quality assurance to maintain skills.



Figure 9.1: Lack of correlation between PICC line tip position on plain radiographs (A: AP view and B: lateral view, black arrows) and NPE (C: subcostal apical view, and D: long axis right atrial view, white arrows)

The increasing use of functional echocardiography in the NICU has led to an increased detection rate of intravascular thrombi associated with umbilical artery catheters [137, 138]. There is however, no consensus to guide the management of this incidental finding. Local experience shows that the majority of these thrombi resolve spontaneously once the catheters are removed. Intra-cardiac vegetations in association with long lines and UVCs may also be detected in infants with persistently positive cultures and persistent thrombocytopenia. A paediatric cardiologist opinion is highly recommended for the management of these cases [139] **[Figure 9.2].**



Figure 9.2: Intra-cardiac vegetations in neonates are relatively rare and are usually diagnosed following related symptoms such as persistent thrombocytopenia, a new onset murmur, or persistent sepsis. We observed an intra-cardiac vegetation diagnosed incidentally following routine monitoring of a patent ductus arteriosus in a 25+2 week preterm neonate with a birth weight of 840 grams, and bilateral grade IV haemorrhages on day 17 of life. Of note, a PICC line was inserted the previous day with tip seen to touch the inter-atrial septum. Echocardiography revealed a vegetative mass extending to both atria with its centre attached to the atrial septum at the foramen ovale level. This vegetation carries a high risk of embolization to the brain due to its unique position. The neonate was commenced on a 6-week course of antibiotics, with good response.

APPENDIX

I. NPE STANDARD NEONATAL FUNCTIONAL PROTOCOL

This protocol is the reference protocol for image acquisition to exclude major congenital heart disease and evaluate neonatal cardiac function and hemodynamics. It should also be considered the reference protocol for the other studies, which may be adapted to satisfy the unique examination. In the other protocols, knowledge of the basic imaging views is assumed and they will focus more specifically on the particular information to be obtained with each different lesion.

Key Elements

• Sweeps

 \circ Subcostal long & short axis in 2D and colour

- \circ Parasternal long & short axis in 2D and colour
- $_{\odot}$ Apical four chamber in 2D and colour
- \circ Supra-sternal; superiorly for arch sidedness; laterally for LSVC

Measurements

- All valve annuli
 Branch PAs
 Arch
 Chamber and wall dimensions
- Define pulmonary and systemic venous return
- Shunts: atrial, ventricular, ductal
- Systolic and diastolic ventricular function

Principles of Imaging

- 1. Warm sterile ultrasound gel should be used for all imaging
- 2. Ensure that patient well-being is conducive to the performance of a complete study
- 3. The target duration for a standard examination is no greater than 30 minutes
- 4. A clear ECG signal should be obtained on the imaging screen
- 5. Time should be taken to ensure the optimal environment for imaging
- 6. A neck roll should be available for high or supra-sternal evaluations
- 7. The order of image acquisition may be adapted to the stability of the patient
- 8. Lighting in the room should be low to avoid using too much gain
- 9. Infant should be in a supine position
- 10. EGC leads should be away from the echo windows
- 11. For the assessment of regurgitant jets the Nyquist limit should be set at 70 cm/sec
- 12. Measurements should ideally done at the end of the exam to minimise discomfort
- 13. Patients' blood pressure, gestational age and weight should be recorded

SPECIFIC IMAGING WINDOWS

<u>SUBCOSTAL</u>

Situs view + sweep in transverse plane: cross-section of spine, abdominal Ao + IVC (single sweep with colour doppler)

Abdominal Ao and IVC long axis

- colour IVC + PW hepatic veins
- colour + PW Doppler in abdominal aorta ensuring minimum angle correction possible

Measurements:Descending aortic diastolic flow (level of the diaphragm)Peak, mean, and end diastolic velocity of celiac trunk. Celiac VTI.

Long-axis views with sweep from posterior to anterior. Acquire one colour Doppler sweep to screen for atrial communication (if present) and demonstrating atrio-ventricular and ventriculo-arterial connections. Specific interrogation (using 2D, color/ PW/ CW Doppler) may be needed if abnormalities are detected.

- Posterior view: atrial septum: 2D + colour
- Measure, colour, Doppler ASD / PFO if present
- RV inflow, 2D + colour
- LVOT / Aortic valve, 2D + colour
- RV outflow, 2D + colour

Measurements:ASD size, shunt direction and gradient (2D, PWD)Evaluation valvular gradient (where relevant)

Short axis subcostal views: rotate clockwise

- Bicaval view SVC and IVC (acquire 2D then colour Doppler)
- One sweep from right to left with color box covering the interventricular septum.
- Doppler at any level if pathology is suspected or turbulent / abnormal flow on colour Doppler is detected.
- Superior mesenteric, celiac or renal artery 2D, color and PWD evaluation

Measurements:Evaluation valvular gradient (where relevant)IVC diameter and respiratory variation (2D)SMA, celiac, renal peak systolic and end-diastolic velocity, resistance and
pulsatility index

PARASTERNAL LONG AXIS

Long axis (PLAX):

- 2D PLAX image
- Zoom on the aortic valve;
- Zoom on the MV
- Colour aortic valve and mitral valves
- M-mode of LV at the level of tip of mitral valve leaflets with line of interrogation perpendicular to IVS.
- M-mode through aortic valve leaflets with line of interrogation perpendicular to aorta
- Acquire one colour sweep covering entire IVS from anterior (PA) to posterior (TV) to rule out VSDs

Measurements:	Aortic valve annulus diameter (2D)
	Evaluation valvular gradient (where relevant)
	LV cavity and wall dimensions
	LV fractional shortening
	LA: Ao ratio, LVET, R-R interval
	Subjective evaluation of RV systolic performance

RV inflow in 2D:

- Zoom on the TV
- RV inflow view: colour + Doppler

Measurements: RVSp calculation (CWD)

RV outflow in 2D:

- Zoom the PV
- PW Doppler in RVOT and MPA / CW for PAp
- Measurements:Pulmonary valve annulus diameter (2D)
Evaluation valvular gradient (where relevant)
RV VTI (PWD) for RVO calculation
Pulmonary artery acceleration time, RVET
Subjective evaluation of RV systolic performance

PARASTERNAL SHORT AXIS

Short axis (SAX):

Level of aortic valve

- aortic valve , zoom valve, define cusps, colour
- image right and left coronary artery origins: 2D + color (lower Nyquist)
- tricuspid valve: 2D + colour + CW Doppler
- pulmonary valve + colour + PW (+ CW where relevant)

Measurements:RVSp calculation – if superior trace (CWD)Evaluation valvular gradient (CWD where relevant)MPA VTI (PWD) for RVO calculation – if superior traceSVC diameter (M-mode or 2D) – angle counterclockwise and anterior

Level of LV: multiple levels 2D and colour flow Doppler screen

- the mitral valve; 2D + colour
- basal LV in short axis with M-mode measurements
- the papillary muscles
- LV apex.
- Single colour sweep of IVS from base to apex to exclude VSDs. Adapt color scales to lower levels (40-60 cm/s)

APICAL

Apical four chamber (A4C)

- 4-chamber view in 2D
- 4-chamber view sweep in colour from anterior to posterior to check for VSDs

A4C View, LV

- 2D view of LA / LV
- Zoom MV: 2D with annular measurement
- LV inflow: Colour, PWD and/or CWD
- Colour and PW pulmonary vein for velocities

Measurements: Mitral valve annulus diameter (2D)

Transmitral flow (PWD) - E wave, A wave, deceleration time, A-duration Transmitral flow (CWD) if valvular regurgitation or if inflow obstruction present, measure peak and mean gradients

Pulmonary vein flow (PWD) - S wave, D wave, A wave reversal velocity, A wave duration

Subjective evaluation of RV systolic performance

Ejection fraction (as indicated below) according to biplane Simpson's method

Apical five chamber

- 2D of LVOT + colour
- Doppler of LVOT: PW (+ CW where relevant)

Measurements: Isovolumic relaxation time (TDI) LVOT VTI for LVO calculation (PWD)

Evaluation valvular gradient (CWD where relevant)

A4C view, RV

- 2D image of RA / RV
- Zoom TV: 2D
- colour RV inflow
- M-mode of tricuspid valve annulus
- PW + CW of TV
 - measure: E wave velocity from PW
 - if TR is present, do CW and measure

Measurements:Tricuspid valve annulus diameter (2D)Trans-tricuspid flow (PWD) - E wave, A waveTrans-tricuspid flow (CWD) if valvular regurgitation to estimate RVSPTAPSE (M-mode)

Apical two chamber

- 2D of LA / LV plus colour Doppler and for Simpsons Biplane Calculation

SUPRASTERNAL

- In short axis: 2D + colour Doppler + PW SVC and ductus arteriosus (ductal sweep)
- Short axis arch sidedness sweep using colour Doppler
- Short axis sweep for left SVC using colour Doppler
- Arch long axis: 2D + colour + Doppler
- Measurements:PDA diameter pulmonary and aortic end (2D and Color Doppler)Direction of ductal flowPeak and mean velocity of tranductal flow (PWD)Pre- and post-ductal aortic arch gradient (PWD or CWD where relevant)

HIGH PARASTERNAL LONG AXIS

- Define pulmonary artery branches
- Define four pulmonary veins (crab view, in small children), acquire 2D image and colour flow Doppler. Do PW Doppler if turbulent flow is detected.

Measurements:Pulmonary artery branch diameter (2D)Pulmonary artery peak velocity and gradient (PWD)Pulmonary venous peak velocity and gradient (PWD where relevant)

CRANIAL AXIAL VIEW

- Define middle cerebral artery (2D, color and PWD evaluation)

Measurements: MCA peak systolic and diastolic velocity, resistance and pulsatility index

CALCULATE biplane Simpson's if

- ➢ If M-mode is abnormal (FS<25%)</p>
- If regional wall motion abnormalities
- > If paradoxical motion of the interventricular septum
- When abnormal geometry

ADVANCED FUNCTIONAL IMAGING

Principles:

- > 2D imaging: frame rates 60 110 fps for Speckle tracking, record 2 beat loops.
- > Color TDI: highest frame rates possible (at least 150 fps); record 4 beat loops.

TDI from A4C view

- Tissue Doppler e', a' and s' tracings and velocity measurements at TV annulus, basal septum and lateral MV annulus

II. ASSESSMENT OF A PATENT DUCTUS ARTERIOSUS PROTOCOL

Preamble: NPE may be performed in premature infants with respiratory failure or hemodynamic instability, where congenital heart disease is not suspected by the attending clinical team.

Goals of PDA evaluation

- 1. Document patency of the ductus arteriosus
- 2. Exclude congenital heart disease that is duct-dependant (First study)
- 3. Characterize hemodynamic significance according to echocardiography markers which are surrogates of the magnitude of the ductal shunt.
- 4. It must be recognized that determination of hemodynamic significance requires integration of echocardiography markers in the context of the clinical scenario.

Indications

- 1. Premature infant with clinical signs of pulmonary overcirculation or systemic hypoperfusion thought to be attributable to a hemodynamically significant ductus arteriosus
- 2. Premature infant with a murmur or signs of a PDA, and no suspicion of congenital heart disease
- 3. Longitudinal evaluation of hemodynamic significance in a patient with known PDA
- 4. Postoperative evaluation following surgical ligation of the ductus arteriosus

Study type

First study: Comprehensive NPE study to exclude duct-dependent lesions and characterize hemodynamic significance of the ductus arteriosus where relevant.

Repeat study: Standard NPE study characterize hemodynamic significance of the ductus arteriosus through surrogate echocardiography markers of pulmonary overcirculation and systemic hypoperfusion. Attention should also be paid to the aortic arch to exclude coarctation and branch pulmonary artery stenosis. This study still will be reviewed and reported by a neonatal echocardiographer who has completed advanced training.

Pre-intervention assessment

Morphology

- PDA: location, size
- Aortic arch: sidedness, arch anomalies (IAA, coarctation)
- PA branches: confluent PAs, LPA/RPA stenosis
- EXCLUDE: RVOTO/LVOTO
- Any associated CHD

Functional

- 1. **PDA** *morphology*: shunt size (pulmonary and aortic end), direction (L-R-bidirectional), gradient (mean + peak)
- 2. *Left Heart Volume Loading*: LV dimensions (LVEDD), LA dimensions (LA size, LA:Ao ratio), Pulmonary artery diastolic flow (Level of MPA, Left branch), Right upper pulmonary vein peak diastolic velocity. Mitral valve inflow VTI.
- 3. *Left Heart Function*: systolic (LV FS and/or EF) and diastolic (E/A ratio, IVRT) function, left ventricular output (LVO)
- 4. **Systemic Hypoperfusion**: Diastolic flow in post-ductal aorta, SMA, celiac and middle cerebral arterial diastolic flow, LVO: SVC flow ratio

Follow-up PDA assessment

Functional	
1.	PDA morphology: shunt size (pulmonary and aortic end), direction (L-R-
	bidirectional), gradient (mean + peak)
2.	Left Heart Volume Loading: LV dimensions (LVEDD), LA dimensions (LA size, LA:Ao
	ratio), ASD size, flow direction and gradient, Pulmonary artery diastolic flow (Level of
	MPA, Left branch),
3.	Left Heart Function: systolic (LV FS and/or EF) and diastolic (E/A ratio, IVRT)
	function, left ventricular output (LVO)
4.	Systemic Hypoperfusion: Diastolic flow in post-ductal aorta, SMA, celiac and middle
	cerebral arterial diastolic flow, LVO:SVC flow ratio
5.	Aortic Arch: Arch compromise following PDA closure

Post-Ligation assessment

Morphol	ogy	
- Resid	- Residual PDA	
- Aort	- Aortic arch obstruction	
- PA b	- PA branches: LPA/RPA stenosis	
Functiona	al	
1.	PDA morphology (where relevant): shunt size (pulmonary and aortic end), direction	
	(L-R-bidirectional), gradient (mean + peak)	
2.	Left Heart Volume Loading: LV dimensions (LVEDD), LA dimensions (LA size, LA:Ao	
	ratio), Pulmonary artery diastolic flow (Level of MPA, Left branch), RV dimensions	
	(RVEDD) and RV pressure (RVSp)	
3.	Left Heart Function: systolic (LV FS and/or EF) and diastolic (E/A ratio, IVRT)	
	function, <u>left ventricular output</u> (LVO)	
4.	Systemic Hypoperfusion: Diastolic flow in post-ductal aorta, SMA, celiac and middle	
	cerebral arterial diastolic flow	

Note 1: Evaluation of left ventricular output critical in the management of postoperative cardio-respiratory instability

Note 2: Emphasis should be placed on assessing the presence of aortic arch and left pulmonary artery turbulence attributable to possible tethering of these vessels following clipping of the duct. The assessment of pericardial effusion should also be carried out.

COMPREHENSIVE STRUCTURAL AND FUNCTIONAL IMAGING PROTOCOL OF PDA ASSESSMENT

SUBCOSTAL

- Situs view + sweep in transverse plane: cross-section of spine, abdominal Ao + IVC (2D + colour)
- Abdominal Ao and IVC long axis
 - colour IVC + PW hepatic veins
 - colour + PW Doppler in abdominal aorta
 - colour and PW Doppler of the celiac trunk.

Measurements: Descending aortic diastolic flow reversal (level of the diaphragm) Peak, mean, and end diastolic velocity of celiac trunk. Celiac VTI.

- Long-axis views with sweep from posterior to anterior. Acquire one colour Doppler sweep to screen for atrial communication (if present) and demonstrating atrioventricular and ventriculo-arterial connections. Specific interrogation (using 2D, color/ PW/ CW Doppler) may be needed if abnormalities are detected.
 - Posterior view: atrial septum: 2D + colour
 - Measure, colour, Doppler ASD / PFO if present
 - RV inflow, 2D + colour
 - LVOT / Aortic valve, 2D + colour
 - RV outflow, 2D + colour

Measurements:ASD size, shunt direction and gradient (2D, PWD)Evaluation valvular gradient (where relevant)

Short axis subcostal views: rotate clockwise

- Bicaval view SVC and IVC (acquire 2D then colour Doppler)
- Sweep from right to left: 2D + colour
- RVOT + pulmonary valve: 2D + colour
- Doppler at any level if pathology is suspected or turbulent / abnormal flow on colour Doppler is detected.
- Superior mesenteric, celiac or renal artery 2D, color and PWD evaluation

Measurements:	Evaluation valvular gradient (where relevant)
	SVC VTI (PWD)
	IVC diameter and respiratory variation (2D)
	SMA, celiac, renal peak systolic and diastolic velocity, resistance and
	pulsatility index

PARASTERNAL

Long axis (PLAX):

- 2D PLAX image
- Zoom on the aortic valve;
- Zoom on the MV
- Colour aortic valve and mitral valves
- M-mode of LV at the level of tip of mitral valve leaflets with line of interrogation perpendicular to IVS.
- M-mode through aortic valve leaflets with line of interrogation perpendicular to aorta
- Acquire one colour sweep covering entire IVS from anterior to posterior to rule out VSDs

Measurements:	Aortic valve annulus diameter (2D)
	Evaluation valvular gradient (where relevant)
	LV [LVEDD (2D) – z scores], RV cavity and wall dimensions
	LV fractional shortening
	LA: Ao ratio, LVET, R-R interval
	Subjective evaluation of RV systolic performance

RV inflow in 2D:

- Zoom on the TV
- RV inflow view: colour + Doppler

Measurements: RVSp calculation (CWD)

RV outflow in 2D:

- Zoom the PV (2D & color) exclude stenosis and/or atresia
- PW Doppler in RVOT and MPA / CW for PAp

Measurements:Pulmonary valve annulus diameter (2D)
Evaluation valvular gradient (where relevant)
RV VTI (PWD) for RVO calculation
Pulmonary artery acceleration time, RVET
Subjective evaluation of RV systolic performance
Assess pulmonary regurgitation, if present measure early diastolic
pressure gradient as estimate for mean PA pressure

Short axis (SAX):

Level of aortic valve

- aortic valve , zoom valve, define cusps, colour
- tricuspid valve: 2D + colour + CW Doppler
- pulmonary valve + colour + PW (+ CW where relevant)

Measurements:RVSp calculation – if superior trace (CWD)
Evaluation valvular gradient (CWD where relevant)
RV VTI (PWD) for RVO calculation – if superior trace
SVC diameter (M-mode or 2D) – angle counterclockwise and anterior

Level of LV: multiple levels 2D and colour flow Doppler screen

- the mitral valve; 2D + colour. M-mode at mitral valve tips.
- basal LV in short axis with M-mode measurements
- the papillary muscles
- LV apex.
- Single colour sweep of IVS from base to apex to exclude VSDs. Adapt color scales to lower levels (40-60 cm/s)

Measurement: FS%, LV wall and cavity dimensions in diastole.

<u>APICAL</u>

Apical four chamber (A4C)

- 4-chamber view in 2D
- 4-chamber view sweep in colour from anterior to posterior to check for VSDs

A4C View, LV

- 2D view of LA / LV
- Zoom MV: 2D with annular measurement
- LV inflow: Colour, PWD and/or CWD
- Colour and PW pulmonary vein for velocities
- Note the presence of pericardial effusion (post PDA ligation)

Measurements:

5: Mitral valve annulus diameter

Trans-mitral flow (PWD) - E wave, A wave, deceleration time, A-duration, MV VTI

Trans-mitral flow (CWD) if valvular regurgitation or if inflow obstruction present, measure peak and mean gradients

Pulmonary vein (RUPV) flow (PWD) - S wave, D wave, A wave reversal velocity, A wave duration

Subjective evaluation of RV systolic performance

Ejection fraction (if indicated) according to biplane Simpson's method

Apical five chamber

- 2D of LVOT + colour
- Doppler of LVOT: PW (+ CW where elevant)

Measurements: Isovolumic relaxation time (PWD or CWD) LVOT VTI for LVO calculation (PWD) Evaluation valvular gradient (CWD where relevant)

A4C view, RV

- 2D image of RA / RV
- Zoom TV: 2D
- M-mode of tricuspid valve annulus
- colour RV inflow
- PW + CW of TV
- TV VTI.
 - measure: E wave velocity from PW
 - if TR is present, do CW and measure

Measurements:Tricuspid valve annulus diameter (2D)
RVEDD (z score)
Trans-tricuspid flow (PWD) - E wave, A wave
Trans-tricuspid flow (CWD) if valvular regurgitation to estimate RVSP
TAPSE (M-mode)

Apical two chamber

- 2D of LA / LV plus colour Doppler
- Ejection fraction to complete simpson's biplane measurement

SUPRASTERNAL

- In short axis: 2D + colour Doppler + PW SVC and ductus arteriosus (ductal sweep)
- Short axis arch sidedness sweep using colour Doppler
- Short axis sweep for left SVC using colour Doppler
- Arch long axis: 2D + colour + Doppler

Measurements:PDA diameter – pulmonary and aortic end (2D and Color Doppler)
Direction of ductal flow
Peak and mean velocity of tranductal flow (PWD)
Pre- and post-ductal aortic arch gradient (PWD or CWD where relevant)
to rule out obstruction
SVC VTI (PWD)

HIGH PARASTERNAL LONG AXIS

- Define pulmonary artery branches
- Define four pulmonary veins (crab view) and their drainage, acquire 2 D image and colour flow Doppler. Do PW Doppler if turbulent flow is detected.
- Measurements:Pulmonary artery (R+L) branch diameter z score (2D)Pulmonary artery branches peak velocity and gradient (PWD ± CWD)Pulmonary venous peak velocity and gradient (PWD where relevant)

CRANIAL AXIAL VIEW

Measurements: MCA peak systolic and end diastolic velocity

III. APPROACH TO THE ASSESSMENT OF PPHN PROTOCOL

Preamble: NPE may be performed in patients with oxygenation failure or hemodynamic instability, where PPHN is suspected or known but congenital heart disease is not suspected by the attending clinical team.

Goals of PPHN evaluation

- 1. Confirm the diagnosis of PPHN
- 2. Exclude congenital heart disease that is duct-dependant (First study)
- 3. Evaluate the severity of PPHN
- 4. Evaluate impact of PPHN on myocardial performance and systemic blood flow
- 5. Facilitate selection of volume vs cardiotrope vs pulmonary vasodilator therapy.

It must be recognized that determination of hemodynamic significance requires integration of echocardiography markers in the context of the clinical scenario.

Indications

- 1. Neonate with clinical signs of hypoxemic respiratory failure, and no clinical suspicion of congenital heart disease
- 2. Longitudinal evaluation a patient with PPHN to evaluate response to treatment in

Study type

First study: Comprehensive NPE study to exclude duct-dependent lesions and characterize severity and hemodynamic impact of PPHN. This study <u>must</u> be reviewed and reported by a pediatric cardiologist.

Repeat study: Standard TNE study to characterize ongoing severity and hemodynamic consequences of PPHN after therapeutic intervention. This still will be reviewed and reported by a neonatal echocardiographer who has completed advanced training.

KEY ELEMENTS

Morphology

- Rule out congenital heart disease- first study
- RV size: TV annulus

Functional

- Atrial/PDA/VSD Shunts: L-R-bidirectional
- Tricuspid valve regurgitation: RVSp
- PAAT:RVET index
- Pulmonary regurgitation: PA mean pressure
- Pulmonary venous return: RUPV Vmax
- LV systolic function: biplane Simpson's, LVO
- LV diastolic function: usual protocol
- RV function: Subjective impression, RVO, TAPSE, images for FAC, RV diastolic function

COMPREHENSIVE STRUCTURAL AND FUNCTIONAL IMAGING PROTOCOL

SUBCOSTAL

- Situs view + sweep in transverse plane: cross-section of spine, abdominal Ao + IVC (single sweep with colour doppler)
- Abdominal Ao and IVC long axis
 - colour IVC + PW hepatic veins
 - colour + PW Doppler in abdominal aorta ensuring minimum angle correction possible

Measurements:

- Long-axis views with sweep from posterior to anterior. Acquire one colour Doppler sweep to screen for atrial communication (if present) and demonstrating atrioventricular and ventriculo-arterial connections. Specific interrogation (using 2D, color/ PW/ CW Doppler) may be needed if abnormalities are detected.
 - Posterior view: atrial septum: 2D + colour
 - Measure, colour, Doppler ASD / PFO if present
 - RV inflow, 2D + colour
 - LVOT / Aortic valve, 2D + colour
 - RV outflow, 2D + colour

Measurements:ASD size, shunt direction and gradient (2D, PWD)Evaluation valvular gradient (where relevant)

• Short axis subcostal views: rotate clockwise

- Bicaval view SVC and IVC (acquire 2D then colour Doppler)
- One sweep from right to left with color box covering the interventricular septum.
- Doppler at any level if pathology is suspected or turbulent / abnormal flow on colour Doppler is detected.
- Superior mesenteric, celiac or renal artery color and PWD evaluation

Measurements:Evaluation valvular gradient (where relevant)SVC VTI (PWD)IVC diameter and respiratory variation (2D)SMA, celiac, renal peak systolic and diastolic velocity, resistance andpulsatility index

PARASTERNAL

Long axis (PLAX):

- 2D PLAX image
- Zoom on the aortic valve;
- Zoom on the MV
- Colour aortic valve and mitral valves
- M-mode of LV distal to mitral valve
- M-mode through aortic valve
- Acquire colour sweep of IVS from anterior to posterior to rule out VSDs

Measurements: Aortic valve annulus diameter (2D)

Evaluation valvular gradient (where relevant) LV [LVEDD (2D) – z scores], RV cavity and wall dimensions LV fractional shortening LA: Ao ratio, LVET, R-R interval Subjective evaluation of IVS morphology (flattening, bulging in to LV) in systole (pressure loading) and diastole (volume loading) Subjective evaluation of RV systolic performance

RV inflow in 2D:

- Zoom on the TV
- RV inflow view: colour + Doppler

Measurements: RVSp calculation (CWD)

RV outflow in 2D:

- Zoom the PV (2D & color) exclude stenosis and/or atresia
- PW Doppler in RVOT and MPA / CW for PAp
- Measurements:Pulmonary valve annulus diameter (2D)
Evaluation valvular gradient (where relevant)
RV VTI (PWD) for RVO calculation
Pulmonary artery acceleration time, RVET
Subjective evaluation of RV systolic performance
Assess pulmonary regurgitation, if present measure early diastolic
pressure gradient as estimate for mean PA pressure

Short axis (SAX):

Level of aortic valve

- aortic valve , zoom valve, define cusps, colour
- image right and left coronary artery origins: 2D + color (lower Nyquist)
- tricuspid valve: 2D + colour + Doppler
- pulmonary valve + colour + PW (+ CW where relevant)

Measurements:	RVSp calculation – if superior trace (CWD)
	Evaluation valvular gradient (CWD where relevant)
	RV VTI (PWD) for RVO calculation – if superior trace
	SVC diameter (M-mode or 2D) – angle counter clockwise and anterior

Level of LV: multiple levels 2D and colour flow Doppler screen

- the mitral valve; 2D + colour
- basal LV in short axis with M-mode measurements
- the papillary muscles
- LV apex.
- Single colour sweep of IVS from base to apex to exclude VSDs. Adapt color scales to lower levels (40-60 cm/s)
- Subjective evaluation of IVS morphology (flattening, bulging in to LV) in systole (pressure loading) and diastole (volume loading)

<u>APICAL</u>

- 4-chamber view in 2D
- 4-chamber view sweep in colour from anterior to posterior to check for VSDs

A4C View, LV

- 2D view of LA / LV
- Zoom MV: 2D with annular measurement
- LV inflow: Colour, PWD and/or CWD
- Colour and PW pulmonary vein for velocities

Measurements:Mitral valve annulus diameter
Transmitral flow (PWD) - E wave, A wave, deceleration time, A-duration
Transmitral flow (CWD) if valvular regurgitation or if inflow obstruction
present, measure peak and mean gradients
TAPSE: M-mode through tricuspid annulus
Pulmonary vein (RUPV) flow (PWD) - S wave, D wave, A wave reversal
velocity, A wave duration
Subjective evaluation of RV systolic performance
Ejection fraction (if indicated) according to biplane Simpson's method

Apical five chamber

- 2D of LVOT + colour
- Doppler of LVOT: PW (+ CW where relevant)

Measurements:Isovolumic relaxation time (PWD)LVOT VTI for LVO calculation (PWD)Evaluation valvular gradient (CWD where relevant) for stenosis or
regurgitation

A4C view, RV

- 2D image of RA / RV
- Zoom TV: 2D
- colour RV inflow
- M-mode of tricuspid valve annulus
- PW + CW of TV
 - measure: E wave velocity from PW
 - if TR is present, do CW and measure

Measurements:Tricuspid valve annulus diameter (2D)RVEDD (z score), Measure RV1 + RV lengthMeasure tricuspid closure to opening time, calculate RV MPI: myocardialperformance index = (TCOT-ET)/ET
Measure RA minor + major axis & TAPSE (M-mode) Trans-tricuspid flow (PWD) - E wave, A wave Trans-tricuspid flow (CWD) if valvular regurgitation to estimate RVSP

Apical two chamber

- 2D of LA / LV plus colour Doppler
- Measure ejection fraction to complete simpson's biplane calculation

Apical three chamber

- A3C view in 2D + colour

SUPRASTERNAL

- In short axis: 2D + colour Doppler + PW SVC and ductus arteriosus (ductal sweep)
- Short axis arch sidedness sweep using colour Doppler
- Short axis sweep for left SVC using colour Doppler
- Arch long axis: 2D + colour + Doppler

Measurements:PDA diameter – pulmonary and aortic end (2D and Color Doppler)
Direction of ductal flow
Peak and mean velocity of tranductal flow (PWD)
Pre- and post-ductal aortic arch gradient (PWD or CWD where relevant)
to rule out obstruction
SVC VTI (PWD)

HIGH PARASTERNAL LONG AXIS

- Define pulmonary artery branches
- Define four pulmonary veins (crab view, in small children) and their drainage, acquire 2
 D image and colour flow Doppler. Do PW Doppler if turbulent flow is detected.
- Measurements:Pulmonary artery (R+L) branch diameter z score (2D)Pulmonary artery branches peak velocity and gradient (PWD and/or CWD)Pulmonary venous peak velocity and gradient (PWD where relevant)

CRANIAL AXIAL VIEW

- Define middle cerebral artery (color and PWD evaluation)

Measurements: MCA peak systolic and end diastolic velocity, resistance and pulsatility index

Additional notes:

CALCULATE biplane Simpson's if

- ➢ If M-mode is abnormal (Fs < 25%)</p>
- If regional wall motion abnormalities
- > If paradoxical motion of the interventricular septum
- When abnormal geometry

Systolic RV function

- visual assessment

ADVANCED FUNCTIONAL IMAGING

Addendum: The following measurements should be considered in patients with impaired myocardial performance or as part of an approved prospective research study. Normative data has not been well defined; hence, the value of these measurements as part of a routine clinical study has not been established.

Principles:

- > 2D imaging: frame rates 60 110 fps for Speckle tracking, record 2 beat loops.
- Color TDI: highest frame rates possible (at least 150 fps); record 4 beat loops.

TDI from A4C view

- Tissue Doppler E', A' and S' tracings and velocity measurements at TV annulus, basal septum and lateral MV annulus
- Ensure entire LV is covered with tissue colour map

IV. INDWELLING CATHETER EVALUATION

Goals of evaluation

- 1. Document location of tip of catheter
- 2. A comprehensive TNE should be performed if the patient is symptomatic
- 3. Exclude complications related to catheter tip e.g. effusions, vegetations.
- 4. Studies to exclude vegetations must be performed by a pediatric cardiologist.

Study type

Focused study: A focused evaluation, where congenital heart disease is not suspected clinically, that is performed to define line position or exclude an effusion.

Comprehensive study: A comprehensive evaluation should be performed in symptomatic patients or if an effusion is confirmed on a focused evaluation.

Note: The process of locating the catheter tip is very challenging and requires skill and patience. Incorrect alignment of the ultrasound beam with respect to the path of the catheter within the vessels and heart chambers may result in underestimation of the catheter length and erroneous conclusion of the position of the catheter tip. The use of small volume saline boluses and imaging the resultant jet by ultrasound may sometimes help in locating tip position.

KEY ELEMENTS

Specific Imaging

Umbilical arterial catheter:

View: Subxiphoid long-axis view below and above the diaphragm *Technique*: Color and PWD (or CWD) should be performed to ensure laminar flow

Umbilical venous catheter:

View: Subxiphoid long-axis view below and above the diaphragm. The location of the hepatic segment of the inferior vena cava, hepatic vein, and ductus venosus are determined *Technique*: Color and PWD (or CWD) should be performed to ensure laminar flow

<u>Central venous catheters:</u>

Line tip in IVC

View: Subxiphoid long-axis view below and above the diaphragm. The location of the hepatic segment of the inferior vena cava, hepatic vein, and ductus venosus are determined. *Technique:* Color and PWD (or CWD) should be performed to ensure laminar flow

Line tip in SVC:

View: The SVC can be imaged from any of the following views: subxiphoid "bicaval" view; high right parasternal view; suprasternal view. The suprasternal coronal or short-axis plane is used to visualize the left innominate vein and its connection to the superior vena cava. The presence of a left SVC should be excluded by suprasternal views with leftward angulation. In the same view, blood return from left subclavian vein can be detected by color flow mapping. Suprasternal coronal and sagittal views tilted rightward are used to determine the connection of the right superior vena cava with the right atrium. Suprasternal coronal view with right and superior angulation can also be used to visualize right innominate vein and its continuation into SVC using 2D and Color Doppler.

Technique: Color and PWD (or CWD) should be performed to ensure laminar flow

Imaging for Pericardial Effusions

View: The presence of an effusion may be confirmed on 4 chamber, long-axis or short axis sweeps. Larger effusions are commonly seen on more than one view. The depth of the effusion may be recorded, although the accuracy of this technique is poor. In an emergency situation (pre-arrest) the purpose of the echocardiogram is to document the presence of an effusion and guide emergency pericardiocentesis. In a non-emergent situation, where the patient is thought to be symptomatic, a standard TNE evaluation should be performed to evaluate the impact on pulmonary and systemic hemodynamics, and myocardial performance.

Measurements: As per pulmonary hypertension or systemic hypoperfusion protocol

NORMATIVE VALUES

Left Ventricle							
	Prer Dev 1	nature (< 29 weeks)		Ierm			
Committeest	Day 1	Da	iy 2	Day 1	Day 2		
Conventional	4.2 (0.5)						
Aortic diameter (mm)	4.2 (0.5)	4.4	(0.5)	6.9 (0.6)	6.9 (0.5)		
1)/O(mlo/kg/min)	165 (93)	- PDA	+ PDA	129 (29)	127 (29)		
LVO (mis/kg/min)	24 (6)	24 (7)	245 (120)	120 (20)	157 (20)		
Shortening Fraction (%)	54 (0)	54 (7)	57 (0)	39(7) FF(7)	59 (8)		
Ejection Fraction (%)	57 (7)	58 (6)	0.47(0.16)	55 (7) 0 EC (0.08)	53 (6) 0 EC (0.08)		
	0.35 (0.11)	0.41 (0.16)	0.47 (0.16)	0.56 (0.08)	0.56 (0.08)		
IVIV A wave (m/s)	0.48 (0.12)	0.50 (0.13)	0.56 (0.11)	0.50 (0.08)	0.49 (0.09)		
E:A ratio	0.75 (0.19)	0.85 (0.45)	0.83 (0.27)	1.1 (1.0-1.2)	1.1 (0.9-1.3)		
MVVII	4.8 (1.3)	5.3 (1.4)	5.9 (1.4)	9.1 (1.5)	8.6 (1.7)		
	1	r		r	1		
LV IDI (cm/s)							
s'	2.8 (0.9)	3.3 (0.7)		4.9 (0.8)	4.6 (0.6)		
e'	3.6 (1.4)	4.2 (1.3)		6.7 (1.4)	6.5 (1.2)		
a'	4.0 (1.5)	4.8 (1.4)		5.5 (1.3)	5.4 (1.3)		
e':a' ratio	0.95 (0.36)	0.91 (0.25)		1.3 (0.4)	1.3 (0.4)		
Septal TDI (cm/s)		P			P		
s'	2.4 (0.6)	3.0 (0.6)		3.6 (0.6)	3.5 (0.5)		
e'	2.8 (0.8)	3.6 (1.1)		4.7 (1.1)	4.8 (0.9)		
a'	3.9 (1.1)	4.7 (1.4)		4.2 (0.8)	4.4 (0.8)		
e':a' ratio	0.76 (0.21)	0.91 (0.25)		1.1 (0.9-1.3)	1.1 (0.9-1.3)		
LV Free Wall Strain & SR TD							
Strain (%)	12.8 (3.3)	13.1 (3.6)		24.5 (3.8)	-		
Systolic SR (1/s)	1.5 (0.6)	1.6 (0.5)		1.8 (0.4)	-		
Diastolic E' SR (1/s)	1.8 (0.8)	2.0 (0.8)		3.2 (1.5)	-		
Diastolic A' SR (1/s)	2.3 (0.7)	2.7 (1.2)		2.1 (1.3)			
Septal Strain & SR TD		_					
Strain (%)	15.8 (2.8)	16.8 (3.6)		25.9 (4.8)	-		
Systolic SR (1/s)	1.6 (0.3)	1.8 (0.5)		1.9 (0.6)	-		
Diastolic E' SR (1/s)	1.7 (0.6)	2.2 (0.6)		3.2 (1.6)	-		
Diastolic A' SR (1/s)	2.3 (0.7)	2.6 (1.2)		2.4 (0.9)	-		
LV Dimensions							
Septal wall diameter (mm)	2.7 (0.6)	2.6	(0.6)	-	-		
LV internal diameter (mm)	11.0 (2.2)	11.7	(2.1)	18 (3)	17 (2)		
LV posterior wall diameter (mm)	2.5 (0.6)	2.4	(0.6)	-	-		
LV length (mm)	17.7 (1.6)	18.4	(1.8)	30.8 (2.6)	30.7 (2.6)		
LV Event Times							
IVCT (ms)	56 (13)	46	(11)	65 (14)	65 (12)		
IVRT (ms)	58 (13)	52	(12)	53 (12)	52 (10)		
Systolic time (ms)	147 (20)	150	(18)	188 (172-203)	184 (172-195)		
Diastolic time (ms)	131 (22)	126	(22)	199 (42)	195 (44)		
SD ratio	1.16 (0.17)	1.29	(0.23)	0.98 (0.24)	0.98 (0.19)		
Myocardial performance index	0.87 (0.2)	0.72 (0.17)		0.61 (0.53-0.7)	0.61 (0.54-0,7)		
Deformation STE							
LV GLS (%)	18.4 (3.5)	20.3	(3.2)	21.7 (1.9)	21.2 (1.8)		
LV GLSRs (1/sec)	1.8 (0.3)	2.1	(0.3)	2.05 (1.9-2.28)	2.17 (1.93-2.43)		

Right Ventricle								
	Premature	(<29 weeks)	Term					
	D1	D2	D1	D2				
Conventional								
Pulmonary Artery Diameter (mm)	5.7 (0.7)	5.6 (0.7)	9.0 (1.0)	9.5 (1.0)				
PAAT (ms)	42 (10)	45 (12)	49 (17)	59 (15)				
RVET (ms)	151 (21)	157 (29)	216 (24)	216 (23)				
TDI								
RV TDI (cm/s)								
s'	3.6 (0.9)	4.4 (1.0)	6.55 (1.12)	6.54 (1.1)				
e'	3.9 (1.3)	4.5 (1.1)	7.99 (1.6)	7.33 (1.3)				
a'	6.7 (1.8)	8.6 (2.6)	8.27 (1.6)	8.01 (1.3)				
e'/a'	-	-	0.99 (0.2)	0.93 (0.2)				
RV strain & SR TD								
Strain (%)	22.1 (5.1)	23.1 (4.7)	28.3 (4.9)	-				
Systolic strain rate (1/s)	2.0 (0.6)	2.4 (0.6)	1.9 (0.5)	-				
Diastolic E' SR (1/s)	2.4 (0.9)	2.5 (0.6)	2.8 (0.8)	-				
Diastolic A' SR (1/s)	3.4 (1.0)	4.4 (1.4)	2.1 (0.9)	-				
RV TAPSE & FAC								
TD TAPSE (mm)	5.1 (1.0)	5.9 (1.1)	9.2 (1.4)	9.1 (1.3)				
3D Chamber FAC (%)	43 (8)	48 (7)	39 (7)	38(6)				
4D Chamber FAC (%)	37 (8)	43 (8)	26 (7)	27 (8)				
Global FAC (%)	40 (7)	46 (6)	33 (5)	33 (4)				
RV Dimensions								
Tricuspid valve annular diameter (mm)	6.4 (1.0)	6.4 (0.9)	12.9 (1.5)	13.1 (1.5)				
Right ventricular basal diameter (mm)	11.1 (1.3)	10.9 (1.4)	17.1 (1.7)	17.4 (2.1)				
Right ventricular mid cavity diameter (mm)	9.9 (1.6)	9.6 (1.6)	15.5 (1.9)	16.7 (1.7)				
Right ventricular length (mm)	18.7 (2.2)	18.7 (2.4)	30.6 (2.3)	30.5 (2.3)				
RV Event Times								
IVCV (cm/sec)	-	-	4.88 (1.52)	4.84 (1.39)				
IVRT (msec)	-	-	41.38 (17.09)	43.32 (15.55)				
Myocardial performance index	-	-	0.42 (0.15)	0.42 (0.12)				
S'D' ratio	-	-	1.08 (0.26)	1.11 (0.31)				
Deformation STE								
RV FWLS (%)	18.1 (4.0)	20.3 (3.2)	21. 2 (5.3)	21.3 (5.4)				
RV FWLSRs (1/sec)	1.9 (0.5)	2.2 (0.6)	-	-				

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