21 Coronary Angiography and Intravascular Imaging

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Coronary angiography consists of the visualization of the coronary anatomy under fluoroscopy, facilitated by direct injection of contrast media into the epicardial coronary arteries through a catheter advanced from a peripheral artery to the aortic root and into the coronary ostia.

The history of coronary angiography starts in the 19th century with the discovery of x-rays by Roentgen in 1895. One month later, Haschek and Lindenthal injected a mixture of calcium carbonate in the blood vessels of an amputated hand and were able to visualize the vascular bed using a roentgenogram. Meanwhile, Andre Cournand and Dickinson Richards at Columbia University performed the first experiments on cardiac catheterization in animals, which led to the description of heart hemodynamics and the application to humans of crucial techniques and principles, such as the Fick method to measure cardiac output and pressure manometry (see Chapter 22). Forssmann performed the first human cardiac catheterization on himself in 1928, advancing a catheter through an antecubital vein into his right atrium, and acquired roentgenograms to document it.

Selective coronary angiography was first attempted in 1958 by Mason Sones, who cannulated a right coronary artery with a catheter inserted through a brachial artery.[1] In the 1960s, angiographic studies for the determination of coronary artery disease (CAD) were performed in extremely ill patients in the few tertiary care centers in the United States with the necessary resources. Coronary angiography remained a purely diagnostic technique until 1977, when Gruentzig performed the first percutaneous transcatheter coronary angioplasty (see Classic References, Ryan). In the early 1990s the field of coronary angiography entered a period of explosive growth, such that by 2010, an estimated 1,029,000 inpatient diagnostic cardiac catheterization procedures and 954,000 inpatient percutaneous coronary intervention (PCI) procedures (see Chapter 41) were performed per year in the United States alone.[2] Recent years have seen rapid development and maturation of the field, with continuous introduction of new materials, techniques, and innovations for coronary angiography and intracoronary interventions.

Despite the availability of noninvasive imaging techniques such as computed tomographic coronary angiography (CTCA) and magnetic resonance coronary angiography (MRCA) that allow visualization of the coronary anatomy without the risks related to an invasive percutaneous procedure (see Chapters 19 and 20), selective coronary angiography remains the gold standard to determine the extent of CAD because it is the only technique that can simultaneously provide both functional and anatomic information for the estimation of ischemic burden of CAD. Although coronary angiography technique is well established, it is important to keep in mind that it is an invasive procedure with potential complications. Therefore, indications for coronary angiography are clearly defined in the current American Heart Association and American College of Cardiology (AHA/ACC) clinical practice guidelines.[3,4] This chapter reviews the indications for coronary angiography, the basic technique, and interpretation of angiographic images, with an overview of the available intravascular imaging techniques.

INDICATIONS FOR CORONARY ANGIOGRAPHY

Selection of candidates for invasive coronary angiography is based on the pretest probability of CAD, which is estimated on the basis of the clinical evaluation of the patient, the patient's clinical presentation, and the results of noninvasive diagnostic testing such as electrocardiography, echocardiography, blood tests, stress test, and CTCA or MRCA if performed[5,6] (see Chapters 15, 16, and 18 to 20). Current guidelines and indications for coronary angiography by clinical presentation are summarized in Chapters 37 to 40 (eTable 21.1).[3,7]

In patients with low pretest probability of CAD, first-line noninvasive assessment of cardiovascular risk is necessary to decide whether to proceed to coronary angiography. Traditionally, stress test findings can be defined as low, intermediate, or high risk, which are associated with a cardiac mortality of less than 1%, 1% to 3%, and greater than 3% per year, respectively. For patients with intermediate-risk pretest probability, coronary angiography may be considered, whereas for patients with high-risk pretest probability, angiography should be performed without delay and with no need for further testing. Patients presenting with acute coronary syndrome (ACS), unstable angina (UA), or non–ST-segment elevation myocardial infarction (NSTEMI) with hemodynamic instability or who are at high clinical risk (as determined by the presence of any of the risk factors listed in eTable 21.2) should undergo early invasive evaluation. For hemodynamically stable UA/NSTEMI patients without high clinical risk, a delayed invasive strategy may be justified, although an initially noninvasive risk stratification may be practiced outside the United States. Patients presenting with ST-segment elevation myocardial infarction (STEMI) should generally undergo urgent invasive intervention as

ETABLE 21.1 Current Clinical Practice Guidelines on the Indications for Coronary Angiography in Stable CAD, UA/NSTEMI, and STEMI

CLASS I	CLASS IIA	CLASS IIB	CLASS III
Stable CAD			
1. Patients with SIHD who have survived sudden cardiac death or potentially life-threatening ventricular arrhythmia. (*LOE: B*) 2. Patients with SIHD who develop symptoms and signs of HF should be evaluated to determine whether coronary angiography should be performed for risk assessment. (*LOE: B*) 3. Patients whose clinical characteristics and results of noninvasive testing indicate a high likelihood of severe IHD and in whom the benefits are deemed to exceed risk. (*LOE: C*) 4. Patients with presumed SIHD who have unacceptable ischemic symptoms despite optimal medical therapy and who are amenable to, and candidates for, coronary revascularization. (*LOE: C*)	1. Patients with suspected SIHD whose clinical characteristics and results of noninvasive testing (exclusive of stress testing) indicate a high likelihood of severe IHD and who are amenable to, and candidates for, coronary revascularization. (*LOE: C*) 2. Patients with suspected symptomatic SIHD who cannot undergo diagnostic stress testing, or have indeterminate or nondiagnostic stress tests, when there is a high likelihood that the findings will result in important changes to therapy. (*LOE: C*) 3. Patients with SIHD who have depressed LV function (EF <50%) and moderate-risk criteria on noninvasive testing with demonstrable ischemia. (*LOE: C*) 4. Patients with SIHD and inconclusive prognostic information after noninvasive testing or patients for whom noninvasive testing is contraindicated or inadequate. (*LOE: C*) 5. Patients with SIHD who have unsatisfactory quality of life due to angina, have preserved LV function (EF >50%), and have intermediate-risk criteria on noninvasive testing. (*LOE: C*)	1. Patients with stress test results of acceptable quality that do not suggest the presence of CAD when clinical suspicion of CAD remains high and there is a high likelihood that the findings will result in important changes to therapy. (*LOE: C*)	1. Patients with SIHD who elect not to undergo revascularization or who are not candidates for revascularization because of comorbidities or individual preferences. (*LOE: B*) 2. Patients with SIHD who have preserved LV function (EF >50%) and low-risk criteria on noninvasive testing. (*LOE: B*) 3. Patients who are at low risk according to clinical criteria and who have not undergone noninvasive risk testing. (*LOE: C*) 4. Coronary angiography is not recommended to assess risk in asymptomatic patients with no evidence of ischemia on noninvasive testing. (*LOE: C*)
ACS—UA AND NSTEMI			
1. An urgent/immediate invasive strategy (diagnostic angiography with revascularization if appropriate) is indicated in patients with NSTE-ACS who have refractory angina or hemodynamic or electrical instability (without serious comorbidities or contraindications to such procedures). (*LOE: A*) 2. An early invasive strategy (diagnostic angiography with revascularization if appropriate) is indicated in initially stabilized patients with NSTE-ACS (without serious comorbidities or contraindications to such procedures) who have an elevated risk for clinical events. (*LOE: B*)	1. It is reasonable to choose an early invasive strategy (within 24 hours of admission) over a delayed invasive strategy (within 25 to 72 hours) for initially stabilized high-risk patients with NSTE-ACS. For those not at high/intermediate risk, a delayed invasive approach is reasonable. (*LOE: B*)	1. An ischemia-guided strategy may be considered for initially stabilized patients with NSTE-ACS (without serious comorbidities or contraindications to this approach) who have an elevated risk for clinical events. (*LOE: B*) 2. An ischemia-guided strategy in initially stabilized patients (without serious comorbidities or contraindications to this approach) may be reasonable after considering clinician and patient preference. (*LOE: C*)	1. An early invasive strategy (i.e., diagnostic angiography with intent to perform revascularization) is not recommended in patients with: a. Extensive comorbidities (e.g., hepatic, renal, or pulmonary failure; cancer), in whom the risks of revascularization and comorbid conditions are likely to outweigh the benefits of revascularization. (*LOE: C*) b. Acute chest pain and a low likelihood of ACS who are troponin negative (*LOE: C*), especially women. (*LOE: B*)
ACS—STEMI			
1. Immediate angiography and PCI when indicated should be performed in resuscitated out-of-hospital cardiac arrest patients whose initial ECG shows STEMI. (*LOE: B*) 2. Primary PCI should be performed in patients with STEMI and ischemic symptoms of less than 12 hours' duration. (*LOE: A*) 3. Primary PCI should be performed in patients with STEMI and ischemic symptoms of less than 12 hours' duration who have contraindications to fibrinolytic therapy, irrespective of the time delay from first medical contact. (*LOE: B*) 4. Primary PCI should be performed in patients with STEMI and cardiogenic shock or acute severe HF, irrespective of time delay from MI onset. (*LOE: B*)	1. Primary PCI is reasonable in patients with STEMI if there is clinical and/or ECG evidence of ongoing ischemia between 12 and 24 hours after symptom onset. (*LOE: B*)		1. PCI should not be performed in a noninfarct artery at the time of primary PCI in patients with STEMI who are hemodynamically stable. (*LOE: B*)

ACS, Acute coronary syndrome; *CAD*, coronary artery disease; *ECG*, electrocardiogram; *EF*, ejection fraction; *HF*, heart failure; *IHD*, ischemic heart disease; *LOE*, level of evidence; *LV*, left ventricular; *MI*, myocardial infarction; *NSTE-ACS*, non–ST-segment elevation acute coronary syndrome; *NSTEMI*, non–ST-segment elevation myocardial infarction; *PCI*, percutaneous coronary intervention; *SIHD*, stable ischemic heart disease; *STEMI*, ST-segment elevation myocardial infarction; *UA*, unstable angina.

ETABLE 21.2 Risk Factors That Support Early Invasive Evaluation of Patients Presenting with ACS

Significant troponin increase
Diagnostic ST or T wave changes
GRACE score >140
Diabetes mellitus
Reduced LV function (ejection fraction <40%)
Early postinfarction angina
Recent PCI
Prior CABG
Intermediate to high GRACE risk score

ACS, Acute coronary syndrome; *CABG*, coronary artery bypass graft surgery; *GRACE*, Global Registry of Acute Coronary Events; *LV*, left ventricular; *PCI*, percutaneous coronary intervention.

soon as possible after symptom onset.[7] Patients with delayed cases may be treated conservatively, as described in other chapters.

Appropriate Use Criteria

In 2012 the appropriate use criteria (AUC) for diagnostic coronary angiography were released.[4] This and a more recent focused update document provide a classification schema for procedures into *appropriate*, *may be appropriate*, and *rarely appropriate* care based on specific criteria. The proportion of "inappropriate" nonacute PCI has been reduced overall.[8] Clinical indications for PCI are beyond the scope of this chapter, but the AUC for diagnostic catheterization are mentioned here to highlight the appropriate selection of patients referred for coronary angiography for diagnostic purposes, since coronary angiography itself may be an unnecessary invasive procedure that could trigger an inappropriate coronary intervention in some cases.[9] The rate of angiographically normal or minimally diseased coronary arteries in patients undergoing elective procedures is approximately 39%.[10] In particular, the use of coronary angiography and PCI in asymptomatic patients is uncertain. A recent study showed that among a sample of 300,000 patients receiving coronary angiography in the United States, 25% were asymptomatic at the time of the elective coronary angiography. Furthermore, the rate of angiographic procedures in asymptomatic patients directly correlated with the number of inappropriate PCI procedures performed.[9] Therefore, strategies to verify the correct referral of patients for diagnostic coronary angiography are required to avoid unnecessary procedures, reduce health care costs, and prevent the therapeutic cascade that may lead from diagnostic angiography to inappropriate PCI.

Contraindications to Coronary Angiography

There are no absolute contraindications to coronary angiography listed in the clinical practice guidelines. However, specific conditions should be taken into account when weighing risks and benefits of the procedure. Based on the patient's cardiovascular risk and the clinical presentation, a decision should be made whether to avoid or postpone the procedure or proceed with coronary angiography using prophylactic measures to reduce the probability of periprocedural complications. Relative contraindications that should be taken into account are known anaphylactoid reaction to contrast media, moderate to severe kidney impairment, decompensated heart failure and pulmonary edema that prevent the patient from lying down during the procedure, uncontrolled hypertension, active infection, coagulopathy, and gastrointestinal bleeding.[11] In addition, coronary angiography requires the use of radiation to visualize the wires and catheters advanced through the blood vessels and to obtain images of the coronary arteries. Therefore, pregnant women should not undergo angiography unless strictly necessary and on exhaustive explanation of the risks related to radiation exposure, medications, and contrast media for both the mother and the fetus.[12] The presence of comorbidities that can increase the risk of complications should be critically considered before referring patients for coronary angiography.[13]

Complications of Coronary Angiography

Complications during coronary angiography are rare, occurring in approximately 2% of patients, with serious complications such as cerebrovascular accident (CVA), or stroke, or myocardial infarction (MI) accounting for less than 1% of all patients. Mortality rate is lower than 0.1%.[13] Complications during PCI are more common (see Chapter 41). Table 21.1 lists complications that may be encountered during coronary angiography.

Although rare, the most common complications are allergic reactions to contrast, vascular complications, and worsening of kidney function (see next section). Vascular complications at the access site include hematoma, pseudoaneurysm, aneurysm, and dissection. The risk of a vascular complication increases with the diameter of the sheath used, age of the patient, and degree of local calcifications. Iatrogenic coronary dissection or perforation occurs infrequently but is potentially life-threatening and could require urgent coronary stenting[14] (Fig. 21.1). Ventricular and atrial arrhythmias are relatively common. Intracoronary injection of contrast media itself can induce arrhythmias. In particular, during injection of contrast media into the right coronary artery (RCA), one should take care to avoid deep cannulation of the RCA and injection of contrast media directly into the conus branch because this can result in ventricular fibrillation (VF).[15] In addition, when performing ventriculography, the mechanical stress of the catheter on the ventricular walls can trigger ventricular arrhythmias ranging from isolated

premature ventricular complexes (PVCs) to runs of ventricular tachycardia (VT). Usually, these arrhythmias are self-resolving with catheter relocation and do not require medical intervention. Embolic events are rare but can occur and may involve the coronary arteries, central nervous system, or peripheral arteries.[16] Highly calcific axillary or subclavian arteries can increase the likelihood of embolization.

In addition, advanced age, diabetes mellitus, emergency coronary angiography, prior stroke, renal failure, and congestive heart failure (CHF) have been reported as risk factors for periprocedural stroke.[16] Infections are exceptionally rare in immunocompetent patients, and prophylactic antibiotic therapy is not usually required. Bleeding is usually minor, except when precipitated by vascular complications. In general, the use of anticoagulation during diagnostic angiography should be dosed based on the length of the procedure, weight of the patient, and presence of comorbidities such as kidney impairment to avoid the risk of bleeding when the sheath is removed from the access site. Use of radial access rather than femoral access has significantly reduced the rate of vascular and bleeding complications[17] (see Chapter 41).

Contrast-Induced Acute Kidney Injury. Contrast-induced acute kidney injury (CI-AKI) is defined as an acute deterioration of renal function, defined as an increase in creatinine of 0.5 mg/dL or more or 25% or greater compared with baseline.[18] It generally develops 24 to 72 hours after administration of an intravascular contrast agent in the absence of other identifiable causes (see Classic References, Goldenberg and Matetzky). This complication significantly impacts the duration of hospital stay and related health care costs. CI-AKI also has marked repercussions on short- and long-term morbidity and mortality.[19] In particular, studies in patients with moderate to severe renal dysfunction (estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m^2) undergoing coronary angiography or angioplasty show that the development of CI-AKI in such patients is a negative prognostic factor of clinical outcome both short and long term.[20] The incidence of CI-AKI ranges from 2% in low-risk patients to 12% to 50% in patients with diabetes and known chronic kidney disease (CKD) (see Chapters 31 and 101). The mechanisms of CI-AKI are only partially understood. Certainly, toxic damage caused by the passage of iodine molecules in the interstitial kidney is one of the causes. Another mechanism is related to the redistribution of flow in the kidney tissue secondary to contrast administration. In particular, after injection of contrast media, blood flow increases in the cortex and decreases in the medulla. Unfortunately, the medulla is particularly vulnerable to ischemic injury for the basal hypoxic condition (Po$_2$ = 20 mm Hg) because of high metabolic activity (e.g., sodium transporter channels). Therefore, blood flow reduction in the medulla after contrast injection further decreases oxygen tension, leading to endothelial dysfunction. Other important elements affecting kidney function are the physical and chemical characteristics of the contrast agents, in particular osmolality and viscosity. Contrast agents with a high osmolality and viscosity significantly increase hypoxemia and tubular stress. The downstream effect consists of an increase of free radicals, a reduction of nitric oxide (NO) bioavailability, and an increase in cellular death.[19,20]

The risk of CI-AKI depends largely on baseline renal function. The eGFR is a valid index to describe the level of renal function. Patients with an eGFR value below 60 mL/min are at high risk of CI-AKI. However, eGFR is not able to identify subclinical or latent forms of renal dysfunction. Therefore, a careful assessment of CI-AKI risk is essential, particularly before interventional procedures that may require high contrast medium volume (Fig. 21.2) (see Classic References, Mehran et al.).

TABLE 21.1 Risks Associated with Coronary Angiography

COMPLICATION	RISK (%)
Mortality	0.11
Myocardial infarction	0.05
Cerebrovascular accident	0.07
Arrhythmias	0.38
Vascular complications	0.43
Contrast agent reaction	0.37
Hemodynamic complications	0.26
Perforation of heart chamber	0.03
Other complications	0.28
Total of major complications	1.70

Modified from Scanlon P, et al. ACC/AHA guidelines for coronary angiography. J Am Coll Cardiol 1999;33:1756.

Risk of CI-AKI can be stratified using a risk score model that includes patients' baseline and procedural characteristics.[21]

In high-risk patients, prevention is crucial and consists of pharmacologic and nonpharmacologic measures. Individual risk-benefit ratios should be carefully estimated for each patient, and the utility of an alternative noninvasive diagnostic test should be evaluated. If the use of contrast medium is necessary for diagnostic purposes, the volume used should be minimized, and the use of monomeric low- or iso-osmolality contrast agents is recommended. Hydration plays a pivotal role in reducing the incidence of CI-AKI. Depending on the clinical condition (e.g., CHF), the Contrast-Induced Nephropathy (CIN) Consensus Working Panel recommendations state that an infusion of 1.0 to 1.5 mL/kg/hr of isotonic saline solution, from 3 to 12 hours before until 6 to 24 hours after the procedure, is suitable to minimize the incidence of CIN.[22] Recently, a clinical trial specifically investigated the efficacy and safety of a left ventricular (LV) end-diastolic pressure–guided hydration protocol with good results; thus filling pressure–guided fast hydration may be employed in the catheterization laboratory.[23] Moreover, to obtain effective hydration, devices have been developed that balance the volume of infusion and fluids lost through diuresis.[24] N-Acetylcysteine has been considered for the prevention of CI-AKI for years. In animal models of ischemia-reperfusion injury, the use of N-acetylcysteine significantly limited kidney damage mainly through its antioxidant properties.[25] However, the efficacy of N-acetylcysteine in humans in clinical studies remains unclear, given the high heterogeneity in study protocols and populations.[26] Similarly, some studies report that the use of isotonic sodium bicarbonate is associated with a higher reduction in the incidence of CI-AKI than saline solution. These findings were attributed to a potential reduction in the production of reactive oxygen species in the renal parenchyma. However, recent meta-analyses did not show superiority of sodium bicarbonate over saline solution.[27,28] For this reason, both N-acetylcysteine and sodium bicarbonate have minimal roles in the latest guidelines on prevention (i.e., no benefit) and the routine prevention of CIN in patients undergoing percutaneous coronary angiography and interventions.
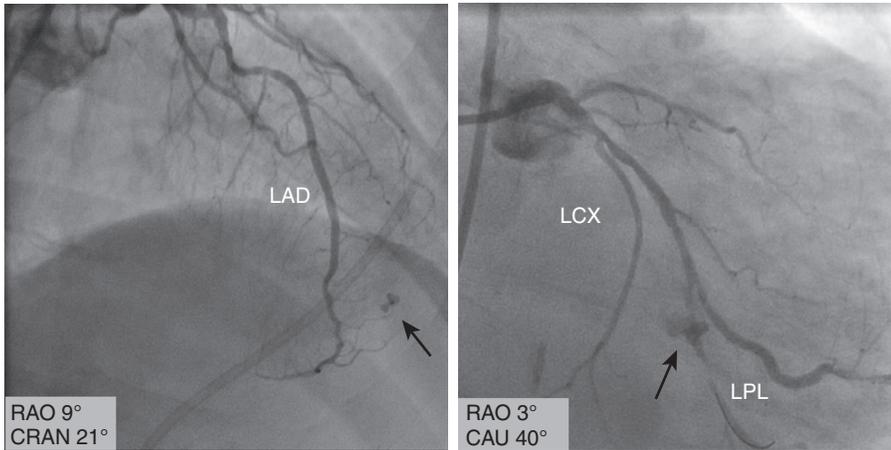
Risks Related to Radiation Exposure

Coronary catheterization may result in radiation-related injury, which although infrequent, may be potentially serious. Radiation injury may be *deterministic* (i.e., dose-dependent), which can present weeks after exposure, or *stochastic,* which is genetically determined and not dose-dependent. Stochastic injury can result in cancer, pregnancy complications, and inheritable diseases. Deterministic injury may result in skin injury, hair loss, and lens injury. However, the
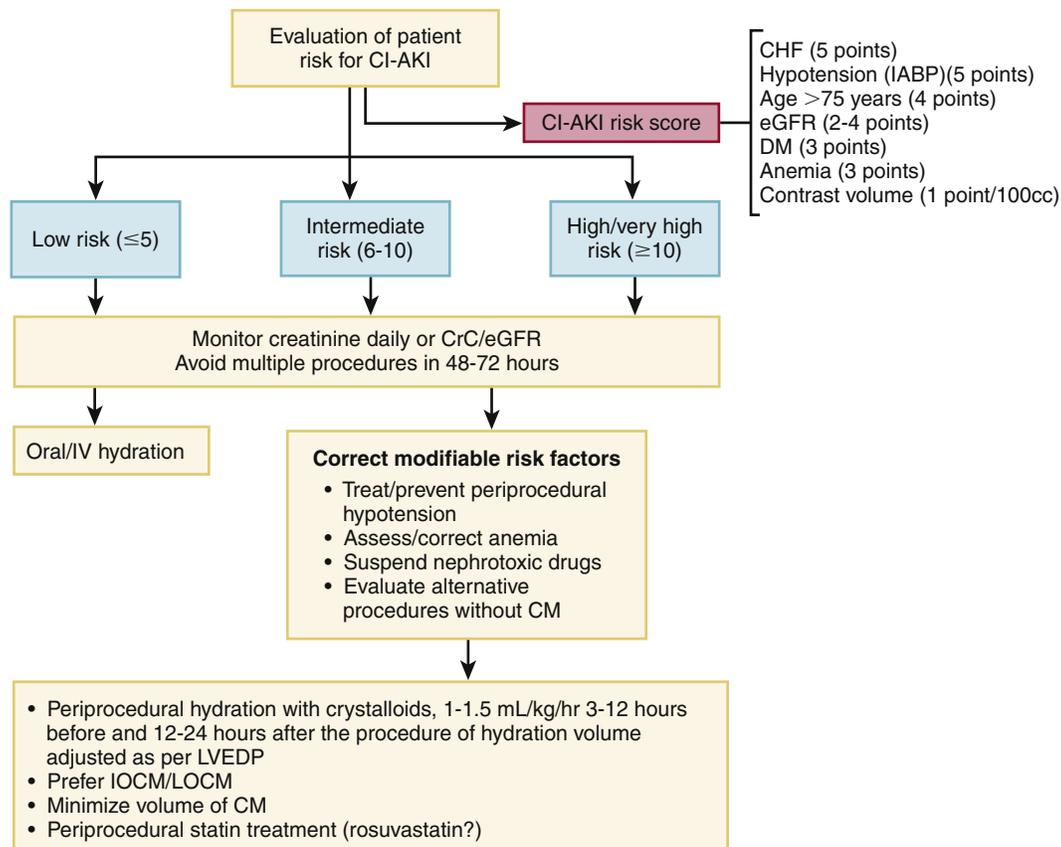

FIGURE 21.1 **Iatrogenic coronary perforations. Left,** Wire perforation of distal left anterior descending artery (*LAD*). **Right,** Perforation of a left posterolateral branch (*LPL*) after rotational atherectomy. *Black arrows* indicate contrast media extravasation. *CAU,* Caudal; *CRAN,* cranial; *LCX,* left circumflex artery; *RAO,* right anterior oblique. (Angiographic images courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)

FIGURE 21.2 Risk score to determine the probability of contrast-induced acute kidney injury. *BID,* Twice daily; *CHF,* congestive heart failure; *CI-AKI,* contrast-induced acute kidney injury; *CM,* contrast media; *CrC,* creatinine clearance; *DM,* diabetes mellitus; *eGFR,* estimated glomerular filtration rate; *IOCM,* iso-osmolar contrast media; *IV,* intravenous; *LOCM,* low-osmolar contrast media; *LVEDP,* left ventricular end-diastolic pressure. See also Chapter 101 and Figure 101.7 for a management strategy for CI-AKI.

most common location of radiation-induced lesions in cardiac catheterization is the skin of the back, and common patterns include erythema, telangiectasia, and plaques.[29] The sensitivity of the skin to radiation exposure is differentiated by site; areas at risk in decreasing order of sensitivity include anterior neck, antecubital and popliteal areas, flexor extremities, chest and abdomen, face, back, extensors, nape of the neck, scalp, palms, and soles.[30] Although uncommon in contemporary practice, early reports from coronary catheterization indicate deep and extensive skin rashes and burns at the site of radiation exposure, some requiring skin grafting.

PCI procedures may result in 10-fold higher radiation exposure compared with diagnostic catheterization (see Chapter 41). An average PCI results in 150 times more exposure than a chest radiograph and five times the annual radiation exposure received as environmental background radiation.[31] Measures used to assess patient dose include dose-area product (DAP; the absorbed dose multiplied by the area irradiated), air kerma (AK; *kinetic energy released per unit mass* of air), and fluoroscopy time (FT), which are routinely measured and documented.[32] All procedures should be performed using the ALARA (as low as reasonably achievable) principle.[33] Exposure can be minimized in several ways: reduced FT and acquisition time, use of multiple angles rather than a single working camera position, reduced fluoroscopy dose, avoidance of high magnification, use of collimator beams and filters, avoidance of high angulation, and reduction in the flat-panel image detector as much as possible. For exposures of absorbed radiation greater than 5 Gy, patients should be advised to watch for areas of erythema; for those greater than 10 Gy, a medical physicist should be consulted to calculate the peak dose in 2 to 4 weeks; greater than 15 Gy is regarded as a hospital risk management event. Similarly, in the event that FT exceeds 60 minutes, physicians must be vigilant for late radiation effects.

From the perspective of occupational radiation exposure, operators should be cognizant of the need to wear protective personal equipment during catheterization procedures, including a lead apron, thyroid drape, lead eyeglasses, and dosimeters.[33] Table height and distance from the x-ray source are important, and radiation risk decreases as the inverse square of distance from the source. Operators should also optimally position lead shields and skirts and should be compliant with use of radiation dosimeters for monitoring exposure to the whole body (chest) and eye. Novel dosimeters providing real-time monitoring and alerts can serve to decrease operator radiation exposure.[34] Monitoring, reporting, and audit of radiation exposure can promote improved awareness and practice in the operator and catheterization laboratory staff. Systematic tracking of FT and radiation exposure is expanding through inclusion in the procedure report as well as in quality assurance databases (national/statewide).

CORONARY ARTERIOGRAPHY TECHNIQUE

Patient Preparation

Patients should receive a comprehensive explanation of the diagnostic angiographic procedure and of the coronary intervention potentially required. Risks of angiography should be discussed in-depth and weighed against both the clinical benefit and the risks related to refusal of the procedure. Patients are required to provide written informed consent before coronary angiography. Women of childbearing age should be questioned on their pregnancy status and advised on the additional risks of radiation exposure for pregnant women. A thorough medical history, including comorbidities, current medications, and allergies, needs to be obtained before the procedure. In the event of an emergency procedure, as with a STEMI presentation, a brief evaluation of the patient history with particular attention to known CKD and known allergies to contrast media should be obtained if possible. In patients with prior coronary artery bypass graft (CABG) procedure, a report stating the type, arterial or venous graft(s), and position of the graft(s) should be attained if available to facilitate the cannulation and subsequent imaging of the grafts. Patients may receive mild sedation with a benzodiazepine before the procedure according to the hospital standard practice.[35] In case of hemodynamic instability or respiratory distress, anesthesiologist support might be necessary. In most patients, however, general anesthesia and deep sedation are unnecessary for coronary angiography. Conscious sedation with short-term agents such as midazolam or fentanyl is most common. Constant monitoring of the patient's ECG, heart rate, blood pressure, respiratory rate, and oxygen saturation is required periprocedurally. A venous access line should be readily available for the infusion of fluids or medications. Local anesthesia with topical anesthetic cream or subcutaneous injection of 1% lidocaine or mepivacaine (0.5 to 1 mL for radial access and 2 to 5 mL for femoral access) should be performed in all patients before puncturing the peripheral artery and introducing the sheath.[36] An adequate local anesthetic will not only make the patient more comfortable but, by reducing the pain during the arterial cannulation, also reduce the risk of peripheral artery spasm.

Access Sites (see Chapter 41)

Possible access sites for coronary angiography are the femoral artery and the radial artery. Although the radial access approach is associated with fewer vascular and bleeding complications, femoral access is still commonly used in the United States. Femoral access allows for larger-diameter equipment that could be necessary in case of PCI. In addition, accessing from the femoral artery usually grants an easier advancement of the catheter to the aortic root due to the lack of tortuosity in the descending aorta. After disinfection and appropriate local anesthesia at the access site, the common femoral artery (CFA) is punctured with a base-metal needle approximately 1 cm below the inguinal line with a 45- to 60-degree angulation.[35] In obese patients, the ideal puncture site is sometimes difficult to determine. The head of the femur, visualized under fluoroscopy, can be used as a landmark (eFig. 21.1). Ultrasound can localize the common femoral artery and its bifurcation (see eFig. 41.4 for the use of ultrasound guidance for femoral access). Puncture should be performed with the needle leveled at half the head of the femur. Multiple punctures should be avoided to reduce the risk of bleeding and vascular damage. A J-tip flexible guide is inserted through the needle into the CFA. The needle is then removed and a sheath advanced around the wire into the artery (eFig. 21.2). Once the sheath is fully advanced in the artery, the dilator and wire are removed, and the sheath is flushed with saline.[37] Usually, a 6 French (6F) sheath (French units: F = 0.33 mm) is used for coronary angiography and coronary interventions. Verification of the correct position of the sheath in the vessel can be ascertained simply by drawing blood from the sheath.

Radial access should always be considered first, before resorting to the femoral approach, especially for diagnostic coronary angiography.[38] The procedure for the sheath insertion is similar to that described for the femoral artery. The modified Allen test is performed by applying pressure on both the ulnar and the radial artery of one wrist to occlude them while the patient keeps the hand elevated with the fist clenched for approximately 30 seconds. Once opened, the hand appears pale. The compression on the ulnar artery is then removed while pressure is maintained on the radial artery. If the ulnar artery supply to the hand is adequate, the color quickly returns to the hand and the test is normal. Conversely, if color does not return, the ulnar artery supply is insufficient, meaning that the radial artery supports the entire circulation of the hand. In this case the radial artery should not be punctured, because this may compromise the blood flow to the hand. This rule may be bypassed if an oximeter is placed in the thumb during radial artery occlusion, and resurgence of pulsation and oxygenation is documented after its initial disappearance ("Barbeau method").

When both radial arteries are acceptable access sites, the patient's right, closer to the operator, is preferred for technical reasons. However, the left subclavian artery may be less tortuous than the innominate artery. The ideal puncture site is 1 to 2 cm proximal to the radial styloid with the wrist slightly hyperextended. After local anesthesia, usually 0.5 to 1 mL of 1% lidocaine, the needle is advanced angled 30 to 45 degrees to the skin until a flashback of blood is visualized. A straight-tip wire is gently inserted through the needle. After removing the needle, a 5F or 6F sheath is inserted in the radial artery over the wire. A small incision 1 mm long can be made on the skin to facilitate advancement of the sheath. Because the radial artery is extremely vasoactive, the risk of spasm is high, especially in women; therefore, as soon as access is obtained, an intra-arterial spasmolytic agent such as nitroglycerin (100 to 200 µg) or verapamil (2.5 mg) diluted into 10 mL of saline should be administered.[35] A hydrophilic-coated sheath can further reduce the likelihood of spasm and regional pain. To prevent thromboembolic
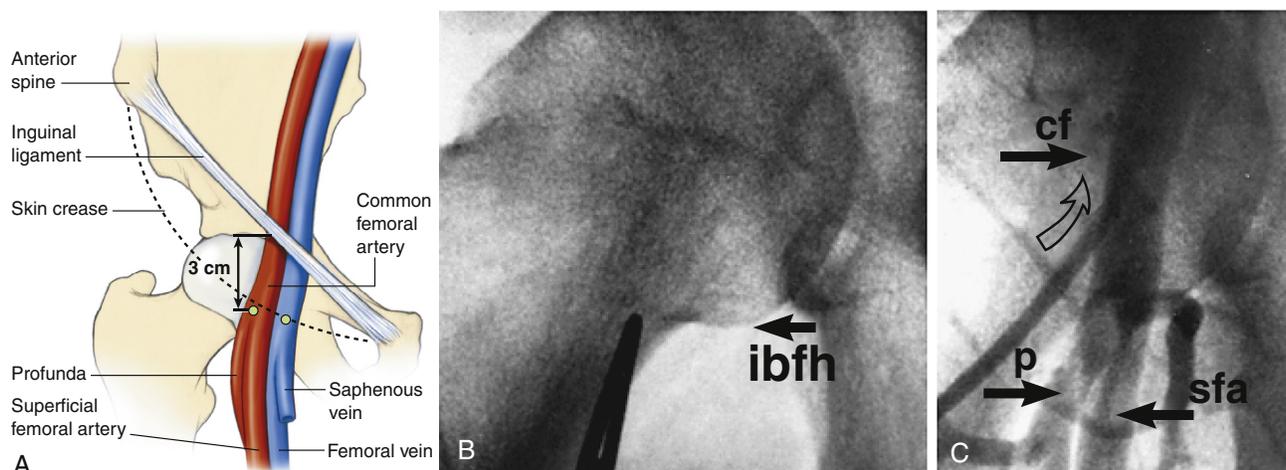
EFIGURE 21.1 (See eFig. 41.4 for the use of ultrasound guidance for femoral access.) **A,** Diagram of femoral artery and vein anatomy. The arterial skin nick should be placed approximately 3 cm below the inguinal ligament and directly over the femoral arterial pulsation; the venous skin nick should be placed at the same or lower level but approximately one fingerbreadth more medially. **B,** Localization of the skin nick by fluoroscopy and use of a hemostat, the top of which should point to the inferior border of the femoral head (*ibfh*). **C,** Catheter insertion (*open arrow*) into the common femoral artery (*cf*), above the bifurcation into the superficial femoral artery (*sfa*) and profunda (*p*) branches. (From Baim DS, Grossman W. Percutaneous approach, including transseptal and apical puncture. In Baim DS, Grossman W, editors. Cardiac Catheterization, Angiography, and Intervention. 7th ed. Philadelphia: Lea & Febiger; 2006,p 81.)
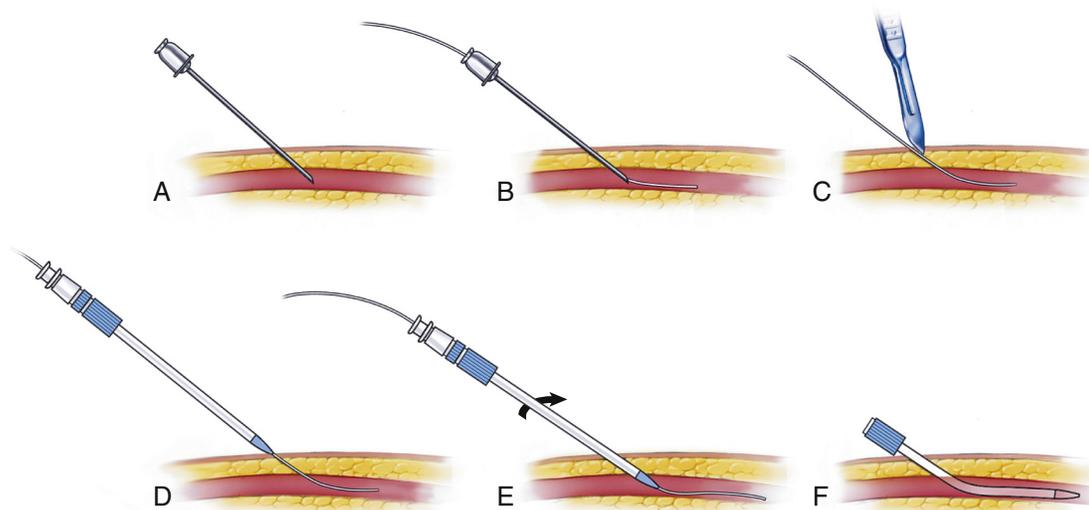
EFIGURE 21.2 Modified Seldinger technique for percutaneous introduction of the catheter sheath. **A,** Vessel punctured by the needle. **B,** Flexible guidewire placed into the vessel through the needle. **C,** Needle removed, guidewire left in place, and hole in skin around wire enlarged with a scalpel. **D,** Sheath and dilator placed over guidewire. **E,** Sheath and dilator advanced over guidewire and into the vessel. **F,** Dilator and guidewire removed while sheath remains in the vessel. (From Hill JA, Lambert CR, Vlietstra RE, Pepine CJ. Review of general catheterization techniques. In Pepine CJ, Hill JA, Lambert CR, editors. Diagnostic and Therapeutic Cardiac Catheterization. 3rd ed. Baltimore: Williams & Wilkins; 1998, p 107.)

events and radial artery occlusion, weight-adjusted unfractionated heparin (UFH), 40 to 70 U/kg up to 5000 U, is administered either intravenously or intra-arterially.[39]

Radial access appears associated with fewer periprocedural events and should be preferred whenever possible. It should be noted, however, that the axillary-subclavian axis can be tortuous and calcific, particularly in elderly patients, and it can therefore be technically difficult to advance the catheter to the aortic root. Brachial access is very uncommon, but unlike radial access, it avoids the small-caliber arteries in the forearm and therefore may be required in the event that radial access is not available or fails. Brachial access can be obtained with a percutaneous or cutdown approach. On the other hand, there is no alternative blood supply to the forearm in case of closure.

Basic Technique

Coronary angiography is an invasive procedure based on the intravascular advancement of angiographic guidewires and catheters from a percutaneous access using the Seldinger technique. After a valved sheath is inserted into the access site artery (see Access Sites), a flexible metallic J-tipped guidewire is inserted through the sheath and advanced slowly under fluoroscopic imaging through the arterial axis until the aortic root is reached. A fluid-filled catheter is then advanced over the angiographic guidewire, while the wire itself is maintained in place. Once the catheter is in the aortic root, the wire is fully extracted from the sheath, and the catheter is flushed and connected to the contrast media injection apparatus. Under fluoroscopic imaging, and with the help of small injections of contrast, the coronary ostium is engaged with the tip of the catheter.[40] At this point, the x-ray tube is positioned appropriately (see Projection), and angiographic images are obtained while injecting contrast directly into the cannulated coronary artery.

Catheters for Diagnostic Procedures

There are several types of diagnostic catheters, characterized by differing lengths, diameters, and shapes. In general, catheters are composed of an external layer, which is not thrombogenic or lubricious, and by a lubricious inner layer. These two layers include a fine metallic core required to confer stability, improve maneuverability, and reduce the risks of kinking. Lengthwise, the catheter is divided into three parts: hub, body, and tip. Through a female Luer-Lok, the *hub* connects the catheter to the contrast injection system and facilitates the catheter grip and rotation with winged tips. The *body*, mostly strong and rigid, transmits to the tip the movements impressed on the hub by the operator. The *tip* can be divided, starting from the distal end, into three curves: primary, secondary, and tertiary, which allows the best possible fit to the aortic root curvature. The size of the catheter is another important characteristic. Compared with guiding catheters used for PCI (see Chapter 41), diagnostic catheters have a thicker wall, which considerably reduces their internal lumen. The 5F catheter allows an optimal balancing between contrast flow and satisfactory catheter manipulation, particularly for the radial approach. Catheter length can vary from 80 to 110 cm (32 to 44 inches), depending on the anatomic characteristics and the access site (radial, brachial, or femoral). However, the standard length for adult left-heart catheterization by both the radial and the femoral approach is 100 cm (40 inches), while 80 cm is suitable for brachial access.

Among the diagnostic catheters, the most commonly used are the Judkins and the Amplatz catheters. *Judkins catheters* can be used both for the femoral and for the right/left radial approach. A preformed left Judkins (JL) presents a primary curve of 90 degrees and a secondary curve of 180 degrees, whereas the right Judkins (JR) presents a primary curve of 90 degrees and secondary curve of 30 degrees (Fig. 21.3). Since the JL is preformed, after removing the angiographic guide, it automatically engages the ostium of the left coronary artery (LCA). The JR, in contrast, once positioned in the right coronary sinus, requires a clockwise rotation to engage the ostium of the RCA from any vascular approach. In both JL and JR catheters, the distance between the primary and secondary curves (termed *arm*) is variable; for example, JL4 has a 4.2-cm length arm, and JL5 and JL6 have 5.2- and 6.2-cm-long
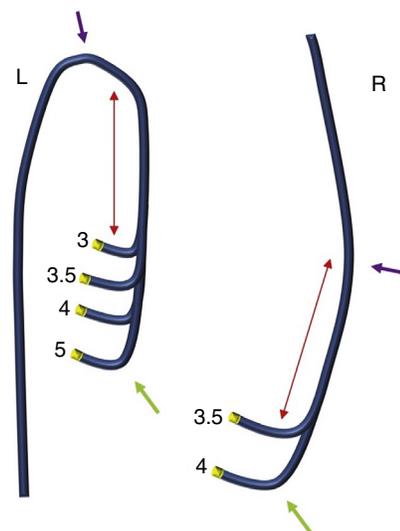

FIGURE 21.3 Judkins catheters. *Left* (L), for left coronary artery. *Right* (R), for right coronary artery. *Green arrows* indicate the primary curve. *Purple arrows* show the secondary curve. *Red arrows* indicate the distance between the primary and the secondary curve. To determine the correct catheter's tip, the operator should evaluate the approach (femoral or radial), the patient's height, and diameter of the aortic root. In particular, it would be helpful to add 0.5 cm for a femoral approach and for a dilated or horizontal aorta.

arms, respectively (see Fig. 21.3). Catheter selection depends on the approach (radial or femoral), the height of the patient, and the aortic diameter and curvature. For example, when using a femoral access, the JL4 is the most adaptable catheter for the LCA, whereas for the radial access, the JL3.5 catheter may be more suitable. Moreover, the presence of a dilated aortic root or the anatomy of particularly tall patients (>180 cm [72 inches]) may increase the length required between the primary and secondary curves and might require the selection of a catheter with a longer arm. In addition to their conventional use, JR catheters may be used for saphenous vein graft (SVG) and left internal mammary artery graft study through femoral and left radial approach.

Amplatz catheters for the LCA (AL) and RCA (AR) represent a valid alternative to Judkins catheters (Fig. 21.4). The available lengths and sizes are the same as for the Judkins catheters, but the tip morphology of the left Amplatz (AL) catheter differs, allowing for easier coronary engagement in specific settings, such as short left main ostium, separate ostium of circumflex (Cx)–left anterior descending (LAD) artery branches, and RCA with anterior-high origin. Conversely, the right Amplatz (AR) catheter allows engagement of RCAs with inferior orientation. Amplatz catheters may also be used with confidence for the study of SVGs. *Multipurpose* (MP) *catheters* present a single bend (MPA 1 and 2 have a 45- to 60-degree primary curve, while MPB 1 and 2 have approximately an 80-degree primary curve) and may be used for the cannulation of coronary ostia that are difficult to reach with other catheters, as well as for engagement of SVGs. *Internal mammary artery* (IMA) *catheters* have a high angulated primary curve tip (80 degrees) to facilitate the engagement of the IMA through either the femoral or the radial approach. These catheters can also be used to engage the upward-pointing RCA (see Fig. 21.4). It should be specified that the catheters just described are the ones most frequently used to perform diagnostic coronary angiography. Additional catheter types are available, although less frequently used, in case of specific coronary anatomic variables.

Selective Coronary Artery Cannulation
Left Coronary Artery. The JL4.0 coronary catheter is used most often to engage the LCA (Fig. 21.5). The catheter is advanced over the guidewire until it reaches the aortic root. There, the catheter is rotated clockwise to direct it toward the left sinus of Valsalva. Once in position, the wire is removed, and the catheter regains its primary bent and should engage the ostium of the LCA. When the ascending aorta is dilated or the aortic arch is unfolded, advancement of the JL4.0 or JL5.0 might be necessary. If the tip of the JL catheter advances beyond the ostium of the LCA without engaging the ostium, the catheter can be advanced
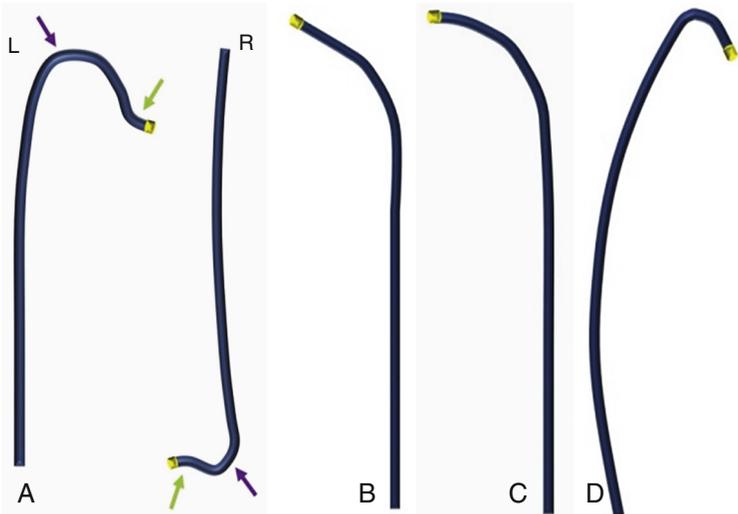
FIGURE 21.4 A, Amplatz catheters, left (L), for left coronary artery; right (R), for right coronary artery. *Green arrows* indicate the primary curve. *Purple arrows* show the secondary curve. **B,** Multipurpose A catheter. **C,** Multipurpose B catheter. **D,** Internal mammary artery catheter.
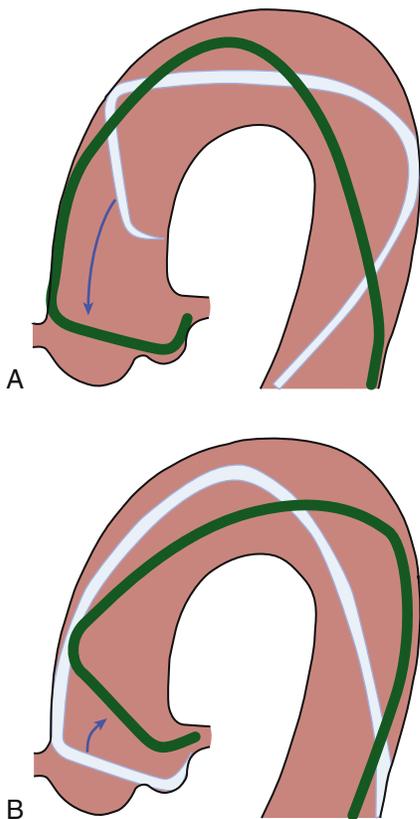

FIGURE 21.5 A, Push-pull technique for catheterization of the left coronary artery (LCA) with the Judkins left catheter. In the LAO view, the coronary catheter is positioned in the ascending aorta over a guidewire, and the guidewire is removed. The catheter is advanced so that the tip enters the left sinus of Valsalva. **B,** If the catheter does not selectively engage the ostium of the LCA, further slow advancement into the left sinus of Valsalva creates a temporary acute angle at the catheter. Prompt withdrawal of the catheter allows easy entry into the artery. (From Popma JJ, et al. Coronary angiography and intracoronary imaging. In Mann D, et al, editors: Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 10th ed. Philadelphia: Elsevier; 2014.)

farther until the tip enters the left sinus and the catheter body assumes an acute angle. At that point, prompt withdrawal of the catheter should allow the tip to "pop" into the ostium of the LCA.

Right Coronary Artery. The RCA is cannulated in the left anterior oblique (LAO) position (see later, Angiographic Projections). Once the JR or modified Amplatz catheter reaches the aortic root, it must be rotated clockwise to engage the vessel. The height of the catheter during the rotation may need to be adjusted by gently withdrawing the catheter to engage the ostium.

In patients with prior CABG, cannulation might be challenging because the locations of graft ostia are more variable, even when surgical clips or ostia markers are used. Whenever possible, the number, type, and course of the bypass grafts should be obtained before the procedure.

Saphenous Vein Grafts

SVGs from the aorta to the distal RCA or posterior descending artery (PDA) originate from the right anterolateral aspect of the aorta approximately 5 cm (2 inches) superior to the sinotubular ridge. SVGs to the LAD artery (or diagonal branches) originate from the anterior portion of the aorta approximately 7 cm superior to the sinotubular ridge (Fig. 21.6). SVGs to the obtuse marginal branches arise from the left anterolateral aspect of the aorta 9 to 10 cm superior to the sinotubular ridge. In most patients, all SVGs can be engaged with a single catheter, such as a JR4.0 or a modified Amplatz right 1 or 2.

Viewed in the LAO projection, the catheter should be rotated anteriorly from the leftward position as it is rotated in a clockwise direction. This movement should be repeated with the catheter at various heights in the ascending aorta, 5 to 10 cm above the sinotubular ridge, and with various degrees of rotation. Small test injections of contrast media can be used to verify that the catheter is in the SVG. If the graft is occluded, usually it is possible to visualize a "stump" during contrast injection. The surgical clips can be used to verify that all the grafts have been visualized. If one or more SVGs cannot be visualized, it can be useful to perform an ascending aortogram (preferably in biplane) to visualize all SVGs and their course to the coronary arteries. When visualizing an SVG, it is important to evaluate the ostium and the anastomotic site for irregularities or stenosis. It is also important to evaluate the flow distal to the anastomosis. *Sequential grafts* are those that supply two different epicardial branches in a side-to-side fashion (for the more proximal epicardial artery) and terminate in an end-to-side anastomosis (for the more distal epicardial artery). A Y graft is characterized by a proximal anastomosis in an end-to-side fashion to another saphenous vein or arterial graft, with two distal end-to-side anastomoses to the two epicardial grafts from these two grafts. It should be noted that with severe calcifications of the ascending aorta, the SVG could depart from the descending aorta to reach lateral wall branches.

Internal Mammary Artery Grafts. The left IMA (LIMA) can be cannulated with a specially designed J-tip IMA catheter. The catheter is advanced into the aortic arch distal to the origin of the left subclavian artery, then rotated counterclockwise and gently withdrawn with the tip pointing in a cranial direction, allowing entry into the left subclavian artery. The right anterior oblique (RAO) or anteroposterior (AP) projections can be used to visualize the IMA (Fig. 21.7 and eFig. 21.3). For the right IMA (RIMA), first the innominate artery is entered with the guidewire in the LAO projection, then the IMA catheter is advanced to a point distal to the expected origin of the RIMA. The catheter is withdrawn slowly in the LAO view and rotated to cannulate the RIMA. Small injections of contrast are used to assess the position and the cannulation of the IMA. If the IMA cannot be selectively engaged and arteriography of the subclavian artery can be used, this usually allows for the opacification of all or most of the IMA, although weak (eFig. 21.4). The IMA can also be visualized with semiselective contrast injection; to avoid injury of the ostium, the catheter can simply be oriented toward the IMA without cannulating it. The correct orientation can be obtained by advancing a guidewire in the IMA to stabilize the position of the catheter during injection.

Radial Grafts

Radial artery (RA) grafts represent the most popular arterial grafts after the LIMA and RIMA. Similar to SVGs, radial grafts require a double anastomosis, one on the aorta and one on the coronary vessel. Because of potential early spasm, RA grafts were abandoned in the 1970s and 1980s. In the 1990s, however, this procedure was rediscovered, and with specific surgical techniques and pharmacologic prophylaxis, it has safely been used with good short- and long-term results (eFig. 21.5).

Gastroepiploic Artery. Rarely the right gastroepiploic artery (GEA) can be used for CABGs. To cannulate the GEA, first a special catheter called the "cobra" is inserted into the common hepatic artery. Next, a hydrophilic-coated guidewire is advanced to the gastroduodenal artery and then to the right GEA. The cobra catheter is then exchanged for an MP or JR catheter, which is used for the selective cannulation of the GEA (Fig. 21.8).
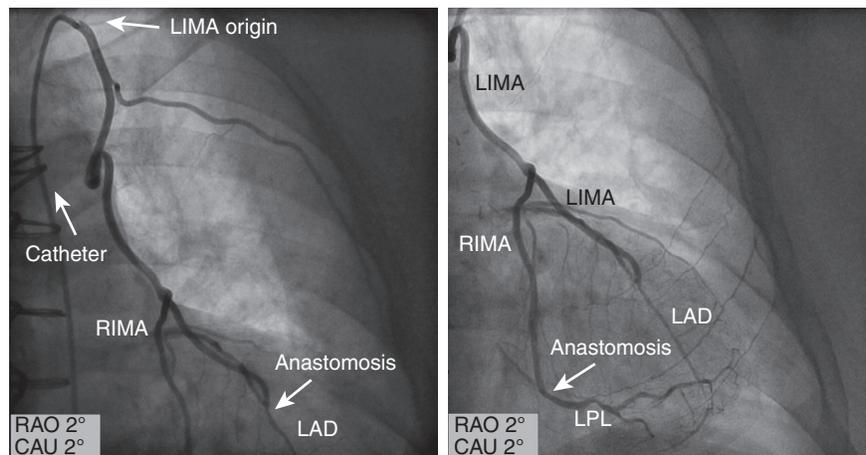
EFIGURE 21.3 Y graft of the left internal mammary artery (*LIMA*) to the left anterior descending artery (*LAD*) and the free right internal mammary artery graft (*RIMA*) to the left posterolateral branch (*LPL*). *CAU,* Caudal; *RAO,* right anterior oblique. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
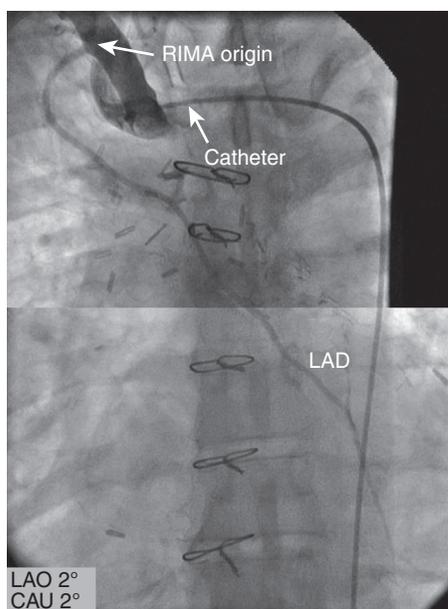

EFIGURE 21.4 Nonselective cannulation of the right internal mammary artery (*RIMA*) anastomosed to the left anterior descending artery (*LAD*). *CAU,* Caudal; *LAO,* left anterior oblique. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
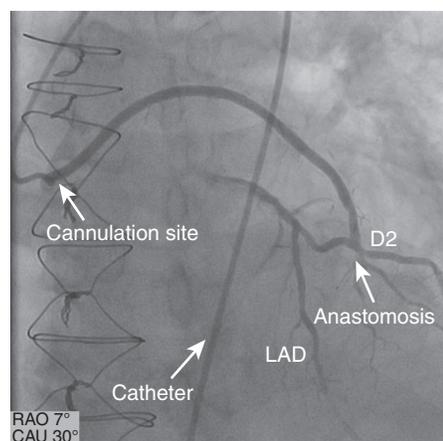

EFIGURE 21.5 Free radial graft to large diagonal branch. *CAU,* Caudal; *D2,* second diagonal branch; *LAD,* left anterior descending artery; *RAO,* right anterior oblique. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
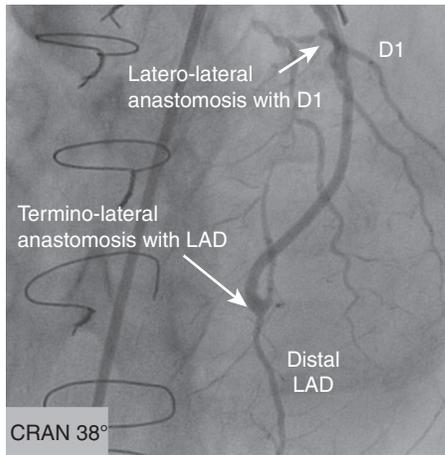
FIGURE 21.6 Sequential saphenous vein graft to the first diagonal branch (*D1*) and left anterior descending artery (*LAD*) with latero-lateral anastomosis to D1 and termino-lateral anastomosis to the distal LAD. *CRAN,* Cranial. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York.)
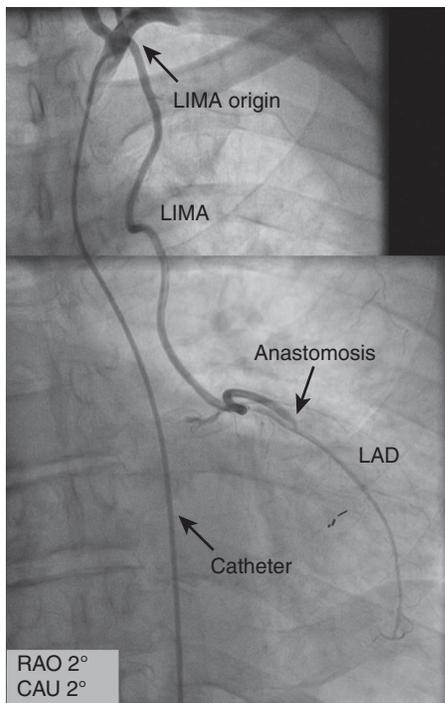

FIGURE 21.7 Arterial graft of left internal mammary artery (*LIMA*) to the left anterior descending artery (*LAD*). RAO, Right anterior oblique; CAU, caudal. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)

Ventriculography
Left Ventriculography

Left ventriculography provides important information about volumes, global and segmental function, and anatomic abnormalities such as ventricular septal defect, ventricular thrombus, and valvular dysfunction. However, it is not routinely performed in the current era given the continuous evolution of noninvasive technologies such as echocardiography, CT, or MRI and concerns for complications and contrast volume. Incomplete ventricular opacification with hand-injection of up to 10 cc of contrast through a JR catheter has been become popular as a method to verify an already known normal LV function based on earlier noninvasive studies.

Since the physiologic high pressure developed during each cycle in the left ventricle, the operator should inject a rather high volume of contrast agent in a rather short time for an effective opacification. Accordingly, 6F to 8F catheters with multiple lateral holes are the best option since the single end-hole catheter could be unstable during the
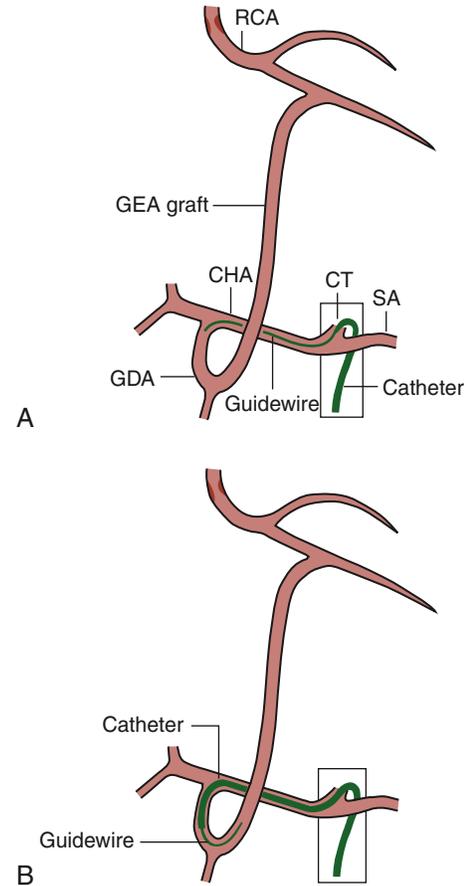

FIGURE 21.8 Catheterization of right gastroepiploic artery (*GEA*) graft. A, The celiac trunk (*CT*) is selectively engaged with a cobra catheter, and a guidewire is gently advanced to the gastroduodenal artery (*GDA*) and the GEA. **B,** The catheter is advanced over the guidewire for selective arteriography of the GEA graft. *CHA,* Common hepatic artery; *SA,* splenic artery. (From Popma JJ, et al. Coronary angiography and intracoronary imaging. In Mann D et al, editors. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 10th ed. Philadelphia: Elsevier; 2014.)

high-pressure injection, thus increasing the risk of arrhythmias or inadequate ventricle opacification. The pigtail catheter, including multiple side holes and a "pigtail-like" end-configuration, is frequently used for several reasons. First, usually, the pigtail catheter easily crosses the aortic valve, either directly or by prolapsing across the valve leaflets. Second, the loop shape keeps the end-hole of the catheter away from the cardiac wall, thus decreasing the risk of endocardium trauma, intramyocardial ventricular staining, and arrhythmias. Third, the simultaneous delivery of the contrast agent along the numerous side holes allows a correct opacification of the left ventricle and a further stabilization of the catheter. The pigtail catheter is available with a preformed straight shaft or with a 145- to 155-degree angled shaft, allowing a central position also for that ventricle having an accentuate angle between the aortic root and long axis of the chamber. Crossing the aortic valve requires careful movements, despite the safety profile of the pigtail catheter, and watchful rhythm observation since VT occurrence may require immediate wire/catheter manipulations and even retraction (eFig. 21.6). A common approach is advancing the pigtail close to the aortic valve with a 0.035-inch J-tip guidewire up to the end of the straight catheter section and rotate the catheter to achieve a "6" shape on a RAO projection. Then the catheter should be pushed against the aortic plane to obtain a U-shape curve, and following a deep inspiration or under pullback and clockwise rotation, the tip of the catheter usually falls into the left ventricle. An alternative to the pigtail could be the Halo-type catheters, constituted by a perpendicular helix, inwardly and upwardly directed, and a single end-hole, thus decreasing the risk of ectopic beats and allowing a superior pressure measurement when necessary (e.g., hypertrophic cardiomyopathy). Other catheters can be used to better suit the anatomic variability and facilitate the crossing through the aortic valve. The Judkins catheter for the RCA may be more appropriate for the small aortic roots, whereas
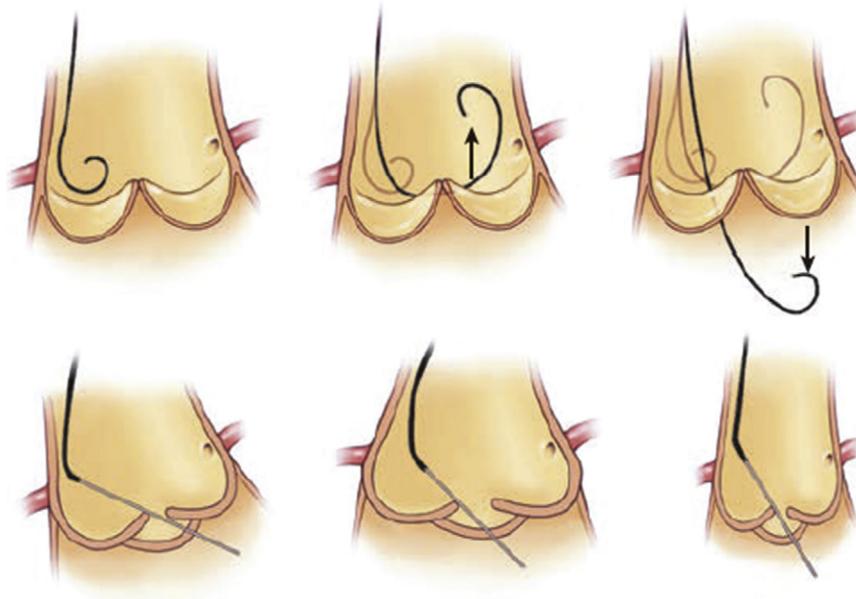
EFIGURE 21.6 Technique for retrograde crossing an aortic valve. **Left,** Normal aortic root. **Middle,** Large aortic root. **Right,** Small aortic root. **Top row,** Crossing of normal aortic valve (pigtail catheter and angled wire used). **Bottom row,** Crossing of stenotic aortic valve with straight wire and Amplatz Right-2, Amplatz Left 1 or 2, and Judkins right (or Amplatz Right-1) catheters from left to right. (From Baim DS, Grossman W. Percutaneous approach including transseptal and apical puncture. In Baim DS, Grossman W, editors: Cardiac Catheterization, Angiography, and Intervention. 6th ed. Philadelphia: Lea & Febiger; 2006, p 93.)

TABLE 21.2 Settings, Suggested Projection and Structure Observed in Patients Undergoing Left or Right Ventriculography

	SETTINGS	SUGGESTED PROJECTION	STRUCTURES OBSERVED
Left Ventricle	Flow rate 10-15 mL/sec Total contrast volume 30-45 mL Pressure limit 750-1200 psi 0- to 0.5-second rise	30-degree right anterior oblique and 0-degree cranial angulation	• Global ventricular function • Segmental wall motion (anterobasal, anterolateral, apical, diaphragmatic, and inferobasal) • Mitral valve
		60-degree left anterior oblique and 25-degree cranial angulation	• Segmental wall motion (lateral, posterolateral, apical septal, and basal septal) • Interventricular septum integrity • Aortic valve
Right Ventricle	Flow rate 8-10 mL/sec Total contrast volume 20-30 mL Pressure limit 750 psi	30-degree right anterior oblique and 0-degree cranial angulation	• Global ventricular function • Segmental wall motion (right ventricle dysplasia)
		Anteroposterior view	• Congenital heart disease evaluation

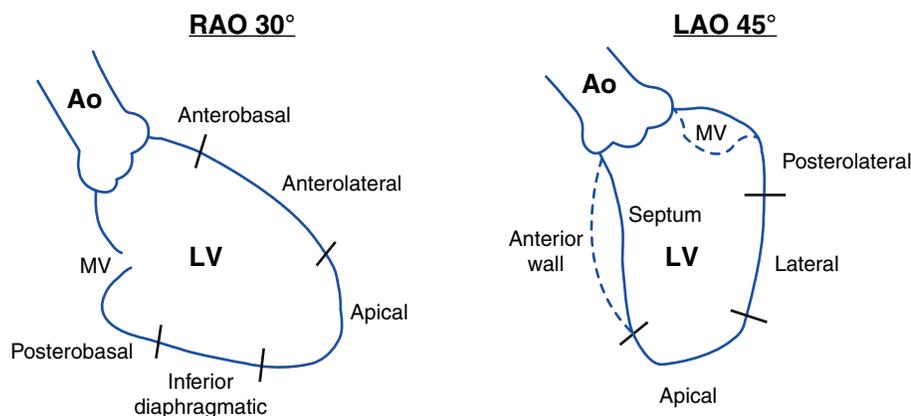*PSI,* Pounds per square inch.

FIGURE 21.9 **Projections for left ventriculography.** *Ao,* Aorta; *LAO,* left anterior oblique; *LV,* left ventricle; *MV,* mitral valve; *RAO,* right anterior oblique.

the AL or multipurpose catheters might be used to cross bicuspid valves or stenotic aortas. In severe aortic valve stenosis, straight rather than J-tipped guidewires are used, including the straight Glidewire, which may afford faster crossing but also requires greater care to avoid microperforations.[41] Of note, regardless of the type of catheter used to cross the valve, it may need to be exchanged over a 0.035-inch J-tip guidewire with a Pigtail catheter for the following indications: (1) the complete ventriculography via power-injector, (2) detailed hemodynamic assessment of stenosis (dual-lumen pigtail) particularly with excessive femoral pressure amplification of any significant aortoiliac arterial stenosis, (3) if an end-hole catheter is specifically required (e.g., Halo or multipurpose) for slow pull-back hemodynamic measurements, and (4) for advancement of the stiff pigtail-end guidewires to the ventricular apex, as necessary for aortic valve interventions. For optimal ventriculography technique, the catheter should be in midcavity and the RAO projection selected. Table 21.2 and Fig. 21.9 summarize settings and other structures that can be evaluated. Both qualitative and quantitative assessment requires at least two free extra-beats periods since the evaluation of ectopic or post ectopic beats will over- or underestimate the ventricular function and regurgitation entities as well.

Complications related to left ventriculography are as follows: (1) cardiac arrhythmias (both supraventricular and ventricular) often requiring dynamic repositioning, (2) microembolization, (3) intramyocardial contrast staining, (4) contrast associated issues, including nephropathy or high volume load in end-stage heart failure or dialysis patients.

The wall motion pattern is graded from normokinesis, hypokinesis, akinesis, and dyskinesis. Anterobasal, anterolateral, apical, diaphragmatic, and inferobasal segments can be evaluated in RAO projection; lateral, posterolateral, apical septal, and basal septal are viewed in LAO projection. Ejection fraction can be determined qualitatively with a visual estimation or quantitatively assessing end-diastolic and end-systolic contours (centerline method).

The degree of mitral regurgitation can be scored by Sellers classification (see Classic References, Sellers et al.).

Trivial (+1): A minimal jet with a brief and incomplete atrial opacification during systole, rapidly clearing during each cycle without atrial enlargement.

Mild (+2): A moderate opacification of the left atrium with each cycle, clearing with the subsequent beats. The atrium is less opacified than the left ventricle, usually with preserved dimensions.

Moderate (+3): A complete opacification of the left atrium, equal intensity to ventricular opacification. There is delayed atrial clearing over several cycles and a significant enlargement of the left atrium.

Severe (+4): A complete and immediate opacification of the left atrium, even denser than the ventricle. The left atrium is typically severely enlarged and opacification of pulmonary veins may be visible.

Aortography

Dos Santos first described aortography in 1929 by a direct abdominal aorta puncture. Ascending aortography, as practiced by Sones, is indicated to assess the following: (1) aortic valve regurgitation, (2) dimensions, (3) aortic coarctation, (4) sub- or supravalve aortic stenosis, (5) shunts, and (6) identification of bypass grafts.

The standard approach of LAO 30-degree projection allows the best view of ascending aorta, aortic arch, the innominate artery, and the left subclavian and carotid arteries; RAO is preferred for aortic valve evaluation and related interventions. The typical set up for aortic injection is flow rate 15 to 20 mL/sec, volume of the contrast agent 30 to 45 mL, rate of rising 0 to 0.5 s, and pressure limit 750 to 1000 psi.

The less traumatic side-hole pigtail catheter should be preferred for complete opacification. After tight connection of the catheter to the power injector with high-pressure tubing, the operator should ensure any air bubbles are removed from the injector system. The loop of the pigtail catheter must *not* be in Valsalva sinus and the operator should avoid iatrogenic regurgitation minimizing catheter-valve contact.

Aortic regurgitation may be trivial, mild, moderate, or severe depending on ventricular opacification after the third cycle following contrast injection.

Trivial or grade 1 (1+): minimal regurgitation jet with a brief and incomplete left ventricle opacification during diastole and fast clearance of the contrast agent.

Mild or grade 2 (+2): regurgitation jet causing a moderate ventricular opacification, which less dense than in the ascending aorta and is cleared within one to two cardiac cycles.

Moderate or grade 3 (+3): regurgitation jet causing complete ventricular opacification within two cycles, as dense as in the ascending aorta and with delayed clearing from the ventricle over several cycles, often associated with dilated left ventricle.

Severe or grade 4 (+4): complete and immediate opacification of the left ventricle, denser than observed in the ascending aorta.

Right Ventriculography

The optimal position is the midcavity that allows only few ventricular premature beats. Right ventriculography is indicated to assess right-to-left ventricular shunts, right ventricle dimensions or dysplasia, abnormalities of the RV outflow tract (RVOT), and pulmonary stenosis or global and segmental ventricular function. However, it is not valuable for assessing tricuspid regurgitation due to the presence of the catheter across that valve. A multiple-hole pigtail might be used. The 7F Berman balloon-directed multiple-sidehole catheter is frequently used. The septum and RVOT can be evaluated using an AP cranial or AP lateral projections. Typically, 20 to 30 mL of contrast material is injected at 8 to 10 mL/sec (but if the ventricle is severely dilated, the volume could be increased up to 40 to 50 mL at 12 to 18 mL/sec).

Selection of Contrast Media

Since the introduction of intravascular contrast agents (ICAs) in the 1950s, clinical practice has become increasingly dependent on their use, particularly as the use of computed tomography (CT) and cardiac catheterization procedures has expanded markedly in recent years. All currently used ICAs are classified on the basis of their physical and chemical structure, specifically osmolality, iodine content, ionization in solution, and viscosity (eTable 21.3). The most useful classification in clinical practice divides available ICAs into high-osmolar contrast agents (HOCAs), low-osmolar contrast agents (LOCAs), and iso-osmolar contrast agents (IOCAs). The HOCAs have an osmolality four to five times higher than blood (300 Osm). LOCAs have an osmolality twice as high as blood. The latest-generation IOCAs have the same osmolality as blood. Ionic high-osmolality ICAs were the first class of ICA used. However, the high-osmolality and calcium-chelating proprieties often resulted in heart rhythm disorders (sinus bradycardia, atrioventricular blocks, QRS prolongation, long QT, ST-T, giant T-wave inversion, and extremely rarely, VT and VF) and altered LV contractility. Therefore, in recent decades, new-generation ICAs have been developed with low osmolality and neutral chemical characteristics that allow a significant reduction of adverse events.[42] In large cohort studies, the incidence of all types of adverse reactions to contrast was approximately 12% with a high-osmolality agent, compared with only 3% with a low-osmolality ICA (see Classic References, Katayama et al.). For this reason, LOCAs and IOCAs are now considered the safest ICAs to use for vascular diagnostic procedures.

Automatic and Manual Injection of Contrast Media

Manual contrast injection with a manifold permits a constant modulation of the pressure of the injection and allows the operator to feel the resistance of the vessel to the injection. However, careful evaluation of the line should be performed before the injection to ensure the absence of air bubbles in the system. Manual injection was the only technique used to deliver contrast media until 10 years ago, when power injections were introduced. These automatic systems can detect air bubbles in the tubes and stop the injection accordingly. The maximum volume of contrast delivered, as well as the maximum pressure, can be preset to reduce the risk of iatrogenic artery dissection. Current systems also allow for operator touch-sensitive, variable-volume, and pressure injections. For the RCA, 4 to 6 mL/sec is usually injected to optimally visualize the entire vessel, with a maximal pressure of 450 psi. For the LCA, a volume of 6 to 8 mL/sec is injected at a pressure of 450 to 600 psi.

The use of automatic injection systems is now preferred in most catheterization laboratories in Europe, whereas in the United States, 50% of sites still use manual injection. Automatic injections can significantly reduce the volume of contrast used for coronary procedures, and some studies report that they might reduce the risk of CI-AKI.[43,44]

Adverse Reactions to Contrast Media and Prophylactic Therapy

Adverse reactions after injection of ICA may be acute or delayed and can further be classified as allergic or allergic-like (physiologic). *Allergic reactions* can present with a variety of clinical symptoms, ranging from itching to skin rash, local edema, asthma, and full-blown anaphylactoid reaction. The pathophysiologic mechanisms hinge on the activation of different components of the immune system. *Allergic-like reactions* have a similar clinical presentation as the classic allergic response but are independent of immune system activation. Allergic-like reactions revolve around a physiologic response to contrast (e.g., nausea, vomiting, vasovagal reaction, hypertension, flushing).[45] The incidence of acute adverse reactions is related to the chemical and physical characteristics of ICAs (eTable 21.4). In particular, as previously described, high-osmolar ICAs have approximately a 12% rate of acute adverse events, whereas that of low- or iso-osmolality ICAs is significantly lower (see Classic References, Katayama et al.). In a cohort of 545 patients undergoing CT, the use of nonionic ICAs led to an allergic reaction rate of only 0.6%, of which only 23% were graded moderate to severe.[46]

Temporally, acute reactions occur within seconds or minutes of contact with the ICA. Delayed reactions, on the other hand, may develop from 30 minutes up to 1 week after injection of ICA and usually present with cutaneous manifestations (eTable 21.5). A prospective study of 539 patients by Loh and colleagues demonstrated that the percentage of delayed adverse events with the use of the dimeric low-molecular group (iohexol) is 14.3% compared with 2.5% observed in the no-contrast group.[47] Moreover, among the different types of ICA, nonionic dimeric agents show a higher percentage of delayed events than nonionic monomer agents. Because the rate of true allergic reaction to contrast is so low, prophylactic therapy is indicated only in patients with a history of allergic adverse events. In elective patients at risk for allergic reactions, in particular those with a history of anaphylactic reaction, prophylactic treatment must include prednisone, 50 mg by mouth (PO), or hydrocortisone, 200 mg intravenous (IV) at 13 hours, 7 hours, and 1 hour before ICA injection, plus diphenhydramine, 50 mg IV, intramuscularly (IM), or PO, 1 hour before ICA administration (see Classic References, Lasser et al.). Methylprednisolone, 32 mg PO, 12 hours and 2 hours before ICA injection, plus an antihistamine can also be used. In addition, careful selection of ICA in addition to prophylactic therapy can help to further reduce the risk of adverse reactions, which are very uncommon (0.2% to 1.6%). Reactions to contrast agents may be more difficult to manage in patients receiving beta-blocker therapy. Recurrence rates may approach 50% on repeat exposure to contrast agents, and prophylactic use of H_1 and H_2 histamine receptor–blocking agents and aspirin therapy has been recommended.

ANGIOGRAPHIC PROJECTIONS

To identify and interpret the severity of coronary lesions, proper visualization of every segment of the main epicardial vessels and their branches is crucial. Although the coronary anatomy has a certain degree of variability, specific angulations of the x-ray tube are typically used during coronary angiography to ensure that vessel segments are not foreshortened or overlapping. The projections depend on the position of the x-ray tube and image intensifier. The AP view is obtained with the image intensifier in perpendicular position above the patient, with the x-ray beam traveling back to front. The intensifier can then be angled toward the patient's left or right side to obtain LAO and RAO views. The beam can be angulated cranially if the intensifier is tilted toward the head of the patient and caudally if it is moved toward the patient's feet. The degree of angulation can be changed to prevent overlapping of vessels or obstruction of vessel segments caused by superimposition of implantable devices or other structures, such as spine, bone, or diaphragm. As a general rule, in LAO views, the LAD is visible on the right side of the spinal column. Conversely, in RAO projections, the LAD is on the left side of the spinal column. Cranial and caudal tilting is used to "open" overlapped segments. Caudal views are mostly used for the proximal segment of the LCA, whereas cranial views avoid foreshortening and allow for the evaluation of the

ETABLE 21.3 Intravascular Iodinated Contrast Agents: Characteristics

	GENERIC NAME	OSMOLALITY RANGE (mOsm/kg H$_2$O)	VISCOSITY RANGE (cP or mPa-s*) 37°C	IONICITY
High osmolarity	Diatrizoate/meglumine Diatrizoate/sodium (ionic compounds)	1500-2000	4.1-10.5	Ionic
	Iothalamate (ionic compound)	600-1400	1.5-4	
Low osmolarity	Ioxaglate (ionic compound)	600	7.5	
	Iodipamide	664	5.6	
	Iohexol	322-844	1.5-10.4	Nonionic
	Iopamidol	413-796	3.0-9.4	
	Iopromide	330-770	1.5-10	
	Ioversol	502-792	3-9	
	Ioxilan	610-721	5.1-8.1	
Iso-osmolarity	Iodixanol	270-320	6.3-11.8	

*Centipoise or millipascal-second
Data from Manual on Contrast Media of the American College of Radiology (ACR) Committee on Drugs and Contrast Media. Version 10.2, 2016.

ETABLE 21.4 Classification of Acute Adverse Reactions After Injection of Intravascular Iodinated Contrast Agents

MILD*	MODERATE†	SEVERE‡
Allergic-Like		
Urticaria or pruritus (+) Cutaneous edema (+) Throat discomfort ("itching") Nasal congestion Sneezing, conjunctivitis, rhinorrhea	Urticaria or pruritus (++) Diffuse erythema (++) Facial edema (++) Wheezing or bronchospasm (++) Throat discomfort ("tightness or hoarseness")	Diffuse edema (+++) Facial edema and dyspnea (+++) Diffuse erythema and hypotension (+++) Wheezing or bronchospasm and hypoxia (+++) Anaphylactic shock
Physiologic		
Nausea or vomiting (+) Self-limiting vasovagal reaction (+) Hypertension (+) Flushing or warmth (+) Headache or dizziness Altered sense of taste Anxiety	Nausea or vomiting (++) Vasovagal reaction (++) Hypertension urgency (++) Chest pain	Vasovagal reaction, resistant to treatment (+++) Hypertension emergency (++) Arrhythmia Convulsion

*Self-limited adverse effects without evidence of progression.
†More pronounced adverse effects that require medical therapy.
‡High risk of permanent morbidity and mortality if not adequately treated.
Data from Manual on Contrast Media of the American College of Radiology (ACR) Committee on Drugs and Contrast Media. Version 10.2, 2016.

ETABLE 21.5 Classification of Delayed Adverse Reactions After Injection of Intravascular Contrast Agents

MOST FREQUENT	RARE
Urticaria Persistent rash Maculopapular exanthema Exanthema pustulosis Urticaria or pruritus Angioedema or pruritus Pruritus alone	Severe cutaneous reactions in patients with systemic lupus erythematosus (SLE) Cutaneous reactions in sun-exposed areas of body Inflammation and swelling of salivary glands (parotitis or mumps) Acute polyarthropathy Nausea or vomiting Fever Drowsiness Headache Severe hypotension* Cardiopulmonary arrest*

*Extremely rare (only in part referable to administration of contrast agents).
Data from Manual on Contrast Media of the American College of Radiology (ACR) Committee on Drugs and Contrast Media. Version 10.2, 2016.

mid- and distal portion of the vessel and its bifurcations. Table 21.3 lists common projections for every coronary artery, and Figs. 21.10 and 21.11 provide examples for the LCA and RCA, respectively.

CORONARY ANATOMY

The heart vasculature comprises three main epicardial arteries that divide into smaller, thinner branches that eventually form the arterioles. The arterioles have a muscular wall and are the main site of vascular resistance that can modulate the blood pressure reaching the capillary net downstream (see Chapter 36). This section reviews the coronary anatomy of the main epicardial vessels that can be visualized with coronary angiography.

The main epicardial vessels are the left main coronary artery (LMCA) and the RCA. The LMCA originates from the left sinus of Valsalva and divides into the LAD and the Cx arteries. Occasionally, a third branch can originate from the LMCA, the ramus intermedius (RI), usually attributed to the Cx artery.

The LAD artery runs along the anterior interventricular sulcus and provides circulation for the anterior and anterolateral wall of the left ventricle with diagonal vessels and the anterior two-thirds of the interventricular septum with the septal branches. The number of diagonal and septal branches may vary greatly, and for the purpose of coronary description, they are simply numbered sequentially (D1, D2 … S1, S2, S3). Based on the length of the vessel, the LAD can be classified into type 1 if it does not reach the LV apex, type 2 if it reaches the LV apex, and type 3 if it reaches and wraps around the LV apex, supplying also the posterior apex. The Cx artery courses along the left atrioventricular (AV) groove and provides branches for the left atrium, occasionally giving rise to the sinoatrial (SA) branch (40% of cases). The Cx also supplies the LV lateral and posterior walls with branches called *obtuse marginal* (OM) branches, which are numbered sequentially similar to the diagonal branches (see Fig. 21.10). There is high anatomic variability in the number of diagonal, septal, and OM branches present in the LCA.

The RCA originates from the right sinus of Valsalva and courses across the right AV groove. The proximal branches provided by the RCA are atrial branches for the right atrium, the SA node in 60% of cases, and the branch to the conus that supplies the right ventricular outflow tract. Once it reaches the acute margin of the ventricle, the RCA provides the acute margin branch. The RCA then continues to the crux cordis (where the AV groove intersects the posterior interventricular sulcus), where it branches into the PDA and the posterolateral (PL) branches (see Fig. 21.11). This anatomy is the most common and is termed *right coronary dominance.* Dominance can also be left or balanced, based on the origin of the PDA and the PL branches. Approximately 80% of the population displays a right dominance, meaning both the PDA and the PL branches are supplied by the RCA, while 10% of the population has a *left coronary dominance,* with PDA and PL branches deriving from the Cx artery. The remaining 10% display *codominance,* or *balanced coronary dominance,* with the PDA arising from the RCA and the PL branches arising from the Cx (eFig. 21.7).

The subdivision of the coronary arteries into segments is crucial to describe the localization of lesions during angiography. eTable 21.6 lists
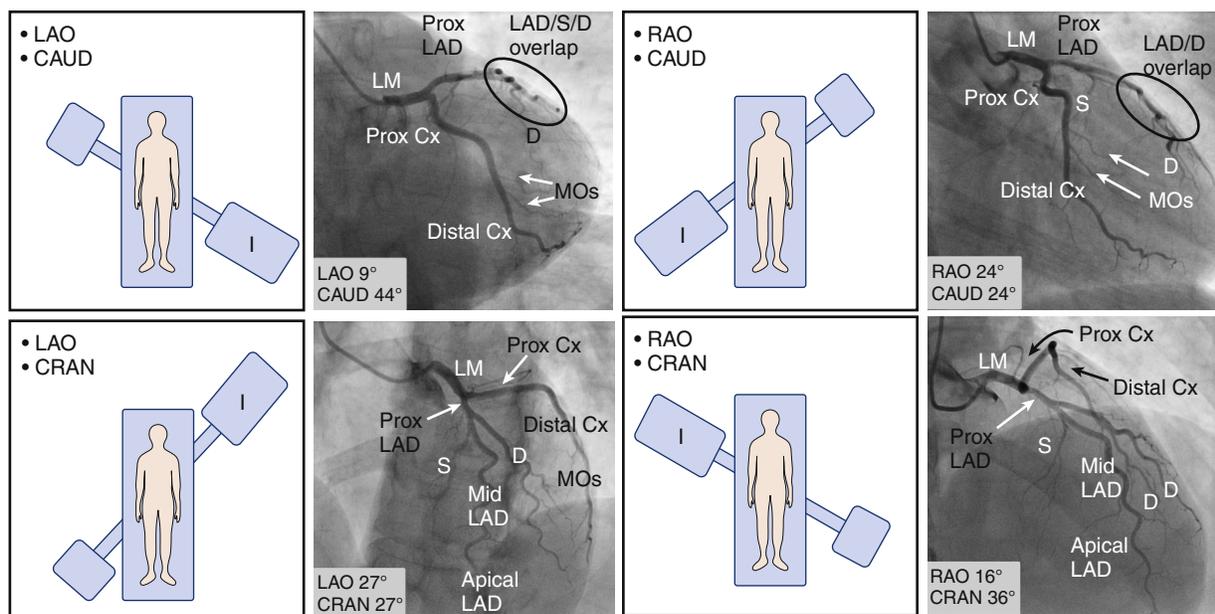
TABLE 21.3 Standard Angiographic Projections

PROJECTION/DEGREES	ANATOMIC DESCRIPTION
Right Coronary Artery	
LAO 45	Vessel engagement projection
	Ostium and RCA along AV sulcus
LAO10-30, CRAN 30	PDA, PL branches, and RCA after crux
RAO 30	PDA ostium, PDA septal branches, right ventricular branches, acute margin branches
Left Coronary Artery	
Anteroposterior, CAUD 10	LMCA engagement projection
LAO 20-45, CAUD 30-45	"Spider projection": LMCA and proximal segment of LAD, Cx, and ramus (if present)
LAO 20-45, CRAN 30-60	Mid- and distal LAD and its branches, Cx PDA, and Cx PL branches if present
RAO 15-30, CAUD 10-30	All LAD and branches, Cx and OM branches
RAO 15-30, CRAN 10-30	Mid- and distal LAD and branches, mid-Cx and branches

AV, Atrioventricular; *CAUD,* caudal; *CRAN,* cranial; *Cx,* circumflex artery; *LAO,* left anterior oblique; *LMCA,* left main coronary artery; *OM,* obtuse marginal; *PDA,* posterior descending artery; *PL,* posterolateral; *RAO,* right anterior oblique; *RCA,* right coronary artery.

FIGURE 21.10 Angiographic projection for the left coronary artery and anatomic evaluation. *CAUD,* Caudal; *CRAN,* cranial; *Cx,* circumflex artery; *D,* diagonal branch(es); *I,* intensifier; *LAD,* left anterior descending artery; *LAO,* left anterior oblique; *LM,* left main coronary artery; *MOs,* obtuse marginal branch(es); *Prox,* proximal; *RAO,* right anterior oblique; *S,* septal branch(es). (Angiographic images courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
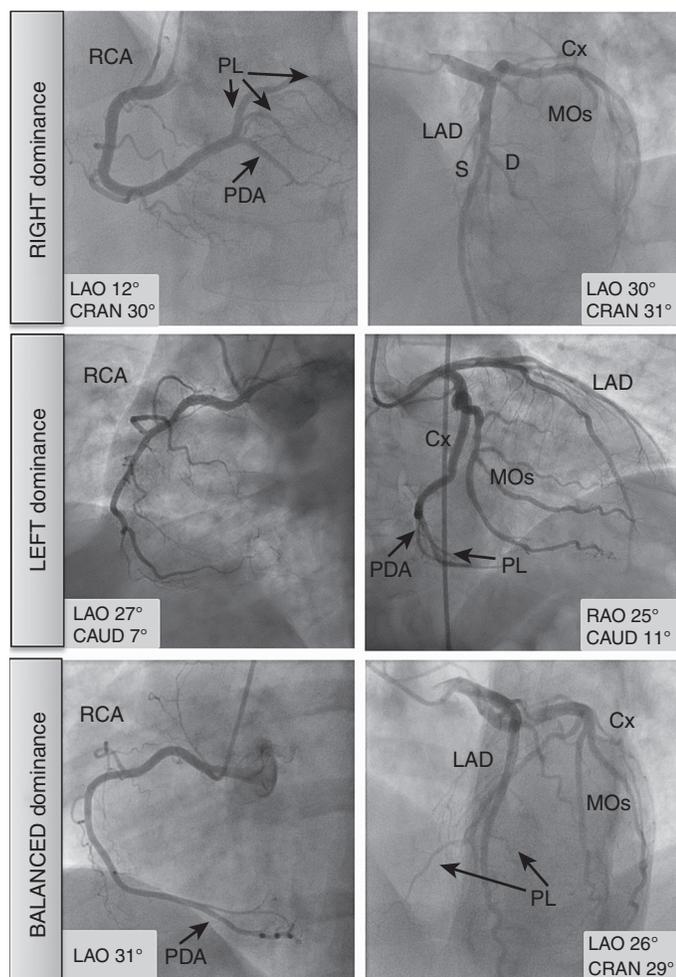
EFIGURE 21.7 Coronary artery dominance. **Top,** Example of right coronary dominance. **Middle,** Left coronary dominance. **Bottom,** Balanced dominance. *CAUD,* Caudal; *CRAN,* cranial; *Cx,* circumflex artery; *D,* diagonal branch(es); *LAD,* left anterior descending artery; *LAO,* left anterior oblique; *MOs,* obtuse marginal branch(es); *PDA,* posterior descending artery; *PL,* posterolateral branches; *RAO,* right anterior oblique; *RCA,* right coronary artery; *S,* septal branch(es). (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)

ETABLE 21.6 Classification of Coronary Segments from SYNTAX Score

SEGMENT	DESCRIPTION	CASS NUMBER
Left main	From ostium of LCA until bifurcation into LAD and left Cx branches	11
LAD proximal	Proximal to, and including, first major septal branch	12
LAD middle	LAD immediately distal to origin of first septal branch and extending to the point where LAD forms an angle (RAO view). If this angle is not identifiable, this segment ends at one-half the distance from the first septal to the apex of the heart.	13
LAD distal	Terminal portion of LAD, beginning at end of previous segment and extending to or beyond apex	14
Major diagonal branches	LAD branches, sequentially numbered	15 first diagonal 16 second diagonal 29 third diagonal
Intermediate ramus	Branch from trifurcating left main other than proximal LAD or Cx; belongs to Cx territory	28
Proximal Cx	Main stem of Cx from its origin from left main to and including origin of first OM branch	18
Distal Cx	Stem of Cx distal to origin of most distal OM branch and running along posterior left atrioventricular grooves. Caliber may be small or artery absent.	19
OM branches	Cx branches, sequentially numbered	20 first OM 21 second OM 22 third OM
PL branches from Cx	PL branch originating from distal Cx	24 first PL 25 second PL 26 third PL
RCA proximal	From ostium to one-half the distance to acute margin of heart	1
RCA mid	From end of first segment to acute margin of heart	2
RCA distal	From acute margin of heart to origin of posterior descending artery	3
Posterior descending	Branch running in the posterior interventricular sulcus	4 if from RCA 27 if from Cx
PL branches from RCA	Posterolateral branch originating from distal coronary artery distal to crux	6 first PL 7 second PL 8 third PL

CASS, Coronary artery surgery study; *Cx,* circumflex artery; *LAD,* left anterior descending artery; *OM,* obtuse marginal; *PL,* posterolateral; *RAO,* right anterior oblique; *RCA,* right coronary artery.
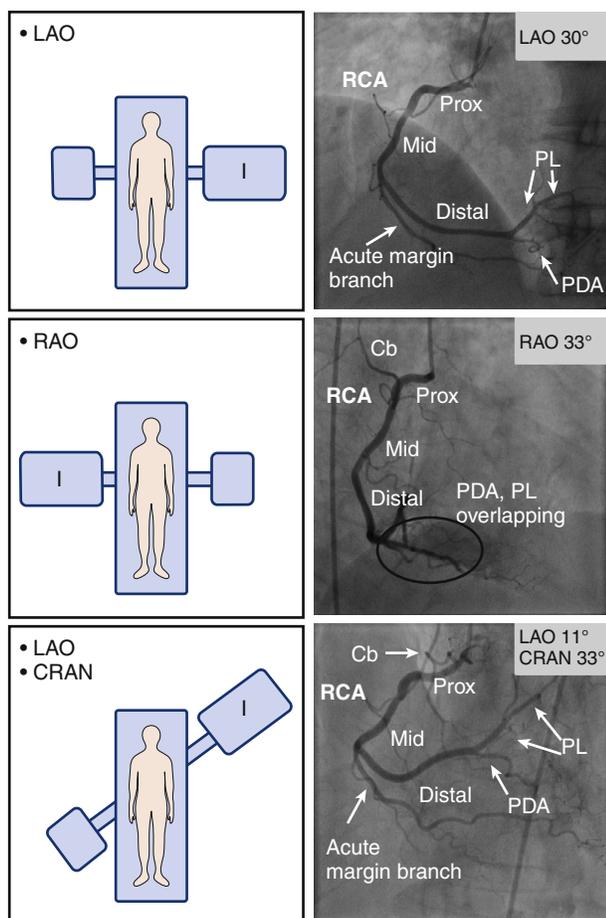Modified from https://www.syntaxscore.org.

FIGURE 21.11 Angiographic projection for the right coronary artery (*RCA*) and anatomic evaluation. *Cb,* Conus branch; *CRAN,* cranial; *I,* intensifier; *LAO,* left anterior oblique; *PDA,* posterior descending artery, *PL,* posterolateral branches; *prox,* proximal; *RAO,* right anterior oblique. (Angiographic images courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)

the definitions of the coronary segments adapted from the SYNTAX Trial, with the corresponding CASS (coronary artery surgery study) number.

CORONARY ARTERY ANOMALIES

The prevalence of coronary artery anomalies (CAAs) in patients undergoing coronary angiography averages 1% to 5%[48] (Table 21.4). Despite being rare in the general population, CAAs are the second most common cause of sudden cardiac death (SCD) among young athletes.[49]

There are many ways to classify CAAs. From a clinical standpoint, CAAs can be divided based on the presence of myocardial ischemia, into anomalies without ischemia, anomalies with episodic ischemia, and anomalies with obligatory ischemia (Table 21.5). Despite this important functional assessment, physicians often categorize CAAs based on anatomic characteristics. Use of CTCA and MRCA have increased the capability to detect and characterize anatomic abnormalities and help to determine optimal management of patients with a CAA. The most common anatomic classification of CAAs includes anomalies of ostium, anomalous origin of coronary artery, anomalous termination, congenital absence, and hypoplasia.[49]

Congenital Atresia of Coronary Ostium
Coronary ostial hypoplasia or atresia can occur as an isolated lesion or as a concomitant anomaly with other CAAs. The life expectancy of patients with coronary ostial hypoplasia or atresia depends on the presence of collateral circulation from other vessels that can supply the distal coronary bed.

TABLE 21.4 Incidence of Coronary Anomalies in 1950 Angiograms

VARIABLE	NUMBER	FREQUENCY (%)
Coronary anomalies	110	5.64
Split RCA	24	1.23
Ectopic RCA (right cusp)	22	1.13
Ectopic RCA (left cusp)	18	0.92
Fistulas	17	0.87
Absent left main coronary artery	13	0.67
LCx arising from right cusp	13	0.67
LCA arising from right cusp	3	0.15
Low origin of RCA	2	0.1
Other anomalies	3	0.15

LCA, Left coronary artery; *LCx,* left circumflex artery; *RCA,* right coronary artery.
From Angelini P, editor. Coronary Artery Anomalies: A Comprehensive Approach. Philadelphia: Lippincott Williams & Wilkins; 1999, p 42.

TABLE 21.5 Classification of Coronary Anomalies Based on Ischemia

ISCHEMIA	CLASSIFICATION
Absence of ischemia	Most anomalies (split RCA, ectopic RCA from right cusp; ectopic RCA from left cusp)
Episodic ischemia	Anomalous origin of a coronary artery from the opposite sinus (ACAOS); coronary artery fistulas; myocardial bridge
Typical ischemia	Anomalous left coronary artery from the pulmonary artery (ALCAPA); coronary ostial atresia or severe stenosis

Anomalous Origin of Coronary Artery
Anomalous origin of coronary arteries is a common type of CAA. Coronary arteries with ectopic origin can arise either from the wrong sinus of Valsalva (e.g., the Cx artery arising from the right coronary sinus) (eFig. 21.8) or from a different structure, including the pulmonary artery (PA), a branch of another coronary artery, or even a ventricular chamber.[49] The course of the anomalous coronary arteries can be assessed by angiography in the RAO view. The LCA arising from the right aortic sinus usually follows one of these four courses: prepulmonic, retroaortic, interarterial, or transseptal (Fig. 21.12). The interarterial course of an anomalous LCA from the right sinus is associated with SCD during or shortly after exercise in young individuals. The hemodynamic mechanism underlying the risk of SCD remains unclear. Some authors hypothesize that distention of the aortic root and the pulmonary trunk during exercise or stress might exacerbate the preexisting angulation of the anomalous coronary artery, resulting in compression of the coronary artery lumen. In other cases the vessel might have an aberrant course within the aortic wall that favors compression of the coronary artery. Similarly, origin of the RCA from the left aortic sinus with an interarterial course is associated with myocardial ischemia and SCD. Once this anomaly is diagnosed, CABG is recommended, although a stenting strategy has also been reported. A benign variation of the RCA origin is represented by the high anterior origin. This variation has no hemodynamic significance but might result in a challenging cannulation.

Anomalous pulmonary origin of any coronary artery (APOCA) is a very rare occurrence (eFigs. 21.9 and 21.10). If all three coronary arteries arise from the PA, prognosis is poor; patients with this anomaly usually die within the first month of life (see Classic References, Yamanaka and Hobbs). Anomalous origin of the LCA from PA (ALCAPA), also known as Bland-White-Garland syndrome, was reported for the first time in 1956 and represents the most common APOCA. Almost 90% of patients with this CAA die during the first year of life. Only very few, with extensive collateral circulation from the RCA, survive into adulthood. If diagnosed in time, the preferred treatment for APOCA is CABG or unroofing and re-implantation (with or without a patch). Partial ALCAPA (e.g., only of the LAD) has also been reported.[50]
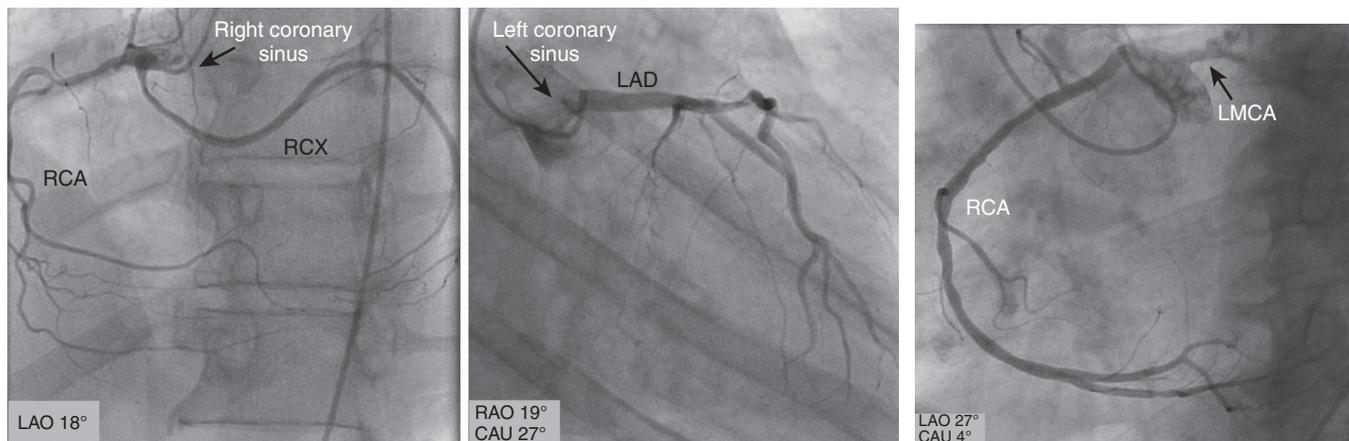
EFIGURE 21.8 A, *left,* Anomalous origin of circumflex artery from right coronary sinus. *Right,* Only the left anterior descending artery (LAD) arises from the left coronary sinus. *CAU,* Caudal; *LAO,* left anterior oblique; *RAO,* right anterior oblique; *RCA,* right coronary artery; *RCX,* right circumflex artery. **B,** Anomalous origin of right coronary artery (*RCA*) from left coronary sinus. The left main coronary artery (*LMCA*) has a separate ostium in the left coronary sinus and can be seen in the upper right corner. *CAU,* Caudal; *LAO,* left anterior oblique. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
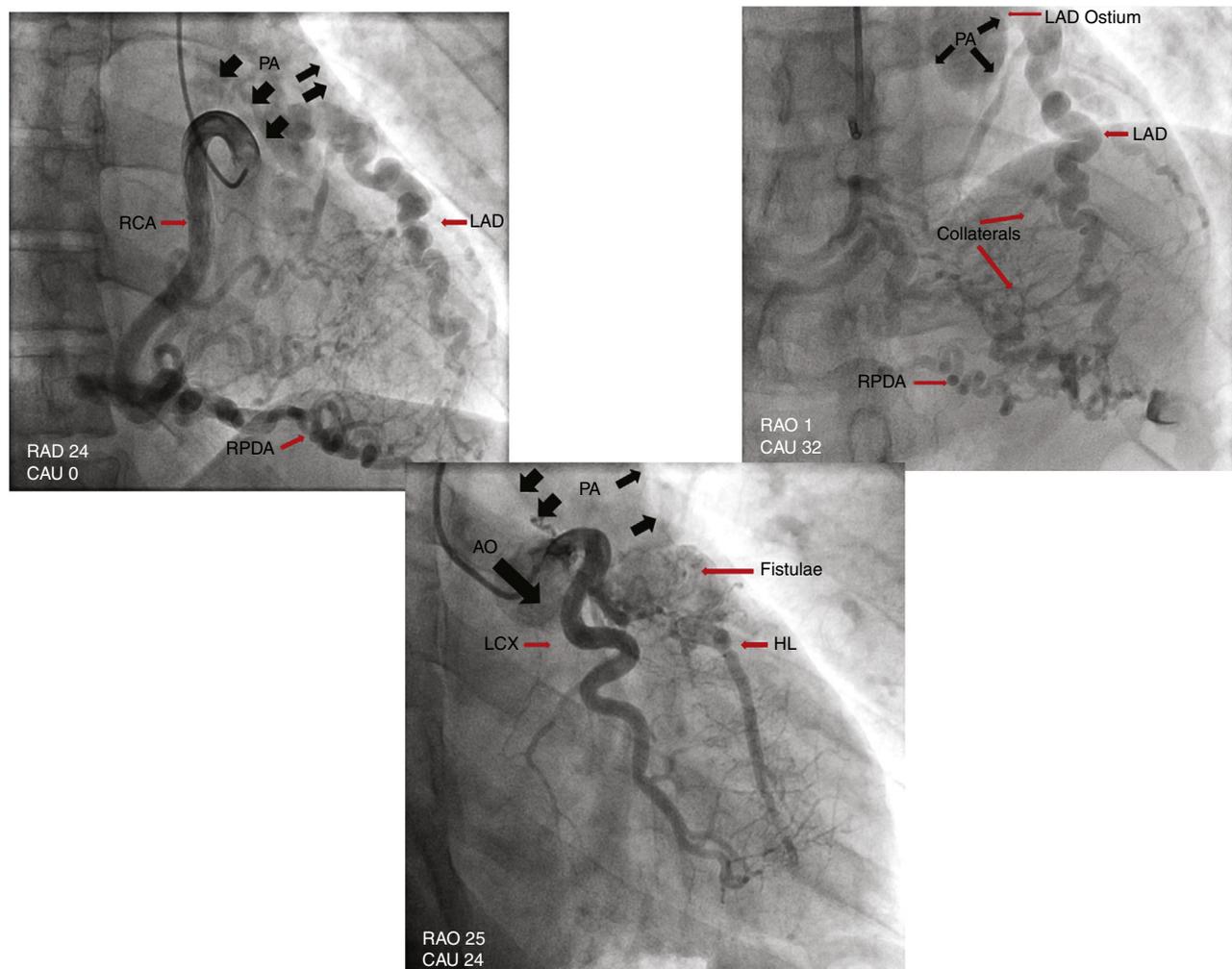

EFIGURE 21.9 Partial anomalous left coronary artery origin (LAD branch only) from the main pulmonary artery (PA) in an adult patient with positive stress test and scar evidence of cardiac magnetic resonance imaging. **Top,** Large RCA giving collaterals filling LAD (Rentrop 3) and drains to the pulmonary artery (PA). Significant coronary ectasia and tortuosity are evident in many segments. This patient also has a set of fistulae between the high lateral branch (HLB) and the PA. Detailed characterization of myocardial ischemia and scar led to surgical treatment with coronary reimplantation. **Bottom,** Fistulae communication between the high lateral (HL) branch and the pulmonary artery (PA). Clear separation aorta (AO)-PA separation is documented with carefully angulated projections. *LAD,* Left anterior descending coronary artery; *LCX,* left circumflex coronary artery; *RCA,* right coronary artery; *RPDA,* right posterior descending artery.
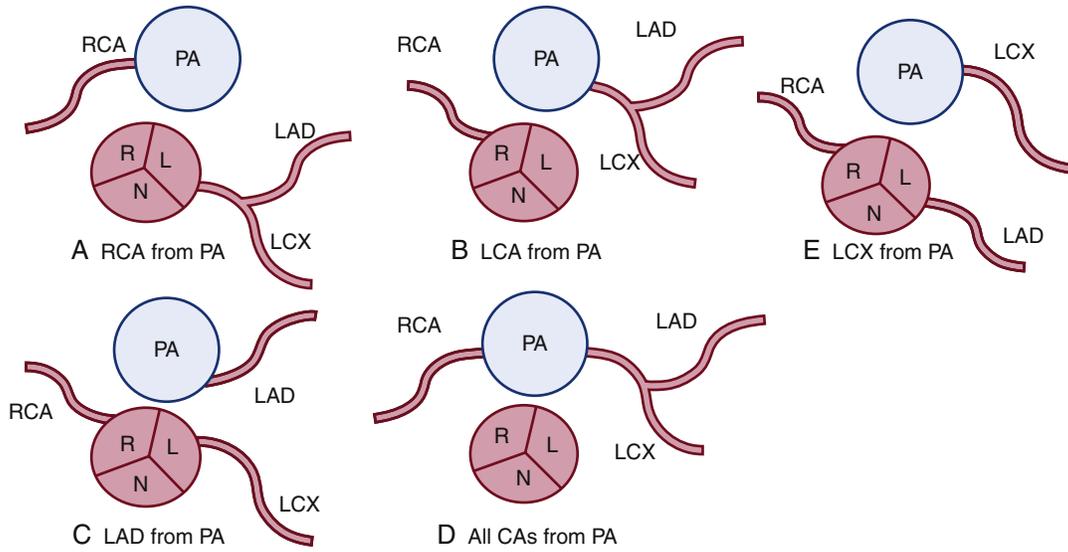
EFIGURE 21.10 **A** to **E,** Anomalies of coronary origin from pulmonary artery (*PA*). *CAs,* Coronary arteries; *L,* left sinus of Valsalva; *LAD,* left anterior descending artery; *LCA,* left coronary artery; *LCX,* left circumflex; *N,* noncoronary sinus; *R,* right sinus of Valsalva; *RCA,* right coronary artery.
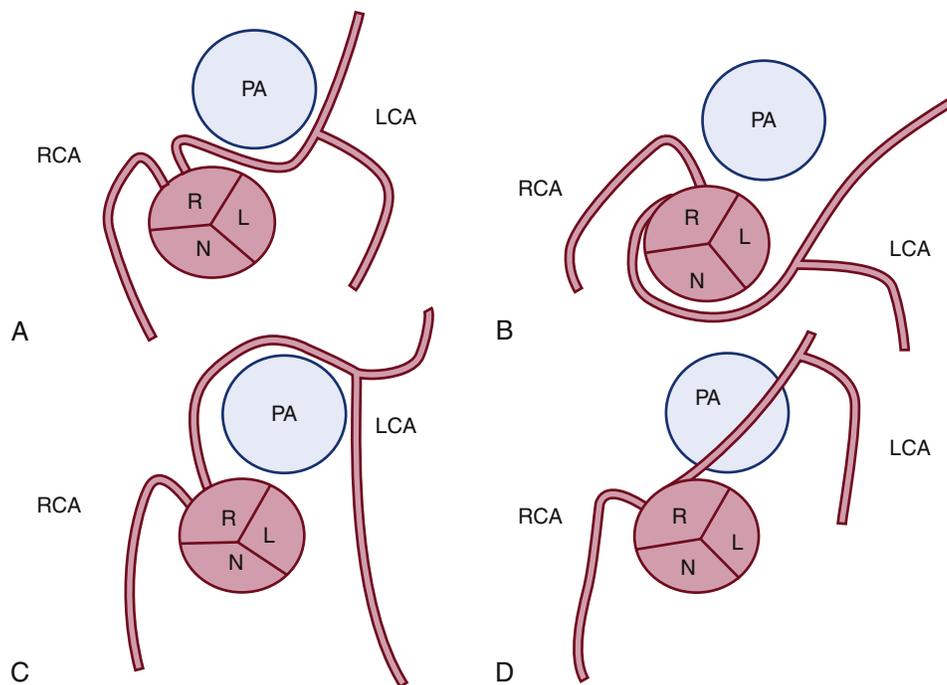
FIGURE 21.12 Four possible courses of the anomalous left coronary artery (*LCA*) arising from the right coronary sinus: **A,** Interarterial. **B,** Retroaortic. **C,** Prepulmonic. **D,** Transseptal. *L,* Left sinus of Valsalva; *N,* noncoronary sinus; *PA,* pulmonary artery; *R,* right sinus of Valsalva; *RCA,* right coronary artery.

Congenital Absence

Lack of an LMCA is the most common form of congenital coronary absence, with a rate of 0.41% to 0.67% in the general population. In the absence of LMCA, the LAD and Cx arteries simply arise directly from the left sinus of Valsalva with separate origins. This anomaly is considered a benign condition and is an occasional finding during coronary angiography. The congenital absence of either the Cx or the RCA has been reported and associated with a benign prognosis.[51]

Hypoplasia

Hypoplasia of a coronary artery is defined as the maldevelopment of at least one of the major epicardial arteries or its branches. One, two, or all three coronary territories can be involved. Hypoplastic coronary arteries usually have a small diameter and a shortened course. A luminal diameter of less than 1.5 mm in a major epicardial vessel, with no nearby compensatory branches, has been proposed as the threshold for diagnosis. The prognosis of single-vessel hypoplasia of the Cx or RCA is relatively good, but SCD can occur in two-vessel hypoplasia.

Anomalous Termination

Congenital coronary artery fistulas (CAFs) are rare anomalies, with an estimated incidence in the general population of approximately 0.002%. As an incidental finding, CAFs are reported in 0.3% to 0.8% of patients undergoing coronary angiography for any indication. CAFs are defined as abnormal direct communication between one or more coronary arteries with another major vessel or a chamber, such as the vena cava, left or right ventricle, pulmonary vein, or PA (Fig. 21.13).

CAFs can originate from any of the major epicardial vessels and involve the RCA in 33% to 55%, the LAD in 35% to 49%, and the Cx in 17% to 18% of cases. Simultaneous involvement of both the left and the right coronary system exists in about 4% to 18% of CAFs.[52,53] Most of the fistulas drain into low-pressure structures, such as the right ventricle (40%), right atrium (26%), PA (17%), coronary sinus (7%), and superior vena cava (1%). Although possible, drainage of CAFs into left-sided chambers is less frequent (left atrium 5%, left ventricle 3%).[52,54]

Coronary angiography is the gold standard for the diagnosis of CAFs. However, in clinical practice, most CAFs are incidental findings during CTCA in low-risk patients. The clinical presentation of patients with CAF depends on size and volume of the shunt, location of the shunt, and concomitance with other cardiac disease. Approximately 50% of patients with CAF are asymptomatic. When present, common symptoms are dyspnea, fatigue, palpitation, and chest pain. The first manifestation of CAF can also include CHF, arrhythmias, SCD, and infective endocarditis. Symptomatic patients with large fistulas should be treated with surgical closure or interventional closure.

PITFALLS OF CORONARY ANGIOGRAPHY

Improper interpretation of angiographic images can result from the use of inadequate projection views, CAAs, vessel foreshortening or superimposition of branches (eFig. 21.11), and deep engagement of the catheter into the vessel, potentially resulting in oversight of ostial lesions. In addition, obesity or instrument malfunctioning can lead to low image quality and erroneous image interpretation. Inadequate vessel opacification because of enhanced blood flow or competitive flow from a bypass graft might result in oversight of stenosis in collateral branches or in overestimation of the degree of thrombosis in a vessel. Also, when reading coronary angiograms, borderline lesions may require multiple views and potentially intracoronary imaging or evaluation of the fractional flow reserve (FFR) to adequately assess the severity of the lesion. eFig. 21.12 shows an example of an eccentric lesion of the proximal LAD that is not visible in the LAO 34-degree, cranial 28-degree projection but becomes evident in the RAO 24-degree, caudal 21-degree projection. Moreover, a myocardial bridge or a coronary spasm can result in a minus defect in the coronary artery that can be misinterpreted as atherosclerotic disease, leading to unnecessary treatment (see next section). In the case of ostial occlusion of a vessel, especially for primary or secondary branches of main epicardial vessels, it can be challenging to notice the missing vessel unless a collateral perfusion is present that allows for partial visualization of the downstream portion of the occluded vessel.[55]

Myocardial Bridging

Myocardial bridging is not a coronary lesion per se, although in the long term it can lead to local coronary damage. It can also be mistaken for a coronary stenosis because bridging might cause filling defects. Myocardial bridging consists of a segment of an epicardial artery that descends into the myocardium for a variable distance (Fig. 21.14). It occurs in approximately 5% to 10% of patients and usually involves the LAD. As it runs in the myocardium, during systole the arterial segment is constricted by the muscle fibers and appears as a narrowing on the angiogram. However, these segments are usually easily identifiable because the narrowing disappears during diastole. Although bridging is not thought to be of any hemodynamic significance in most cases, myocardial bridging has been associated with angina, arrhythmia, depressed LV function, myocardial stunning, early death after cardiac transplantation, and SCD.[56] Treatment with beta blockers can be considered. Alternatively, surgical treatment can be attempted in selected cases.

Coronary Artery Spasm

Coronary spasm is a dynamic reversible focal restriction or occlusion of a coronary artery caused by the constriction of the smooth muscle cells in the vessel wall (Fig. 21.15) (see Chapter 36). Coronary spasm, when prolonged, can cause Prinzmetal angina and lead to transitory ECG changes. Cigarette smoking, cocaine use, alcohol, intracoronary irradiation, and administration of catecholamines can promote
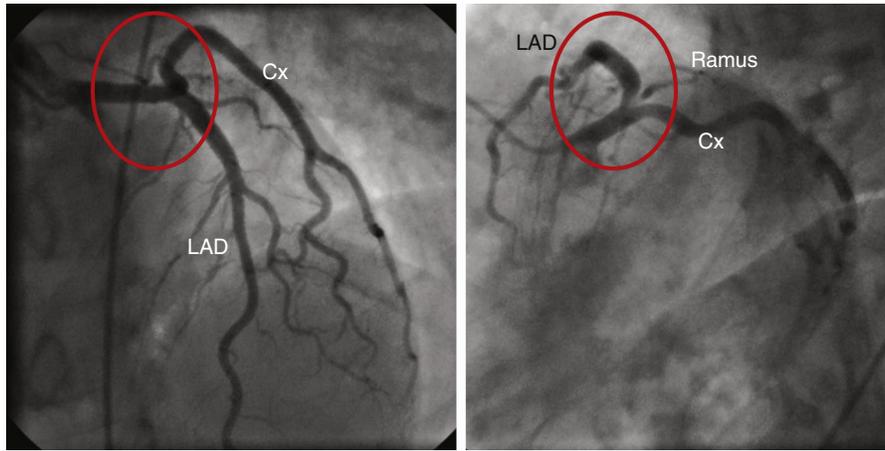
EFIGURE 21.11 **Left,** Erroneous (cranial) projection with overlapping of coronary vessels. **Right,** With a different projection (LAO caudal "spider"), the trifurcation of the left main coronary artery becomes visible and can be evaluated for the presence of coronary stenosis. *Cx,* Circumflex artery; *LAD,* left anterior descending artery. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
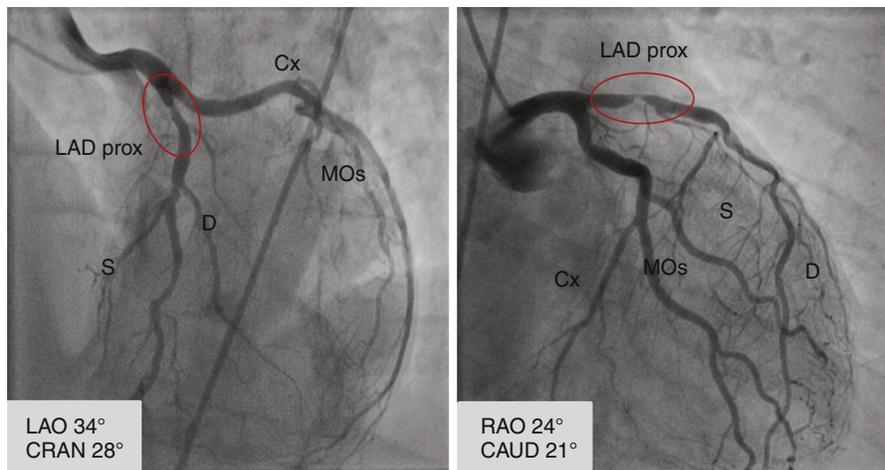
EFIGURE 21.12 Example of eccentric coronary lesion in the proximal LAD, uncovered with the use of different angiographic projections. *Cx,* Circumflex artery; *D,* diagonal branch(es); *LAD prox,* proximal segment of left anterior descending artery; *MO,* obtuse marginal branch(es); *S,* septal branch(es). (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
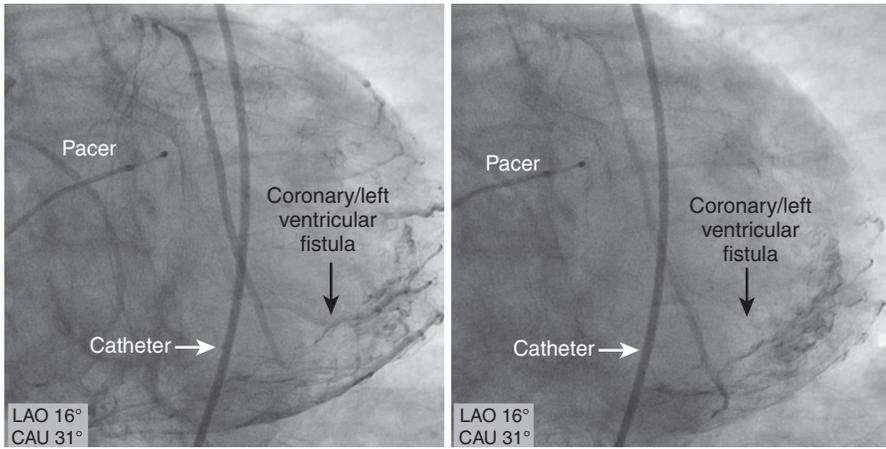
FIGURE 21.13 **Coronary fistula with the left ventricle.** *CAU,* Caudal; *LAO,* Left anterior oblique. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
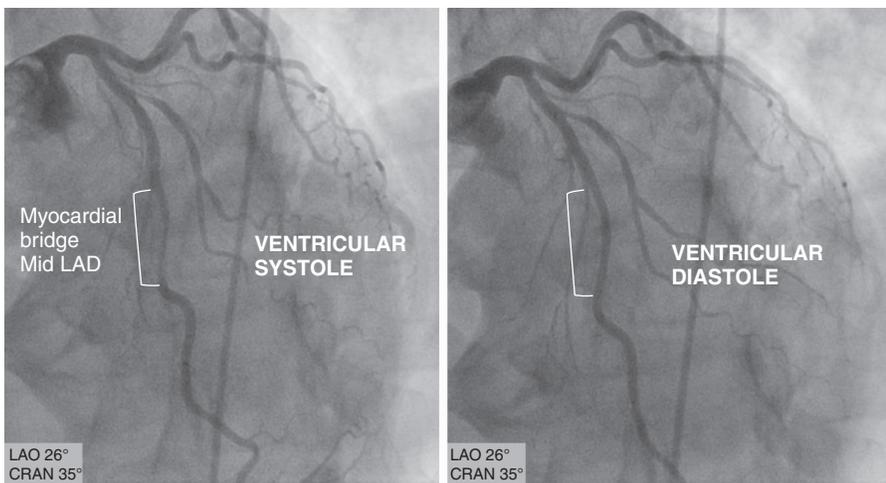

FIGURE 21.14 **Myocardial bridge. Left,** Narrowing of the middle left anterior descending artery (*LAD*) can be observed during the ventricular systolic phase. **Right,** The vessel diameter returns to normal during the ventricular diastolic phase. *CRAN,* Cranial; *LAO,* left anterior oblique. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
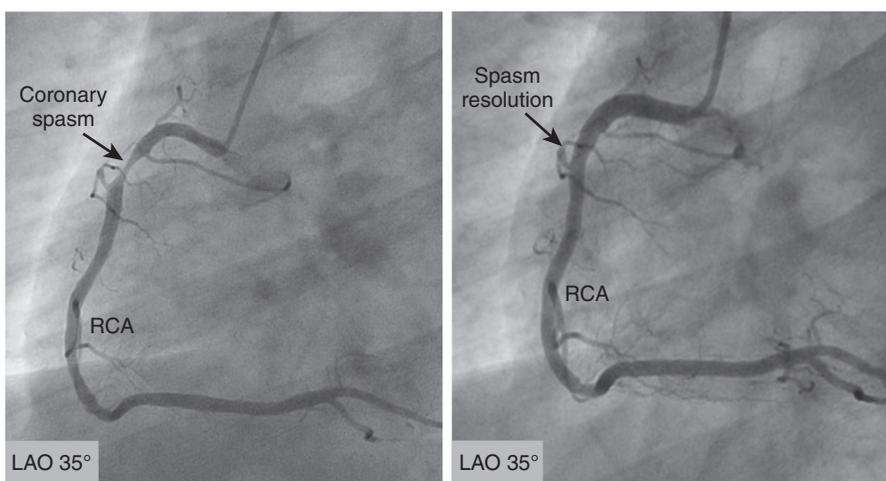

FIGURE 21.15 **Left,** Coronary spasm in the proximal segment of the right coronary artery (*RCA*). **Right,** Resolution of the spasm. *LAO,* Left anterior oblique. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)

focal coronary spasm often associated with chest pain and ECG changes. Intracoronary nitroglycerin is used to relieve the spasm. Acetylcholine (ACh) is a vasodilator acting on the muscarinic receptors of the vascular smooth muscle cells. Incremental doses of ACh (20, 30, and 50 μg) are injected directly into the coronary artery. In the presence of endothelial dysfunction, cells cannot produce NO in response to ACh, resulting in local vasoconstriction. Adverse reactions to ACh include hypotension, bradycardia, dyspnea, and flushing. Also, hyperventilation during coronary angiography can elicit spasm, although it is a much less sensitive test compared with the others. If no spasm can be documented, the diagnosis relies instead on clinical features and the response to treatment with nitrates and calcium channel blockers.

ANGIOGRAM EVALUATION

When reading coronary angiograms, the entire extension of every coronary artery and its branches should be carefully evaluated in all the acquired views. First, the coronary dominance can be assessed. Next, the presence of abnormalities in the course of the coronary arteries should be investigated. The following elements should be part of the evaluation of diseased coronary vessels: (1) extension and localization of the lesion, (2) severity of the stenosis, (3) morphologic characteristics of the lesion, (4) evaluation of the downstream flow, (5) presence of collateral blood vessel circles, and (6) changes compared with previous angiograms, if available (eFig. 21.13).

SYNTAX SCORE

The SYNTAX score is a valuable tool for the assessment of CAD severity. Developed in the context of the eponymous trial, this algorithm integrates several historical anatomical scores including the ACC/AHA, Medina bifurcation, and CTO classifications, as well as the AHA categorization of the three coronary segments and finally the modified Leaman score.[57,58] Although the primary purpose of this score was not to assess prognosis, several trials and prospective registries have shown a significant correlation between the high score tertiles and worse outcomes, irrespective of clinical presentation and follow-up length. Therefore, in patients with LM or multivessel disease, current guidelines recommend SYNTAX score to assess the anatomical complexity of CAD, as well as the long-term risk of mortality and morbidity after PCI. Accordingly, higher tertiles move indication for surgery, while low score tertile for PCI.

Even the residual SYNTAX score has been found strongly related to long-term adverse events. In particular, a post-hoc analysis from the SYNTAX trial has shown that a residual SYNTAX score >8 was an independent predictor of 5-year mortality; observation corroborated in different clinical contexts including patients with ACS.[59,60] This finding has important clinical implications. In patients with multivessel disease in which

coronary artery spasm. If a coronary spasm is suspected, a diagnosis can be made with several provocative tests, most often IV ergonovine maleate, IV acetylcholine, and hyperventilation. The physiologic response to ergonovine is a diffuse coronary vasoconstriction in all epicardial vessels. In patients with coronary spasm, however, ergonovine can induce

Severity of the stenosis

- Stenosis percentage (0-90%)
- Lesions >90% can be divided into 95% stenosis if the contrast media (CM) is visible in the lesion; 99% stenosis if CM is not visible in the lesion although there is antegrade filling; 100% stenosis for total occlusions (no anterograde filling)
- Visual assessment/QCA
- Minimal lumen diameter (MLD, in mm)

Morphologic characteristics

- ACC/AHA lesion classification
- SCAI lesion classification
- Ellis lesion classification

Extension and localization of the coronary disease

- Number of diseased vessels. Left main involvement
- Number of lesions in the same vessel and distance between the lesions (<2 cm or >2 cm)
- Lesion length
- Ostial involvement (ostial lesion if <3 mm from ostium)
- Bifurcation or trifurcation lesions (Medina classification)

Peripheral blood flow evaluation

- TIMI classification
- TIMI frame count (TFM) classification
- Myocardial blush grade
- Rentrop coronary collateral classification

Evaluation of collateral circulation

- Arteriogenesis: structural growth of preexisting arterioles promoted by the transstenosis gradient that favors flux across the anastomotic vessels (not visible for stenosis <90%)
- Angiogenesis: neoformation from a capillary net
- Collateral vessels:
    Intracoronaric (RCA-->RCA; LAD<-->LCX)
    Intercoronaric (Left <--> Right)
- Rentrop classification

Changes compared to previous angiographies

- Degree of disease progression
- Type of stents implanted during previous PCI
- Prior stent's size

Overall patient assessment

- SYNTAX Score
- Global risk classification (GRC): a combination of SYNTAX score and EuroSCORE
- Clinical SYNTAX score (CSS): a combination of SYNTAX score and ACEF score (age, creatinine, ejection fraction)
- Functional SYNTAX score (FSS): a combination of SYNTAX score and FFR
- Residual SYNTAX score: SYNTAX score after coronary revascularization (measure if incomplete revascularization)

EFIGURE 21.13 Evaluation of coronary stenosis. Multiple aspects are required for complete and clinically meaningful characterization.

complete revascularization is not possible with PCI, physicians should prefer surgical revascularization upfront.

Quantification of the Stenosis

A coronary stenosis is a reduction of the caliber of the vessel that is not caused by the progressive thinning of the vessel along its course but rather by pathologic local conditions. The degree of the stenosis can be evaluated by comparing the minimum diameter of the vessel at the level of the lesion to the diameter of the adjacent segment upstream of the stenosis. The degree of stenosis is usually underestimated compared with postmortem evaluation or intravascular ultrasound (IVUS) because the adjacent healthy lumen to which the stenosis is compared might present with vasospasm or diffuse atherosclerosis despite appearing normal on the angiogram. This often leads to underestimation of the stenosis. In addition, it is particularly difficult to evaluate long lesions since the arteries physiologically narrow during their course, and there might be a marked mismatch between the diameters of the normal segment upstream and downstream of a long stenosis.

Stenoses are defined as *minimal* if the narrowing is visually less than 50%, *moderate* between 50% and 70%, and *severe* with diameter reduction 70% or more.[55] Evaluation of stenosis severity can be estimated visually by the interventional cardiologist reading the angiogram, or it can be measured with quantitative coronary angiography (QCA) methodologies based on the selection of the area of interest and vessel diameter measurements, which can be automatic, semiautomatic, or manual. Most programs can be calibrated using the diameter of the catheter and can automatically detect the edge of the vessel across its length and measure the minimum diameter of the stenosis and the length of the stenosis. Alternatively, rather than edge detection, densitometric methodology can be used. This technique avoids the errors of edge detection caused by geometric assumptions required for software calculations. Densitometry measures the stenosis based on the area containing ICA when the vessel is fully opaque. There is usually good agreement between edge detection and densitometry techniques. QCA reduces interoperator variability of reading, which is estimated around 20%, and usually results in 10% to 20% lower values than visual stenosis estimation.[61]

When evaluating a coronary lesion, the diameter and length of the stenosis are only two of many characteristics to consider. Also important are morphologic characteristics of the lesion, including the presence of thrombus, extent of calcification, and tortuosity of the vessel involved. The AHA has classified coronary artery lesions into three main types based on easily identifiable characteristics on the angiogram. This classification has predictive value for the success of a PCI procedure (see Chapter 41). Type A lesions have a procedural success rate of 92% and a low complication rate, type B lesions have a 72% success rate with a 10% rate of complications, and type C lesions have only a 61% success rate and a 21% rate of complications (Table 21.6). Additional classifications of lesion severity are the Society for Cardiovascular Angiography and Interventions (SCAI) and the Ellis systems.[62]

Evaluation of Microvascular Blood Flow

Evaluation of the downstream flow provides additional information not only on the severity of the stenosis but also on the status of the microcirculation in the affected territory. It has been proven that often the microcirculation is impaired in the territory affected by epicardial vessel lesions. Prognostic information can be obtained from the degree of blood flow through the lesion. The most common classification is the Thrombolysis in Myocardial Ischemia/Infarction (TIMI) flow grade[35] (Table 21.7). In the presence of good blood flow in the coronary artery (TIMI 3) after PCI, patients can additionally be stratified using the TIMI frame count (TFC) score based on the number of angiographic frames necessary for the contrast to reach a standardized distal point in the vessel. The angiographic film should be acquired at 30 frames per second and contrast injection performed with a 6F catheter to measure TFC. The first frame is where the origin

of the vessel appears fully opacified. The last frame is predefined for each coronary vessel: For the LAD and Cx arteries, it is the most distal bifurcation, whereas for the RCA, it is the emergence of the first PL branch. For the LAD, the apical segment is the milestone for the TFC. Because the LAD is usually longer than the other vessels, a correction factor needs to be used when calculating this score in the LAD by dividing TFC in the LAD by 1.7. Normal TFCs are 36 ± 3 (or 21 ± 2 if corrected) for the LAD, 22 ± 4 for the Cx, and 20 ± 3 for the RCA.[37] This score provides quantitative information on the status of the microcirculation in the infarcted areas and is a predictor of functional recovery and clinical outcomes after primary PCI. In fact, while most primary PCIs obtain patency of the epicardial flow and a TIMI flow grade 3, the tissue-level perfusion will determine the extent of the myocardial damage or the muscle recovery. Similarly, the *myocardial blush* score provides a semiquantitative measure of peripheral perfusion (Table 21.8). It represents the arrival of the contrast in the capillaries and therefore can be appreciated only with angiographic acquisitions prolonged after the contrast has washed out of the main epicardial vessel. The myocardial blush grade is superior to TIMI flow grade for predicting postprocedural cardiac death and major adverse cardiovascular event (MACE).[63]

TABLE 21.6 AHA/ACC Lesion Classification

Type A	• Length <10 mm	• Little or no calcification
	• Discrete	• Less than totally occluded
	• Concentric readily accessible	• Not ostial
	• <45-degree angle	• No major side branch involvement
	• Smooth contour	• Absence of thrombus
Type B B1 if only one characteristic is present B2 if two or more characteristics are present	• Length 10-20 mm	• Moderate or heavy calcification
	• Eccentric	• Total occlusion <3 months old
	• Moderate tortuosity of proximal segment	• Ostial lesion
	• 45- to 90-degree angle	• Bifurcation lesion requiring two guidewires
	• Irregular contour	
	• Presence of any thrombus grade	
Type C	• Length >20 mm	
	• Diffuse	
	• Excessive tortuosity of proximal segment	
	• >90-degree angle	
	• Total occlusion >3 months old and/or bridging collaterals inability to protect major side branches	
	• Degenerated vein graft with friable lesions	

TABLE 21.7 Thrombolysis in Myocardial Ischemia/Infarction (TIMI) Flow Rate

TIMI 0 Flow	No penetration of contrast beyond the stenosis (100% stenosis, occlusion)
TIMI 1 Flow	Penetration of contrast beyond the stenosis but no perfusion of the distal vessel (99% stenosis, subtotal occlusion)
TIMI 2 Flow	Contrast reaches the distal vessel but at reduced rate of filling or clearing compared with other coronary arteries (partial perfusion)
TIMI 3 Flow	Contrast reached the distal vessel and clear at the same rate as the other coronary arteries

Collateral Vessel Circulation

The coronary arteries represent the end circulation of the heart, and thus there is very little redundancy in the vascularization of each myocardial territory. However, collateral vessels can form under specific circumstances. Collateral blood vessels are anastomotic connections between two segments of the same artery or between different native coronary arteries. They function as natural bypasses and represent an alternative source of blood supply for a coronary territory. Clearly, collateral circulation becomes very important in the event that the main vessel serving the territory becomes occluded. There are two main mechanisms by which collateral vessels can be formed: arteriogenesis and angiogenesis. *Arteriogenesis* is the growth of preexisting arterioles that transform into functional collateral arteries, as a muscular layer forms and viscoelastic and vasomotor properties are acquired. Arteriogenesis is promoted by the pressure gradient across the stenosis that favors the blood flow through the small, preexisting anastomotic vessels upstream of the stenosis. *Angiogenesis,* on the other hand, involves the de novo formation of vessels starting from primitive postcapillary venules. The process is favored by hypoxic stimuli such as local production of vascular endothelial growth factor (VEGF) and hypoxia-inducible factors (HIFs)[64] (see Chapter 36). The collateral vessel net can be intracoronary if it connects different segments of the same coronary artery or the two LCAs and intercoronary if it connects the RCA with one or both of the LCAs.

When evaluating coronary stenosis, it is important to take into account the presence of collateral vessels that may have formed over time. Collateral flow can allow visualization of an occluded vessel by retrograde opacification of the vessel downstream of the occlusion. Based on the presence of contrast in the collateral vessels and the degree of retrograde opacification of the epicardial vessel, collateral circulation can be classified with the Rentrop grade[65] (see Classic References) (eTable 21.7; Fig. 21.16, and eFig. 21.14).

SPECIAL LESION CONSIDERATIONS

Chronic Total Occlusion

A chronic total occlusion (CTO) is the complete or almost-complete blockage of a coronary artery for 30 or more days. It can be an incidental finding in patients referred for diagnostic angiography. To visualize the vessel downstream to the CTO, a retrograde technique can be used by injecting the patent coronary artery; if collateral vessels are present between the two arteries, the vessel downstream of the CTO can be visualized (see Rentrop classification for collateral vessels previously described). CTOs are considered very complex lesions and contribute greatly to the SYNTAX score (see Chapters 40 and 41); less than 50% of CTO lesions in the SYNTAX trial were successfully treated by PCI. A specific score, the J-CTO, has been developed to predict the probability of successful guidewire CTO crossing within 30 minutes; independent predictors were previously failed lesion, blunt stump type, vessel bending, presence of calcification, and occlusion length of 20 mm or more. For the purpose of CTO angioplasty, another way to visualize the vessel distal to the CTO is the preprocedural use of CTCA. Using co-registration software, the vessel portion that is "missing" in the coronary angiogram is integrated with the CT image, thus providing guidance for the advancement of the intracoronary guidewire.

Calcific Lesions

Atherosclerotic calcifications are an important predictor of successful PCI. Although invasive coronary angiography can detect calcific coronary lesions, it has a low sensitivity for calcium and can only detect moderate to severe calcifications[66] (eFigs. 21.15 and 21.16). The gold standard for the evaluation of calcific lesions is CTCA (see Chapter 20). The extent of CAC correlates with the plaque burden (eTable 21.8), and because of the high sensitivity of CT scan for calcium, this imaging modality can detect plaque burden at a very early stage. As an alternative to CTCA, IVUS has been shown to have significantly higher sensitivity to detect coronary calcification than standard angiography, especially for milder calcifications.[66] Presence of a calcific arc greater than 180 degrees by IVUS is considered a severe calcification.[67]

The correct assessment of the calcium burden of a coronary lesion is important to determine the most appropriate treatment strategy. Highly calcific lesions are not compliant, and despite dilation before stent deployment, the risk of suboptimal stent apposition is high. Vessel dissection and distal embolization with aggressive vessel dilation before or after stent deployment are also possible complications. CABG might not be a valid alternative to PCI with extensive calcifications that do not allow for graft insertion on the native coronary artery, particularly in multivessel calcific disease. Atherectomy (rotational or orbital) may specifically treat calcific lesions during PCI (see Chapter 41).

Thrombotic Lesions

Presence of thrombus is usually associated with plaque rupture observed during ACSs (see Chapters 24 and 37 to 39). However, patients with generalized prothrombotic states can develop thrombus in the absence of plaque rupture. Thrombi are associated with higher rates of periprocedural complications. Thrombus load has been graded with the TIMI score as follows:

Grade 0, no cineangiographic characteristics of thrombus present;

Grade 1, images suggestive but not diagnostic for thrombus: reduced contrast density, haziness, and irregular lesion contour;

Grade 2, small thrombus present that is one-half or less the vessel diameter;

Grade 3, moderate-size thrombus present with greatest linear dimension more than one-half the vessel diameter but less than two vessel diameters (Fig. 21.17);

Grade 4, large thrombus present with a dimension that is two vessel diameters or greater;

Grade 5, recent total occlusion, which can involve some collateralization but usually does not involve extensive collateralization and tends to have a "beak" shape and a hazy edge or appearance of distinct thrombus; and

Grade 6, CTO, which usually involves extensive collateralization, tends to have a distinct, blunt cutoff or edge and will generally clot to the nearest proximal side branch.

TABLE 21.8 Myocardial Blush Score

| Grade 0	No myocardial blush or contrast density
Grade 1	Minimal myocardial blush or contrast density
Grade 2	Moderate myocardial blush but less than that obtained from the ipsilateral non–infarct-related coronary artery
Grade 3	Normal myocardial blush or contrast density comparable to that obtained during angiography of a contralateral or ipsilateral non–infarct-related artery
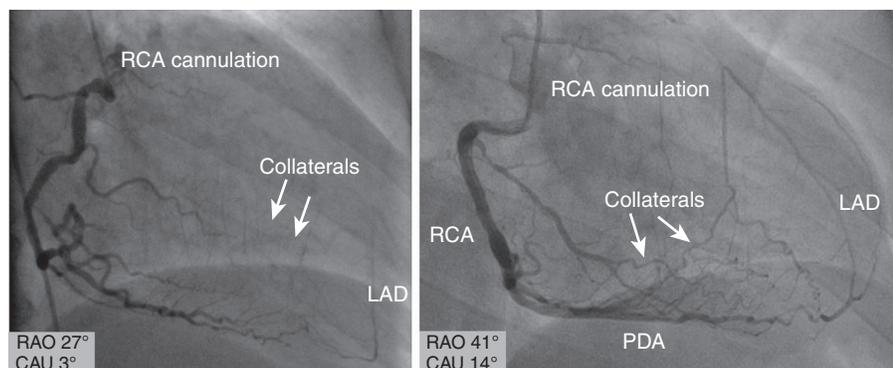
FIGURE 21.16 Collateral circulation from the right coronary artery to the left coronary artery. Left, Rentrop 2. **Right,** Rentrop 3. *CAU,* Caudal; *LAD,* left anterior descending coronary artery; *PDA,* posterior descending artery, *RAO,* right anterior oblique; *RCA,* right coronary artery. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)

ETABLE 21.7 Rentrop Classification of Coronary Collateral Classification

Grade 0	No filling of collateral circulation
Grade 1	Minor filling of collateral vessels with no retrograde visualization of the epicardial vessel
Grade 2	Partial retrograde opacification by the collateral vessels of the epicardial artery
Grade 3	Complete retrograde opacification by the collateral vessels of the epicardial vessel
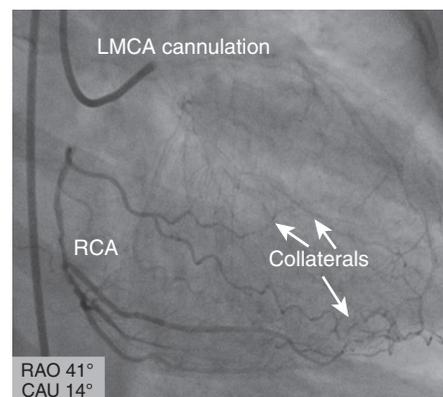
EFIGURE 21.14 Rentrop 3 collaterals. The left coronary artery provides collateral vessels to the right coronary artery (*RCA*); *CAU,* Caudal; *LMCA,* left main coronary artery; *RAO,* right anterior oblique. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
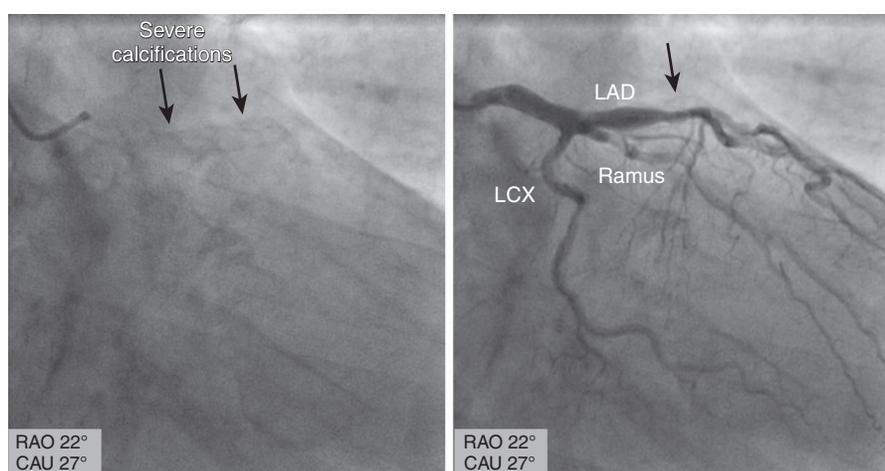
EFIGURE 21.15 Severe calcifications in the proximal and middle left anterior descending artery (*LAD*). **Left,** Calcifications can be seen before contrast injection. **Right,** Marked irregularities of the vessel diameter in the segments with severe calcifications. *CAU,* Caudal; *LCX,* left circumflex artery; *RAO,* right anterior oblique. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
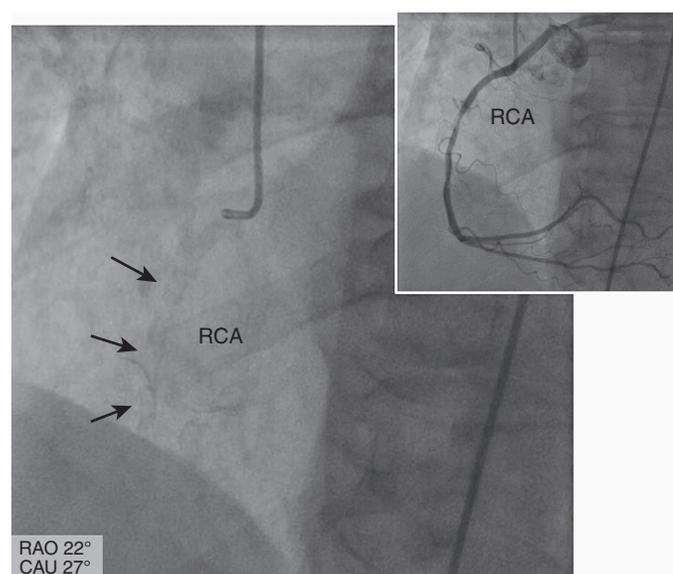
EFIGURE 21.16 Severe calcifications in the right coronary artery (*RCA*). **Left,** Calcification can be seen before contrast injection. **Right inset,** Marked irregularities of the vessel diameter in the segments with severe calcifications. *CAU,* Caudal; *RAO,* right anterior oblique. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)

ETABLE 21.8 Coronary Artery Calcium (CAC) Score

| SCORE (AGASTON)	PLAQUE BURDEN	DESCRIPTION/PROBABILITY OF CORONARY ARTERY DISEASE
0	Nonidentified	Negative test: very low risk of having a cardiovascular event in the next 10 years (<5%).
1-10	Minimal	Minimal atherosclerosis is present. Findings are consistent with a low risk of having a cardiovascular event in the next 10 years (<10%).
11-100	Mild	Mild coronary atherosclerosis is present. Mild or minimal coronary stenosis is likely.
101-400	Moderate	Moderate calcium is detected in the coronary arteries. There is a moderate risk of having a cardiovascular event within 10 years.
>400	Extensive	High risk of having at least one significant coronary stenosis (>90%). Significant risk of having a cardiovascular event within the next 10 years.
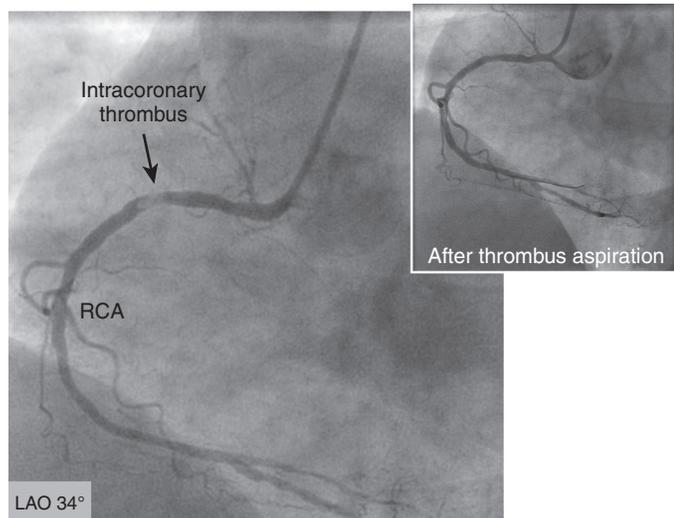
FIGURE 21.17 Grade 3 intracoronary thrombus in the proximal segment of the right coronary artery (*RCA*). **Right inset,** Absence of visible thrombus after aspiration. *LAO,* Left anterior oblique. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)

FIGURE 21.18 Type B coronary dissection. The *arrows* show two dissection sites in the diagonal branch. *CRAN,* Cranial; *RAO,* right anterior oblique. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)

Bifurcation Lesions

Bifurcation lesions account for approximately 15% of lesions requiring PCI. Bifurcation lesions are difficult to assess and treat because they may require intervention not only on the main vessel but also on the side branch as well. Thus, these lesions are associated with increased complications during and after PCI. During coronary angiography, bifurcations are evaluated according to the Medina classification, a three-digit system based on the evaluation of three distinct vessel segments in the following order: main artery in the segment proximal to the bifurcation, main artery in the segment distal to the bifurcation, and the side branch. To each segment, the operator can assign 0 if no significant CAD or 1 if a significant stenosis is present.

Coronary Dissections

Coronary artery dissection can be a life-threatening complication during PCI or a spontaneous event. Iatrogenic dissections can be caused by the advancement of the guidewire into the coronary artery or by plaque fracture after intracoronary balloon inflation. Based on their angiographic appearance, dissections can be classified (eTable 21.9 and Fig. 21.18). Not all dissections require treatment. Type A and B dissections are usually considered benign and might not require intervention, whereas types C and F are often major dissections associated with morbidity and mortality. Whenever necessary, the management of coronary dissection is stent deployment.

Spontaneous coronary artery dissections (SCADs) are rare. Their pathophysiology is not clear, but since they are more common in young women age 40 to 50 without any other cardiovascular risk factors, the etiology of SCAD has been associated with steroid hormones (see Chapter 91). In accordance with this theory, SCADs are more common within 2 weeks postpartum, when marked changes in hormonal levels are usually observed. Another possible explanation is the presence of undetected fibromuscular dysplasia (FMD), an arteriopathy that can involve different vascular districts, including renal arteries and coronary arteries (see Chapter 43). FMD can cause intramural hematomas that may result in SCADs. For example, in a study of 50 patients with SCAD, 86% were found to have FMD.[68]

CORONARY INTRAVASCULAR IMAGING

The diffusion of techniques for intravascular imaging has advanced the understanding of coronary atherosclerotic disease and has provid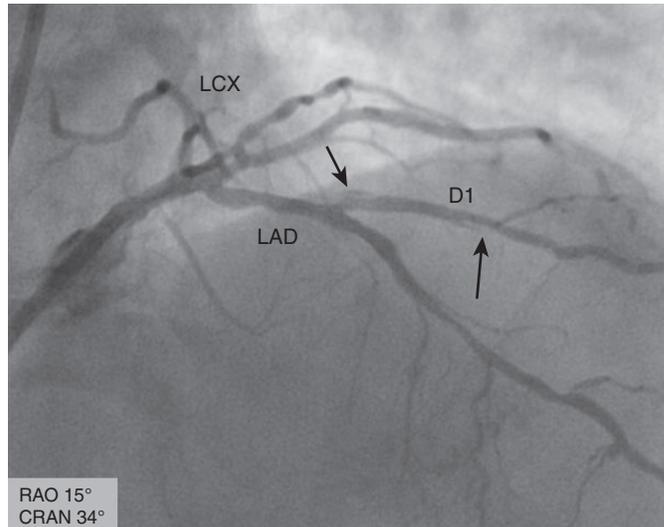ed additional information to angiography for the guidance of intracoronary stenting. IVUS and OCT are the main imaging modalities currently available in the catheterization laboratory for intravascular imaging.

Intravascular Ultrasound

An invasive coronary angiogram is a luminogram with poor specificity. Intravascular imaging such as IVUS and OCT can facilitate detailed assessment and characterization of CAD and aid optimization of revascularization with stent implantation. OCT provides better definition of the vascular endothelium and fibrous cap of atheromas,[69] while IVUS has higher vessel wall penetration that ensures a more detailed characterization of the atheroma core.

Principles. IVUS employs an intracoronary catheter with a transducer at the tip, which generates sound waves by converting electrical energy into acoustic energy.[70] The waves are reflected off arterial vessel walls, returned to the transducer, and subsequently converted into a working image for qualitative and quantitative evaluation. Contemporary IVUS catheters include transducers emitting sound waves at frequencies of 20 to 60 MHz, which provide high penetration (5 to 10 mm) for accurate assessment of vessel size and plaque burden. However, the low resolution (70 to 200 μ; 100-μ micron axial resolution parallel to radius and 200-μ lateral resolution perpendicular to radius) of gray-scale IVUS results in imperfect plaque characterization.[71] Virtual histology IVUS (VH-IVUS) overcomes the drawback of gray-scale IVUS and allows detailed interpretation of plaque morphology in the different stages of phenotypic plaque evolution, namely, pathologic intimal thickening, fibrotic plaque, thick- and thin-cap fibroatheroma, and fibrocalcific plaque.[72] VH-IVUS also clearly demonstrates necrotic core, dense calcium, and areas of plaque rupture. Comparatively, OCT using light wave technology permits a higher resolution of 5 to 10 μ, although with low penetration for optimal assessment of plaque morphology, as well as differentiation between thrombus and plaque.[73] Finally, near-infrared spectroscopy (NIRS) technology promotes understanding of coronary plaque lipid burden and may be used in conjunction with IVUS or OCT.[74]
Technology. There are two types of IVUS systems: single-element transducers and phased array transducers with multiple crystals arranged around the end of the delivery catheter.[70] A single-element transducer uses one element that generates and receives sound waves; a phased array system uses multiple transducers, which can be pulsed separately. The single-element type of catheter is commercially available with a transducer frequency of 40 to 60 MHz and a crossing profile of 2.9F to 3.2F compatible with 5F and 6F guides. Two such catheters are the Revolution (Volcano, California) and the Opticross (Boston Scientific). In contrast, the Eagle Eye Platinum catheter (Volcano) employs a phased array transducer with 20-MHz frequency and 2.9F crossing profile compatible with 5F guides. This catheter combines gray-scale and radiofrequency VH-IVUS assessment. The working length of the

ETABLE 21.9 Classification of Coronary Dissections

Type A	Minor radiolucent areas within the coronary lumen during contrast injection with no persistence of the contrast after dye has cleared from the lumen
Type B	Dissections are parallel tract or double lumen separated by a radiolucent area during contrast injection with minimal or no persistence after dye clearance
Type C	Presence of contrast outside the coronary lumen ("extraluminal cap") with persistence of contrast after dye has cleared from the lumen
Type D	Spiral ("barbershop pole") luminal filling defects frequently with excessive contrast staining in the dissected false lumen
Type E	Dissection appears as new, persistent filling defects within the coronary lumen
Type F	Dissection that leads to total occlusion of the coronary lumen without distal antegrade flow

Modified from the National Heart, Lung and Blood Institute (NHLBI) classification system for intimal tears.

catheter is 150 cm (60 inches), and the proximal end is connected to the IVUS console for image reconstruction, which may be operated within the catheterization laboratory by radiation scientists. A console connected to the angiography table permits the operator to obtain measurements online during the procedure.

Indications for Use. Intracoronary imaging is used in the vast majority of PCI procedures in Japan. Current guidelines on the use of IVUS[75] are summarized in eTable 21.10. ACC/AHA recommends IVUS use for assessment of indeterminate lesions in the LMCA (class IIa, level of evidence B) and non-LMCA (IIb, B) coronary arteries to determine the need for revascularization. IVUS is also recommended for optimization of stent implantation, particularly in the LMCA (IIa, B). Indeed, the use of IVUS in observational data has been associated with implantation of larger and longer stents and higher pressures for postprocedural dilation.[76] After PCI, IVUS is recommended for the investigation of stent failure to determine the mechanism of both in-stent restenosis (IIa, C) and stent thrombosis (IIb, C). Some investigators have also advocated IVUS use for the assessment and diagnosis of SCAD to visualize the tissue flap, true and false lumens, and intramural hematoma, thereby facilitating more accurate diagnoses.[77]

The European guidelines recommend use of IVUS to assess lesion severity and optimize the treatment for unprotected left main coronary lesions (Class IIa, level of evidence B). Furthermore, IVUS should be considered to detect stent-related mechanical problems leading to restenosis (Class IIa, level of evidence C) and to optimize stent implantation in selected patients (Class IIa, level of evidence B).[78]

Procedure

Similar to a standard PCI procedure, IVUS examination is performed through a coronary guide catheter system over a 0.0014-inch guidewire using standard techniques. The crossing profile of the IVUS catheter varies from 2.9F to 3.2F, which is compatible with a 5F to 6F guide catheter. It is conventional an adequate dose of anticoagulation for thrombus prevention and a bolus dose of intracoronary nitroglycerin to prevent arterial spasm and allow better imaging assessment.[62] Once at the desired location distal to the lesion, pullback of the catheter is initiated, which may be automated or manual, with a typical pullback rate of 0.5 mm/sec. IVUS-related complications are rare and usually self-resolving. The risk of coronary dissection or perforation with IVUS use is estimated at 1.6%.[79] Complications with IVUS catheter use may be related to size of the vessel and force used to advance the catheter (see eTable 21.11).

Interpretation

IVUS identifies three layers in normal vessel architecture, including the intima, media, and adventitia (Fig. 21.19). The *intima* is an echogenic, bright inner layer. The *media* is a hypoechoic, homogeneous area between the intima and adventitia composed of smooth muscle cells, collagen, elastic tissue, and proteoglycans. The *adventitia* is the outer reflective layer.[70] In the presence of atherosclerosis, there is evidence of medial thinning and deposition of plaque in the intima. This is typically noted to be heterogeneous due to variable impedance of the different plaque components (Fig. 21.20). Thrombus in the lumen may appear similar to plaque and cannot be clearly differentiated on gray-scale IVUS in the absence of a distinct interface between thrombus and plaque. Occasionally, IVUS may indicate the presence of blood flow through luminal thrombus. VH-IVUS identifies different plaque morphologies in a color-coded manner, and necrotic core, dense calcification, and fibrous and fibrofatty areas are all clearly noted.[72]

A coronary dissection may be diagnosed on IVUS with documentation of tissue flap, true and false lumens, and intramural hematoma.[80] Implanted coronary stents can be assessed using IVUS for both expansion and apposition. A gap between the stent struts and the vessel wall indicates malapposition; the greater the distance between the stent strut and the vessel wall, the worse the malapposition. Stent underexpansion and

malapposition are correlated with long-term adverse outcomes, including stent thrombosis. Real-time assessment of stent apposition and the need for post-dilation can be made online to allow specific management during PCI. Post-PCI neointimal hyperplasia caused by in-stent restenosis can be assessed using IVUS and appears as a hypoechoic area within the stent.[70]

In addition to immediate qualitative assessment of images for nature and extent of CAD, automated software analysis is available for both online and offline quantitative measurement of plaque burden and vessel size. Several validated measurements may be taken for evaluation of minimum lumen area, minimum lumen diameter, external elastic membrane (EEM) area, EEM diameter, plaque and media area (EEM area–lumen area), and plaque burden (plaque and media area/EEM area)[71] (Fig. 21.21). General criteria for significant obstructive disease include minimum lumen area less than 6 mm^2 in the LMCA or less than 4 mm^2 in the proximal LAD and other major vessels.[81]

For VH-IVUS, the gray-scale IVUS images recorded during pullback are combined with raw radiofrequency data captured on top of the R wave and reconstructed in a color-coded map by the IVUS-VH data recorder. The color-coded map identifies necrotic core (red), dense calcium (white), fibrofatty tissue (light green), and fibrous tissue (dark green). Thin-cap fibroatheroma on VH-IVUS is diagnosed in the presence of a greater than 30-degree arc of necrotic core abutting the lumen in three consecutive slices.[71]

Clinical Data

Several observational and randomized trial have shown long-term benefit from IVUS use for PCI attributed to greater minimum stent area and lower MACE. In the Assessment of Dual Antiplatelet Therapy with Drug-Eluting Stents (ADAPT-DES) study, IVUS was used in 39% of cases and was associated with longer stents, larger stent diameters, and higher inflation pressures in 74% of IVUS-guided cases.[76] The MATRIX (Comprehensive Assessment of Sirolimus-Eluting Stents in Complex
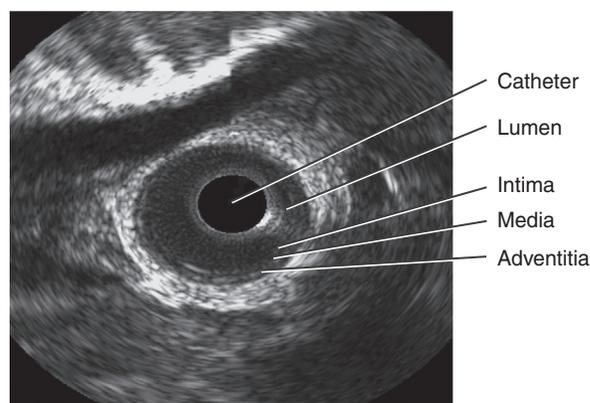

FIGURE 21.19 Normal vessel architecture on intravascular ultrasound (IVUS) demonstrating three layers: intima, media, and adventitia. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)

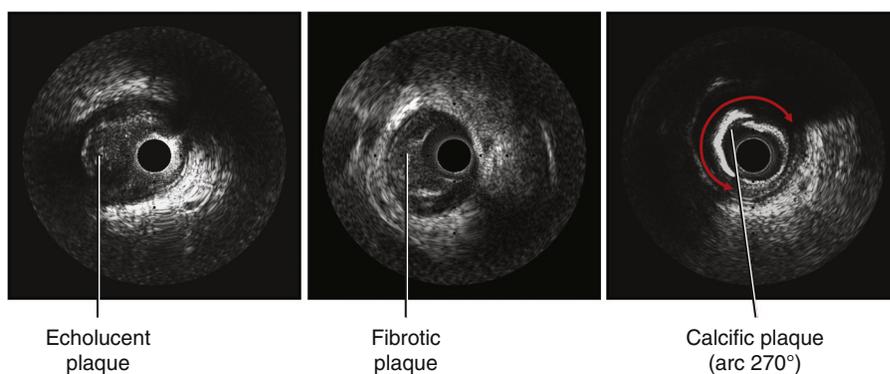Echolucent plaque   Fibrotic plaque   Calcific plaque (arc 270°)

FIGURE 21.20 Heterogeneous nature of different plaque components caused by variable impedance on IVUS. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)

ETABLE 21.10 Current Guidelines for Use of IVUS

EUROPEAN SOCIETY OF CARDIOLOGY[78]	AMERICAN HEART ASSOCIATION/AMERICAN COLLEGE OF CARDIOLOGY[75]
Diagnosis	
Class IIa (level of evidence: B)	***Class IIa (level of evidence: B)***
• IVUS should be considered to assess the severity of unprotected left main lesions	• IVUS is a reasonable option to assess angiographically indeterminant left main CAD
	• IVUS and coronary angiography are within reason 4 to 6 weeks and 1-year post cardiac transplantation to rule out donor CAD, detect rapidly progressive cardiac allograft vasculopathy, and provide prognostic information
Class IIa (level of evidence: C)	***Class IIa (level of evidence: C)***
• IVUS should be considered to detect stent-related mechanical problems leading to restenosis	• IVUS is a reasonable option to determine the mechanism of stent restenosis
	Class IIb (level of evidence: b)
	• IVUS may be reasonable in assessing non–left main coronary arteries possessing angiographically intermediate coronary stenoses (i.e., 50% to 70% diameter stenosis)
	Class IIb (level of evidence: C)
	• IVUS may be reasonable for the determination of the mechanism of stent thrombosis
Intervention	
Class IIa (level of evidence: B)	***Class IIb (level of evidence: b)***
• IVUS or OCT should be considered in selected patients to optimize stent implantation	• IVUS may be considered for the guidance of coronary stent implantation, especially in cases of left main coronary artery (LMCA) stenting
• IVUS should be considered to optimize treatment of unprotected left main lesions	***Class III***
	• IVUS for routine lesion assessment is not a recommendation if revascularization with PCI or CABG is not being contemplated

ETABLE 21.11 General Characteristics of Tissue Types by Optical Coherence Tomography (OCT)

TISSUE TYPE	BACKSCATTERING	ATTENUATION	GENERAL ASPECTS
Calcium	+	+	Sharp borders, low signal, with heterogeneous regions
Lipid	++	+++	Irregular borders, superficial high signal followed by very low signal
Fibrotic	++	+	Homogeneous bright tissue
Red thrombus	+++	+++	Superficial signal rich, low penetration, signal-free shadowing
White thrombus	+++	+	Signal rich, more penetration than for red thrombus
Media layer	+	+	Low signal region, limited by two signal-rich lines (IEL/EEL)
IEL/EEL	+++	+	High signal lines (20 µ)

IEL/EEL, Internal/external elastic lamina; +, low; ++, moderate; +++, high.
Modified from Bezerra HG, et al. Intracoronary optical coherence tomography: a comprehensive review clinical and research applications. JACC Cardiovasc Interv 2009;2:1035-1046.
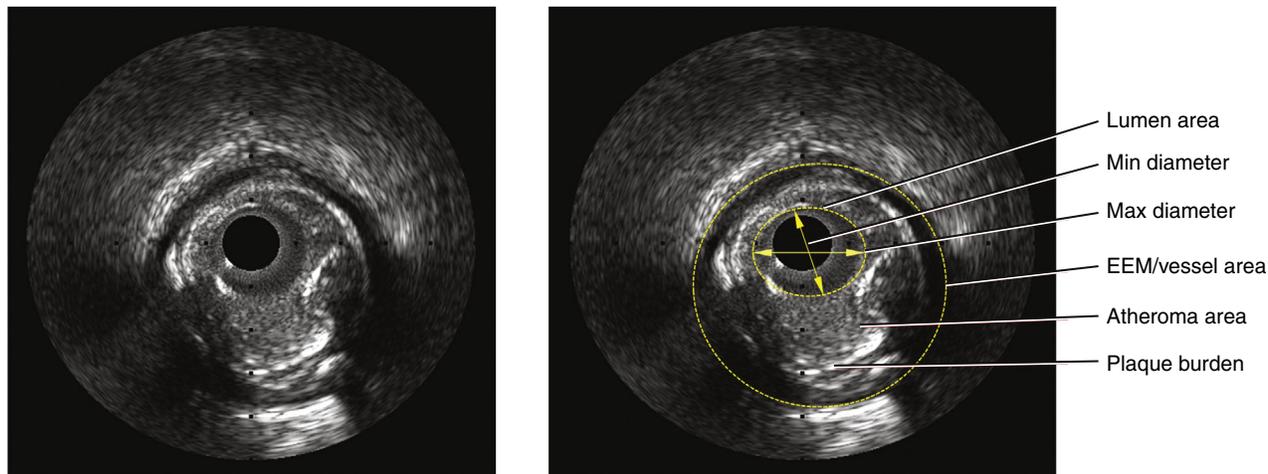
FIGURE 21.21 IVUS quantitative measurements for evaluation of lumen diameter and lumen area, external elastic membrane (EEM) area, and plaque burden. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)

Lesions) registry compared patients undergoing IVUS-guided versus non-IVUS-guided PCI. Both short- and long-term outcomes were significantly reduced with IVUS use.[82]

Furthermore, several randomized clinical trials have compared IVUS-guided with angiography-guided PCI. A meta-analysis summarizing those evidences confirmed benefits of IVUS guided PCI compared with PCI alone with a reduction in major adverse events, including cardiovascular death, MI, and target lesion revascularization.[83] Results confirmed in the following published Intravascular Ultrasound Guided Drug Eluting Stents Implantation in "All-comers" Coronary Lesions (ULTIMATE) trial, randomized a total of 1448 all-comer patients undergoing PCI to IVUS-guided PCI or angiography-guided PCI. At 12-month follow-up, this study showed that IVUS-guided DES implantation was associated with reduction in target vessel failure (0.530 [0.312 to 0.901]; $P = 0.019$).

The greater the complexity or lesion burden, the higher should be the use of intravascular imaging. For example, the EXCEL trial comparing 1905 patients with left main disease to PCI with cobalt-chromium everolimus-eluting stents versus CABG has shown an extensive use of intravascular imaging, pre- and post-stent implantation. In particular, IVUS guidance was performed in 722 of 935 (77.2%) patients who underwent PCI. Furthermore, in the Providing Regional Observations to Study Predictors of Events in the Coronary Tree (PROSPECT) study, almost 700 patients presenting with ACS underwent three-vessel coronary angiography and IVUS after PCI. The study showed that nonculprit lesion–related MACE (composite of all-cause death, cardiac arrest, MI, or rehospitalization due to unstable or progressive angina) was associated with plaque burden of 70% or more, minimum lumen area of 4 mm² or less, and thin-cap fibroatheroma less than 65 μ.[79] However, at 3 years, MACE was equally related to culprit and nonculprit vessel lesions. Use of intracoronary imaging may facilitate early detection and treatment of vulnerable plaque in nonculprit lesions and decrease long-term MACE.

An important limitation of IVUS interpretation is the need for coaxial catheter position during image acquisition.[84] However, dedicated software that allows real-time co-registration between angiogram and intravascular images has significantly improved this technique limitation (see paragraph Co-registration of Intravascular Imaging and X-Ray Angiography for Patients Undergoing PCI). The low resolution prevents clear differentiation between thrombus and plaque burden. In regard to applicability to the workflow of a busy catheterization laboratory, routine IVUS use is perceived to be expensive, time-consuming, and limited by operator skill. Further, IVUS does not allow visualization of the plaque lipid content, which might have important prognostic repercussions. To overcome this limitation, NIRS can be used.

Plaque Lipid Core Detection

The NIRS catheter emits near-infrared waves with a wavelength of 0.8 to 2.5 μ. Based on differences in absorption pattern of the light, different components of plaque and lipid are demonstrated in a map or chemogram of lipid deposition along the coronary artery.[85] The TVC Insight Catheter (Infraredx, Massachusetts) combines NIRS and IVUS (40 MHz), with a crossing profile of 3.2F compatible with 6F guide catheter systems. The TVC composite system allows superimposed imaging from NIRS-IVUS, which can provide information on vessel size, plaque burden, and areas of lipid-rich plaque.[86]

Hybrid catheters are also available, combining FFR-IVUS and IVUS-OCT to provide complementary data from these dual technologies. NIRS can be used before PCI to identify lipid-rich plaques that might be at risk of periprocedural myonecrosis and distal embolization, to evaluate the necessity of distal protection filters.[87] The Coronary Assessment by Near-infrared of Atherosclerotic Rupture-prone Yellow (CANARY) Trial was a randomized clinical study on 57 patients undergoing coronary angiography and NIRS-IVUS imaging. Patients were randomized to angioplasty with or without a distal embolic protection device. The results showed that lipid-rich plaques identified by NIRS are associated with higher rates of periprocedural MI. However, the use of a distal protection filter did not prevent myonecrosis after PCI at lipid-rich plaques.[88]

Optical Coherence Tomography

Cardiovascular OCT is a catheter-based imaging technique that uses light and its reflection to create images of the coronary wall. Initially developed to perform imaging of the retina, OCT technology rapidly expanded to various biomedical and clinical applications.

Principles. OCT is based on a fiberoptic wire with a rotating lens that emits near-infrared light (approximately 1300 nm) and records the light reflected from the analyzed tissue. One of the most valuable properties of OCT is its high resolution, up to 10 μ for axial resolution and 20 μ for lateral resolution (i.e., superior to IVUS). Although resolution is high, tissue penetration ranges from 1.0 to 3.5 mm (i.e., inferior to IVUS).

The images created by OCT are derived from the delay that results from the light traveling to the target tissue and back to the lens. Images are generated by measuring the echo time delay and the intensity of reflected light. The speed of light does not allow direct measurement of the echo time delay, so a technique known as *interferometry* has been developed to analyze the reflected light signal. With this technique the light reflected from target tissue is measured by correlating it with light that has traveled a known reference distance. Cross-sectional images of the vessel are created by obtaining multiple axial scans as the fiberoptic wire is simultaneously rotating and pulled back rapidly along the vessel.

Two types of OCT imaging systems have been developed: *time-domain* OCT (TD-OCT) and Fourier-domain OCT, also known as

frequency-domain OCT (FD-OCT). Using a novel wavelength-swept laser as a light source, FD-OCT imaging systems provide superior signal-to-noise ratio and allow significantly faster imaging speed compared with the earlier time-domain technology. Recent FD-OCT imaging systems are capable of acquiring images at a rate of 180 frames/second at a pullback speed of up to 36 mm/sec. One single pullback allows imaging of up to 75 mm of the vessel.

Early OCT technology required a complete displacement of blood from the viewing field to generate high-quality images. An over-the-wire low-pressure occlusion balloon catheter with distal flush ports to infuse saline or Ringer lactate can be used to remove erythrocytes from the viewing field. However, the accelerated pullback speed provided by FD-OCT no longer requires occlusion of the vessel, with a shift toward a nonocclusive approach with flushing of contrast.

Clinical Applications

OCT can be used to guide diagnosis during coronary angiography as well as procedure planning and assessment of PCI, as indicated in an initial clinical study.[89]

Normal Vessel Wall

In a healthy vessel, OCT visualizes the coronary artery wall as a three layered structure (Fig. 21.22). The intima appears as a thin, highly reflective, and signal-rich layer. Although not able to visualize the "healthy" intima layer since that is beyond its resolution, OCT can identify intimal thickening: an early stage of atherosclerosis that appears as a signal-rich, homogeneous, thin rim of tissue. The media layer appears as a dark, low-reflective band with a mean media thickness of 200 μm delimited by the internal elastic lamina, an adluminal signal-rich line, and the external elastic lamina, an abluminal signal-rich line. With its limited tissue penetration (1 to 1.5 mm), OCT is not able to characterize vessel remodeling. Finally, the adventitia appears as a signal-rich, heterogeneously textured outer layer.

Stable Coronary Artery Disease

In patients with stable CAD, OCT imaging is used for quantitative assessment of the lesion by measuring the minimal lumen area (MLA). For the identification of hemodynamically severe coronary stenosis, OCT was shown to have only moderate diagnostic efficiency, when using the gold standard FFR as a reference, and similar accuracy compared with IVUS.[90]

Plaque Morphology

High-risk features of plaques, including a large lipid core, thin fibrous cap, and increased macrophage infiltration, can be detected by OCT.[91]

First, OCT provides the possibility to distinguish between fibrotic, lipid-rich, and calcified lesions (eTable 20.11). Lipids are signal-poor regions with diffuse borders, while fibrous tissue appears as a signal-rich homogenous region, and fibrocalcific or calcific tissue appear as well-delineated, signal-poor regions with sharp borders.

Second, OCT is the only imaging technique that in vivo allows an accurate evaluation of the fibrous cap and macrophage content. Smooth muscle cells organized in a collagenous-proteoglycan matrix, with varying degrees of infiltration by macrophages and lymphocytes, compose the fibrous cap of the plaque. Thin fibrous cap, lower collagen density, thinner collagen fibers, or low number of smooth muscle cells (SMCs) are highly related to plaque rupture. OCT has shown high accuracy in detecting thin fibrous cap, with a specificity of 79% and sensitivity of 90%.[92] The implemented

polarization-sensitive OCT (PS-OCT) technology is able to assess collagen density and its polarization as well as quantify the presence of the SMCs. In particular, PS-OCT allows measurement of birefringence, a property that is elevated in tissues containing proteins with an ordered structure such as collagen and SMCs actin/myosin. Accordingly, a high positive correlation between PS-OCT with thick collagen fiber content and SMC density has been demonstrated.

Finally, OCT may allow visualization of plaque's macrophages that appear as a signal-rich punctate dots, distinct or confluent, which exceed the intensity of background speckle noise. Macrophages may often be distributing at the boundary between the bottom of the cap and the top of a necrotic core. Also for the evaluation of macrophages, dedicated software has been developed that provides a higher accuracy than simple visual inspection.

Acute Coronary Syndrome

In patients with ACS, OCT has not only high sensitivity to detect intraluminal thrombus but also the capability of discriminating between red and white thrombus (Fig. 21.23). Furthermore, OCT has higher sensitivity in detecting fibrous cap rupture (Fig. 21.24) and fibrous cap erosion compared with IVUS.[89] The capability of OCT to discriminate the underlying mechanism of ACS has direct impact on further treatment
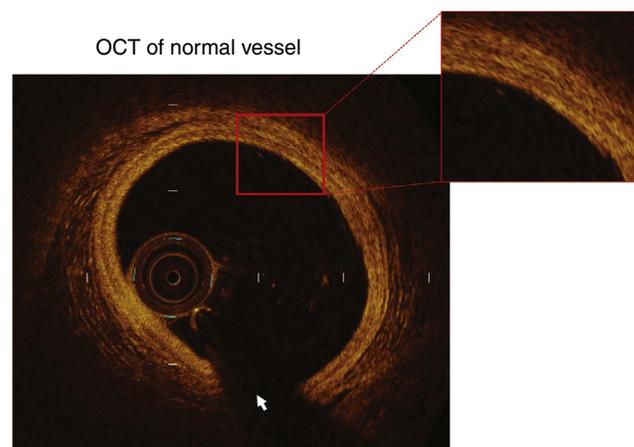

OCT of normal vessel

FIGURE 21.22 Optical coherence tomography (OCT) of a healthy vessel: The coronary artery wall is visualized as a layered structure. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
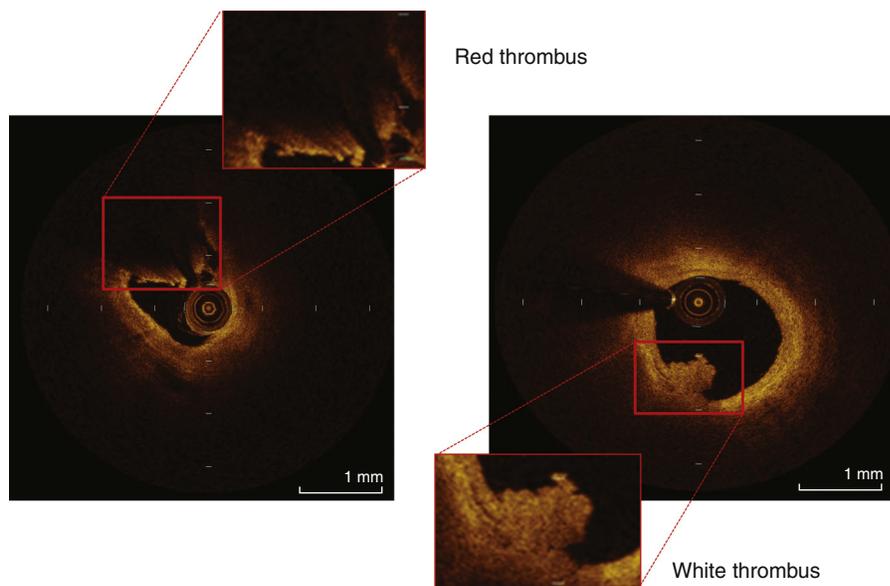

Red thrombus

White thrombus

FIGURE 21.23 OCT is capable of discriminating between red **(left)** and white **(right)** thrombus. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
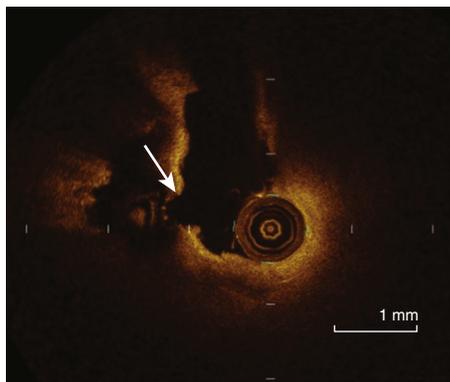
FIGURE 21.24 OCT of a ruptured fibrous cap. *Arrow* indicates the rupture site. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
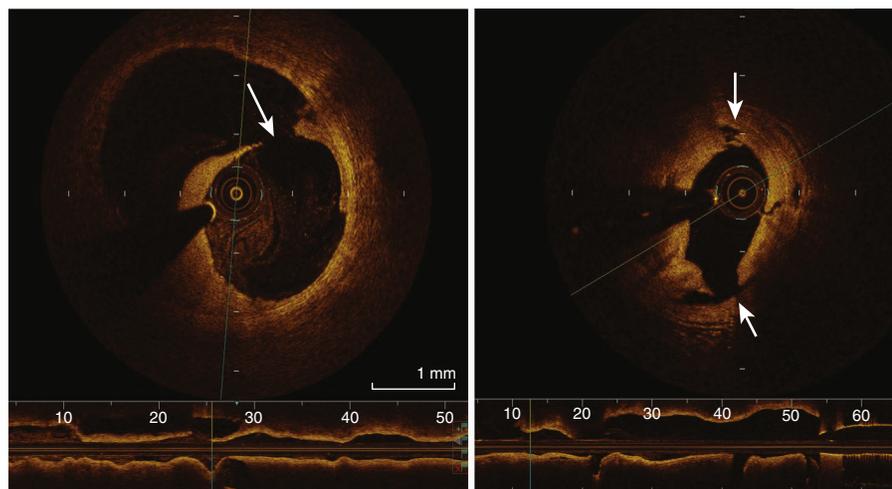

FIGURE 21.25 OCT of a dissected vessel. **Left,** Spontaneous coronary artery dissection (SCAD). **Right,** Dissection after balloon pre-dilation. *Arrows* indicate the sites of rupture. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)
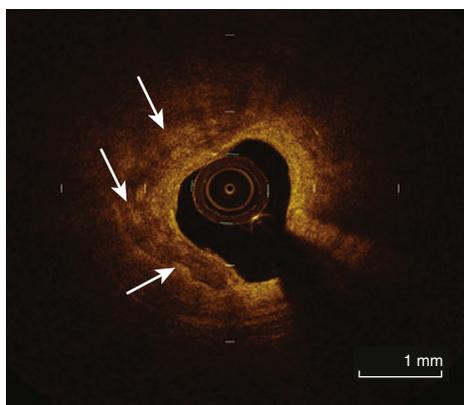

FIGURE 21.26 OCT of a severely calcified lesion. *Arrows* indicate some of the calcifications. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)

strategy. Furthermore, the possibility to detect vulnerable plaques among the nonculprit lesions is also extremely important to prevent recurrence of ischemic events. In SCAD (Fig. 21.25), one of the non-CAD-related causes that can be detected by OCT, unnecessary stent implantation, can be avoided.

Procedure Planning and Lesion Preparation
In procedural planning for PCI, OCT is a valuable tool for assessing the landing zone and especially for measuring calcium thickness.

Concentric but thin calcium allows the use of regular or scoring balloons, whereas thicker concentric calcium may require atherectomy[93] (Fig. 21.26). OCT imaging can guide adequate lesion preparation, which is crucial for optimal stent deployment, but it can also be helpful for stent selection. Stent diameter, as well as length, can be chosen according to measurements of the reference vessel diameter both proximal and distal to the target lesion, as well as the lesion length. The fast-pullback acquisition of images makes FD-OCT less susceptible to artifacts resulting from heart motion, and therefore an optimal tool for accurate measurement of lesion length.

Assessment After Percutaneous Coronary Intervention
Post-PCI OCT offers the possibility to detect postprocedural complications and to provide information on the potential need for further procedural steps. OCT is used for ensuring appropriate stent expansion and evaluating apposition of the stent with the vessel wall (Fig. 21.27). Stent underexpansion, associated with small minimal stent area measured by OCT, was shown to be an independent predictor of device-oriented clinical endpoints, including cardiac death, target vessel–related MI, target lesion revascularization, and stent thrombosis.[94] By allowing the determination of the distance of each stent strut from the vessel wall, OCT is capable of detecting the percentage of malapposed stent struts, which were shown to be associated with delayed neointimal coverage.[95] The presence of uncovered stent struts detected by OCT was proposed as an independent predictor of late stent thrombosis in drug-eluting stents.[96] In particular, for bioresorbable scaffolds, the rate of stent thrombosis seems to increase significantly in malapposition. Therefore, use of OCT is strongly recommended after deployment of such a stent. *Stent edge dissection* (SED) is another post-PCI complication that is detectable by OCT that has been shown to be associated with adverse clinical outcomes.[97] However, the vast majority of SEDs diagnosed by OCT heal without further treatment, and additional stenting should be reserved for the presence of intramural hematoma, as recently suggested.[93] Deployment of stent edges within the normal vessel wall and appropriate selection of stent diameter may help to avoid SED.[97] Compared with SED, tissue protrusion is a less investigated post-PCI complication. Irregular tissue protrusion was shown to be associated with device-related clinical endpoints, which were primarily driven by target lesion revascularization.[94] However, the further management of tissue protrusion detected by OCT is not yet clear.

CO-REGISTRATION OF INTRAVASCULAR IMAGING AND X-RAY ANGIOGRAPHY FOR PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION. During coronary invasive procedures, it may be difficult to identify corresponding segments between intracoronary imaging and angiography. To overcome this limitation, several tools have been recently developed, providing a real-time point-to-point co-registration that allow a precise integration of angiographic and intravascular imaging. Co-registration tools are available for both IVUS and OCT. These technologies offer more precise localization and characterization of the lesions (eFig. 21.17) and support an optimal stent implantation (eFig. 21.18). To understand the impact of co-registration on the angiographic results, several studies have been conducted. The prospective single-arm DOCTOR (Does Optical Coherence Tomography Optimize Revascularization) study, including patients admitted for elective PCI, assessed the relevance of co-registration for a correct stent implantation. Without access to co-registered data, the segment of the target lesion indicated by OCT was left uncovered by the stent in approximately 70% of the stented population.[98]

EFIGURE 21.17 Two different OCT imaging cases before PCI to clarify angiographic haziness: calcified bifurcation lesion (**A**) and a large red thrombus in another (**B**).

EFIGURE 21.18 Two post-stent images. **A,** Well-expanded and apposed stent (no red marks on three-dimensional stent reconstruction shown in the longitudinal view). **B,** Well-expanded stent with a small malapposition (only few struts shown in red on stent reconstruction).

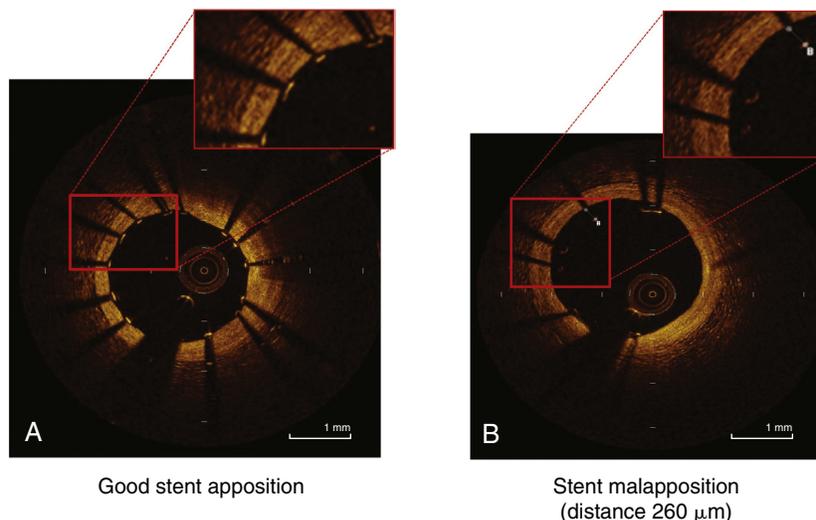**Good stent apposition** **Stent malapposition**
(distance 260 μm)

FIGURE 21.27 OCT is capable of evaluating apposition of a stent. **Left,** Good stent apposition. **Right,** Stent malapposition. (Courtesy Dr. Annapoorna Kini, Icahn School of Medicine at Mount Sinai, New York, NY.)

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