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Diagnostic approach of coronary atherosclerosis through invasive procedures: indications and applications of coronary angiography

Abordaje diagnóstico de la aterosclerosis coronaria mediante procedimientos invasivos: indicaciones y aplicaciones de la angiografía coronaria

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The cardiac catheter was… the key in the lock.
André F. Cournand
1956 Lecture Nobel Prize for Medicine

INTRODUCTION

Coronary angiography is understood as the visualization of the coronary arteries through the injection of a radiopaque contrast material and recorded in radiographic images in digital form. This technique is now the most reliable way to identify coronary anatomy and pathology for therapeutic decision making in patients with myocardial ischemia. Over the next chapter we shall review the most important aspects about its indications and clinical applications in diagnosis and therapeutics for coronary heart disease.

THE PROCEDURE

The pioneering studies in cardiac catheterization by Forssmann, Cournand, and Richards, earned them the Nobel Prize in Physiology or Medicine in 1956. A few years later, Mason Sones performed an aortography by injection in which the catheter accidentally slipped into the right coronary artery, thus giving the first direct angiographic image of a coronary artery in a live patient. The technique was then methodically developed by Sones himself through brachial dissection and later through percutaneous femoral approach by Melvin Judkins.[1] From then on, important breakthroughs in the methodology, mainly the radial artery approach, and the technological advances in guidewire and high flow catheters, as well as digital imaging techniques have made the coronary angiography one of the most used clinical methods in ischemic heart disease. This procedure is safe, very well tolerated and it usually takes between 20 to 40 minutes to be done. In brief, using local anesthesia, a vascular catheter is inserted through the radial or femoral artery employing a percutaneous technique and a 2 mm vascular introducer. With preformed catheters coronary arteries can be easily engaged and images are obtained using a contrast agent. Patients could be sedated, if necessary, pre-treated with heparin 50-100 U/kg and intracoronary nitroglycerin as needed. Images of both coronary arteries in different angles are recorded in a digital radiographic system. At the end of the procedure or intervention, the catheters and introducers are removed, and external arterial compression is applied, preferably with pneumatic compressors. Cardiac complications in a diagnostic procedure are infrequent and they occur in less than 1% of all cases, including acute myocardial infarction, unscheduled revascularization, stroke, coronary dissection,

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pericardial effusion or even death (0.01%).[2] Major hemorrhage occurs, including subjects undergoing coronary intervention, in 1.3% of patients with a radial approach and 2.5% with a femoral one.[3] The patient usually remains under hospital surveillance until the next day, but in low-risk patients without complications from the procedure, an «outpatient» protocol with early discharge within 24 hours may be considered. It is concluded that diagnostic coronary angiography is a safe and well-tolerated procedure with a very low incidence of complications and short hospital stay.

ANGIOGRAPHIC EVALUATION OF CORONARY ATHEROSCLEROSIS

The images obtained of the coronary arteries by angiography only show the vascular lumen, seen in a two-plane projection. This allows the cardiologist to assess and measure the magnitude of the coronary lesions according to the degree of stenosis of the vascular lumen in relation to the «healthy» reference segments *(Figure 1A)*.

Therefore, it is not possible to visualize the arterial wall, the degree of vascular remodeling, and the characteristics and volume of the plaque. Furthermore, it is necessary to obtain images in complementary projections to visually «reconstruct» the lesions when these are asymmetrical or eccentric. A stenosis is considered «significant» when it is > 50% of the visible diameter or if it obstructs > 75% of the vascular lumen area. Greater obstructions above these percentages have shown a reduction of the distal and reserve flow, as well as a high clinical correlation and with non-invasive ischemia stimulation studies.[4] The direct subjective assessment of the occlusion magnitude will depend on the characteristics of the lesion, the quality of the radiographic images, angulation or the presence of secondary vessel branches or bifurcation. All this factors explain that a great intra and inter-observer variations could exist. The use of quantitative coronary angiography or coronary intravascular ultrasound may be necessary for a more precise characterization and evaluation of the plaque, especially in borderline, complex or difficult to assess lesions *(Figure 1B)*. Even more, it would be ideal whenever possible, the use of functional tests such as the measurement of the pressure differences across a coronary artery stenosis through the «fractional flow reserve» (or FFR) with or without pharmacological therapy to evaluate the significance of the obstruction. This has proven not only to be a better form of identification of the repercussion of coronary stenosis, but also may establish therapeutic indication and prognosis in a more precise way. The cost and time of the procedure, however, has made its use infrequent in routine practice.

In addition to the magnitude and degree of stenosis, the coronary angiography allows to establish various aspects of the morphology and complexity of the plaques. The length of the lesion, its relationship with other vessel branches, eccentricity, ulceration, areas of calcification, dissection or thrombus, should always be considered. In case of total occlusion, it is important to evaluate the degree of distal flow or perfusion, as well as the presence of collateral circulation. For each of these variables there are numerous classifications that extend beyond the scope of this review. Finally, it is important to establish the location and extension of the disease and the identified lesions, for which it is not only useful the correct knowledge of the anatomy but the use of the international nomenclature and definition of the different segments of the coronary tree.[4] With the information of morphology, complexity and extension, the risk for every case may be established using different risk scores for decision-making. One of the most used risk calculators is the SYNTAX score; that has been thoroughly validated, is easy to do at the website (www.syntaxscore.com), and it may estimate the risk of clinical events and the prognosis with the different revascularization treatment alternatives.[5]

CORONARY INTRAVASCULAR ULTRASOUND (IVUS)

As mentioned, the main limitation of coronary angiography is that the images only depict the vascular lumen, creating a «luminogram». The IVUS permits the direct visualization from the

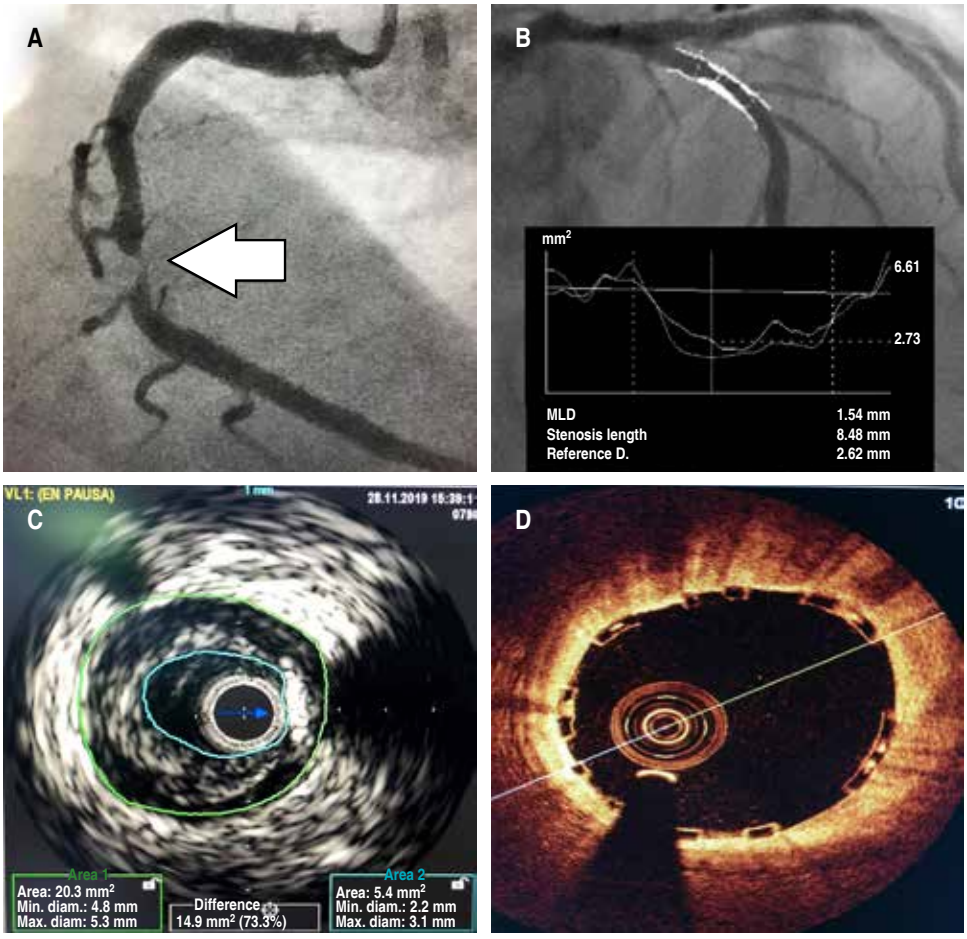

Figure 1:

Images of atherosclerotic plaques through invasive procedures: **A)** Angiography of a critical lesion of the right coronary artery (arrow). **B)** Quantitative coronary angiography of a borderline lesion in the proximal left anterior descending coronary artery with measurements. **C)** Intravascular ultrasound showing a significant obstructive stable plaque. **D)** Optic coherence tomography after placement of a coronary stent.

interior of the vessel, enabling a circumferential analysis of the vascular wall. The procedure is done using a guiding catheter for coronary angioplasty and a 0.014" coronary guide wire. A special catheter containing the miniaturized ultrasound transducer of < 1 mm is then advanced to the distal segment of the coronary artery and a slow pullback is done, usually by a mechanical retraction system at a rate of 0.5 mm/s. The images obtained with transducers of 40 to 60 MHz, allow a full vision of the vascular wall at high resolution *(Figure 1C)*. The procedure lasts an additional 10 to 15 minutes, and it may be performed as many times as necessary in a single intervention. The complications are quite uncommon with experienced hands, being coronary vasospasm the most frequent (1%). The information gathered represents a considerable segment of the entire length of the coronary vessel and it reveals the extension, magnitude, and characteristics of the disease with great detail, being important in the decision-making process. The measurement at the reference segments, and at the level of stenosis called «minimal luminal area» shows the severity of the lesion, being less than 4.0 mm^2 a significant obstruction in non-left-main lesions. The length, volume, plaque characteristics, areas of dissection, vulnerable plaques or calcifications can be seen with great detail and may prove to be important in the decision-making process. In case of a percutaneous coronary intervention with a stent, it enables a better selection of the material and a better outcome through the optimal placement, attachment and post-dilation that decreases the complications of thrombosis and restenosis in the medium or long-term follow up. Undoubtedly, it is a great advance in the assessment of ischemic

heart disease, and it let to make better therapeutic decisions.[6]

OPTICAL COHERENCE TOMOGRAPHY (OCT)

This novel imaging technique generates tomographic images from almost-infrared light produced by a rotational optic fiber. The images have a significantly higher resolution (10-20 µm) but less penetration. The technique to perform the procedure is similar to the one described for the intravascular ultrasound. The difference is that in order to avoid the interference of the red blood cells, it becomes necessary the administration of a contrast agent, synchronized with a rapid automated retraction system that obtains and reconstructs the images in seconds. It is ideal for visualizing the intimal layer, dissection areas and vulnerable plaques. The adequate placement and attachment of stents may be clearly seen even in longitudinal and even tridimensional reconstruction *(Figure 1D)*. Although it is less used than IVUS, both techniques are useful and complementary.[6]

INDICATIONS OF CORONARY ANGIOGRAPHY

The indication for invasive coronary angiography will essentially depend on the patient's clinical status. In all cases the goal is to establish the diagnosis, prognosis, and the type of treatment with or without coronary revascularization. We may distinguish three types of indications: acute coronary syndromes, chronic coronary syndromes or as a routine procedure for direct diagnosis *(Table 1)*.

ACUTE CORONARY SYNDROMES

This may be the clearest indication for an invasive coronary angiography. The proven benefit of arterial reperfusion therapy in this clinical condition and the importance of timing have been deemed essential in the treatment of coronary syndromes. In case of a ST-segment elevation myocardial infarction the early coronary angiography, whether in the context of primary angioplasty or following fibrinolysis, have a clear recommendation in international guidelines (class I, level A). The procedure should also be done between 12 to 24 hours if the patient remains symptomatic, clinically unstable or with signs of important residual ischemia (class I, level C).[7] In patients with very high-risk non-ST-segment elevation myocardial infarction, immediate (within 2 hours) coronary angiography with an invasive strategy is suggested, or within 24 h in patients with high risk, including ST-segment depression or dynamic EKG changes, cardiac biomarkers, signs of ischemia or with any other high-risk clinical variables (GRACE score > 140).[8] After this period of time, the decision will depend on the clinical condition, evolution and the level of induced ischemia.

Table 1: Indications for invasive coronary angiography.

ACS-STEMI	Angiography and primary angioplasty are recommended over fibrinolysis in patients with < 12 hours of onset of symptoms or in > 12 hours, after fibrinolysis, if symptoms persist, or there are hemodynamic instability or severe arrhythmias
ACS-NSTEMI	Urgent angiography (< 2 h) is indicated in very high-risk patients. Within 24 hours at high risk: persistent angina, ECG changes or enzyme elevation. In 12-48 h if symptoms persist, or there are severe ischemia or LV dysfunction
CCS	Persistence of symptoms after optimal medical treatment. Severe ischemia unveiled with non-invasive studies, or inconclusive results with a high probability of the disease. Significant high-risk lesions on coronary CT angiography
Direct	Before high-risk heart surgery, or organ transplantation. Prior to surgery for aneurysm or aortic dissection. Hypertrophic cardiomyopathy with angina or Kawasaki disease with documented coronary aneurysms

Indications for invasive coronary angiography: ACS-STEMI = ST segment elevation acute coronary syndrome; ACS-NSTEMI = non-ST segment elevation acute coronary syndrome; CCS = chronic coronary syndrome; EKG = electrocardiogram; LV = left ventricular.[7-9]

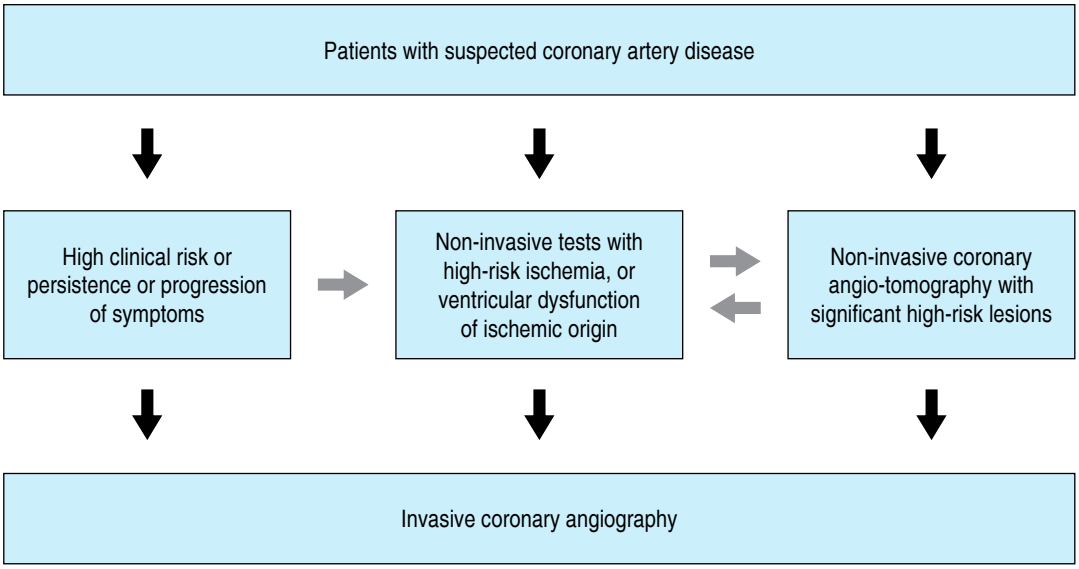

Figure 2: Diagnostic pathways in patients with suspected coronary artery disease. Solid black arrows show the preferred decision algorithm, and alterative personalized options in gray arrows.

CHRONIC ISCHEMIC HEART DISEASE (CHRONIC CORONARY SYNDROME)

It is this condition the one with greater difficulty for clinical decision-making within the diagnostic algorithm of ischemic heart disease *(Figure 2)*.

In high or very high-risk patients, whether because of symptom persistence (severe, progressive, or refractory angina) or severe ischemia with high-risk markers put in evidence through non-invasive tests, it becomes clear that an invasive coronary angiography with eventual subsequent revascularization is the step to follow. With low-risk or low probability of coronary atherosclerosis patients, the recommended diagnostic study is a non-invasive CT coronary angiogram. However, if extensive or critical proximal high-risk disease is documented with this diagnostic study, the patient must be referred for an invasive coronary angiography. The same applies to patients with documented ventricular dysfunction and a history or suspicion of chronic ischemic heart disease where invasive coronary angiography is indicated because of the probability of high-risk lesions, and the benefit of revascularization in most of these cases.[9] The more difficult decision lies in the intermediate-risk group, in which it is necessary to consider not just the risk profile but the co-morbidities, characteristics of the symptoms, the grade and extension of ischemia in each case, and of course the patient's preference. The ischemia trial compared conservative treatment with optimal medical management versus an initial invasive strategy in 5,179 patients with chronic ischemic heart disease, without finding significant differences in the occurrence of major clinical events in both study groups after three years of follow-up.[10] This demonstrates the efficacy of an adequate medical treatment and it shows that an invasive strategy, either with angioplasty or surgery, must be reserved for those patients that remain symptomatic or that exhibit severe ischemia or high-risk coronary stenosis with a poor prognosis. Finally, it may become necessary to perform and invasive coronary angiography if the symptoms or the non-invasive studies are inconclusive and if the clinical conditions of the patient suggest the likelihood of coronary artery disease or possible benefit of revascularization. Certainly, in the absence of symptoms, without significant documented ischemia or the absence of obstructive lesions by non-invasive angio-tomography, there is no indication to perform an invasive coronary angiography.

DIRECT DIAGNOSTIC STUDY

Some critical clinical conditions may indicate a direct coronary angiography as a routine procedure. Some of them are the preoperative evaluation before cardiac surgery in heart valve disease, before cardiac or organ transplantation, patients with proximal aortic disease with dissection or aneurysm subject to surgery, hypertrophic cardiomyopathy with persistent angina or asymptomatic Kawasaki disease with documentation of coronary aneurysms. In some countries, certain labor regulatory conditions in high-risk jobs, may indicate an invasive procedure but in this instance CT non-invasive coronary angiography has become the first line diagnostic study.

PERSPECTIVE AND CONCLUSIONS

Under the Hippocratic precept *primum-non-nocere* or first, do no harm, any clinical study, especially if it is invasive, must have a clear indication and a prognostic and therapeutic objective. The technological advances are surprising; they have resulted in the ability to see the coronary anatomy rapidly, and directly, with great accuracy and precision. The great progress with non-invasive studies, especially CT angiogram, has also yielded impressive results, is necessary to consider the best alternative for each case. It should be emphasized that cardiac catheterization and invasive angiography entail high costs, potential complications and may lead to specific therapeutic decisions. Therefore, the indication must be substantiated by risk determinants that put the need for subsequent revascularization in the therapeutic scenario, counting with the empowerment of the patient to participate in this decision. For interventional cardiologists, few moments are as intense and as satisfying as being in the cardiac catheterization laboratory. They will give what they were to be in the catheterization room every day, but at the same time will do everything possible to ensure that patients who do not require an invasive study were in the same room. If the catheter was «the key in the lock», let us use it wisely.

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