From Massachusetts General Hospital, Boston (O.O.Y.).

1. Prager GW, Taieb J, Fakih M, et al. Trifluridine–tipiracil and bevacizumab in refractory metastatic colorectal cancer. N Engl J Med 2023;388:1657-67.
2. Temmink OH, Emura T, de Bruin M, Fukushima M, Peters GJ. Therapeutic potential of the dual-targeted TAS-102 formulation in the treatment of gastrointestinal malignancies. Cancer Sci 2007;98:779-89.
3. Wilson PM, Danenberg PV, Johnston PG, Lenz H-J, Ladner RD. Standing the test of time: targeting thymidylate biosynthesis in cancer therapy. Nat Rev Clin Oncol 2014;11:282-98.
4. Heidelberger C, Boohar J, Kampschroer B. Fluorinated pyrimidines: XXIV. In vivo metabolism of 5-trifluoromethyluracil-2-C-14 and 5-trifluoromethyl-2′-deoxyuridine-2-C-14. Cancer Res 1965;25:377-81.
5. Matsushita S, Nitanda T, Furukawa T, et al. The effect of a thymidine phosphorylase inhibitor on angiogenesis and apoptosis in tumors. Cancer Res 1999;59:1911-6.
6. Lee S, Chen TT, Barber CL, et al. Autocrine VEGF signaling is required for vascular homeostasis. Cell 2007;130:691-703.
7. Folkman J. Tumor angiogenesis: therapeutic implications. N Engl J Med 1971;285:1182-6.
8. Mayer RJ, Van Cutsem E, Falcone A, et al. Randomized trial of TAS-102 for refractory metastatic colorectal cancer. N Engl J Med 2015;372:1909-19.
9. Sommerhäuser G, Kurreck A, Stintzing S, et al. Study protocol of the FIRE-8 (AIO-KRK/YMO-0519) trial: a prospective, randomized, open-label, multicenter phase II trial investigating the efficacy of trifluridine/tipiracil plus panitumumab versus trifluridine/tipiracil plus bevacizumab as first-line treatment in patients with metastatic colorectal cancer. BMC Cancer 2022;22:820.

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When Images Speak, Listen

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Although revascularization with percutaneous coronary intervention (PCI) was initially reserved for patients with simple coronary artery disease, PCI has now become the norm for patients with acute or chronic coronary artery disease who have complex coronary-artery anatomy or are at high risk for coronary-artery bypass surgery. Advances in the design of guiding catheters, coronary guide wires and balloons, and stents; in techniques to perform PCI; and in the effectiveness of procedure-related anticoagulant and antiplatelet medications have improved clinical outcomes. These advances have led to high procedural success rates with low incidences of serious complications.[1]

Intravascular imaging, an established catheterization laboratory tool, provides details of coronary-artery anatomy that are not seen on angiography. Coronary-artery dimensions and features of plaque and the artery wall can be determined by intravascular imaging. Intravascular imaging has been available for more than 20 years but has not been widely adopted. For example, intravascular ultrasonography, the most common type of intracoronary imaging, is used in only 16.5% of PCI procedures.[2] Intracoronary optical coherence tomography (OCT) is more complicated to use than intravascular ultrasonography but provides enhanced image resolution and greater anatomical detail, although its use during coronary procedures remains infrequent. Current cardiology society guidelines suggest a limited role for intracoronary imaging, stating that it is useful for procedural guidance only in patients with left main artery disease or complex coronary disease who are undergoing stent implantation.[3]

In this issue of the *Journal*, Lee et al.[4] report the results of a large, randomized clinical trial (RENOVATE-COMPLEX-PCI; Randomized Controlled Trial of Intravascular Imaging Guidance versus Angiography-Guidance on Clinical Outcomes after Complex Percutaneous Coronary Intervention) that showed a lower risk of target-vessel failure (defined as a composite of death from cardiac causes, target-vessel–related myocardial infarction, or clinically driven target-vessel revascularization) among patients with complex coronary artery disease who underwent stent implantation with intra-

coronary imaging guidance than among those who underwent PCI with angiographic guidance only. The absolute between-group difference in the cumulative incidence of the composite end point was 4.6 percentage points. In addition, for each of the individual components of the primary end point, hazard ratios favored patients in the intravascular imaging group. A prespecified subgroup analysis of the primary end point suggested that for some complex coronary-lesion types and for some subgroups of patients, such as those with stable ischemic heart disease or without diabetes, there was benefit regardless of whether imaging was done with intravascular ultrasonography or OCT.

Several features of this trial are noteworthy, including the large patient sample, minimal crossover, and excellent completeness of follow-up. Several types of complex coronary-artery lesions were included, which reflects what is encountered in current clinical practice. On the other hand, the ability to broadly generalize the trial findings is limited by the enrollment of participants from a single country, with one site responsible for enrolling most of the trial participants.

Previous trials have shown that intracoronary imaging improves patient outcomes by reducing the risk of repeat target-lesion revascularization.[5] The proposed mechanism by which intracoronary imaging improves outcomes is by the provision of an accurate determination of vessel size, which leads to greater stent expansion and contact with the vessel wall as well as to the identification of any complications such as dissections; this information results in a lower risk of lesion recurrence or restenosis.[6] In the present trial, the cumulative incidence of target-lesion revascularization was lower in the intravascular imaging group than in the angiography group, but only minimally so. However, the cumulative incidence of target-lesion revascularization was quite low in the angiography group, a finding that limits the opportunity for a substantial benefit to be seen with intracoronary imaging.

Unlike many previous investigations of imaging-guided PCI, the RENOVATE-COMPLEX-PCI trial enrolled only patients with complex coronary disease. The criteria for optimized stent deployment in both the intravascular imaging group and the angiography group were strict and often not achieved. These goals were met in only 45.4% of the patients in the intravascular imaging group and in 58.9% of those in the angiography group. The low percentages of patients with stent optimization may relate to the structure and composition of the coronary lesions that were treated in this trial. For example, physical or anatomical constraints may limit stent expansion in heavily calcified lesions or in lesions that occur at coronary-artery bifurcations. Despite the low percentages of patients with stent optimization, the cumulative incidences of target-lesion revascularization were also low, which suggests that stent optimization (according to the criteria prespecified in this trial) in complex coronary-artery lesions may not be essential for achieving excellent clinical results.

What are the clinical implications of this trial? Imaging-guided PCI improves clinical outcomes, and its routine use should be considered by interventional cardiologists when treating patients with complex coronary artery disease.

Disclosure forms provided by the author are available with the full text of this editorial at NEJM.org.

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1. Venkitachalam L, Kip KE, Selzer F, et al. Twenty-year evolution of percutaneous coronary intervention and its impact on clinical outcomes: a report from the National Heart, Lung, and Blood Institute–sponsored, multicenter 1985–1986 PTCA and 1997–2006 Dynamic Registries. Circ Cardiovasc Interv 2009;2:6-13.

2. Hannan EL, Zhong Y, Reddy P, et al. Percutaneous coronary intervention with and without intravascular ultrasound for patients with complex lesions: utilization, mortality, and target vessel revascularization. Circ Cardiovasc Interv 2022;15(6):e011687.

3. Lawton JS, Tamis-Holland JE, Bangalore S, et al. 2021 ACC/AHA/SCAI guideline for coronary artery revascularization: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 2022;145(3):e18-e114.

4. Lee JM, Choi KH, Song YB, et al. Intravascular imaging–guided or angiography-guided complex PCI. N Engl J Med 2023;388:1668-79.
5. Elgendy IY, Mahmoud AN, Elgendy AY, Bavry AA. Outcomes with intravascular ultrasound-guided stent implantation: a meta-analysis of randomized trials in the era of drug-eluting stents. Circ Cardiovasc Interv 2016;9(4):e003700.
6. Shlofmitz E, Iantorno M, Waksman R. Restenosis of drug-eluting stents: a new classification system based on disease mechanism to guide treatment and state-of-the-art review. Circ Cardiovasc Interv 2019;12(8):e007023.

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