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Current Cardiology Reviews, **2016,** *12,* **155-162**

Diagnostic Cardiac Catheterization in the Pediatric Population

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Abstract: Although the utility of diagnostic cardiac catheterization in the clinical setting has diminished over the last years, due to the emergence of noninvasive imaging modalities, such as echocardiography, magnetic resonance imaging and computed tomography, catheterization for diagnostic reasons still constitutes a valuable tool in certain parts in the workup of pediatric heart disease. As a result, awareness of the main aspects of diagnostic catheterization is of great importance for the clinical cardiologist. In this article, the main variables measured and the main actions performed during diagnostic cardiac catheterization in children are discussed.

Keywords: Cardiac, catheterization, children, diagnostic, heart, pediatric.

1. INTRODUCTION

With the advent of advanced noninvasive imaging modalities (echocardiography, cardiac MRI - cMRI), multislice CT - msCT), the value of cardiac catheterization in the diagnosis, anatomic and hemodynamic assessment of heart disease has decreased. However, due to its preciseness and more direct concept as an investigational modality, there are still cases, in which diagnostic catheterization can offer valuable data about structure and pathophysiology of the underlying cardiac lesion. Such cases may be 1) diagnostic measurements before an interventional cardiac catheterization for the acquisition of useful data, 2) insufficient or equivocal information from noninvasive tests, 3) complex lesions (e.g. pulmonary atresia with aortopulmonary collateral arteries for the depiction of the collateral network, pulmonary atresia with intact ventricular septum and ventricular-coronary connections), 4) decision making on pharmacological or surgical treatment in patients with pulmonary hypertension, 5) endomyocardial biopsy for the assessment of myocardial rejection, genetic testing in cardiomyopathies or diagnosis of myocarditis, 6) surveillance of graft vasculopathy in post-transplant patients, 7) electrophysiologic studies. This article discusses the main process around diagnostic cardiac catheterization in the pediatric population and focuses on several measurements derived during the procedure, including cardiac output/index, evaluation of shunts, vascular resistances, valve areas, pressure gradients and delineation of cardiac and vascular anatomy via injection of contrast materials. A referral to endomyocardial biopsy is also made.

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2. PREOPERATIVE, PERIOPERATIVE AND POST-OPERATIVE MANAGEMENT

2.1. Preoperative Clinical Assessment

History taking and physical examination remain integral parts of the patient's precatheterization evaluation. A detailed history focuses not only on the pediatric patient's symptomatology and course of disease, but also on the maternal and family history. Maternal illness or medications during pregnancy, congenital or acquired heart disease in the family, as well as coexisting congenital anomalies and/or genetic or chromosomal abnormalities, should be sought.

2.2. Preoperative Laboratory Assessment

Noninvasive imaging prior to catheterization is the "gold standard" method for the evaluation of the pediatric patient with heart disease in most cases. This involves all types of echocardiography, cMRI or msCT. The noninvasive depiction of cardiac structure and function is useful regardless the diagnostic nature of the catheterization procedure, since it provides a more comprehensive picture of the underlying anatomy and pathophysiology, without burdening the patient. Furthermore, electrocardiogram for heart rhythm evaluation and the exclusion of arrhythmias and/or chest X-ray for cardiac silhouette and lung vascularity delineation can often prove useful. Finally, routine hematological exams are performed, so that hematocrit, BUN and creatinine are measured, among other variables. Cyanotic patients with polycythemia may require hydration or partial exchange transfusion, while anemic patients may need blood transfusion [1].

2.3. Complementary Preoperative Preparation

In addition to the aforementioned parameters, adequate hydration has to be ensured and intravenous fluids can be

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given, if needed. The patient must also be kept nil per os at least 2 hours before the procedure concerning clear liquids, 4 hours concerning breast milk and 6-8 hours concerning solids, nonhuman milk and infant formula, according to the American Society of Anesthesiologists Committee practice guidelines for reducing the risk of pulmonary aspiration [2].

Table 1. American Society of Anesthesiologists guidelines for preoperative fasting [2].

Ingested material	Minimum fasting time
Clear liquids	2
Breast milk	4
Infant formula	6
Nonhuman milk	6
Solids	6-8

An intravenous line has to be placed and patients, especially neonates and infants, must be kept warm during the intervention with blankets and room air-conditioning. A written consent is always signed prior to the procedure.

2.4. Premedication, Sedation and Anesthesia

Premedication, sedation and anesthesia are the means of securing a motionless patient, facilitating the catheterization, providing amnesia, analgesia and anxiolysis and making separation from family easier. Factors that have to be considered by the anesthesia operator include the reason for the procedure, the pathophysiologic state of the cardiac lesion and the effect of anesthesia on the hemodynamic and respiratory function, so that the optimum regimen is selected and no unreliable data are collected. Additionally, many patients are oxygenated with room air, in order to preserve the underlying acid-base and blood gases homeostasis. Unlike adults, children usually require deep sedation to ensure immobility. However, diagnostic catheterization is preferably performed under minimal sedation so that hemodynamic variables are hardly distorted. Should deep sedation be needed, sedative agent is selected with consideration. The complexity and special needs of pediatric sedation require expertise in the anesthetic practice and thus a well-trained and experienced practitioner is necessary, especially in very sick patients.

Monitoring and perioperative care of the sedated patient includes baseline EKG, pulse oxymetry, noninvasive blood pressure count, capnography for respiratory monitoring, preparation of resuscitation drugs prior to the catheterization and availability of a defibrillator [3]. The most popular score for quick assessment of the level of sedation is the Ramsay sedation scale [4].

Premedication is the first step to relax the patient, facilitate separation from parents, and enhance their composure having their child calm before the procedure. Local anesthesia at the site of the impending cannulation is the next step and lidocaine is the most common anesthetic agent; usually, a topical cream (eutectic mixture of lidocaine and prilocaine) is applied in advance, so that the needle insertion of lidocaine becomes less painful. There is not clear indication concerning the optimal sedative medication and the choice is based on the goals and special needs of each case.

Midazolam is one of the most commonly used premedication agents in sedation, because of its anxiolytic and amnesic effect, the rapid onset of action and predictable wear-off time, the multiple routes of administration (oral, nasal, rectal, intramuscular), the absence of considerable cardiac and respiratory effect and – for some practitioners – its property to keep the child calm postoperatively [5]. Clonidine is also used, proven to be superior to midazolam in sedation provision, postoperative analgesic properties, emergence agitation and, possibly, in preventing postoperative nausea and vomiting [6]. It constitutes a safe agent, although little hemodynamic alterations may be noticed. Relative drawback is the prolonged onset of action time. Consequently, we can say that midazolam can be selected when prompt sedation is needed, while clonidine is useful when postoperative analgesia is desired. Ketamine has been a popular hypnotic and analgesic medication for many years with minimal influence on respiratory function and airway reflexes, although silent aspiration cannot be ruled out, possibly because of its hypersalivative effect [7]. for which an antisialagogue can be coadministered. Other adverse effects of ketamine constitute its anticholinergic symptomatology (e.g. tachycardia) and the emergence reactions, although the latter are less pronounced in children [7, 8]. Ketamine's property of inducing tachycardia makes it useful for patients, in high-afterload-needing patients, such as in aortic stenosis and right-to-left shunts [9]. Another handy anesthetic agent is propofol, very often

Table 2. Ramsay sedation scale.

	Ramsay sedation scale
1	Patient anxious and agitated or restless, or both
2	Patient cooperative, oriented and calm
3	Patient responsive to verbal commands only
4	Patient exhibiting brisk response to light glabellar tap or to an auditory stimulus
5	Patient exhibiting a sluggish response to light glabellar tap or to an auditory stimulus
6	Patient unresponsive to stimuli of items 4 or 5

used for general anesthesia, because of its short onset of action, rapid recovery time and easy titratability. Drawback of propofol is the respiratory depression and the decrease in blood pressure and heart rate. Usually propofol is used in conjunction with an analgesic (e.g. opioids) to provide desired analgesia, since it has been advocated to cause hyperalgesia [10]. Such conjunction should be strictly monitored, due to the respiratory effect of both drugs. Dexmedetomidine has the same mechanism of action as clonidine, although it acts more rapidly – though still slower than midazolam – and also has shorter recovery time. It causes no respiratory depression. Notable drawback is the low per os bioavailability, thus, intranasal or transmucosal administration is preferred.

Sedative combinations are often favored, since they can match properties of multiple agents in one regimen plus they reduce the need for high doses of a single drug. A common combination is ketamine-propofol, two agents with oppositional effect on heart rate and blood pressure, which could contribute to hemodynamic stability and has been shown to maintain respiratory function [11-13]. Dexmedetomidine is usually used in combination with another sedative drug, such as ketamine. In a study of Mester *et al*. [14] this scheme was proved to be effective for the sedation of infants and children undergoing cardiac catheterization. However, Tosun *et al*. [13] found dexmedetomidine-ketamine combination to induce less sufficient sedation and analgesia than propofol-ketamine and having longer recovery time. Midazolam-ketamine combination was found to achieve better children cooperation in the dental setting than midazolam alone [15, 16]. The need for adding opioids in the sedation scheme can be minimized with the use of topical anesthetic cream and subcutaneous topical infiltration with lidocaine, combined with adequate sedation. Midazolam can be supplemented with opioids, due to lack of analgesic effect.

When general anesthesia with endotracheal intubation is indicated, inhaled anesthetics can be used. The most common agents are sevoflurane and halothane. Russell *et al*. [17] characterized sevoflurane as superior to halothane in the anesthetic practice of infants and children with congenital heart disease, because of the former's less hypotension and bradycardia episodes and a lower incidence of emergent drug use.

2.5. Vascular Access

The entry site of the needle is of fundamental importance in order to put through the whole intervention with ease and avoid adverse events. Especially in children, in whom vascular walls are thinner, tissue easier intersected, a small amount of blood loss can represent a large percentage of their total blood volume and lengthy manipulations are less well tolerated, puncture site should be correctly settled from the beginning. In some cases, this is achieved via simple palpation of the target vessel and/or inspection of landmarks around, but ultrasonographic guidance may be necessary to facilitate correct puncture, as in the case of internal jugular vein (IJV) access [18]. Access to the heart can be antegrade (venous) for right heart catheterization or retrograde (arterial) for left heart catheterization, or even antegrade with left heart access through a transseptal puncture. Venous access is usually femoral, jugular or subclavian, because of the less tortuous route to the right atrium, while arterial is mostly femoral, although other sites are occasionally used (e.g. carotid). In newborns, umbilical vein and arteries are also an attractive alternative up to 1-week postpartum. Transhepatic approach is frequently considered in patients with both femoral veins occluded and for securing other vascular entries for future interventions [19].

Table 3. Vascular access sites in pediatric cardiac catheterization.

Anterograde access	Retrograde access
Femoral vein	Femoral artery
Internal jugular vein	Carotid artery
Subclavian vein	Umbilical artery
Hepatic veins	
Umbilical veins	

Femoral vessels are approached with the Seldinger technique [20]. Intravascular guidewire entrance may be confirmed with fluoroscopy. During IJV access, general anesthesia and intubation may be necessary, especially in very young patients, while ultrasonograhic guidance constitutes a common practice. It is a common choice for endomyocardial biopsy and patients with bi-directional Glenn shunt. Subclavian approach carries the risk for pneumothorax and air embolization due to the negative intrathoracic pressure. Umbilical vessels can be cannulated in the newborn with a 3.5 or 5-Fr catheter, although smaller catheters used for femoral access make the latter preferable, due to the less tortuous vascular route. In transhepatic approach contrast injection is performed to confirm entrance in the hepatic, and not the portal vasculature [18, 19].

2.6. Postoperative Care

After catheterization, the patient is closely monitored. Recovery from sedation or anesthesia is accomplished with simultaneous vital signs surveillance. Vital signs are obtained frequently during the first hour (3-4 times) and more sparsely when assured that the patient is hemodynamically stable. Unstable patients or those with difficulty recovering should be monitored for complications (e.g. vascular rupture, embolization, arrhythmia), cardiac defect deterioration or pathology triggered from another system (e.g. respiratory compromise, neurologic damage). Noninvasive imaging modalities (echocardiography, cMRI, msCT) can be used to diagnose possible adverse phenomena and in carefully selected cases (e.g. critically ill patients, unavailable noninvasive imaging tests, strong suspicion for a lesion that could require intervention) repeat catheterization may be performed [21]. Such patients may be admitted to the ICU for further stabilization and constant monitoring. Fluid intake should be affluent to replace blood loss and help the excretion of contrast materials. Care at puncture site includes application of gauze pads and firm bandage, in order to avoid bleeding. Wide-range moves are avoided in the first couple of hours. Peripheral limb pulses are frequently checked to

confirm distal perfusion. The child may stay in the hospital, depending on its general health status, and, prior to discharge, instructions are given for rest in the following days, possible medications prescribed and puncture site self-care.

3. PERIPROCEDURAL MEASUREMENTS DERIVED AND ACTIONS PERFORMED

The measurements derived during diagnostic cardiac catheterization are discussed, a brief synopsis of which is depicted in Fig. (**1**).

3.1. Cardiac Output/Index

Cardiac output (CO) expresses the blood volume pumped by the left or right ventricle per unit time (L blood/min). In children cardiac index (CI) is a useful tool, since it relates CO with body surface area (L/min/m^2), enabling comparison between patients. There are two ways to determine CO, the thermodilution method and the Fick method. The former is performed with a pulmonary artery catheter. Saline colder than blood temperature is injected in the right atrium and is mixed with the blood. Downstream in the pulmonary artery a thermistor on the distal part of the catheter detects the temperature change and a temperature-time graph is designed by a computer. The area under the curve is inversely proportional to the CO. This technique is not applicable when intracardiac shunts, tricuspid or pulmonary regurgitation are present and it is less accurate when CO is low. These limitations can be overcome by estimating CO using the Fick principle:

$$CO = \frac{oxygen\ consumption}{arterial\ blood\ oxygen\ content - mixed\ venous\ blood\ oxygen\ content}$$

OR

$$CO(L/min) = \frac{VO_2(mL/min)}{C_aO_2 - C_vO_2}$$

Due to practical difficulties in measuring VO_2 during the catheterization procedure, VO_2 is routinely estimated using the LaFarge and Miettinen equations [22]:

Male patients: $VO_2(mL/min/m^2) = 138.1 - (11.49 \times \ln(age)) + (0.378 \times heart\ rate)$

Female patients: $VO_2(mL/min/m^2) = 138.1 - (17.04 \times \ln(age)) + (0.378 \times heart\ rate)$

However, oxygen consumption estimation using this formula is poorer for children <3 years old [23, 24]. In this age group we can approximately calculate VO_2 according to weight (2-5kg → 10-14mL/min/m^2, 5-8kg → 7-10mL/min/m^2) [18]. A more precise and rapid method includes the direct measurement of oxygen consumption with a tight-fitting mask via respiratory mass spectrometry [23].

Oxygen content in a sample of blood is the sum of the oxygen amount bound to hemoglobin plus the amount of oxygen dissolved in the plasma. The amount of oxygen

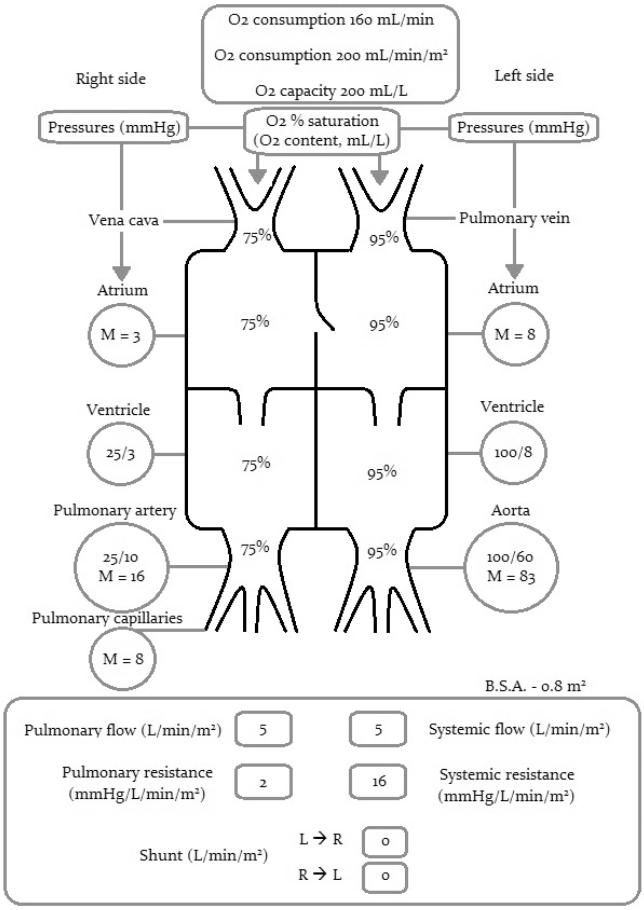

Fig. (1). Diagrammatic depiction of the normal values of variables determined during the diagnostic part of cardiac catheterization. (Nadas AS, Fyler DC: Pediatric cardiology, Edition 3, Philadelphia, 1972, WB Saunders).

bound to hemoglobin is the product of multiplying oxygen capacity (mL O_2/L blood), which is the maximum amount of oxygen that can be bound to hemoglobin, by oxygen saturation. Moreover, oxygen capacity is the amount of oxygen that can be bound to 1g of hemoglobin multiplied by the total amount of hemoglobin in g/dL and multiplied by 10, in order to receive the grams of hemoglobin per L. In addition, each gram of hemoglobin can carry up to 1.34 to 1.39 mL of oxygen (we calculate as if it was 1.34) [25]. Finally, according to Henry's law, the amount of a gas dissolved in a specific amount of liquid is directly proportional to the partial pressure of that gas in the liquid and, thus, dissolved oxygen in the blood (mL O_2/dL blood) equals to the partial pressure of oxygen (mmHg) in the blood multiplied by the constant 0.003 (mL/mmHg O_2/dL blood) and multiplied by 10, in order to receive the mL of oxygen per L [25]. Considering all the above:

$$oxygen\ content = oxygen\ capacity \times oxygen\ saturation + dissolved\ oxygen$$

$$oxygen\ content\ (mL\ O_2/L) = 1.34\ (mL/g) \times \text{hemoglobin (g/dL)} \times 10 \times oxygen\ saturation + oxygen\ partial\ pressure\ (mmHg) \times 0.003\ (\text{mL/mmHg/dL}) \times 10$$

Oxygen saturation is commonly measured by spectrophotometry taking advantage of the distant spectral absorptions of oxidized hemoglobin and reduced hemoglobin. The amount of oxidized hemoglobin and the total amount of hemoglobin can therefore be measured and the ratio between the two reveals the oxygen saturation. In room air ventilation (O_2 concentration ~ 21%) the dissolved amount of oxygen in the plasma slightly contributes to oxygen content of blood (~ 3mL/L, which is about 1% of oxygen content) and, thus, it is many times ignored. The amount of oxygen dissolved in blood increases when higher concentrations of oxygen are administered and in these cases it should be counted in the total oxygen content.

3.2. Shunts

The evaluation of intracardiac and extracardiac shunts includes a quantitative and a qualitative method. Qualitative assessment involves heart chamber oxygen saturation measurements and calculates the difference between a single chamber's oxygen saturation and the pulmonary artery (PA) saturation, in search for a possible step-up, when examining the right heart chambers, or a step-down, if left heart is investigated. As far as the right heart is concerned, the saturation results obtained by the superior vena cava (SVC), right atrium (RA) and right ventricle (RV) are subtracted from the PA oxygen saturation. A left-to-right shunt is presumed if there is a remarkable step-up between two successive chambers. In 1979 [26], Freed et al. examined a population of 1121 children with aortic or pulmonary stenosis, but without intracardiac shunt (excluded by indicator dye curves or angiocardiography), who underwent cardiac catheterization. Assessing a normal distribution, they concluded that, in the absence of intracardiac shunts, the differences between oxygen saturation in the SVC and the PA, the RA and the PA, and the RV and the PA, are found to be ≥8.7%, ≥5.6% and ≥5.2%, respectively, in 1% of the cases. Greater step-up occurs in less than 1%, making the presence of an intracardiac shunt highly likely. It should be mentioned that this study does not provide criteria to exclude a shunt, merely only to determine if one is present. For right-to-left shunts, no relevant data exists on the saturation step-downs in the left heart chambers. An assessable left heart desaturation is ≥3% or an absolute value of aortic saturation <92% at sea level and room air breathing [27]. When examining the left heart, desaturation (step-down) at the level of the pulmonary veins (PV) may be due to parenchymal lung disease or hypoventilation (e.g. anesthesia complication), as well as, a right-to-left shunting lesion. Administering 100% oxygen helps to distinguish between these potentials, since no increase in saturation occurs in the case of an intracardiac shunt, in contrast to the lung disease. A step-down at a lower level [left atrium (LA), left ventricle (LV), aorta] with normal PV saturation indicates a right-to-left shunting lesion at that level.

During quantitative assessment the systemic and pulmonary blood flows (Q_s, Q_p) are defined using the Fick principle. For the systemic blood flow the oxygen content of blood flowing towards the systemic circulation (aortic oxygen content – C_aO_2) and the oxygen content of blood returning from the systemic circulation (mixed venous oxygen content – C_vO_2) are needed, while for the pulmonary blood flow the oxygen content of blood flowing towards the pulmonary circulation (pulmonary artery oxygen content – $C_{pa}O_2$) and the oxygen content of blood returning from the pulmonary circulation (pulmonary veins – $C_{pv}O_2$) are needed. Therefore:

$$Q_s(L/min/m^2) = \frac{VO_2(mL/min/m^2)}{C_aO_2 - C_vO_2}$$

$$Q_p(L/min/m^2) = \frac{VO_2(mL/min/m^2)}{C_{pv}O_2 - C_{pa}O_2}$$

When there is increased oxygen saturation at some point across the chambers of the right heart or decreased saturation across the left heart chambers, the Q_p/Q_s ratio is calculated. From the above equations it is inferred that:

$$\frac{Q_p}{Q_s} = \frac{C_aO_2 - C_vO_2}{C_{pv}O_2 - C_{pa}O_2}$$

Assuming that the patient is breathing in room air, the ratio can be expressed with saturations, instead of oxygen contents, as follows:

$$\frac{Q_p}{Q_s} = \frac{S_aO_2 - S_vO_2}{S_{pv}O_2 - S_{pa}O_2}$$

Normally, in the absence of intracardiac shunts, the blood volume flowing towards the systemic circulation per unit time is the same as the blood volume flowing towards the pulmonary circulation in the same time period, which mathematically is expressed as $Q_s = Q_p$. When a left-to-right shunt is present, $Q_p > Q_s$, since there is an oxygenated blood volume that recirculates through the pulmonary circulation. On the other hand, when a right-to-left shunt is present, $Q_s > Q_p$, because of the deoxygenated blood volume that escapes the pulmonary circulation entering the systemic one.

In order to quantitate a left-to-right, right-to-left or bidirectional shunt the effective pulmonary blood flow (Q_{ep}) and the effective systemic blood flow (Q_{es}) must be calculated. Q_{ep} expresses the volume of blood returning from the systemic venous circulation to the right heart that passes to the lungs, in order to be oxygenated, whereas Q_{es} expresses the volume of blood flowing from the pulmonary veins to the systemic circulation. But for any patient in steady state the volume of blood that flows to the lungs per unit time is equal to the volume of blood that flows out of the lungs and into the systemic circulation per unit time, which is mathematically expressed as $Q_{ep} = Q_{es}$. Q_{ep} can be determined according to the Fick principle:

$$Q_{ep} = \frac{VO_2}{C_{pv}O_2 - C_vO_2}$$

With all these variables known we can therefore calculate an intracardiac shunt as below:

$$Left\text{-}to\text{-}right\ shunt = Q_p - Q_{ep}$$

$$Right\text{-}to\text{-}left\ shunt = Q_s - Q_{es}$$

3.3. Pressure Measurements

Determination of pressures in the heart chambers and the great vessels consists an integral part of diagnostic catheterization. The pressures are measured via a stiff, fluid-filled (saline or blood) catheter with a transducer applied at its distal tip. A diaphragm on the transducer is deflected according to pressure alterations and this mechanical stimulus is transmitted to an electronic strain gage, which converts the pressure signal to an electric signal, which is then displayed as a waveform. The system is calibrated to zero before the procedure. Errors that result in inaccurate calculations are permeation of air in the system (air is compressible, in contrast to saline or blood, and thus signal transmission is distorted), loose connections of the system, clot formation in the tube of the catheter, catheter kinking and improper calibration prior to the procedure [28].

A brief description of the heart chamber pressures is illustrated in (Fig. **2**).

Pressure changes in the right atrium are expressed in the form of waves (Fig. **2**). The "a" wave is an upward deflection representing the atrial systole. Shortly after, the "c" wave follows indicating the upward movement of the tricuspid leaflets during closure of the tricuspid valve. Then, a downward wave, called the "x" wave, is created by the descent of the tricuspid valve ring as a part of the ventricular systole. An upward wave, the "v" wave, is generated as the intra-atrial pressure increases in the end of the ventricular systole with the tricuspid valve closed. Finally, the downward "y" wave represents the intra-atrial pressure drop as blood flows from the right atrium towards the right ventricle after the opening of the tricuspid valve. The left atrial waveform is similar to that of the right atrium with slightly higher pressures and a more prominent "v" wave, in contrast to the right atrium, which has a more prominent "a" wave. In the right atrium abnormal prevalence of "a" wave is seen in cases of forceful atrial systole, such as in tricuspid stenosis, right ventricular hypertrophy, impaired right ventricle diastolic function, right outflow tract obstruction or pulmonary hypertension. Elevated "v" waves are observed in tricuspid regurgitation, Ebstein anomaly or left-ventricular-to-right-atrial shunt. As far as the left atrium is concerned, high "a" waves are present with mitral stenosis, aortic stenosis, coarctation of the aorta. High "v" waves are commonly a result of mitral regurgitation. Sharper "cannon a" waves are present in arrhythmias where atrial systole is performed with the atrioventricular valves closed at the same time with ventricular systole (e.g. complete heart block). Mean atrial pressure is elevated in the aforementioned situations and in the presence of heart failure. Decreased atrial pressure is indicative of hypovolemia.

Right ventricular pressure tracing begins with a steep elevation of intraventricular pressure during isovolumic systole followed by a dome-shaped striping of the tracing during ejection and an abrupt downfall during isovolumic relaxation. Throughout diastole intraventricular pressure rises slowly and slightly and the cardiac cycle is repeated this way. Left ventricular pressure reflection follows the same pattern as that of the right ventricle, but with significantly higher pressures and an earlier peak pressure during ejection, in part due to high systemic vascular resistance. Right ventricular pressure is increased in the presence of a ventricular septal defect, right ventricular outflow tract obstruction, pulmonary hypertension or myocardial failure and, similarly, left ventricular pressure is elevated in aortic stenosis, coarctation of the aorta or left ventricular failure.

3.4. Pressure Gradients and Valve Areas

Normally, RV and PA systolic pressures equal. A systolic pressure gradient between RV and PA is usually caused by right outflow tract obstruction (e.g. pulmonary stenosis). Lower systolic pressure gradients with normal right outflow

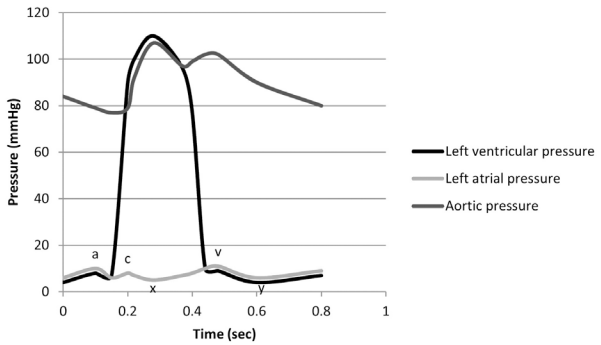

Fig. (2). Left atrial, left ventricular and aortic pressure waveform.

tract and pulmonary valve may be due to increased blood flow through the valve orifice (e.g. atrial septal defect, ventricular septal defect) and minimal gradients (<5mmHg) may be normal. In the left heart, LV end-diastolic pressure equals LA end-diastolic pressure and, in case of a pressure gradient, mitral stenosis may be present. Lower gradients may be functional (e.g. increased blood flow through the mitral valve due to a large ventricular septal defect). Finally, LV systolic pressure equals aortic systolic pressure and a pressure gradient may be caused by left outflow tract obstruction (aortic stenosis) or secondary stenosis in the context of hypertrophic cardiomyopathy. A gradient between the ascending and the descending aorta is indicative of aortic coarctation. When determining the gradients the operating physician has to keep in mind the dependence of the gradients' calculation on the blood flow. Increased flow (e.g. large shunts) may create gradients in the context of normally structured valves, whereas low flow (e.g. myocardial failure, hypovolemia) may underestimate an existing gradient resulting from an abnormal structure. For this reason, it is possible to measure a stenotic valve area, in order to characterize and describe a stenotic valve. This is accomplished via the Gorlin formula:

$$A = \frac{CO}{Kx\sqrt{\Delta P}}$$

where A = valve area, CO = cardiac output, K = an empirical constant for each valve, ΔP = transvalvular gradient [29].

3.5. Vascular Resistance

Determination of vascular resistance, especially pulmonary, is important especially for management planning, in order to determine operability or medical management in pulmonary hypertension etc. In children, pulmonary vascular resistance (PVR) and systemic vascular resistance (SVR) are calculated in Wood units indexed for body surface area (mmHg/L/min/m^2) using the following equations:

$$PVR = \frac{meanPAP - meanLAP}{Q_p}$$

$$SVR = \frac{MAP - meanRAP}{Q_s}$$

where meanPAP = mean pulmonary artery pressure, meanLAP = mean left atrial pressure (can be substituted with PCWP), Q_p = pulmonary blood flow, MAP = mean arterial pressure, meanRAP = mean right atrial pressure, Q_s = systemic blood flow. The result in Wood units is multiplied by 80, in order to be expressed as dynes × sec × cm^{-5} [18].

Normal PVR values range below 3 Wood units. In the neonatal period and early infancy PVR is remarkably higher and decreases with increasing age. After the first 6 months, PVR values resemble the adult values. If PVR exceeds 4 Wood units/m^2, a vasodilation study with 100% inhaled oxygen or nitric oxide is performed, in order to measure correspondence to specific vasodilators, determine operability or pharmacologic management and define prognosis. Vasoreactivity has been defined as the decrease in meanPAP and PVR by 20% [30]. A newer definition sets vasoreactivity at a meanPAP decrease by 10mmHg or more to below 40mmHg [31]. These patients should be treated with calcium channel blockers, while patients with no remarkable vasoreactivity should be offered other therapeutic options. Reassessment to ensure benefit from medication is necessary and those who do not respond to any medical treatment are candidates for heart-lung transplantation [32].

3.6. Angiocardiography

Noninvasive technology has supplanted angiocardiography in the structural assessment of cardiac chambers, great vessels and coronary arteries. However, there are cases when delineation of the cardiac anatomy by catheterization may be indicated, such as when exact determination of the anatomy is necessary (e.g. tetralogy of Fallot with pulmonary atresia and aortopulmonary collaterals), when noninvasive modalities fail to provide with sufficient information (e.g. peripheral pulmonary artery stenosis) or when there is potential for a complementary intervention. The catheter is guided with fluoroscopy and, when correctly placed, a contrast media (radiopaque visualized) is injected and an anatomic feature is defined. Different angles can be used to obtain a complete picture of the structures. Biplane angiocardiography allows for more precise depiction in two planes at the same time minimizing the need for contrast injection. Furthermore, the evolution of CT and MRA has offered the opportunity for more accurate imaging and 3D reconstruction of the features delineated. Coronary artery anatomy is evaluated with selective coronary angiography, such as in the presence of a coronary artery fistula, anomalous origin of the left coronary artery or in Kawasaki disease.

The contrast materials used in pediatrics are most commonly of low osmolarity, due to the poorly tolerated side effects of high-osmolar materials, such as hemodynamic depression, reflex tachycardia, interstitial fluid shift intravascularly, increase of pulmonary artery pressure, as well as allergic reactions and acute renal failure. Adequate hydration prior and post-operatively minimizes the renal burden.

3.7. Endomyocardial Biopsy

Endomyocardial biopsy (EMB) has always been questioned as a diagnostic tool for specific types of heart disease and in many centers is not used as a routine modality. However, in other institutions EMB constitutes a valuable means for the identification of heart problems. The most common indication is the monitoring of cardiac allograft rejection after heart transplantation. Biopsies are recommended in an annually-scheduled follow-up of 2-3 years (maybe more frequently during the first year) and in a non-routine base afterwards [33]. The role of EMB is expected to minimize further in the following years as new noninvasive modalities will pass in clinical practice. For the time EMB being the state of art, it is crucial that pathologic interpretation be made guided by the clinical status of the patient and a complete history, something which necessitates close cooperation between the laboratory and the clinical cardiologist.

CONFLICT OF INTEREST

The authors report no financial relationships or conflicts of interest regarding the content herein.

ACKNOWLEDGEMENTS

The authors would like to thank George D. Chloros, MD for his help in reviewing the manuscript.

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Received: May 05, 2015 Revised: September 21, 2015 Accepted: December 22, 2015