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Nikant Sabharwal, Andrew Kelion, Theodoros Karamitos, and Stefan Neubauer 16.3.4 Cardiac catheterization and angiography 3339 Edward D. Folland

16.3.4 Cardiac catheterization and angiography 3339 Takx RA, et al. (2015). Diagnostic accuracy of stress myocar- dial perfusion imaging compared to invasive coronary angiog- raphy with fractional flow reserve meta-analysis. Circ Cardiovasc Imaging, 8, e002666. 16.3.4 Cardiac catheterization
and angiography Edward D. Folland ESSENTIALS Cardiac catheterization/angiography is indicated for evaluation of patients with coronary, valvular, and congenital heart disease in whom diagnostic or therapeutic decisions cannot be made on the basis of noninvasive tests. Most patients presenting for cardiac cath- eterization have coronary artery disease: catheterization and cor- onary angiography are integral parts of interventional treatments for patients experiencing ischaemic coronary syndromes. Technique and diagnostic utility—vascular access is usually

obtained percutaneously from the femoral, radial, or brachial artery (for the left heart), or the femoral, internal jugular, or brachial/antecubital vein (for the right heart). Key information that can be obtained by cardiac catheterization/angiography include (1) pressures within car- diac chambers; (2) cardiac output; (3) quantitative estimation of left ventricular function; (4) diagnosis and quantitation of intracardiac shunts; (5) calculation of systemic and pulmonary vascular resist- ances; (6) assessment of cardiac valves; and (7) details of coronary arterial anatomy and function. Therapeutic utility—cardiac catheterization/angiography permits interventions, particularly coronary angioplasty/stenting that are of great and increasing therapeutic importance. Introduction Invasive cardiac diagnosis by means of catheterization and angiog- raphy developed hand in hand with cardiac surgery throughout the 20th century. It answered the need for precise information about cardiac physiology and anatomy, which arose in the 1940s when surgical techniques for the treatment of congenital and rheumatic heart disease first became available. A few years earlier, in 1929, Werner Forsman of Germany successfully and safely passed a fili- form urinary catheter from a median basilic vein into the right atrium of his own heart and documented it on X-ray film. Although this feat cost him his own job, it enabled Andre Cournand and Dickenson Richards a decade later to use catheters for sampling blood, measuring pressure and flow, and injecting radiopaque contrast medium (angiography) into the intact, beating human heart, ushering in the era of invasive cardiac diagnosis. Cournand, Richards, and Forsman later won the Nobel Prize for their important work. This chapter reviews the diagnostic applications of cardiac catheterization and angiography. Indications for cardiac catheterization
and angiography Catheterization entails some degree of risk and discomfort, and is expensive, hence patients should be carefully selected. In broadest terms, it is indicated for detailed evaluation of those with coronary, valvular, and congenital heart disease, once they have been identi- fied as candidates for surgery or other forms of intervention. It may also be indicated for patients whose diagnosis is uncertain from noninvasive evaluation. Coronary artery disease Most patients presenting for cardiac catheterization have coronary artery disease. Angiography of the coronary arteries performed during cardiac catheterization is essential for patients in whom revascularization is indicated. In spite of the limitations discussed later in this chapter, no other imaging modality, including MRI and CT (see Chapter 16.3.3), can as yet provide the detailed anatomy of the entire coronary circulation that is needed for planning revascularization procedures such as coronary artery bypass surgery and percutaneous intervention. Coronary angiography is indicated for patients with chronic stable angina that persists in spite of reasonable efforts at pharma- cological therapy. It is also indicated for patients whose survival would be improved by revascularization, regardless of symptoms. Such patients are those with severe stenosis of the main left cor- onary artery and those with severe two-and three-vessel coronary artery disease in combination with impaired left ventricular func- tion. These patients may be identified by the following features of stress testing: ischaemia at low workload (especially in stage 1 of the Bruce protocol); marked depression of the electrocardiographic ST segment (>2 mm); failure to augment systolic blood pressure during exercise; and large exercise-induced defects or increased lung up- take during radionuclide perfusion imaging (see Chapters 16.3.1 and 16.3.3). In addition, patients with high-risk clinical presenta- tions such as acute myocardial infarction, unstable angina, and post-myocardial infarction ischaemia are candidates for angiog- raphy. Patients having acute myocardial infarction are best served by immediate percutaneous coronary intervention if this is avail- able in a timely manner (see Chapter 16.13.5). Finally, catheteriza- tion is sometimes indicated to obtain a definitive diagnosis when noninvasive testing has yielded equivocal or inconsistent results. Valvular disease Catheterization was once considered essential prior to the

surgical treatment of valvular heart disease. This is no longer the case because of advances in noninvasive testing using ultrasound and Doppler techniques. Nevertheless, catheterization is often helpful for gath- ering the information needed to properly select patients for surgical therapy, and to guide the surgeon in providing optimum treatment, the most common issue being to assess the need for coronary ar- tery revascularization, particularly among those with aortic sten- osis, who commonly have coronary artery disease. Haemodynamic

 studies may also be necessary in cases where noninvasive diagnostic data are limited or equivocal. By contrast, it is often possible to avoid catheterization in young patients in whom noninvasive studies yield unequivocal conclusions and there is no evidence of coronary artery disease. Congenital disease Most patients with congenital heart defects can be definitively diag- nosed by transthoracic or transoesophageal ultrasound, CT, or MRI (see Chapters 16.3.2 and 16.3.3). As in valvular disease, catheteriza- tion is most useful in cases where the abnormality is unusually com- plex, the noninvasive data are incomplete, or the patient is suspected of having coronary artery disease. Catheterization is particularly useful in quantifying shunt flow and pulmonary vascular resist- ance, both of which are important considerations in the treatment of intracardiac defects. The physical passage of a systemic venous catheter across the atrial septum into a pulmonary vein or the left ventricle is diagnostic of an atrial septal defect. Pericardial disease Pericardial tamponade and constriction lend themselves particu- larly well to diagnosis by catheterization. Although ultrasonography has superseded catheterization as a rapidly available method of con- firming the clinical diagnosis of tamponade, it is usually inconclu- sive for patients with pericardial constriction. At catheterization, patients with both conditions usually demonstrate equalization of all intracardiac diastolic pressures, with unique pressure waveforms ex- hibited in the right atrium and right ventricle usually distinguishing the two diagnoses (Fig. 16.3.4.1). Congestive heart failure The aetiology and pathophysiology of congestive heart failure are readily elucidated by catheterization. States of pressure and volume overload as well as systolic and diastolic dysfunction of the ventricles can be easily identified, as explained in detail later in this chapter. Furthermore, catheterization is uniquely suited for identifying transient or reversible causes of left ventricular dysfunction caused by ischaemia or myocardial hibernation due to underlying cor- onary artery disease. Sometimes exercise or other interventions are performed during a catheter study to elicit transient abnormal haemodynamic function. Myocardial biopsy performed during catheterization can sometimes identify the aetiology of primary myocardial dysfunction. Pulmonary vascular disease Patients with primary pulmonary hypertension (see Chapter 16.15.2) should undergo catheterization to measure pulmonary vascular pressure and resistance. Certain vasodilating drugs may or may not benefit the patient, depending upon their effect on pressure and re- sistance during acute administration. Pulmonary angiography per- formed during right heart catheterization is traditionally regarded as the most definitive test for pulmonary embolism, although in most cases the diagnosis can be secured by CT angiography or radioiso- tope lung scanning. Practicalities of cardiac catheterization Preparing the patient Precatheterization evaluation should consist of a careful history and examination, particularly aimed at eliciting details of prior cardiac procedures, reactions to contrast medium, renal function, periph- eral vascular status, and haemostatic function. The patient should be carefully advised of the indications, alternatives, risks, discom- forts, and expected benefits of the procedure. The skilled clinician does this while building the patient’s confidence and avoids creating undue alarm. Following an uncomplicated diagnostic catheteriza- tion, the patient should usually expect to go home the same day and to resume customary physical activities within a day or two.

Vascular access The traditional approach to vascular access is via a cut-down near the antecubital fossa, with isolation and mobilization of the bra- chial or antecubital vein and the brachial artery for right and left heart catheterization, thereby allowing arterial and venous access. After the procedure, the arterial entry site is repaired by suture and the vein is usually tied off. However, although this approach has the advantage of enabling early post-procedure ambulation and the security of direct arterial closure in anticoagulated patients, it has the disadvantage of being time-consuming for most physicians and less cosmetic for the patient. Hence the cut-down approach is now seldom used, with percutaneous arterial catheterization becoming increasingly popular. Percutaneous vascular access is achieved by direct puncture with a needle, through which a flexible spring guide wire is passed into the vessel. Catheters may then be passed into the vessel over the guide wire. Following the procedure haemostasis is achieved by applying pressure over the puncture site until bleeding stops. Percutaneous access is frequently employed at the femoral site, al- though it may also be used at brachial, axillary, internal jugular, and radial locations. It has the advantage of speed, simplicity, and— when performed from the femoral vessels—frees the upper body 150 100 50 RV LV 1 s Fig. 16.3.4.1 Pericardial constriction. This is a tracing of simultaneous left ventricular (LV) and right ventricular (RV) pressure in a patient with pericardial constriction. Generally, the diastolic pressure of the left ventricle is higher than that of the right ventricle. For patients with a constriction, the pericardium determines the diastolic compliance of both chambers, causing the diastolic pressures to be equal. Note also the typical ‘dip–plateau’ pattern or ‘square-root sign’ of both chambers in diastole. Although diastolic ventricular pressures are also equal for patients having tamponade, the dip–plateau pattern is usually absent.

 and arms during angiographic filming. However, it has the disad- vantage of sometimes requiring several hours’ immobilization of the catheterization site following the procedure. Nevertheless, the femoral approach remains popular, especially when smaller cath- eters (4 and 5 French) and arterial closure devices enable earlier ambulation. In recent years, the percutaneous approach to the ra- dial artery has become the preferred choice of many physicians because it is associated with fewer bleeding complications and shortens hospital time. Right heart catheterization Right heart catheterization can be performed from any of the ap- proaches described earlier. Although traditionally performed with a stiff, woven Dacron, end-hole catheter, it is often done with a flexible, balloon-tip, flow-directed catheter (Swan–Ganz) because this is safer and enables the measurement of cardiac output by thermodilution. Catheterization of the right heart is indicated by itself for the study of pulmonary vascular disease and haemodynamic response to exercise or drug administration. It is indicated in combination with left heart catheterization for patients requiring haemodynamic study of valvular, congenital, or myocardial disease, and for patients being studied primarily for coronary artery disease who also have heart failure, valvular, or pulmonary disease. Left atrial pressure can be measured indirectly via right heart catheterization by wedging the tip of the catheter in a pulmonary ar- teriole, or by occluding a pulmonary artery branch with the inflated balloon at the tip of a Swan–Ganz catheter. In either case, this creates a static column of blood from the tip of the catheter, through the pul- monary capillary bed, to the left atrium. This static column of blood has the effect of extending the tip of the catheter to the left atrium for pressure-measuring purposes. The resulting pressure is iden- tical to the directly measured left atrial pressure, except that it is de- layed temporally by approximately 80 ms. This pressure, commonly known as the pulmonary (artery) capillary wedge (PCW) pressure, is very useful in the management of left heart failure and shock, and for estimating the diastolic gradient across the mitral valve in pa- tients with mitral

stenosis. Left heart catheterization Left heart catheterization is generally performed in conjunction with coronary angiography but is specifically required for the assessment of left ventricular function and assessment of stenosis or regurgita- tion of the left-sided valves (mitral and aortic). It is most often ac- complished by femoral, radial, or brachial arterial access, and by retrograde crossing of the aortic valve to enter the left ventricle. Left heart catheterization may also be achieved by controlled puncture of the interatrial septum with a catheter originating from the right femoral vein (trans-septal left heart catheterization): this can then be used to measure left atrial pressure directly and be passed antegradely through the mitral valve to measure pressure and perform angiog- raphy of the left ventricle. Retrograde access of the left atrium from the left ventricle is technically difficult and seldom done. The left ventricle may also be entered via transthoracic needle puncture. This approach, known as direct left ventricular puncture, is occasionally necessary for studying patients who have both mitral and aortic mechanical prosthetic valves. The passage of the needle into the left ventricle from the cardiac apex is facilitated by echocar- diographic guidance. Information obtained from cardiac catheterization and angiography Intracardiac pressures Methodology Pressure at the tip of the catheter is transmitted through the fluid inside the catheter (usually saline) to a transducer, which converts the pressure signal to an electrical signal that can then be ampli- fied, displayed on a screen, and stored as a digital time recording. Once calibrated, the pressure at the tip of the catheter can be read graphically from the recording screen and analysed electronically. The fidelity of recording depends upon the physical characteristics of the fluid-filled catheter, stopcocks, connecting tubing, and the pressure transducer itself. A fluid-filled system is usually capable of responding to transient pressure changes up to 20 Hz or occasion- ally 30 Hz, which is of sufficient fidelity to reproduce diagnostically useful pressure waveforms from the heart. However, it is not respon- sive enough to accurately reproduce the rate of rise of left ventricular pressure during the isovolumic phase of systole (dP/dt). This re- quires responsiveness to transient pressure changes of at least 60 Hz, of which fluid-filled catheter systems are not capable. For such ap- plications catheter-tip manometers are available (Millar catheters), in which the transducer is placed at the catheter tip, eliminating the need for an intervening column of fluid. These devices are expensive and are used only when such fidelity is required, usually in research applications. Normal intracardiac pressures The upper limits of all normal intracardiac pressures measurable from a right heart catheter are approximate multiples of six, hence they are easily remembered by the ‘rule of sixes’ (Table 16.3.4.1). For example, the mean right atrial pressure is 6 mm Hg or less, mean left Table 16.3.4.1 Normal intracardiac pressuresa Location Phasic pressure (mm Hg) Mean pressure (mm Hg) Right atrium 3 ± 2 Right ventricle Systole 24 ± 4 Diastole 5 ± 3 Pulmonary artery 13 ± 5 Systole 24 ± 6 Diastole 13 ± 5 Pulmonary capillary Wedge 9 ± 3 Left atrium 9 ± 3 Left ventricle Systole 120 ± 18 Diastole 10 ± 5 a These values are derived from 100 consecutive catheterization studies of patients proven to have no evidence of heart disease at the West Roxbury Veterans Administration Hospital from 1955 to 1980. An easy way to remember the upper limits of normal values (≤2 standard deviations above mean) is that they are generally multiples of the number 6.

section 16 Cardiovascular disorders 3342 atrial pressure is 12 mm Hg or less. A further aid to remembering normal pressures is the ‘corollary of continuity’, which means that contiguous chambers have a common pressure when the intervening valve is open. For example, the right ventricle and right atrium are essentially a

common chamber when the tricuspid valve is open in diastole, therefore the upper limit of right ventricular end-diastolic pressure is the same as the upper limit of the normal right atrial pressure, or 6 mm Hg. This assumes there is no significant stenosis or regurgitation across the tricuspid valve, and that the right ventricle has normal

compliance. The same condition applies to the mitral valve in diastole and the pulmonic and aortic valves in systole. Another practical rule is that the pulmonary artery diastolic and pulmonary artery capillary pressures approximate each other in the absence of severe pulmonary vascular disease. Once this has been

established for any given patient, the pulmonary artery diastolic pressure can be followed as a surrogate for pulmonary capillary wedge pressure in situations where a pulmonary artery catheter is used for intensive- care monitoring. All intracardiac pressures rise and fall phasically with breathing due to transmission of shifting

intrapleural pressure during respira- tory effort. Usually this variation is no more than a few mm Hg from inspiration to expiration, but it can be quite marked in patients with obstructive lung disease. Standards of normal pressure are based upon measurements taken during resting respiration, averaging sev- eral respiratory cycles. Pressures

in the catheterization laboratory should be similarly measured: asking a patient to hold their breath may generate misleading data. Waveforms The shape of intracardiac pressure waveforms carries useful diag- nostic information. Atria and ventricles have characteristic wave- forms, the left-sided chambers

normally demonstrating similar patterns at relatively higher pressures than right-sided chambers. The state of volume loading and the relative compliance or ‘stiffness’ of the respective ventricles during diastolic filling determines pres- sures in the right and left atria. The left ventricle is generally thicker, stiffer, and less compliant to the stretch of

increasing volume than the right ventricle; hence the left atrial and left ventricular diastolic pressures are higher than the respective pressures in the right heart. Conditions such as pericardial constriction and tamponade alter this normal relationship (see Fig. 16.3.4.1). Cardiac flow and output Measurement of cardiac output was one of

the earliest applications of catheterization. Most methods entail application of the indicator dilution theory (the Fick principle), summarized graphically in Fig. 16.3.4.2, which can be stated simply as follows: the rate of flow can be measured if an indicator substance is added to the moving vehicle (e.g. blood) at a known rate, and the

concentration of the indicator is also known proximal and distal to the point where the indicator is added. The indicator can be any readily meas- ured substance such as oxygen, indocyanine green dye, or saline, the temperature of which is known and different from that of the bloodstream. Cardiac output by oximetry In this method,

commonly called the Fick method, the indicator is oxygen that is carried physiologically by the blood. The method requires that the subject be in a metabolic steady state where the use of oxygen is constant. Such a steady state exists at rest and also during exercise, provided that the workload is constant for at least 3 min. As seen in Fig. 16.3.4.3,

the pulmonary blood flow can be calculated when the oxygen consumption rate is known and the oxygen contents of blood in systemic and pulmonary arteries are q/min Incomplete mixing Complete mixing conc. q/l F (l/min) F = q/min conc. (q/l) = Litre/min q = indicator q/min = injection rate conc. (q/l) = indicator concentration after

complete mixing

Fig. 16.3.4.2 The Fick principle. The flow rate (F) through a vessel (cardiac output, in this case) can be measured if an indicator is added to the flowing liquid at a known rate (q/min) and the concentration (q/litre) of the indicator is measured after complete mixing has occurred. CO = QO2 SAO2 – PAO2 ccO2/min ccO2/l –

ccO2/l

= Litre/min O2 Tissue SAO2 (ccO2/litres of blood) F (l/min) LV O2 Lungs QO2 (ccO2/min) PAO2 (ccO2/litres of blood) RV VC A O PA PV Fig. 16.3.4.3 Cardiac output measured by oximetry. This is an application of the Fick principle in which oxygen is the indicator carried by flowing blood. The patient’s metabolism must be at steady state, a condition where oxygen consumption and utilization are matched. It requires three measurements: oxygen consumption rate (Qo2), systemic arterial oxygen content (SAo2), and pulmonary arterial oxygen content (PAo2). Ao, aorta; cc, volume in ml; CO, cardiac output; LV, left ventricle; PV, pulmonary vein; RV, right ventricle; VC, vena cava.

16.3.4 Cardiac catheterization and angiography 3343 known. In the absence of intracardiac shunts the pulmonary blood flow equals the systemic blood flow, or cardiac output. Dye dilution This method entails the rapid

injection of a known quantity of indocyanine dye into the pulmonary artery. Blood is then sampled by withdrawal at a constant rate from a systemic artery. The sampled blood passes through a spectrophotometer, which is calibrated to measure the concentration of dye.

A concentration curve is inscribed when the injected bolus of dye passes the

sampling point (Fig. 16.3.4.4). Dividing the quantity of dye injected by the area of the time–concentration curve (corrected for recirculation as indi- cated by the dashed line in Fig. 16.3.4.4) yields the cardiac output. This method is now seldom used.

Thermodilution

Measurement of cardiac output by thermodilution

uses the same principle as dye dilution, with the indicator being ‘negative calories’ (the difference between the caloric content of the injected bolus of cool saline and the caloric content of the same quantity of the subject’s blood). The downstream ‘concentration’ of injected nega- tive calories is measured as a transient drop in

temperature by a thermistor at the tip of the injection catheter several centimetres from the point of injection. Dividing the negative calories injected by the area of the distal time–temperature curve yields cardiac output. The advantages of speed, automaticity, and repeatability of this method make it particularly suitable

for serial measurements during different haemodynamic states. Angiographic output This is the only commonly used method that does not employ the indicator dilution or Fick principle. The left ventricular stroke volume calculated from quantitative angiography is multiplied by the heart rate to yield the left ventricular output. In the

absence of valvular regurgitation, this is the same as cardiac output. As ex- plained in greater detail later in the chapter, this method is particu- larly useful in assessing mitral and aortic valvular regurgitation. Quantitative angiography Quantitative left ventricular angiography enables the measure- ment of left ventricular volume at

instants throughout the car- diac cycle. Radiographic contrast medium is injected rapidly into the left ventricle and the shadow image of the opacified ventricle captured electronically at a particular frame rate in any chosen projection. The most common projection is 30° right anterior ob- lique at a framing rate of 30 images/s. In this view the image of the

left ventricle is parallel to its long axis, resembling an ellipse. Arvidsson and Greene first suggested that the volume of the left ventricle could be calculated from the volume formula for an el- lipsoid, the three-dimensional structure created by rotating an ellipse on its long axis. Dodge and Sandler improved upon this concept

by deriving the minor hemi- axes from an idealized el- lipse of the same length and area as the projected image of the ventricle. This method is still commonly used and is often re- ferred to as the area–length method. Images captured at end diastole and end systole are analysed and corrected for magni- fication to yield end-diastolic and end-systolic volumes,

the dif- ference between these volumes being the stroke volume and the product of the stroke volume and heart rate, the angiographic left ventricular output. These indices are useful in the assessment of left ventricular function and valvular regurgitation as discussed later in this chapter. Intracardiac shunts The same methods of

oximetry and indicator dilution used in measuring cardiac output can be employed for the detection and quantitation of intracardiac shunts. Under normal resting con- ditions, blood is approximately 75% saturated as it returns from the body to the right heart and pulmonary artery. As it leaves the lungs in the pulmonary veins, blood is

99% saturated. Intracardiac shunts can be detected, localized, and quantified by measuring the oxygen saturation in various locations. Left-to-right shunts will cause a step-up in the saturation of the blood at the location of the shunt; for example, in a patient with an atrial septal defect the saturation will rise in the right atrium, whereas with a

ventricular septal defect the saturation will rise in the right ventricle. A pa- tient with Eisenmenger’s syndrome (pulmonary hypertension and right-to-left shunting) will exhibit a drop in saturation at the loca- tion of the shunt, namely at the left atrium or ventricle in the case of atrial and ventricular septal defects, respectively. The

degree of the change in saturation is proportional to the size of the shunt and enables calculation of the shunt flow in either direction in litres/ min. Fig. 16.3.4.5 presents a scheme and formulae for calculating shunt volume. Vascular resistance Blood flow through the pulmonary and systemic circulations can be compared to the flow of an

electric current through a circuit. Pressure is the driving force analogous to voltage, flow rate is analo-gous to current, and the impediment to flow through the vascular Q (g) Sampling point O conc. (g/l) conc.∫o t conc.∫o t Inject 0 Q F =

= l/s g g-s/l Time (s) F (litre/s) Fig. 16.3.4.4 Cardiac output measured by dye curve. The concentration curve of indocyanine green dye generated by sampling distal to an injection point can be analysed to yield cardiac output. See text for more details. Thermodilution cardiac output employs the same principle, except that temperature is the measured indicator. F, flow or cardiac output; Q, quantity of indicator injected.

resistance. Pressure, flow, and resistance relate to each other in a fashion analogous to Ohm’s law:
resistance = pressure/flow.
In this formula, ‘pressure’ is the difference in mean pressure across the systemic vascular bed (systemic arterial pressure − right atrial pressure) or the pulmonary vascular bed (pulmonary artery pres- sure

− left atrial pressure). In the absence of intracardiac shunts ‘flow’ is the same for both circulations and is measured as cardiac output by methods already described. In cases of intracardiac shunting the systemic and pulmonary flows will differ according to the degree of shunting, and can be calculated as described under the section

on cardiac shunts and in Fig. 16.3.4.5. Normal values for pulmonary vascular and systemic vascular resistance are expressed either in dyne s cm–5 or Wood units as shown in Table 16.3.4.2. Total pul- monary resistance is a useful concept for expressing the total resist- ance against which the right ventricle must work, and includes not only the

pulmonary vascular resistance but also the resistance en- gendered by the static pressure in the left atrium. Hence, pulmonary vascular disease, left heart failure, or both, can increase the total pul- monary resistance. Measurement of resistance is useful for assessing the state of the pulmonary circulation in congenital heart disease

with intracardiac shunting: high pulmonary vascular resistance may preclude the safe correction of an intracardiac shunt, particularly if the shunt is from right to left. It is also useful in diagnosing the relative contribution of left heart failure and pulmonary vascular disease in patients with pulmonary hypertension, and is the best

indicator of the effective-ness of vasodilating drugs for patients with pulmonary hypertension. Valvular stenosis Valvular stenosis is assessed by measuring the transvalvular pressure gradient and by calculating the valvular orifice area using a formula introduced in the late 1940s by cardiologist Richard Gorlin and his father, an engineer.

The Gorlin formula for valve area was initially de- veloped for patients with rheumatic mitral stenosis. It is based upon a study which utilized data from right heart catheterization alone, validated by relatively crude intraoperative estimates of valve area using the index finger of surgeon Dwight Harken during closed mi- tral commissurotomy operations

at the Peter Bent Brigham Hospital in Boston, Massachusetts, or by autopsy in some cases. Although its validation was relatively crude, the formula has stood the test of time and remains the standard for the haemodynamic assessment of valvular stenosis. In its generalized form it is expressed as follows: Value area TFR

( ) / , K m where K is a constant unique to mitral or aortic valve analysis (38 and 44.5, respectively), TFR is the transvalvular flow rate, and m is the mean pressure gradient in mm Hg during the time when the valve is open. In aortic valve applications TFR (i.e. cardiac output normalized for the time that the valve is actually open) is the cardiac output div- ided by the product of heart rate and systolic ejection period. In mi- tral valve applications it is the cardiac output divided by the product of heart rate and diastolic filling period. Cardiac output is the ef- fective systemic blood flow as determined by Fick, thermodilution, or dye dilution methods, unless there is associated valvular regur- gitation, in which case it is the total left ventricular output as deter- mined by quantitative left ventricular angiography. Fig. 16.3.4.6 shows tracings that demonstrate typical gradients from patients with aortic and mitral stenosis. The ranges of the cal- culated valve area associated with various levels of stenosis for both aortic and mitral valves are displayed in Table 16.3.4.3. In general, procedures performed for the relief of anatomical stenosis are ex- pected to be beneficial in symptomatic patients with severe valvular obstruction. However, many factors enter into such a decision and Resistance = pressure/flow PBF EPBF SA Mixed venous return EPBF R L R L EPBF (l/min) = O2 consumption (ml/min) (PVO2– mixed VO2) × 10 PBF (l/min) = O2 consumption (ml/min) (PVO2– PAO2) × 10 SBF (l/min) = O2 consumption (ml/min) (SAO2– mixed VO2) × 10 Shunt flow (l/min): PV PA SBF L R = PBF – EPBF R L = SBF – EPBF Fig. 16.3.4.5 Quantitation of intracardiac shunts. Shunts between the left and right sides of the heart due to septal defects can be quantified by oximetry using this scheme. Oxygen content is measured in units of cc oxygen per decilitre of blood. EPBF, effective pulmonary blood flow (i.e. that part of the systemic venous return that actually passes through the lungs and is oxygenated); PBF, pulmonary blood flow; mixed Vo2, mixed systemic venous oxygen content; PAo2, pulmonary artery oxygen content; PVo2, pulmonary vein oxygen content; SAo2, systemic artery oxygen content; SBF, systemic blood flow.
Table 16.3.4.2 Normal vascular resistancea Location Resistance (dynes s cm–5)b Wood units Total systemic resistance 1276 ± 371 16 ± 4.6 Total pulmonary resistance 185 ± 57 2.3 ± 0.7 Pulmonary vascular resistance 55 ± 18 0.7 ± 0.2 a These values are derived from 100 consecutive catheterization studies of patients proven to have no evidence of cardiac disease at the West Roxbury Veterans Administration Hospital during the years 1955–1980. b Divide these values by 10 to obtain values in MPa s m−3.

 individual clinical judgement is required. Although patients with large transvalvular gradients generally experience the best result from intervention, the gradient by itself can be misleading due to its exponential relationship to cardiac output. Valvular regurgitation Qualitative assessment Regurgitation of all four cardiac valves can be qualitatively assessed by angiography. The downstream side of the valve in question is opacified by a rapid injection of radiographic contrast me- dium. Regurgitation is visualized as upstream leakage of contrast across the closed valve. In the case of mitral regurgitation systolic opacification of the left atrium occurs during injection of the left ventricle. In aortic regurgitation diastolic opacification of the left ventricle occurs during supravalvular injection of the aorta. The de- gree of regurgitation is graded on an arbitrary scale from mild (1 +) to severe (4 +). Quantitative assessment Aortic and mitral regurgitation can be quantified in terms of regurgitant flow in litres/min or regurgitant fraction as a percentage of left ventricular output. Regurgitant flow is the difference obtained by subtracting the effective forward flow (Fick method described earlier) from the total left ventricular output (angiographically de- rived). It is the best method for measuring the severity of regurgita- tion, provided that the left ventricular angiogram, which itself may change cardiac output, is performed soon after the Fick measure- ment. Furthermore, both

measurements must be made with consid- erable care to ensure accuracy. Regurgitation is considered clinically severe when 50% or more of the total left ventricular output is simply shuttling or regurgitating across the defective valve. The ability to quantify regurgitation across either valve is lost when both mitral and aortic valves are leaky. Left ventricular function Global function Global function of the left ventricle is broadly described by its ability to generate pressure and flow under particular conditions of preload and afterload. Plotting the pressure and volume of the left ventricle at instants in time for a single cardiac cycle generates a pressure– volume loop displayed in Fig. 16.3.4.7. Most of the commonly used indices of left ventricular function can be derived from such a loop, including end-diastolic volume, end-systolic volume, stroke volume, ejection fraction, end-diastolic pressure, and dP/dt. Of these, the Mitral stenosis Aortic stenosis (b) (a) 200 100 0 mm Hg LV Ao 1 s 40 20 0 mm Hg 1 s PCW LV Fig. 16.3.4.6 Pressure gradients associated with valvular stenosis. The upper panel shows simultaneous tracings of left ventricular (LV) and ascending aortic (Ao) pressure in a patient with severe aortic stenosis. The mean systolic gradient across the aortic valve is 60 mm Hg. The lower panel shows simultaneous tracings of left ventricular (LV) and pulmonary capillary wedge (PCW) pressure in a patient with severe mitral stenosis. The mean diastolic pressure gradient across the valve is 16 mm Hg. The respective valvular gradients are cross-hatched. Table 16.3.4.3 Calculated valve areas associated with various degrees of mitral and aortic stenosis Severity Valve area (cm2) Aortic Mitral Mild

> 1.2 2.0 Moderate 0.8–1.2 1.1–2.0 Severea <0.8 ≤1.0 a Severe stenosis is generally considered to be sufficient to warrant surgical or percutaneous intervention. 0 250 150 250 350 LV volume (ml) A B D C 200 150 100 50 LV pressure (mm Hg) 50 Normal Pressure load Volume load Cardiomyopathy Fig. 16.3.4.7 Pressure–volume loops. Simultaneously plotting the instantaneous pressure and volume of the left ventricle throughout a single cardiac cycle produces these loops. The loop is a synthesis of most information relevant to left ventricular function. In this figure a loop from a normal patient is contrasted with those from patients with pressure load (hypertension or aortic stenosis), volume load (aortic or mitral regurgitation), and cardiomyopathy. Point A represents mitral valve closure; segment A–B, isovolumic contraction; point B, aortic valve opening; segment B–C, systolic ejection; point C, aortic valve closure; segment C–D, isovolumic relaxation; point D, mitral valve opening; and segment D–A, diastolic filling.

section 16 Cardiovascular disorders 3346 ejection fraction is most useful because it correlates with prognosis in a variety of cardiac diseases. Grading angiographic wall motion in various segments of the left ventricle as normal, hypokinetic, akinetic, or dyskinetic assesses the regional function of the left ventricle. Regions of abnormal func- tion generally correspond to locations of infarcted or ischaemic myocardium. Contractility This parameter is difficult to assess in the intact heart because all pressure and volume indices are dependent upon preload and afterload. Although ejection fraction is clinically useful it can be misleading in situations of high afterload (e.g. severe aortic sten- osis) and low afterload (e.g. severe mitral regurgitation). The con- cept of ‘elastance’ has gained favour as a useful index of intrinsic contractility because it is relatively independent of loading condi- tions. Elastance is the slope of the line generated by plotting the end- systolic left

ventricular pressure from a series of pressure–volume loops generated at differing afterloads created by the infusion of pressor or vasodilator drugs. The method is laborious and generally reserved for research applications. Diastolic function Diastolic function of the left ventricle is best appreciated from the slope of the pressure–volume loop during the period from mitral valve opening to its closure at the onset of systole. The curve be- comes steeper as the left ventricle becomes less compliant due to the effects of hypertrophy, ischaemia, or infiltrative disease. In general, left ventricular end-diastolic pressure rises as diastolic compliance falls, accounting for the high left atrial pressure and heart failure seen in diastolic left ventricular dysfunction. Assessment of coronary arterial anatomy and function Disease of the coronary arteries can be characterized at catheteriza- tion by both anatomical and functional assessment. Coronary angi- ography images the lumen of the vessel, which has been rendered radiopaque by injection of radiographic contrast medium. It is a shadowing technique that displays the impact of the lesion on the arterial lumen but does not image the plaque per se. Intracoronary ultrasonography provides a tomographic image of the vessel wall and is capable of demonstrating the thickness and sonic density of the vessel wall and any associated plaque, hence angiography and intravascular ultrasonography are complementary methods of (a) (b) (c) (d) Fig. 16.3.4.8 Normal coronary anatomy. Left coronary angiogram showing main stem, left anterior descending, and left circumflex arteries from right anterior oblique view (a) and left anterior oblique view (b). Right coronary angiogram showing right coronary and posterior descending arteries from right anterior oblique view (c) and left anterior oblique view (d).

16.3.4 Cardiac catheterization and angiography 3347 assessing vascular anatomy. To learn the haemodynamic import- ance of a coronary lesion, it may be necessary to analyse its effect on function by measuring pressure and flow in the affected vessel. All these anatomical and functional modalities may be accomplished by catheterization. Coronary arteriography or angiography Coronary arteriography or angiography is presently the single most essential application of cardiac catheterization. The anatomy of coronary arteries in living, conscious humans was first dem- onstrated by nonselective injection of the aortic root. In the early 1960s David Littmann developed a loop catheter that enabled the injection of contrast medium preferentially in the outer circum- ference of the aortic root, opacifying the left and right coronary arteries simultaneously. At the time it was commonly believed that selective injection of contrast material into a coronary artery would have fatal consequences. This changed when Mason Sones accidentally performed the first selective coronary angiogram without harm. He was intending to inject the left ventricle, but the catheter recoiled across the aortic valve and into the right coronary artery. Sones, a cardiologist by training, went on to develop a safe method of selective coronary angiography from the brachial ar- tery cut-down approach using the flexible-tip catheter bearing his name. At the same time Melvin Judkins, a radiologist by training, was perfecting his own method of selective coronary angiography, using preshaped catheters, from a percutaneous femoral artery ap- proach. Both methods have continued to be practised, although the percutaneous femoral, or Judkins' approach, has become most popular because of its speed and simplicity. However—as stated previously—in recent years there has been a return to the arm approach using percutaneous catheterization of the radial ar- tery, which enables more rapid patient ambulation, and the radial artery approach is also associated with fewer serious access site complications. Normal coronary anatomy is demonstrated in Fig. 16.3.4.8. A patient's anatomy is considered to be right (80%)—or left (20%)—dominant, depending upon whether the posterior descending artery arises from the right or left coronary artery, respectively. Atherosclerotic disease is manifest by lesions that encroach upon the

opacified lumen of the coronary artery (Fig. 16.3.4.9). Various approaches are used to grade the severity of these lesions. Most commonly a visual estimate of the percentage of the stenotic reduction in luminal diameter is given to each lesion, with severity quantified by comparing the minimal lumen diameter within a lesion to the diameter of the nearest normal segment of artery. This can be done manually using callipers or automatically using computer-based systems for edge detection and contrast densi- tometry. Quantitative coronary angiography is a complex subject because it requires attention to many variables, such as selection of view and frame, and choice made from among several analytical techniques. Early work by Lance Gould determined that a lesion must impair coronary blood flow to be clinically important. Although flow at rest is not usually reduced until stenosis reduces vessel diameter by 90%, flow under stress may be impaired when the diameter is reduced by 70%. The clinical impact of a stenosis of any given severity is also dependent upon the degree of collateral flow into the vascular bed distal to the stenosis. Coronary physiological measurements (pressure and flow) Flow and pressure may be directly measured in the coronary artery by means of special guide wires that have pressure transducers or Doppler flow transducers mounted near their tips. As just men- tioned, the flow at rest may be normal across a particular coronary artery stenosis. Coronary flow normally increases after maximal vasodilatation induced by local vasodilators. The quotient of the vasodilated flow divided by the resting flow, which is called the cor- onary flow reserve, is normally greater than 2. If not, the lesion in question is considered to be haemodynamically important. Pressure can be measured in the coronary artery at a location distal to a le- sion using a guide wire with a transducer at its tip. The quotient of pressure distal to a lesion compared to the proximal pressure during maximal vasodilatation is called the fractional flow reserve. A quotient less than 0.75 is considered to be clinically important. The measurement of fractional flow reserve has proven useful in selecting vessels in need of revascularization. Intravascular ultrasonography Intravascular ultrasonography (IVUS; see Fig. 16.3.4.10) is ac- complished by advancing a catheter over a guide wire previously placed into a coronary artery. The catheter has a miniature ultra- sound transducer near its tip, which enables rotational Doppler imaging of the vessel wall in a plane perpendicular to its axis. IVUS is particularly useful for assessing the nature of angio- graphically questionable lesions, determining the true size of the vessel prior to stent deployment, and assessing the complete- ness of stent deployment. It is also probably the best method for Fig. 16.3.4.9 Atherosclerotic coronary artery disease. The constrictions and blunt terminations seen in this patient’s coronary angiogram represent atherosclerotic lesions.

section 16 Cardiovascular disorders 3348 serial studies of coronary anatomy during drug treatment trials because it images the plaque itself and is therefore more sensitive than angiography. Complications of cardiac catheterization Although cardiac catheterization is a relatively safe procedure, it is nevertheless important for both the patient and the referring physician to recognize the nature and likelihood of potential com- plications. Table 16.3.4.4 lists the complications of bilateral heart catheterization, including coronary, left ventricular, and aortic angiography, in a prospective study of valvular heart disease from the United States Veterans Administration. Even though these data were collected over 30 years ago from a particularly high- risk group of patients, the frequency of complication is a realistic estimate of what should currently be expected. The rate of each particular complication will vary with the age and general health of the patient. For example, the risk of vascular complication is considerably increased by the presence of vascular disease, and the risk of renal failure due to contrast medium is particularly high in diabetic patients with pre-existing renal dysfunction. Access site complications (bleeding, haematoma, arteriovenous

fistula, pseudoaneurysm, and occlusion) have received particular atten- tion in recent years because of the use of aggressive anticoagulation and antiplatelet treatments during percutaneous coronary inter- vention. The use of smaller gauge catheters and careful location of the arterial puncture site are important. Vascular closure devices enable earlier ambulation of patients having femoral procedures. In counselling the patient regarding the likelihood of untoward events, it is important to give individualized advice based on the patient's particular circumstances. The decision to recommend catheterization must be based on the anticipation that its benefits justify its risk and cost. Fig. 16.3.4.10 Intravascular ultrasound images. The dark central circles represent the ultrasound catheter. Measurement markers are spaced by 1 mm. The top two panels demonstrate the appearance of a cross- section of a normal coronary artery. The arrows in magnified image on the right point to the intimal layer. The three lower panels demonstrate coronary arteries with soft, mixed fibrous/calcified and hard calcified plaque. Reprinted from Nissen SE, Yock P (2001). Intravascular ultrasound: Novel pathophysiological insights and current clinical applications. Circulation, 103, 604–16.

16.3.4 Cardiac catheterization and angiography 3349 FURTHER READING De Bruyne B, et al. (2012). Fractional flow reserve guided-PCI versus med- ical therapy in stable coronary disease. N Engl J Med, 367, 991–1001. Moscucci M (2014). Grossman and Baim's cardiac catheterization, an- giography and intervention, 8th edition. Lippincott Williams and Wilkins, Baltimore, MD. Nissen SE, York P (2001). Intravascular ultrasound: novel patho- physiological insights and current clinical applications. Circulation, 103, 604–16. Sorajja P, Lim M, Kern M (2019). Kern's cardiac catheterization hand- book, 7th edition. Elsevier, Philadelphia, PA. Tonino PA, et al. (2009). Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med, 360, 213–24. Table 16.3.4.4 Complications of cardiac catheterization from a prospective study of 1559 procedures performed on 1483 United States veterans having valvular heart disease during the years 1977–1982a Type of complication Frequency (%) Death within 24 h 0.1 Death between 24 h and 30 days 0.1 Stroke 0.3 Transient cerebral ischaemia 0.1 Myocardial infarction 0.2 Peripheral arterial embolism 0.1 Access site complications 1.7 Cardiac tamponade 0.3 Ventricular fibrillation 0.5 Arrhythmia other than ventricular fibrillation 1.5 Primary hypotension 0.5 Reaction to contrast medium (allergic and renal) 1.8 Arterial perforation or dissection 0.3 Miscellaneous complications 1.4 Patients having one or more of the above complications 6.9 a Although this is a high-risk group of patients undergoing extensive study, the rates are very comparable to what should be expected today. In fact, some complications, especially bleeding, are now more frequent because of aggressive anticoagulation and antiplatelet treatments given to many patients undergoing percutaneous intervention. Recent data from national registries in the United States indicate frequency of vascular access site injury to be less than 1% for diagnostic procedures.

Revision #1
Created 2026-01-22 16:39:43 UTC by Omar Ayman
Updated 2026-01-22 16:39:43 UTC by Omar Ayman