

81.8% (95% CI: 72.2% to 89.2%), 68.0% (95% CI: 57.5% to 76.9%), and 97.3% (95% CI: 90.3% to 99.3%), and for the detection of obstructive CAD undergoing revascularization within 30 days, 100.0% (95% CI: 79.4% to 100.0%), 68.5% (95% CI: 58.9% to 77.1%), 32.0% (95% CI: 26.3% to 38.3%), and 100.0% (95% CI: 100.0% to 100.0%), respectively.

This single-center experience revealed a good discriminatory capability of CTA to exclude obstructive CAD in approximately two-thirds of patients at intermediate to high risk, with a negative predictive value of 97% for ACS. Clinical factors and biomarkers were essential elements to safely exclude ACS and discharge. Although CTA is established for low-risk patients, CTA was used as an alternative strategy to standard care in intermediate-to-high-risk patients; therefore, we could expect that only a limited number of patients with this particular risk profile were triaged to CTA.

We speculate that CTA may serve as a “gate-keeper” to ICA in patients at higher risk for ACS or inconclusive results. Although this sample showed promising results of a coronary CTA strategy in intermediate-to-high-risk ED patients, it is important to recognize that forthcoming randomized controlled data are necessary to inform care standards (3).

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Building Coronary Lesion-Specific Predictive Models Using the Proper Prognostic Parameters



A Look Into the Computational Hemodynamics of the Matter

We read with interest the paper by Lee et al. (1) on the added value of noninvasive computational hemodynamic assessment of coronary arteries in the relentless pursuit of predicting plaques that are culprits for acute coronary syndromes. The EMERALD (Exploring the Mechanism of Plaque Rupture in Acute Coronary Syndrome Using Coronary CT Angiography and Computational Fluid Dynamic) study (1) comes into a compelling background of clinical studies that have investigated the reasonable hypothesis that integration of computational hemodynamics with anatomical information would enhance our ability to localize high-risk plaques and to predict those plaques that could lead to an acute coronary syndrome. Here the investigators similarly demonstrated the added value of a composite of 4 computationally estimated hemodynamic factors, further suggesting that lesion-specific hemorheology might have a more significant impact on plaque-specific events than global, vessel-specific hemodynamics do (such as computed tomography-derived fractional flow reserve).

When focusing on 1 of the hemodynamic parameters that were investigated, the assessment and implementation of wall shear stress (WSS) in the prognostic model warrants a commentary. The investigators estimated WSS by simulating blood flow in resting state and in stress conditions, approximating maximum hyperemia. High WSS, presumably derived from simulation of stress conditions and by using a binary variable for adverse WSS at a single cutoff value of 154.7 dynes/cm², was

regarded as an adverse hemodynamic parameter. Our knowledge on the relationship between WSS and coronary atherosclerosis comes from animal and clinical studies that have studied the effects of resting state WSS. Values of WSS at both extremes are present throughout the natural history of a coronary plaque. Low resting WSS holds a key role in the initiation and progression of coronary plaques and is closely associated with pathobiological markers of nonstenotic high-risk plaques (2). On the other end, high resting WSS is also present at certain time points in the life course of coronary plaques favoring a longitudinal transformation to high risk.

When compared with studies that have also computationally assessed WSS in the human coronary arteries, the EMERALD study reports strikingly higher absolute WSS values (ranging from 145.5 ± 87.6 dynes/cm² for nonculprit lesions to 221.8 ± 113.2 dynes/cm² for culprit lesions). Although there is not a definite agreement of the normal range of WSS values, these absolute numbers far exceed those reported from the invasive assessment of WSS in human coronaries assuming Poiseuille flow and from the typically used low WSS cutoff value of <10 dynes/cm². Such particularly high absolute WSS range values have been previously reported also by a computed tomography-based computational fluid dynamic study (3) that, similarly to the work by Lee et al. (1), mentions as a computational methodological step the estimation of microvasculature response to adenosine.

The actual prognostic value of computationally simulated hemodynamic parameters, particularly that of WSS, remains vague. That is unless there is a consensus on how coronary blood flow for WSS research should be simulated. When looking into plaque progression, is it perhaps more appropriate to simulate coronary flow and WSS in the physiological resting conditions that flow exhibits its effects in the coronaries? On the other hand, investigating the potential relationship of WSS with coronary plaque-specific acute cardiovascular events is it perhaps more appropriate to simulate flow in hyperemia? These assumptions are just a needle in a haystack within the physiological assumptions in the ever-growing field of coronary flow simulations. Although it is rather exciting and, in a way, expected in the fast-paced preventive cardiology field to develop prognostic models combining several parameters, one must be certain of the validity and the accuracy of each one of these parameters. Until then we should interpret

the favorable or not results of simulation studies with caution.

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THE AUTHORS REPLY:



We thank Drs. Giannopoulos and Chatzizisis for their interest in our study (1) and insightful comments. Drs. Giannopoulos and Chatzizisis pointed out a potentially different role of physiologic flow conditions depending on the nature of clinical events. As we considered the hyperemic wall shear stress (WSS) would be more relevant than resting WSS for explaining vulnerable transformation of plaque, rupture, and subsequent acute coronary syndrome (2,3), hyperemic WSS was included in a prediction model as a binary variable (1). It is reassuring that the overall results were the same as the original ones even when segmental or peak WSS as well as resting WSS were used for model 3 in our study.

Drs. Giannopoulos and Chatzizisis also requested further explanation on the high value of WSS in our study. The value of WSS is dependent on stenosis severity, flow assumption, and post-processing methods that were used to generate 1 numerical