

Investigation of Angiographically Moderate Lesions in the Left Main Coronary Artery. A Clinical Indication for Intracoronary Ultrasound

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Since its implementation, coronary angiography has been the reference test for the diagnosis of coronary disease. Despite the development of several methods for morphological and functional assessment of coronary lesions, angiographic evaluation, whether visual or through programs for digital measurement, is the method used in the majority of procedures undertaken in clinical practice. In most studies, measurement of the angiographic image is considered sufficient to safely determine the significance of a coronary lesion, to orient coronary interventions, to assess the immediate results of a procedure, and to perform follow-up studies.

Although it has an unquestionable, well-recognized value, angiography presents a series of limitations that are a consequence of its inherent characteristics. Among these is the fact that it provides a 2-dimensional view of the vessel lumen, although, an attempt is made to simulate a 3-dimensional study by acquiring several views. The limitations of angiography may even impede correct decision-making in specific situations. The presence of branching vessels, diffuse arteriosclerotic involvement or angles, and location of the lesion in the ostium or bifurcation may make proper lesion assessment impossible. Because of remodeling phenomena, stenosis may be detectable by angiography only when it exceeds 40% to 50% of the total area of the artery,^{1,2} and may go unnoticed in the earliest stages of the disease. In addition, angiography offers little information on the composition of the atheromatous plaque and has little sensitivity for the detection of calcium.³ Angiographic quantification of the degree of stenosis of a lesion, based on ratios established using reference segments considered to be healthy according to the coronary angiography, can sometimes be erroneous. In cases of diffuse involvement, the reference segments may be considerably diseased

and this fact may not be evident on angiography; hence, the grade of stenosis might be underestimated.⁴ Despite the use of automatic measurement methods, the intraobserver and interobserver correlations with this technique remain low, particularly in situations of poor visualization, moderate lesions, in-stent restenosis, or presence of calcium.^{5,6}

Technological developments over the years in catheterization laboratories have provided tools that complement and improve the quality of the information offered by angiography. Although other diagnostic techniques are available and currently in use, only intracoronary pressure measurement with a pressure monitoring guidewire and intracoronary ultrasound are in clinical use for coronary interventions. According to data from the Registro de Actividad de la Sección de Hemodinámica y Cardiología Intervencionista (Activity Registry of the Catheterization and Interventional Cardiology Section) of the Sociedad Española de Cardiología (Spanish Society of Cardiology),⁷ in 2005, 2871 intracoronary ultrasound examinations and 1138 intracoronary pressure measurements were performed among a total of 103 646 coronary angiographies and 51 689 angioplasties. Thus, 2.8% and 5.6% of intracoronary ultrasound studies and 1.1% and 2.2% of pressure guidewire studies were performed over the total of coronary angiographies and angioplasties carried out in that year. Considering that a varying percentage of intracoronary ultrasound use (>50% at some centers) is prompted by research protocols, the use of these ancillary diagnostic techniques is very low, despite the aforementioned limitations of angiography.

Based on the results observed in the CASS⁸ (Coronary Artery Surgery Study), patients with more than 50% angiographic stenosis of the left main coronary artery (LMCA) have traditionally been considered to have greater survival with revascularization than with pharmacological treatment alone. Since then, more than 50% stenosis of the LMCA diameter on angiography has been considered the cut-off for significant disease in this location. In clinical practice there are usually no doubts as to the importance of stenosis observed in the LMCA; nevertheless, situations in which it is difficult to determine the contribution of stenosis to the patient's clinical status

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are not uncommon. In up to 19% of cases in the CASS study, a second observer did not detect significant stenosis in patients considered to have >50% by the first observer.⁵ A number of circumstances can invalidate angiography for treatment decisions, such as moderate stenoses at a range of 35% to 50% in situations of diffuse atheromatosis over the entire LMCA, which precludes availability of a suitable reference segment to perform the measurements, ostial locations in which the angiographic image depends on the position of the catheter, eccentric plaques, particularly those that are strongly calcified, and distal locations in the bifurcation of the left anterior descending and circumflex arteries, with overlapping of these branches.

In this issue of *Revista Española de Cardiología*, de la Torre et al⁹ report the safety results of applying a cut-off value obtained by intracoronary ultrasound (minimal lumen area <6 mm²) to decide treatment for angiographically moderate LMCA lesions. Based on the intracoronary ultrasound findings, the authors reported a rate of events in nonvascularized patients similar to, or lower than, that observed in revascularized cases, and in keeping with the prognosis of patients with chronic ischemic heart disease. Among 31 patients in this study with a minimal lumen area on intracoronary ultrasound indicating significant disease (<6 mm²), angiography had underestimated the importance of the lesion in 18 patients (59%) with angiographic stenosis <50%. Although it is not specified in the study, the most frequent causes of this discrepancy are usually poor visualization or unrecognized disease in the segment considered as the reference.

In LMCA lesions of uncertain significance, a fractional flow reserve >0.75 obtained with an intracoronary pressure guidewire has been associated with an excellent prognosis at 3 and 4 years (100% survival).^{10,11} Measurement of the minimal lumen area by intracoronary ultrasound with a cut-off point similar to that used by de la Torre et al⁹ (5.9 mm²) showed an excellent correlation with the fractional flow reserve obtained by pressure guidewire in these lesions.^{12,13} In addition, another intracoronary ultrasound parameter, minimal lumen diameter >3 mm, was associated with a good long-term prognosis (3% incidence of events at 1 year) in nonrevascularized patients.¹⁴

The study by de la Torre et al,⁹ which is highly interesting because of the subject analyzed and the methods used, also presents some limitations, which were recognized in part by the authors. As in the other related studies, the number of patients included is small. The number of laboratories that have included intracoronary ultrasound in routine clinical practice is limited, and uncertainty as to the significance of LMCA lesions does not occur daily. Currently, the Sección de Hemodinámica y Cardiología Intervencionista de la Sociedad Española de Cardiología is conducting a prospective, multicenter study through its Grupo de Trabajo de Técnicas de

Diagnóstico Intracoronario (Working Group for Intracoronary Diagnostic Techniques), to assess the usefulness of intracoronary ultrasound for evaluating intermediate LMCA lesions in a large series of patients (LITRO study). The results of this effort will undoubtedly help to complement the information provided by the study published in the current issue of *Revista Española de Cardiología*. Another limitation mentioned by the authors is the absence of a comparison group. The indication to revascularize patients with significant LMCA lesions was established on the basis of the poor prognosis of patients with angiographic stenosis greater than 50% treated medically. No studies have analyzed conservative treatment in patients with stenosis less than 50% on angiography, but significant disease on intracoronary ultrasound. It is true that the proven good correlation between intracoronary ultrasound parameters and functional measurements^{12,13} makes these studies difficult to perform. A third aspect, which probably should not be considered a limitation, is that fact that the study design led to the exclusion of a subgroup of patients with greater than 50% stenosis in the LMCA ostium. De la Torre et al⁹ found that 84% (21/25) of moderate lesions located in the LMCA ostium had an area >6 mm² and were not significant. In contrast, 68% of diffuse lesions had an area <6 mm² and revascularization was indicated. In daily practice, the ostium of the LMCA occasionally offers images that are difficult to interpret because of poor coaxiality of the catheter, a certain degree of spasm, or angulated withdrawal of the catheter from a left coronary sinus that is deformed due to several possible causes. As the study of de la Torre et al⁹ shows, in these cases, angiography may overestimate the grade of stenosis and lead to inappropriate indications. It is unknown what percentage of lesions with angiographic stenosis between 50% and 60% in the LMCA ostium might present a minimum lumen area on intracoronary ultrasound >6 mm² and what the prognosis of these patients would be if the decision were based on the more precise measurement obtained with intracoronary ultrasound and not on the grade of stenosis quantified by angiography. The data presented in this study favor the use of intracoronary ultrasound in patients with ostial LMCA lesions even though angiography has quantified them as greater than 50%, in cases when this measurement is not certain.

The need to use invasive diagnostic techniques in daily practice in catheterization laboratories has long been a controversial subject among interventional cardiologists.^{15,16} The application of these techniques in research is unquestionable,¹⁷ but their clinical use continues to be limited. Pressure guidewires and intracoronary ultrasound are accessible to most laboratories and given the advances achieved in these methods, they can be performed with a low rate of complications by operators with sufficient experience.^{18,19} Nonetheless, limited operator experience, cost, time needed to perform these techniques when the

operator lacks sufficient training, and the ease with which uncertain lesions can be treated are some of the reasons cited to justify their limited use.²⁰

Among the 117 public hospitals with a catheterization laboratory in Spain in 2005, only 50% performed intracoronary pressure measurements or intracoronary ultrasound in that year (58 and 59 hospitals, respectively). Studies such as the one by de la Torre et al⁹ support the use of these techniques (perhaps in a small number of cases) because they can be essential to establish a precise diagnosis. In the case of LMCA lesions, for which the therapeutic options may be surgical revascularization or medical follow-up depending on the coronary angiography findings, a diagnosis of moderate or intermediate lesion does not resolve the patient's clinical situation. Although it is possible to carry out non-invasive tests following an ambiguous coronary angiography, the patient and physician requesting catheterization generally expect the technique to yield conclusive information for the diagnosis because of its invasive nature. In these cases, the data presented by studies such as the one published in the current issue of *Revista Española de Cardiología* and future studies in this line can be an aid to effectively diagnosing these patients in the catheterization laboratory and provide the information needed to make appropriate therapeutic decisions.

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