Supplemental Material

Methods 1

The exclusion criteria were angiographically significant left main coronary artery disease, previous coronary artery bypass surgery, renal insufficiency with a baseline creatinine level of >2.0 mg/dl, presence of unstable symptoms (worsening angina or angina at rest within 1 month), a myocardial infarction (MI) episode within 30 days before coronary angiography (CAG), severe valvular heart disease, decompensated heart failure, cardiogenic shock, arrhythmia including atrial fibrillation, and lesions with physiological pressure recordings showing drift of >3 mmHg. For cQFR analysis, we also excluded patients with severe vessel overlap, extremely tortuous or calcified coronary arteries, vessels with previous MI, visible collateral development or ostial stenosis, and poor angiographic images.

Methods 2

Coronary catheterization and physiological measurements

Each patient underwent standard CAG via the radial artery with a 5-French system. All patients received a 5000-IU bolus heparin injection before catheterization and an additional 2000-IU bolus injection every hour if the procedure was >1 h. An intracoronary bolus injection of nitroglycerin (0.2 mg) was administered at the start of the procedure and repeated every 30 min. The contrast medium was injected using a mechanical injector pump (ACIST CVi, Eden Prairie, MN, USA) at a rate of approximately 3 ml/s. Physiological measurements of coronary stenosis were performed according to a previously reported protocol.[1] The pressure–temperature sensor-tipped guide wire (PressureWire™; St. Jude Medical, St. Paul, MN, USA) was zeroed and equalized to the aortic pressure before being positioned far distal to the stenosis, and a baseline recording of aortic and coronary pressures was obtained. The pressure wire was positioned at approximately the distal third of the target lesion and at least

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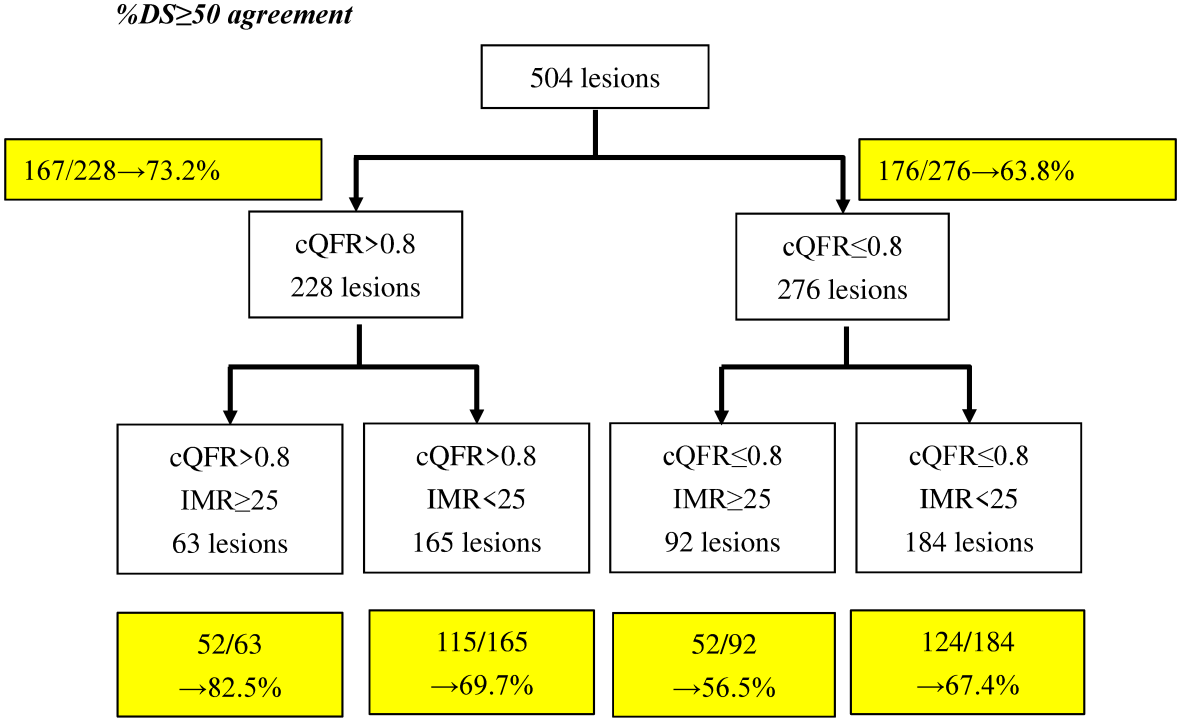
3 cm beyond the target lesion. The sensor position of the wire was documented, and this location was used for quantitative flow ratio (QFR) computation. Subsequently, 3 ml of room-temperature saline was administered three times, and the baseline mean transit time (Tmn) was determined. Because a shorter Tmn has been suggested as a surrogate of higher coronary flow velocity, we also assessed the difference in Tmn among subgroups.[1, 2] Maximal hyperemia was induced by intravenous infusion of adenosine (140 μg/kg/min). The FFR was calculated as the ratio of the mean distal-to-aortic coronary pressure (Pd/Pa) during maximum hyperemia. The coronary flow reserve (CFR) was defined as the resting Tmn divided by the hyperemic Tmn. The IMR was calculated as the product of the distal coronary pressure during maximum hyperemia and the hyperemic mean transit time, and corrected using Yong's formula.[3] The pressure drift was determined by measuring the pressure difference between the aortic pressure and the pressure wire at the tip of the guiding catheter. All patients were instructed to strictly refrain from ingesting caffeinated beverages for >24 hours before catheterization.

Figure 1. The diagnostic performance of angiographic assessments predicting FFR of ≤0.80

The diagnostic performance of the angiographically significant stenosis (%DS ≥50) predicting FFR of ≤0.80 classified by cQFR and IMR (yellow text boxes). In any subsets of these categorizations, cQFR consistently showed better diagnostic performance than angiographic assessment.



References

1 Pijls NH, De Bruyne B, Smith L, et al. Coronary thermodilution to assess flow reserve: validation in humans. *Circulation* 2002;**105**:2482-6.

2 De Bruyne B, Pijls NH, Smith L, et al. Coronary thermodilution to assess flow reserve: experimental validation. *Circulation* 2001;**104**:2003-6.

3 Yong AS, Layland J, Fearon WF, et al. Calculation of the index of microcirculatory resistance without coronary wedge pressure measurement in the presence of epicardial stenosis. *JACC Cardiovasc Interv* 2013;**6**:53-8.