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The Predictive Value of H2FPEF Score for Contrast Induced Nephropathy in Patients Undergoing Coronary Angiography

Mohamed A.Elsharawy, Al-Shimaa M.Sabry, El-Sayed A.ElDarky and Mahmoud S.Abd Al-Naby
Cardiology Depart., Faculty of Medicine, Benha University, Benha, Egypt
E-mail : dr.sh3rawy@gmail.com

Abstract
Coronary calcification is a significant predictor of major adverse cardiac events (MACE) following percutaneous coronary intervention (PCI). This is largely due to the challenges it presents in device delivery, expansion, and apposition, which can predispose stent failure. Recently, intravascular lithotripsy (IVL) has emerged as a novel approach to modifying calcified coronary plaques, overcoming many of the limitations associated with conventional techniques such as non-compliant balloons, cutting and scoring balloons, and rotational/orbital atherectomy. This review discusses the growing body of evidence supporting the use of IVL as a frontline strategy for managing severely calcified coronary arteries prior to stenting. The review highlights the mechanism of action, clinical efficacy, and safety profile of IVL in the treatment of calcified lesions, comparing it to other available methods. Additionally, the review examines clinical outcomes associated with IVL, including its impact on stent expansion, procedural success, and reduction in adverse events. As the use of IVL becomes more widespread, its role in the management of calcified coronary arteries continues to evolve, offering promising results and shaping future guidelines for PCI.

Keywords : intravascular lithotripsy (IVL), percutaneous coronary intervention (PCI), calcified coronary.

Introduction

Calcified lesions are a common symptom of coronary artery disease (CAD) and a major obstacle to percutaneous coronary intervention (PCI). Because these lesions do not respond to conventional balloon angioplasty, stent placement is not optimum, and problems like stent thrombosis are more likely to occur. Modern methods for efficient lesion modification are required due to the rising incidence of hardened coronary lesions in an ageing population. A potential method to tackle these issues is intravascular lithotripsy (IVL). By breaking calcified plaques with acoustic pressure waves, intravascular ligation improves stent expansion and vessel compliance. Discussing the mechanism of action, clinical applications, and results, this chapter delves into the function of intravenous ligation (IVL) in the treatment of calcified coronary lesions. It also highlights the benefits and drawbacks of IVL in comparison to other methods of plaque remodelling, including orbital atherectomy and rotational atherectomy. (1).

The most reliable way to detect the severity of atherosclerotic coronary artery disease (CAD) is via a coronary angiography. There are some inherent risks to the test that depend on the patient and the operation itself, as there are with any invasive surgery. A broad variety of complications might arise, from relatively small issues with temporary effects to potentially fatal ones that, if not treated immediately, could cause permanent harm. Modern technology, better peri-procedural monitoring, and more expertise on the part of diagnostic centres and operators have all contributed to a significant reduction in the dangers associated with coronary arteriography since its introduction (1).

There are no known situations in which coronary arteriography cannot be performed; nonetheless, there are hazards involved, including both cardiac and non-cardiac problems. The patient's risk for complications might be increased by specific disease conditions related to their overall medical profile, such as advanced age, renal insufficiency, uncontrolled diabetes mellitus, and severe obesity. Adverse effects might be exacerbated by the patient's preexisting cardiovascular condition. Heart conditions that may raise the risk of cardiac and vascular problems include advanced coronary artery disease (CAD), congestive heart failure (CHF) with a poor ejection fraction, a history of stroke or myocardial infarction (MI), and an increased tendency to haemorrhage. Diagnostic coronary angiography and further percutaneous coronary intervention are two procedures that vary in the degree to which they change the risk (2).

Points of reference

When improving patient symptoms or prognosis requires information on the existence and severity of coronary artery disease, the internal carotid artery (ICA) is the way to go. Treatment protocols for stable coronary artery disease, acute myocardial infarction with ST-segment elevation, and acute coronary syndromes without ST-segment elevation are all outlined in detail by the European Society of Cardiology (ESC). The basic premise seems to be straightforward: the severity of symptoms and the level of clinical risk determine the strength of the case for internal carotid artery (ICA) (3):

1) Patients without angina who have diminished left ventricular systolic function, arrhythmia (particularly of ventricular origin), a recent diagnosis of heart failure, or coronary artery disease should be evaluated for ICA.

2) To rule out acute coronary artery blockage, which often occurs in the left circumflex area, patients who exhibit persistent symptoms that might indicate an acute myocardial infarction but who do not show any ST-segment elevation on subsequent electrocardiograms should be evaluated for an internal carotid artery (ICA).

3) some individuals have non-invasive tests that provide mixed findings or unusual symptoms. Even a normal result from the internal carotid artery (ICA) may comfort the patient, which in turn improves their quality of life.

4) Non-invasive examination of myocardial ischaemia should be performed before the internal carotid artery (ICA) procedure in patients with minimal clinical risk and moderate non-limiting symptoms. Internal carotid artery (ICA) complications may be hard to explain in this context.

The internal carotid artery (ICA) has no hard and fast rules against its use in an emergency situation. Patients whose cardiac and non-cardiac conditions are not yet stabilised should not have elective internal carotid artery (ICA) procedures (4).

Technique

Crucial is the pre-procedure stage. The obvious thing to do is to get written informed permission, preferably from a member of the medical team that is well-versed in coronary angiography. Before surgery, patients should have standard pre-op testing (complete blood count, electrocardiogram, echocardiography, and other non-invasive diagnostics), which includes a review of their biochemistry (including renal function), anti-allergic medicine, and pre-hydration to preserve their kidneys. It is still not apparent how to best manage patients who are on chronic oral anticoagulant treatment. Should one conduct the ICA (sometimes even followed by ad hoc stenting with a dual antiplatelet treatment) without interrupting the anticoagulation and risk bleeding complications, or should one break the anticoagulation and risk thrombosis? Potentially useful in the future are the newly developed oral anticoagulants that have a short half-life. Without definitive scientific evidence, it is imperative that treatment plans be individualised for each patient (5).

The actual treatment, which usually lasts no more than ten to fifteen minutes, is performed under local anaesthesia in a catheterisation laboratory. Although we do most treatments without conscious sedation (since it is not risk-free for the elderly), we have a low threshold to sedate any patient who is nervous or uncomfortable. A typical Seldinger method is used to acquire artery access. Cannulating both coronary ostia is accomplished by inserting the vascular sheath and using the over-the-wire approach. If the operator feels any resistance, they must continue very gently and only under X-ray visualisation (6).

Most operators utilise 5Fr (1.7 mm) equipment, which clearly indicates a tendency towards using tiny diameter catheters. The viscosity of contrast agents is reduced and coronary artery filling is improved by using pre-warmed contrast agents. In order to fully see the branching and often winding cardiac tree, it is necessary to have several views of both coronary arteries. Each patient's radiation duration and dosage is meticulously documented. The ALARA (As Low As Reasonably Achievable) concept, which allows for independent audits of radiation safety by national agencies, is made possible by this. To prevent radiation-related illnesses and injuries, it is important to adhere to national and local radiological standards (7).

The post-procedure phase consists of removing the vascular sheath and carefully monitoring the patient. Unlike femoral access, which usually requires a few hours of bed rest, radial artery access allows patients to mobilise immediately after the ICA. Patients have been able to experience more comfort and less time to ambulation with the use of femoral vascular closure devices (VCDs) for more than 20 years. The usage of VCDs was shown to result in a reduced rate of bleeding. (8).

Update on coronary angiography

Recognised as unreliable with substantial intra- and inter-observer variability since the late 1970s, visual estimate of stenosis severity is a problem. Quantitative coronary angiography (QCA) offers a reliable, objective approach for assessing the severity of coronary lesions. There are certain drawbacks to quantitative coronary angiography (QCA) despite its widespread usage in clinical and, more often, research settings (9).

• Light curve

The fact that angiography can only show the contrast-filled lumina of the coronary arteries is one of the most glaring restrictions. Because of this, a "Luminogram" cannot assess the whole plaque load (the sum of the vessel area and the lumen area), nor can it detect the pathophysiology of atherosclerosis processes like expansive and constrictive remodelling. To examine this process in real time, it would be possible to use intravascular imaging, particularly intravascular ultrasonography (IVUS). The angiographic Luminogram can only detect the narrowing of the lumen after stent implantation; however, it cannot detect the tissue that has grown in excess of the stent struts or in between them. Optical coherence tomography (OCT) is an infrared-based intravascular imaging technique that has shown the ability to detect neointimal hyperplasia and neoatherosclerosis, among other forms of tissue overgrowth (10).

• A three-dimensional structure captured in two dimensions

The fact that coronary arteries are in fact three-dimensional (3D) structures is another drawback of quantitative coronary angiography. The imaging technique only gives a perspective view. Rotating the C-arm so that the tube is pointed perpendicular to the coronary section of interest minimises foreshortening, a typical difficulty of QCA. The fact that stenosis may be eccentric means that various cameras will capture the same or different diameters of the narrowing. We recommend getting the shots from at least two or three distinct perspectives. Yet, owing to overlapping arteries, this may be difficult at times, particularly in bifurcation lesions (i.e., getting a good look at the side branch ostium without the distal main branch and side branch overlapping, which includes left main lesions) (11).

Repeatability is the focus of quality control analysis (QCA).

The reliability of QCA has been shown to be high both between and among individual observers. But there are a number of things that might affect repeatability; for example, the size of the guiding catheter used for calibration, the projections used, the ability to change contours manually, etc. There is heterogeneity within core laboratories in addition to variability within and between observers. Aiming to provide objective and repeatable outcomes, core labs are autonomous institutions. As a means of reducing the possibility of investigator bias, these core laboratories often conduct QCA analyses as part of clinical studies. Nevertheless, variances in software or variations in standard operating procedures (SOPs) employed for QCA analysis might account for the observed diversity between core labs. Lastly, in order to eliminate any possibility of analyst bias, it is recommended that the analyses be conducted in a blinded method to the best of our ability. This is standard practice for any scientific measurements. In some cases, nevertheless, such as when contrasting bioresorbable scaffolds with metallic stents or stenting with balloon angioplasty, this becomes virtually impossible (12).

• Verification by angiography vs evaluation by physiological measures

It is well-known that quantitative coronary angiography's stenosis severity evaluation does not reliably reflect the degree of ischaemia, or flow limiting, caused by coronary stenoses. Contrasted with angiography-directed PCI, PCI guided by physiological evaluation improved patient outcomes in terms of anginal complaint alleviation and the requirement of (repeat) angiography. Revascularisation decisions should be made with care when using QCA evaluation, despite its usefulness as a proxy for neointimal development over time in clinical studies (e.g., LLL and % diameter stenosis) (13).

The "oculostenotic reflex," first described by Eric Topol, is the tendency of some invasive cardiologists to undergo angioplasty procedures for any stenosis that is considered angiographically significant (i.e., with a diameter stenosis greater than 50%). This tendency causes clinical trials with angiographic follow-up to underestimate the actual clinical benefits by leading to an excessively high rate of repeat revascularizations. Therefore, angiographic follow-up should be done after the official evaluation of the main clinical outcomes in study designs. Furthermore, to minimise needless interventions, it is advised to do a functional evaluation to establish the clinical appropriateness of revascularisation before performing a repeat angiography prior to assessing the clinical objectives (14).

• Bifurcation lesions are not appropriate for conventional QCA.

Coronary vascular trees are defined by their fractal geometry, which is a branching pattern of 3D vessels that is independent of size, recursive, and self-similar (but not identical). Multiple scaling rules (e.g., Murray, Finet, etc.) have been used to characterise the coronary tree's branching at the bifurcations (15). After testing their "Huo-Kassab" (HK) model using human IVUS data and pig coronary micro- and macro-vasculature casts, Huo and Kassab's scaling rule seems to be the most accurate. When they looked at the mother and two daughters' vessel diameters (D) (16), they discovered the following relationship:

• New developments that aim to circumvent these restrictions

Over the last ten years, QCA software has come a long way, with innovations like 3D QCA and specialised bifurcation software addressing the shortcomings of traditional 2D "single vessel" (16).

Specific program for splitting up

Specifically designed algorithms for bifurcation QCA software have been created to address the constraints of using single-vessel QCA software in bifurcations (Figure 1). Despite the fact that several software packages are offered by various businesses, they all adhere to the same fundamental principles:

1) From one end of the vessel to the other, first via the carina to the side branch, second to the proximal main branch, and third to the distal main branch are the three vessel shapes that the program detects automatically. Consequently, unlike traditional software that only detects two vessel contours, our program distinguishes the bifurcation as an anatomical entity without any non-existent contours crossing the ostium of a distant branch.

2) A distinct reconstruction of the interpolated reference diameter is carried out for the proximal main branch, the distal main branch, and the side branch, the three segments that form the bifurcation. Each segment's minimal lumen diameter and stenose diameter are determined independently. The diameter stenosis can't be over- or under-estimated because of this.

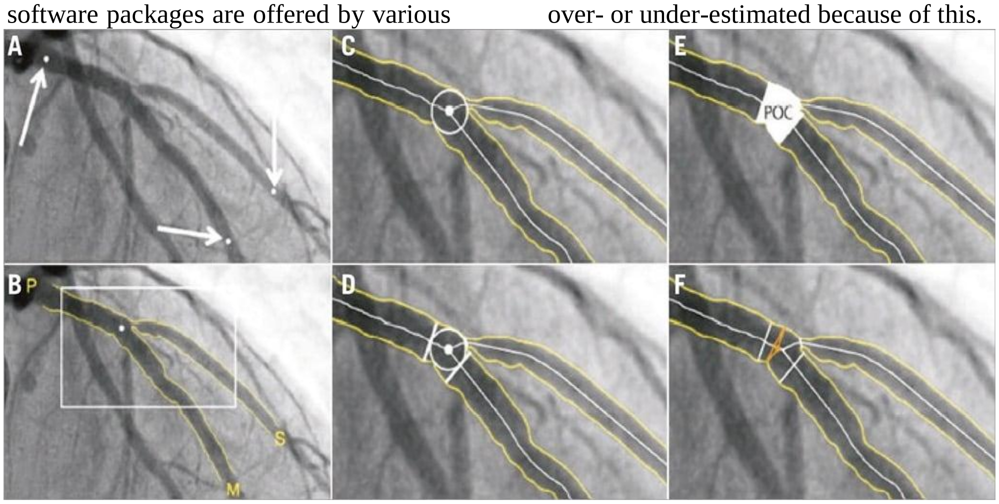

Fig. (1) Dedicated bifurcation QCA analysis with a representative example. One proximal and two distal delimiter points (white arrows, A) represent the section of study in the CAAS QCA bifurcation program (Pie Medical Imaging). The "point of bifurcation" (POB) is the centre of the biggest circle that can touch all three contours (C) after the contours (B) have been automatically detected. E is the polygon of confluence (POC) boundary, which is defined by the points where the circle meets the centerlines (D). The diameter values are calculated in a different way for straight segments outside the POC (F) compared to those within the POC. Similar to the traditional straight-vessel QCA method, diameters outside the POC are calculated by the shortest distance between the vessel's exterior boundaries. But another mathematical procedure, the so-called "minimum freedom" approach, is used inside the POC. (11)

Two existing bifurcation software programs, QAngio XA and CAAS, have been tested using precision-manufactured phantoms for bifurcation and compared to the single-vessel QCA program. There was a great deal of precision and accuracy shown by the bifurcation QCA software algorithms. When compared side by side, the two methods performed similarly. Angiographic evaluation of bifurcation lesions is therefore advised to be performed using bifurcation QCA software, according to the European Bifurcation Club. **(15)**.

QUACA three-dimensional

Another development from the last decade, 3D QCA aims to address some of the issues with 2D QCA. Two angiographic pictures, with a viewing angle of at least 30° between them, are required for every 3D reconstruction. By reducing the likelihood of vessel foreshortening, a problem that may arise in 2D QCA, 3D QCA is able to accurately derive lengths (19).

Importantly, in the case of eccentric lesions, 3D QCA has the additional (theoretical) benefit of stenosis evaluation being unaffected by the projection. The critical viewing angle determines the minimum lumen diameter (MLD) in eccentric lesions with an oval-shaped lumen; a reduced MLD is seen when the projection is perpendicular to the shortest axis of the oval-shaped lumen. This constraint might be circumvented by use of 3D reconstructions. The fact that 3D QCA measures outperformed 2D QCA in predicting functional importance as assessed by invasive FFR in simple, non-bifurcated lesions is notable. Consequently, the functional and anatomical severity of the stenosis may be better understood with the use of 3D data (20)

Additionally, bifurcation lesions have their own 3D QCA program. The capacity to determine the ideal viewing angle—an orthogonal perspective of the lesion that minimises foreshortening and overlap—is another characteristic of 3D QCA. When choosing the optimal projection, this tool might be helpful for the angiographer or interventionist. In bifurcations, where evaluating the three segments of the bifurcation might be challenging in certain circumstances, this can be very valuable. 3D QCA has a few drawbacks, one of which is that it isn't always practical to get two projections at least 30 degrees apart (21).

For example, 3D QCA was only practical in 75.1% of cases in the SYNTAX trial's left major lesion subgroup. However, following rigorous QCA criteria for picture capture might make this better. Lastly, 3D QCA eliminates the need for pressure and/or flow cables by allowing for 3D modelling using computational fluid dynamics, which may mimic physiological evaluation (22).

The fractional flow reserve as determined by angiograms

There have been many efforts to enhance QCA's diagnostic capability to identify functionally relevant lesions since K. Lance Gould's 1978 seminal study detailing the reduction of pressure across a coronary stenosis. Several parameters, including as the entrance and exit angles, lesion length, minimum lumen size, and reference vessel area, influence the functional component of a stenosis, in addition to the conventional angiographic % diameter stenosis evaluation. It is possible to simulate FFR by using 3D QCA-derived coronary geometry and fluid dynamic principles to compute a pressure decrease unique to the lesion. Figure 2 shows the results of the various evaluations of the angiography-derived FFR. Research in the area of "angio FFR" varies greatly in the approach used to determine the pressure drop, which is the most crucial finding. To model the pressure and flow, some writers used on computational fluid dynamics (CFD) that solved the Navier-Stokes equations; others, using a simplified equation derived from the Lance Gould formula, referred to as "rapid CFD" (23).

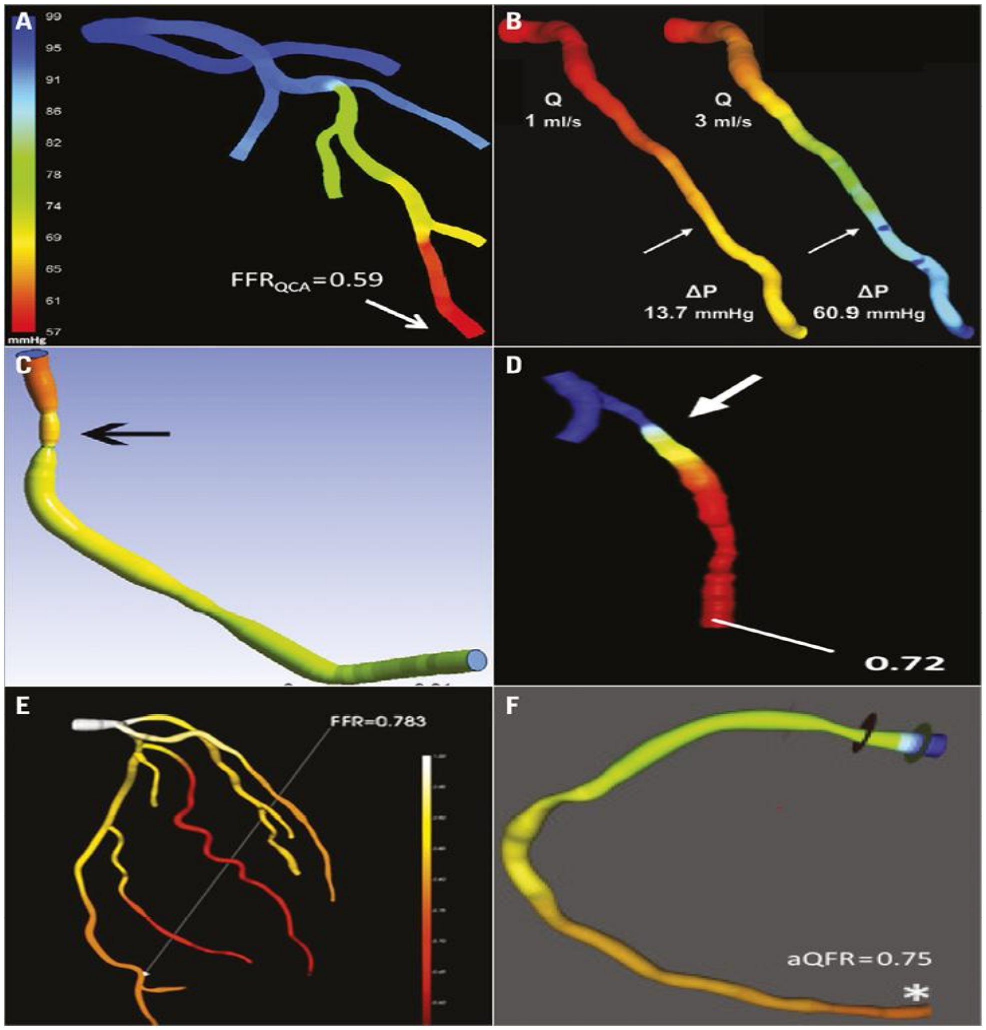

Fig. (2) Technologies exist for angiography-derived fractional flow reserve calculation. Section A: Hyperaemia pressure distribution simulation. A pressure gradient (ΔP) of 13.7 and 60.9 mmHg was produced by two distinct flow rates (Q), as shown in a colour-coded map (B). B) FFR angio, C) Virtual fractional flow reserve, D) etc. A whole coronary tree and bifurcation are included in the angiogram-based FFR (E). Flow ratio that is quantitative (11)

A significant benefit of the simpler method is the time savings in computations. All of these studies consistently referred to invasive FFR. Based on these findings, "angio FFR" could be a useful diagnostic tool for identifying ischemia-producing lesions in non-complex CAD patients. To corroborate this discovery, nevertheless, further research is necessary. **(24)**.

Complications

In the past, there were three broad classes of ICA-related risks: those on the one hand, and those on the other. In **Table 1** we can see the advantages and disadvantages of both methods (25).

Table (1) The femoral and radial artery access comparison, based on subjective author opinion

Empty Cell	**Femoral**	**Radial**	**Comment**
Access site related bleeding	+++	+	Clear benefit of the radial approach

Occlusion of femoral/radial artery	+	++	Most radial occlusions are clinically silent
Access route failure	+	++	Approx. 5% failure rate of radial approach
Radiation dose	+	++	Some conflicting evidence
Pain during procedure	+	++	Occasional radial artery spasm
Post-procedure independence	+	+++	Immediate mobilization after radial access
ICA as a day case	+	++	Radial approach seems safer in this setting

ICA: invasive coronary angiography, PCI: percutaneous coronary intervention.

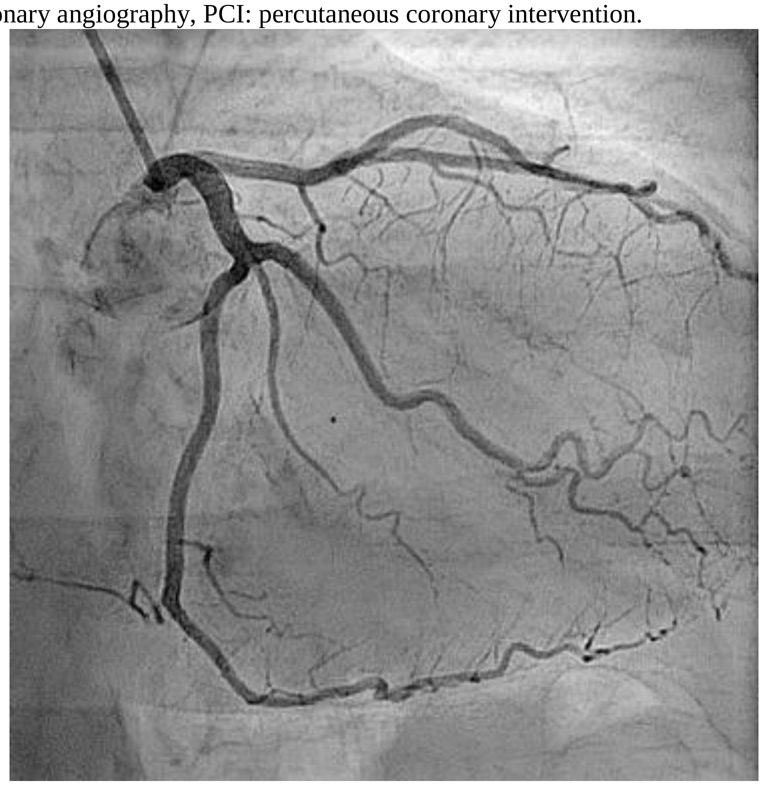

Fig. (3) Excellent spatial resolution of invasive coronary angiography (approx. 100 µm) provides diagnostic information about both proximal and distal part of coronary tree (٢١)

- **Disadvantages (Fig. (4)**
  - The hazards of ionising radiation and the aforementioned complication rate are linked to ICA.
  - ICA's inability to see the vessel wall is due to its two-dimensional nature, which is derived from its reliance on picture summation. Because of this, asymmetric lesions and widespread diseases without a "normal" portion might be difficult to understand. (21).

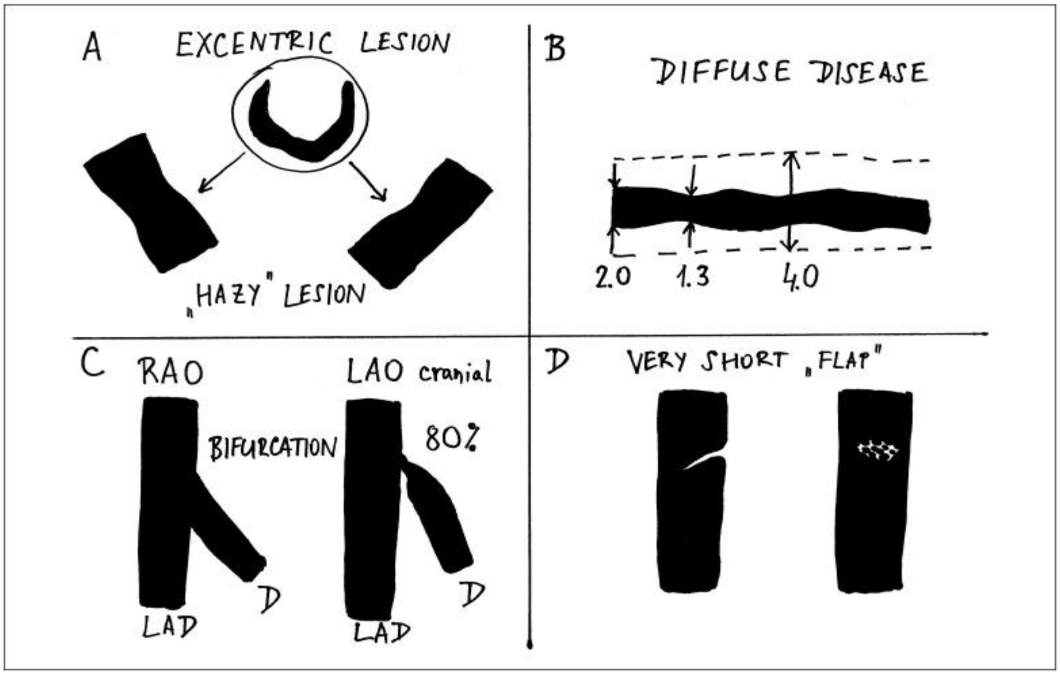

Fig. (4) (A) Diffuse disease without a suitable "normal" segment; (B) Complex, excentric lesions that are difficult to identify with summation imaging and may appear as "haziness" due to the reduced contrast agent density. (A) The interpreter's assumption of 2 mm as a typical vessel size leads to an underestimation of the lesion's severity; (B) In order to "open up" the branching point during bifurcation imaging, the optimal viewing angulation must be maintained; (D) Very short "flap" lesions are also challenging to image; and (E) Only by switching to a coaxial view can the real significance of the lesion's severity be revealed. (25)

- For lesions in tortuous segments, bifurcations, and very short lesions, ICA need good angiographic views.
- The interobserver diversity in ICA interpretation is large. Because of this, quantitative coronary angiography (QCA) with artificial intelligence boundary detection was born. It is common for the visual evaluation to overestimate the severity of lesions. **(22)**.

Conclusion

When it comes to treating calcified coronary lesions, intravascular lithotripsy is a huge step forward. It is a useful technique in percutaneous coronary intervention because it may alter hardened plaques and increase stent expansion. The increasing amount of research demonstrating the efficacy of intravascular ligation (IVL) suggests that this approach will soon be standard equipment in interventional cardiology practices. To further understand IVL's function in the larger framework of coronary artery disease therapy and its possible hazards and long-term benefits, more study is required.

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