recent study showed that analogous rules apply to CT-FFR, and in addition, we showed that CT-FFR when measured at the end of the vessel led to increased sensitivity but significantly decreased both specificity and accuracy, which is exemplified in **Figure 1** (4). These are important considerations for the method, the role of which is to increase specificity of the diagnosis, as the add-on to an already sensitive method of coronary CT angiography. Another important consideration is that due to very low discriminatory power of CT-FFR within the gray zone of 0.75 to 0.85 (the diagnostic value of coin flipping), 0.80 threshold for clinical decision making should be discouraged rather than promoted (5).

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THE AUTHORS REPLY:

We thank Dr. Kruk and colleagues for their thoughtful comments to our reports on computed tomography-fractional flow reserve (CT-FFR) clinical utility (1). Current clinical recommendations for the measurement of invasive FFR are, somewhat paradoxically, based on anatomy ("2 to 3 cm distal to the stenosis"). In contrast to measured FFR, CT-FFR provides simultaneous calculation of pressure and flow across the entire coronary tree. So how is this plethora of data best utilized to optimize management of patients with stable chest pain? It has been demonstrated in patients with ≥1 intermediate range lesions that CT-FFR was positive (lowest value <0.80) in 56% of patients, whereas only 31% were positive for CT-FFR computed 2 to 3 cm distal to stenosis (2). Recently, Solecki et al. (3) demonstrated highest agreement between CT-FFR and stress cardiac magnetic resonance myocardial perfusion imaging when CT-FFR was computed 41 mm distal to stenosis. However, the "optimal" CT-FFR computation point may vary according to the applied CT-FFR methodology and reference standard, which would ideally be invasive physiology and downstream clinical outcomes.

In our reports on clinical utility, CT-FFR was read at the discretion of observers without formal standardization. Following clinical experiences and emerging published data, we agree with Kruk and colleagues that distal vessel CT-FFR positivity as a single interpretation criterion overestimates disease severity by myocardial perfusion imaging or invasive standards. In fact, employment of this interpretation approach during our clinical adoption of CT-FFR may have attenuated its full potential as a gatekeeper to the catheterization laboratory. Accordingly, it may be that some patients with a positive CT-FFR result are best managed by optimal medical treatment without needing further testing. Moreover, we agree with Kruk and colleagues that an absolute CT-FFR threshold of 0.80 should not drive clinical management, nor should it when adjudicated invasively. Accordingly, we propose a binary interpretation strategy only in patients with CT-FFR >0.80 or ≤0.75, whereas in the event of CT-FFR between 0.75 and 0.80, decisions should be based on additional information (1). Moreover, integrating information (beyond the CT-FFR value and pattern of pressure loss) of more patient-specific CT-derived data associated to flow obstruction such as plaque characteristics, myocardium at risk, and vessel-volume relative to myocardial mass may potentially increase the future diagnostic value of coronary CT angiography-CT-FFR testing. CT-FFR is in its infancy and has only recently been introduced for clinical assessment of stable patients. Extensive ongoing research and accumulating data on clinical utility and outcomes will expectedly provide us with information enabling definition of standardized CT-FFR interpretation criteria in the near future.

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Predicting Cardiac Prognosis in Asymptomatic Chronic Kidney Disease Patients

We read with interest the recent study by Winther et al. (1) that addressed the best noninvasive or invasive test for predicting cardiac prognosis in asymptomatic chronic kidney disease (CKD) patients. In this study, 154 patients referred for kidney transplantation assessment underwent coronary artery calcium score, coronary computed tomography angiography, single-photon emission computed tomography, and invasive coronary angiography and were followed up for a mean of 3.7 years. The primary endpoint was major adverse cardiac events (MACE) defined as 1 of the following events: cardiac death, cardiac arrest with successful resuscitation, ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction, or coronary revascularization. The secondary endpoint was all-cause mortality. Coronary artery calcium and abnormal coronary computed tomography angiography and invasive coronary angiography findings were predictive of MACE even after adjustment for renal transplantation and presence of more than 3 risk factors during follow-up.

This study is important, as patients with advanced renal failure have a high cardiovascular risk and cardiovascular mortality accounts for one-half of all deaths in patients with end-stage renal disease receiving dialysis (2,3). Furthermore, although renal transplantation significantly improves survival, cardiovascular disease is still one of the most frequent causes of death accounting for 35% to 50% of all-cause mortality (4). All current screening options have some limitations and there is no consensus about the optimal mode of screening.

The study raises some important questions that require clarification. First, it appears that the treating clinicians were not blinded to the results of the study investigations. Hence, patients who had revascularization procedures in relation to the baseline cardiac evaluation do not appear to have been excluded from follow-up, and these patients (5%) are counted as part of MACE outcome. This is inappropriate and artificially increases the number of MACE events. Second, we are not informed if medical therapy was altered as a result of the study investigations. Third, the units for the laboratory findings are not given, and we are surprised by the very low levels of mean hemoglobin in their population (7.3 g/dl).

Finally, we would like to mention other noninvasive methods of evaluation for coronary artery disease that are being currently studied in the renal failure population. Blood oxygen level-dependent (BOLD) cardiac magnetic resonance (CMR) uses the paramagnetic properties of deoxygenated hemoglobin as an intrinsic contrast and can thus directly indicate the oxygenation status of the myocardium. The BOLD CMR technique can be particularly useful in CKD participants, as it has a high sensitivity to detect myocardial ischemia, and does not involve exposure to radiation or extrinsic contrast agents. In a recent study, BOLD CMR demonstrated significant blunted myocardial oxygenation response to stress in asymptomatic CKD patients (5), and may have prognostic value.

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