found between pCCSA at rest and the presence of cardiovascular risk factors or medical treatment in either of the groups. During adenosine vasodilation, global pCCSA was not significantly different between the groups, and consequently, global CDR was significantly lower in the CAD group than in the non-CAD group (1.18 ± 0.21 vs. 1.43 ± 0.23; p = 0.0003). In both groups, no relationship was found between age, sex, body mass index, hypercholesterolemia, ischemic heart disease in family, or smoking habits and global CDR. Furthermore, in the CAD group, no relationship was found between coronary Agatston score and global CDR.

In this study, we demonstrated that the presence of CAD was associated with a severe impairment of epicardial coronary vasodilatory capacity not related to the degree of coronary artery stenosis or vascular calcification. Impairment of vasodilatory capacity in patients with atherosclerosis appeared to be the consequence of increased coronary vascular size at rest, without a proportionate increase in vessel size during adenosine vasodilation. Because adenosine vasodilation is associated with increased heart rate, effective spatial resolution of MDCT could be reduced, and our results should be interpreted accordingly. However, only the largest and less mobile segments of the coronary vascular tree, the proximal portions, were assessed.

We conclude that the presence of atherosclerosis in epicardial conductance vessels is associated with an impairment of proximal vasodilatory capacity in coronary vessels of the heart, not related to the degree of coronary artery stenosis.

**Patricia M. Udholm, BS***
**Jesper J. Linde, MD, PhD**
**Rachael Barton, AS**
**Jørgen T. Kühl, MD, PhD**
**Jens D. Hove, MD, PhD**
**Mathias Sørgaard, MD**
**Anna F. Thomsen, BS**
**Klaus F. Kofoed, MD, PhD, DmSc**

*Department of Cardiology
Heart Centre
Rigshospitalet
Copenhagen University Hospital
Tagensvej 126, 4, 409
2200 Copenhagen
Denmark
E-mail: patricia.martens.udholm@gmail.com

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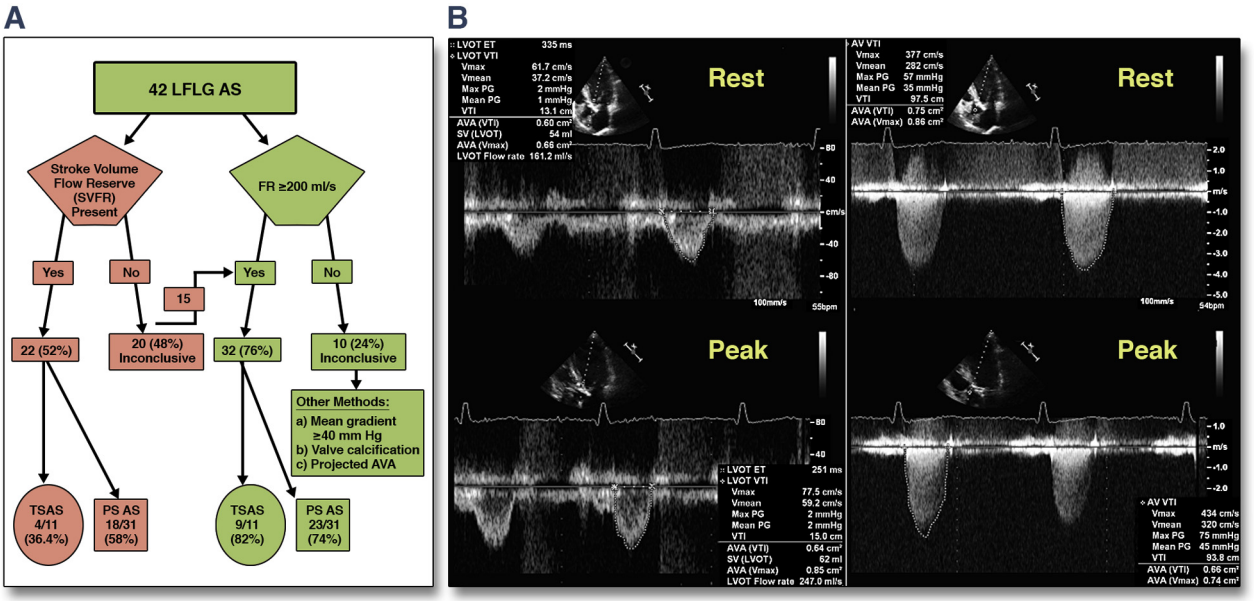
## Lack of Stroke Volume Determined Flow Reserve Does Not Always Preclude Assessment of Severity of Aortic Stenosis in Low-Flow Low-Gradient State During Dobutamine Echocardiography

The severity of low-flow low-gradient (LFLG) aortic stenosis (AS) during low-dose dobutamine stress echocardiography (LDDSE) is deemed assessable only when stroke volume–determined flow reserve (SVFR) (stroke volume [SV] increase ≥20%) is present. However, due to typically frequently exponential increase in heart rate (HR) and the consequent drop in left ventricular (LV) filling time, the SV during LDDSE often drops (1). However, despite lack of SVFR, the transvalvular flow or flow rate (FR) (SV/ejection time) may increase because, with rising HR, ejection time may shorten sufficiently to normalize FR, at which juncture the observed gradient and aortic valve area (AVA) will reflect the true status of AS (2). We thus hypothesized that during LDDSE for the assessment of LFLG AS, even in the absence of SVFR, FR may normalize, which will allow assessment of true severity of AS. FR ≥200 ml/s was considered normal (3,4).

We retrospectively assessed 42 consecutive patients (mean age 75.6 years) with LFLG AS (AVA <1 $cm^2$, mean gradient [MG] <40 mm Hg) who underwent LDDSE of which 33 (79%) demonstrated left ventricular ejection fraction (LVEF) <50%. Dobutamine was infused at 5, 10, 15, and up to 20 μg/kg/min with 5-min increments, and SV, FR, MG, and AVA were assessed at each stage. True severe aortic stenosis (TSAS) was defined as AVA <1 $cm^2$ and MG ≥40 mm Hg during LDDSE. For the comparisons of continuous and categorical variables, the independent Student *t* test and the chi-square/McNemar tests were used. Correlation between continuous variables was assessed by Pearson test.

The changes in HR between patients with SVFR and those without were similar (21 ± 16 beats/min vs. 24 ± 23 beats/min; p = 0.6) and showed similar results

**FIGURE 1 Flow Diagram and an Example for Assessing Severity of AS With SVFR Versus FR ≥200 ml/s**




**(A)** Flow chart for assessment of severity of low-flow low-gradient (LFLG) aortic stenosis (AS) with use of stroke volume–determined flow reserve (SVFR) (stroke volume increase ≥20%) versus attainment of flow rate (FR) ≥200 ml/s. **(B)** Left ventricular outflow tract (LVOT) and aortic valve (AV) Doppler at rest and stress in a patient with LFLG AS. SVFR was 14.8%, whereas FR exceeded 200 ml/s. The aortic valve area (AVA) remained <1 $cm^2$, whereas the mean gradient increased >40 mm Hg, suggesting true severe aortic stenosis (TSAS). PSAS = pseudosevere aortic stenosis.

in patients with LVEF <50%. No correlation between changes in HR and SV was observed, confirming the unpredictable response of SV to variable increments in HR. The changes in MG were similar between patients with SVFR versus those with FR ≥200 ml/s (9.7 ± 9.0 mm Hg vs. 9.8 ± 8.0 mm Hg) and likewise in patients with LVEF <50%. Similar results were obtained in patients with TSAS. Thus the amount of force applied to the AV is similar in patients with SVFR versus those with FR ≥200 ml/s.

However, of the 42 patients, 32 (76%) attained FR ≥200 ml/s versus only 22 (52%) with SVFR ($p = 0.04$). Furthermore, of the 20 patients without SVFR, FR ≥200 ml/s was attained in 15 (75%). Of the 11 patients with TSAS, FR ≥200 ml/s identified 9 (82%) with TSAS, versus only 4 (36.4%) with SVFR ($p = 0.13$). These data support FR ≥200 ml/s as normalized flow. It thus follows that the AS is not severe or is pseudosevere (PSAS) in 23 (74%) of the remaining 31 patients with FR ≥200 ml/s, thus the diagnosis of PSAS was higher ($p = 0.27$) than when SVFR was used (18 patients [58%]). Therefore, although subgroup analysis did not show significant differences in the diagnosis of TSAS and PSAS (lower number of patients in the subgroups), FR ≥200 ml/s during LDDSE resulted overall in significantly more conclusive tests, that is, diagnosis of TSAS and PSAS versus presence of SVFR.

In summary, in patients with LFLG AS undergoing LDDSE, FR-guided assessment allowed more conclusive assessment of severity of AS than an algorithm based on SVFR (Figures 1A and 1B), because more patients can attain a normalized FR ≥200 ml/s—a value also confirmed in a previous study as normal FR at rest—despite no significant change in SV (3). This may also partially explain why even despite lack of SVFR, some patients, possibly those with TSAS, derive prognostic benefit from valve intervention. Whereas it is likely that those with PSAS will not benefit, and this group is best identified using a FR-based algorithm (5). Further evaluation of inconclusive tests may be considered using methods shown in Figure 1A.

**Anastasia Vamvakidou, MBBS**
**Navtej Chahal, MBBS, PhD**
**Roxy Senior, MD, DM***

*Department of Cardiology
Royal Brompton Hospital
Sydney Street

London SW3 6NP
United Kingdom
E-mail: roxysenior@cardiac-research.org

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## Coronary CT Angiography in Asymptomatic Type 2 Diabetic Patients: First Do No Harm?

We read with great interest the article by Kang et al. (1) on the prognostic value of coronary computed tomography angiography (CTA) in asymptomatic type 2 diabetes mellitus. We have several concerns regarding this study. First, the overall event rate was low: 37 cardiac events in 29 patients (an overall event rate of 6.2%). The reported event-free survival rates must be interpreted in the context of the low event rates. Second, the use of medical therapy was low across the study population (<40% for all 3 subgroups). It is also unclear as to why 34.8% of asymptomatic patients with obstructive coronary artery disease (CAD) underwent revascularization. Was the decision to revascularize based on the ocular-stenotic reflex? Of the 10 cardiac deaths, how many of these occurred following revascularization? What is even more perplexing is that for the high-risk subgroup of patients with obstructive CAD, despite some of these patients undergoing revascularization, the use of medical therapy remained suboptimal (only 31.6% were on a lipid-lowering agent).

How would appropriate uptake of optimal medical therapy without screening coronary CTA alter the management and outcomes for this study population? Using the current American College of Cardiology/American Heart Association (ACC/AHA) atherosclerotic cardiovascular disease calculator (2), a typical patient with normal coronary arteries in this study has a 5.6% 10-year risk of heart disease or stroke, with the ACC/AHA recommending moderate-intensity statin therapy; a typical patient with non-obstructive CAD in this study has a 19.4% 10-year risk of heart disease or stroke, with the ACC/AHA recommending high-intensity statin therapy and consideration of aspirin; a typical patient with obstructive CAD in this study has a 23.4% 10-year risk of heart disease or stroke, with the ACC/AHA recommending high-intensity statin therapy and consideration of aspirin (2). One can hypothesize that following current ACC/AHA guidelines, event rates in this study population would have been even lower with appropriate medical therapy alone, without screening coronary CTA. The FACTOR-64 (Screening For Asymptomatic Obstructive Coronary Artery Disease Among High-Risk Diabetic Patients Using CT Angiography, Following Core 64) study was a randomized study examining the role of screening coronary CTA in 900 asymptomatic patients with type 1 or type 2 diabetes mellitus (3). At a mean follow-up duration of 4.0 years, there were no significant differences in the primary composite endpoint of all-cause mortality, nonfatal myocardial infarction, or unstable angina requiring hospitalization between the coronary CTA and control groups (3). It should be emphasized that a high proportion of patients in both the coronary CTA and control groups of the FACTOR-64 study were on statin therapy (76.5% and 72%, respectively) (3). Further evidence against routine screening of diabetic patients for asymptomatic CAD comes from the DIAD (Detection of Ischemia in Asymptomatic Diabetics) study, a randomized controlled trial in which 1,123 patients were randomly assigned to either screening with adenosine stress myocardial perfusion imaging (MPI) or not (4). It was found that screening for asymptomatic CAD with MPI in diabetic patients did not significantly reduce the cardiac event rates (4). During the course of the DIAD study there was a significant increase in the use of statin therapy in both groups (from 41% to 67% for the control group and from 37% to 67% for the MPI group; $p < 0.05$) (4).

Most importantly, retrospective electrocardiogram (ECG) gating was used to perform coronary CTA for the current study. Retrospective ECG gating is associated with significantly higher radiation exposure and potential cancer risk compared with prospective ECG gating (5). The dose-length product and effective radiation dose for each coronary CTA examination were not reported. Given that 52.2% of the patients with normal coronary arteries in this study were middle-aged women, the potential significance of