

# Coronary Sinus Blood Flow (CSBF) and Ejection Fraction (EF) studies before and after – off pump coronary artery bypass (OPCAB) - a literature review

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## Abstract

**Background:** Coronary Artery Bypass Grafting (CABG) Surgery reliably improving survival in patients suffering from coronary artery disease, but what effect it has on cardiac function is still obscure. It is a matter of great interest to review current literature to assess the CSBF and ejection fraction (EF) by transesophageal echocardiography (TEE) in patients before and after off pump coronary artery bypass (OPCAB) grafting.

**Aim:** The purpose of the article is to collect information about Coronary Sinus Blood Flow (CSBF) and Ejection Fraction (EF) studies before and after – off pump coronary artery bypass (OPCAB). Correlating with each other and drawing conclusions.

**Methods:** We analyzed 70 articles regarding to that of cardiac functional activities and coronary blood flow previous and after revascularization procedures.

**Results:** Although recent articles describe changes in coronary flow before and after bypass grafting, the relationship between cardiac functional parameters and blood supply is less well documented, particularly between EF and sinus perfusion.

**Conclusions:** We can conclude that this issue requires further research. (TCM-GMJ June 2025; 10 (1): P57-P64)

**Keywords:** Coronary Sinus Blood Flow (CSBF); Ejection Fraction (EF); Coronary Artery Bypass Grafting (CABG); Transesophageal Echocardiography (TEE)

## Introduction

As it is well known, physiologically coronary sinus (CS) drains the left coronary artery (LCA) basin. Stenosis of the branches of LCA may decrease the coronary sinus blood flow (CSBF). Any intervention that aims at restoring the flow of the stenosed vessel increases coronary artery flow that should consequently increase the CSBF. It is a matter of great interest to review current literature to assess the CSBF before and after each branch of LCA to determine the adequacy of surgical revascularization in patients undergoing elective off pump coronary artery bypass grafting (OPCAB) using transesophageal echocardiography (TEE). Cardiac perfusion can be assessed by coronary sinus blood flow (CSBF). [1] In patients with coronary artery disease, there is reduced CSBF. Any intervention that increases coronary perfusion may also increase CSBF. Measurement of CSBF is by various invasive techniques that require cardiac catheterization using intravascular Doppler flow wire, thermodilution catheter, [2] or digital coronary angi-

ography. It can also be measured by the use of radioisotope dyes such as argon technique or xenon scintigraphy. [1] Feasibility and reproducibility of transesophageal echocardiography (TEE) in measuring CSBF have been previously demonstrated.[3]

However, coronary artery blood flow (CABF) can also be assessed by coronary angiography and Doppler flow measurement in surgically revascularized patients. Unlike CSBF which is simple to demonstrate, obtaining CABF is quite challenging using TEE.

## Methods

We analyzed 70 articles regarding to that of cardiac functional activities and coronary blood flow previous and after revascularization procedures.

## Results and discussion

There has been limited literature available on CSBF for assessment of Coronary artery perfusion after surgical revascularization using TEE. Hence, some studies were undertaken to assess the CSBF before and after each branch of left coronary artery (LCA) to determine the adequacy of surgical revascularization in patients undergoing elective off pump coronary artery bypass grafting (OPCAB) using TEE.

As it was already mentioned, the CS drains the LCA territory. The CS is located 1 cm above and parallel to the left atrioventricular junction. Normally it is 1 cm in diam-

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eter. [1]

Meenakshi *et al.* [5] have estimated CSBF in PTCA patients using TTE and shown an increase of 76 ml in CSBF ( $P = 0.04$ ) post PTCA that was comparable with the present study. The increase in the CSBF was 38 ml post LAD grafting ( $P < 0.0001$ ) and 24 ml after OM grafting ( $P = 0.0002$ ). So, total increase in CSBF was 62 ml after LCA revascularization in their study.

Ng DW *et al.* [1] have studied the usefulness of TTE in demonstrating the CSBF before and after CABG and showed that there was a significant increase in CS VTI from  $10.6 \pm 1.93$  to  $13.4 \pm 2.3$  ( $P = 0.01$ ) with no significant change in CS diameter. Nagaraja P.S. *et al.* [11] reported that VTI after LAD revascularization increased from  $8.93 \pm 4.29$  to  $11.96 \pm 5.68$  ( $P \leq 0.0001$ ) and after OM revascularization, it increased from  $11 \pm 5.53$  to  $12.09 \pm 5.43$  ( $P = 0.002$ ) with no statistically significant change in CS diameter. The total change in the VTI and the change in CS diameter were comparable in both the studies. The advantage of Nagaraja P.S. *et al.* study [11] is that CSBF was estimated before and after each branch of LCA unlike Ng DW *et al.* [1] who estimated the CSBF before and after complete revascularization. Nagaraja P.S. *et al.* study [11] could also demonstrate the correlation between CSBF and adequacy of LIMA to LAD grafting.

Nanda *et al.* [6] have demonstrated left subclavian artery branches using TEE with 53% success rate in identifying LIMA. In the Nagaraja P.S. *et al.* [11], LIMA was demonstrated in 30% of patients post-LAD grafting. Even in the experienced hands, the success rate being only 53%, LIMA flow demonstration is definitely difficult to obtain on a regular basis. Whereas CSBF demonstration was feasible and reproducible (100%) with minimal experience.

Kuroda *et al.* [7] Orihashi *et al.* [8] Calafiore *et al.* [4] have successfully demonstrated LIMA to LAD flow. They have opined that the normal functioning LIMA to LAD graft should have  $Dp/Sp$  and/or  $Dm/Sm > 1$  and/or  $Dvti/Svti > 1.10$ . In the Nagaraja P.S. *et al.* [11] study, LIMA Doppler showed diastolic predominance with  $Dp/Sp$  and/or  $Dm/Sm > 1$  and/or  $Dvti/Svti > 1.10$  after LIMA to LAD revascularization. All patients who had normal functioning LIMA to LAD graft showed a statistically significant increase in the CSBF post grafting without any statistical change in heart rate and CS diameter.

Ng DW *et al.* [1] and Meenakshi *et al.* [5] had no statistically significant change in the heart rate before and after surgical revascularization and PTCA respectively. In the Nagaraja P.S. *et al.* [9] study, there was no statistically significant increase in the heart rate in those 9 patients in whom LIMA flow was demonstrated but when all 30 patients were analyzed, the change in heart rate was statistically significant. The mean heart rate before grafting was  $71.4 \pm 15.01$  and had increased to  $81.80 \pm 13.19$  after complete revascularization. However, the heart rate in only 4 patients had an increase of more than 20% from the baseline values. The increase in the heart rate may be possibly due to the inotropes in these patients. There was also decrease in the ejection fraction in these patients from the preoperative value.

The limitation of the Nagaraja P.S. *et al.* [9] study is that they were not able to compare CSBF with those of any invasive methods. The adequacy of LIMA to LAD flow also haven't been compared with coronary angiography.

Demonstration of CSBF is simple and monitoring the trend of CSBF values before and after each graft of LCA will guide to determine the adequacy of surgical revascularization. Demonstration of LIMA flow is challenging post LIMA to LAD grafting but if obtained will make it easy for correlating CSBF with the adequacy of grafting.

Augmentation of coronary artery flow by surgical grafting increases coronary sinus blood flow (CSBF), which can be quantified on transesophageal echocardiography (TEE). However, transit time flowmetry (TTF) technology remains the most used intraoperative technique for coronary artery graft assessment. The purpose of the pilot study done by Sandeep Joshi *et al.* [10] was to evaluate the predictive value of TEE-based CSBF estimation for identifying favorable TTF graft measurements. The authors [10] concluded that an increase in CSBF on TEE can ensure favorable postoperative TTF graft parameters with high sensitivity and specificity. Their pilot study elucidates the role of TEE in guiding the adequacy of surgical revascularization, which needs to be further investigated in larger studies to improve the reproducibility of this noninvasive matrix. However, the study expands the preexisting literature on the intraoperative graft flow assessment, particularly relevant in the era of alternate revascularization.

Quantifications of CS blood flow changes after CABG can be performed using Echocardiography (11, 12, 13). All three coronary arteries and their segments might be identified but because of accuracy and reliability it is easy to measure flow on venous side of coronary circulation – CS blood flow (11).

CS flow after CABG increase 20% per gram of myocardium per one graft (15). Any sudden decrease during follow up period can suggest new native or bypass flow problem. Normal coronary artery flow is 5% of cardiac output, around 250ml/min (16). Resting flow through normal coronary arteries, according to invasive measurements, is 0.5–1.5 ml/gr/min (0.8-1.2 ml/gr/min). At same time maximal coronary artery flow is 3-4 ml/gr/min.

Resting flow through severely stenotic coronary arteries ( $\geq 80\%$ ), hibernated myocardial segments or infarcted area is  $< 0.5$  ml/min/gr. At same time maximal coronary artery flow is  $< 1$  ml/min/gr.

Resting flow in intermediate stenosis (60-80%) is same as in healthy coronary arteries but slightly near lower value, with differences in published literature (17). Maximal flow through intermediate stenosis strongly correlates with degree of stenosis. Flow started to decrease with stenosis of 40% and become same as resting flow in stenosis  $\geq 80\%$ . Patients with microcirculatory disturbances, even without angiographically evident stenosis also have decreased flow during rest or effort (18). It is mainly because vasodilatory defect of endothelial cells.

After CABG resting net flow increases from 0.65 ml/min/gr to 0.78 ml/min/gr and maximal flow increase from 0.85 ml/min/gr to 1.0 ml/min/gr.

CS flow is lower than sum of coronary arteries flow. It is because there are: alternative drainage route (Thebesian veins and tributaries not connected to CS) and because CS drains mainly left coronary artery territory (19). Severe coronary artery stenosis can decrease the CS blood flow. Revascularization of severely stenotic vessel can increase coronary artery and consequently CS flow. TTE is performed in lateral decubitus position. With B mode, 4 chamber view is used to find CS after dorsal probe angulation. CS can then be found in atrioventricular groove and traced to distal segment. Then probe is rotated until minimal angle of insonation is recorded (about 30 degree). In this position we have to record VTI with Doppler angle of 60° and in B/M mode diameter of CS under same systemic hemodynamic parameters (21). After few cardiac cycles VTI is traced and average value memorized together with CD diameter and systemic hemodynamic data. For recordings in Short Axis View patient is in same position. Distal CS segment is recorded behind mitral valve with minimal probe angulation.

Several studies show usefulness of CS flow measurements using TTE as screening methods of coronary artery disease in specific populations. Even more there are published data about immediate flow changes after CABG recorded using TTE and TEE (16, 17).

Immediate coronary flow increase after triple CABG is up to 50% of native coronary flow. Increase is much higher if there are no micro vascular disturbances. Over time flow increase because graft and capillary bed vasodilatation.

The following formula for flow calculations is frequently used:  $Q = (VTI \times CSA) \times HR$ . Where's Q is flow, (VTI  $\times$  CSA) is stroke volume, HR is heart rate, CSA = cross section area of CS ( $\pi r^2$ , r = radius if vessel is round), VTI is average velocities calculated automatically after tracing heart cycle velocities. Usually above formula is adopted as  $CSA = CSA \times 0,39$ . Reason for this is ellipsoid shape of cross section area of CS with ratio 2:1. B. Banjanovic et al. (20) recorded longer cross section diameter in four chamber view calculation of cross section area was  $\pi ab$  ("a" was half of longer CS diameter, "b" was half of shorter CS diameter that mean "b" was 1/4 of measured diameter);

For LV mass calculations averaging flow rate over gram of myocardium is needed. LV mass was calculated using ASE; Devereux formula:  $LV_{gr} = 0,8(1,04(LVDD + PWTD + IVSTD)^3 - (LVDD)^3) + 0,6$ . Here LVDD is LV diameter in diastole, IVSTD is diastolic diameter of septum, PWTD is diastolic diameter of posterior wall near apex of papillary muscle.

B. Banjanovic, (20) showed statistically significant difference in CS flow during time. Using ANOVA tests for repeated measurements with Sphericity Assumed the author (20) found statistically significant difference during recording periods FVTI (Syst+Diast) (2;180) = 80,5,  $p < 0,001$  with Effect size (Effect Size; Cohen, 1988) of 0,68. So significant difference in CS flow during three time point: (preoperative, at 1 and at 6 postoperative day) is seen. So, the author concluded that there is significantly new

amount of blood in coronary bed after CABG, overall and after classifying per gram of LV and per graft number. And there is constant overall increase in amount of new blood postoperatively first 6 days.

Main variables that influence CS flow are: VTI, diameter of CS and heart rate. In CABG, graft patency is a major factor contributing to cardiac morbidity and mortality, especially in the early follow-up period. At 1-year follow-up, graft occlusion rates of 20.0% for venous and 8.0% for arterial grafts have been reported. Although the cause of late graft failure is attributed to intimal hyperplasia and atherosclerosis, failure within the first year is, thought in part, to be related to technical error that could be corrected at the time of surgery. However, after percutaneous transluminal coronary angioplasty (PTCA), the adequacy of the revascularization could be assessed by fluoroscopic evaluation using intracoronary dye injection; the immediate assessment of grafts following anastomosis is often neglected or performed with crude evaluations such as finger palpation.

As it seems from current literature further research and examination are required for intraoperative graft assessment modalities that could aid the surgeon in decision making regarding graft revision.

Intraoperative assessment tools for measurement of graft patency include transit time flowmetry and intraoperative fluorescence coronary angiography. The predictability for long-term outcomes is variable and inconclusive for both the techniques besides time consumption for performing intraoperative fluorescence coronary angiography, and therefore, both techniques have not gained much popularity.

There are many techniques available to measure the blood flow through the CS. The existing methods include thermodilution; gas clearance; densitometry; electromagnetic and Doppler flow probes; positron-emission tomography; and newer approaches ultrafast computed tomography, contrast echocardiography, and MRI. All the techniques cannot be used intraoperatively for measurement of CSBF.

TEE is a standard monitoring technique in cardiac surgery, and measurement of CS parameters in real time is easy, reliable, and reproducible.

Prajapati et al (27) evaluated the effectiveness of measuring CSBF using TEE during off-pump CABG and the authors found that TEE is a very simple and effective technique for evaluation of adequacy of coronary revascularization in off-pump CABG. Diameter of CS (measured in M-mode), VTI, and derived parameters, which included cross-section area of CS, CSBF per beat, and CSBF per minute using standard formulae, were assessed. All the aforementioned data were collected before commencement of revascularization and after completion of revascularization (before sternal closure). It has been found a significant increase in CS blood flow per minute ( $218.9 \pm 46.61$  vs.  $363.8 \pm 80.55$  ml) ( $P < 0.001$ ) and significant increment in mean CS diameter in post-revascularization phase as compared with pre-



revascularization phase (0.79 vs. 0.68 cm;  $P<0.001$ ).

Meenakshi *et al.* (25) studied transthoracic echocardiography to assess the improvement in CSBF after successful PTCA. CSBF per beat increased from  $3.06\pm1.12$  to  $4.2\pm1.80$  ( $P<0.038$ ), and CSBF per minute increased from  $231.33\pm70.68$  to  $308.20\pm121.32$  ( $P<0.042$ ).

Ng *et al.* (23) have studied the usefulness of TTE in demonstrating the CSBF before and after CABG and showed that there was a significant increase in CSVTI from  $10.6\pm1.93$  to  $13.4\pm2.3$  ( $P=0.01$ ), with no significant change in CS diameter.

Nagaraja *et al.* (24), found that mean heart rate increased after left anterior descending (LAD) and obtuse marginal revascularization, which was statistically significant. They proposed that the rise in the heart rate could be owing to increase in inotrope requirement. Prajapati *et al.* (27) found the average heart rate increased from  $72.51\pm6.33$  to  $74.73\pm8.38$  bpm ( $P=0.016$ ). Post-revascularization mean blood pressure also increased from  $83.44\pm4$  to  $87.01\pm5.46$  mmHg ( $P<0.0001$ ). However, CVP showed post-revascularization decrease from  $5.81\pm1.63$  to  $5.4\pm1.36$  cmH<sub>2</sub>O ( $P=0.01$ ). The aforementioned data were statistically significant; however, it has little relevance clinically, as the post-revascularization hemodynamic alteration was within  $\pm 10\%$  of baseline variation.

The aforementioned finding could be explained by the fact that the systemic blood pressure, heart rate, and CVP are dependent on multiple factors such as fluid status, inotropic/vasopressor requirement, depth of anesthesia, and degree of sympathetic stimulation. However, we tried to maintain the hemodynamics within the baseline range as per our institution's protocol using vasopressors.

Findings by Prajapati *et al.* (27) were comparable to the results of Nagaraja *et al.* (24) who in a similar study evaluated the CSBF in patients undergoing off-pump CABG. They found that the CSBF per beat increased from  $1.28\pm0.71$  to  $1.70\pm0.89$  ( $P<0.0001$ ), CSB per minute increased from  $92.59\pm59.32$  to  $130.72\pm74.22$  ( $P<0.0001$ ), and total VTI increased from  $8.93\pm4.29$  to  $11.96\pm5.68$  ( $P<0.0001$ ) after LAD revascularization. Similarly, the CSBF per beat increased from  $1.67\pm1.03$  to  $1.91\pm1.03$  ( $P<0.001$ ), CSBF per minute increased from  $131.91\pm86.59$  to  $155.20\pm88.70$  ( $P<0.0002$ ), and total VTI increased from  $11.00\pm5.53$  to  $12.09\pm5.43$  ( $P<0.002$ ) after obtuse marginal revascularization.

Similar findings were obtained by Hajaghaei *et al.* (26), who also found comparable results in their study, where they found CS diameter increased from  $8.6\pm1.06$  to  $9.4\pm1.21$  ( $P<0.01$ ) 1 month after CABG.

Coronary flow reserve is defined as a maximum to resting blood flow ratio. Normally, increase in the coronary blood flow is mediated by dilation of arteriolar bed. Coronary Flow Reserve (CFR) measurement is a very helpful clinical tool in several conditions including assessment of intermediate stenosis especially in patients with chest pain syndrome, detection of critical stenosis, and in-stent restenosis, as well as evaluation of graft patency after CABG. There are two major vasodilators for measurement of CFR, adenosine and dipyridamole. [M Hajaghaei \*et al.\* \(26\)](#)

used dipyridamole as a vasodilator and stressor test, mostly because of its prolonged action compared with adenosine (29,30). Dipyridamole blocks the intracellular retransport of adenosine and inhibit adenosine deaminase responsible for intracellular breakdown of adenosine (31). Thus, dipyridamole acts as an indirect coronary arteriolar vasodilator.

Although assessment of CFR via intracoronary Doppler wire is accurate, but this method is invasive with radiation exposure; and makes the follow up study relatively impossible. PET scan is another method with radiation exposure and highly expensive. In the past decade, there were several attempts for measurement of CFR by echocardiography as non-invasive and reproducible results, and mostly performed on coronary arteries by transthoracic or transesophageal approach. Although the coronary arteries (mostly left anterior descending artery) were detected with Doppler and 2-D images, these lacked sufficient clarity for accurate measurement of vessel diameter, thus only the coronary blood velocity could be measured. The flow velocity variation is proportional to total blood flow if vessel lumen is kept constant. Thus, estimation of CFR can be accurate if the coronary artery functions only as a conduit.

4. CFR measurement of the coronary arteries by Doppler echocardiography is therefore limited to the coronary blood velocity. CFR and coronary flow velocity were closely correlated (32), because most of the vasodilation was located in microcirculation and arterioles, but in this study measurement of blood velocity and VTI was done on venous side of the coronary system. Similar to other veins, coronary sinus has a thin wall and highly extensible structure; so, the coronary blood velocity is no longer closely related to CFR. As a result, for measuring CFR in the coronary sinus, measurement of CS diameter at baseline and hyperemic phase is mandatory and ignoring this step may lead to significant error in estimation of CFR. In another study (33) with focus on CS diameter in baseline status before and after CABG, there was no significant increase in CS diameter after surgery. Another difference in CFR estimation on arterial and venous side was based on different shape of flow in the cardiac cycle. Regarding the coronary arteries, there was predominantly diastolic flow with gradual diastolic slope and respective peak diastolic and systolic velocities of  $28\pm9$  cm/sec and  $17\pm4$  cm/sec (34). However, in CS, the pattern of flow was also related to right atrial pressure with two distinct systolic and diastolic waves, considering that systolic wave was dominant in the healthy subjects (35). Therefore, simple CFR assessment by diastolic velocity ratio in the coronary artery could be used with reasonable accuracy (36) but this is not true with respect to CS. Another variable of the coronary blood flow is heart rate. Usually, measurement of CFR was done in two ways:  $\text{CFR}/\text{min} = \text{HR} \times \text{D}^2 / 4 \times (\text{S} + \text{D})$  VTI  $\text{CFR}/\text{beat} = \text{D}^2 / 4 \times (\text{S} + \text{D})$  VTI In the study of M Hajaghaei *et al.* (28), a close relationship between above equations led to CFR/min to be higher than CFR/beat in all cases. Therefore, as the authors concluded, considering these technical points, coronary flow reserve measurement by transthoracic echocardiography can be used as a feasible and reproducible method to monitor the changes in

cardiac perfusion after revascularization.

S. M. Seyedian *et.al* (36) in their study, observed a significant increase in the CSD in each individual compared with the diameter before surgery. The coronary sinus is a tubular structure, about 3 cm in length and 1 cm in caliber, located in the groove between the left atrium and the left ventricle posteriorly. It begins as a continuation of the great cardiac vein and empties the entire blood of the cardiac veins into the right atrium through the ostium of the coronary sinus (37). In 1983, Ishimitsu and colleagues (38) described the detection of the coronary sinus by parasternal 2D echocardiography. A severe dilatation of the coronary sinus compared to normal values is a clue to the presence of a persistent left superior vena cava or more rarely, other congenital anomalies such as coronary arteriovenous fistulae or anomalous pulmonary venous drainage into the coronary sinus (39). Recently, the dilatation of the coronary sinus has also created much interest among echocardiographers as a surrogate echocardiography marker for various conditions such as pulmonary hypertension and tricuspid regurgitation (39;40;41). This is probably related to an elevated pressure in the right atrium, where the coronary sinus is emptied, due to a transfer of the right atrial pressure to the coronary sinus causing dilatation of this vein. Our results revealed an increase in the CSD compared with pre-CABG status in the patients with significant stenosis in 2 or 3 major coronary arteries and without right atrial hypertension, which may have been in consequence of a decrease in venous drainage secondary to a decrease in the coronary artery flow distal to stenosis in per CABG status. Based on such evidence, there may be a positive association between the CSD and the intracoronary flow. In fact, our evaluation of the CSD in the patients before surgery showed that those with severe stenosis in 2 or 3 arteries had a decrease in the CSD compared with post CABG. The CSBF is often used as a measure of cardiac perfusion and it has been shown to increase after CABG in response to a decreased flow by stenosis before surgery. 2,6 The main finding of our study was that the CSD significantly increased after CABG in comparison with the diminished size due to coronary stenosis before surgery; this finding corresponds with the results of other perfusion studies. It might be due to the exposure of the vein to an increased intravascular flow and the coronary sinus pressure after CABG, which subsequently distends the coronary sinus. The aforementioned phenomenon has also been previously reported in the case of the overdilatation of the venous graft after exposure to arterial blood pressure following CABG (41). In another study, Xia et al (41) assessed the CSD and the blood velocity of the coronary sinus post CABG in 78 patients and reported that the difference was more prominent in those with triple-vessel disease than in the ones with double-vessel disease. In our study on 100 patients, we found significant changes in the CSD itself, with 95% confidence intervals ( $6.89 \pm 0.69$  vs  $7.67 \pm 0.65$ ;  $P = 0.0001$ ); additionally, S. M. Seyedian *et.al* (36) observed that the increase in the diameter was more significant in our patients

with triple-vessel disease in comparison with those with double-vessel disease after CABG ( $7.24 \pm 5.83$  vs  $8.06 \pm 7.63$ ;  $P < 0.005$ ; in double-vessel disease and  $6.76 \pm 4.83$  vs  $7.53 \pm 5.43$  in triple-vessel disease). S. M. Seyedian *et.al* (36) finding is in line with that reported by Xia and coworkers. The difference can be explained by the fact that both the flow and the diameter of the coronary sinus are reduced more in triple-vessel disease than in double-vessel disease; therefore, before and after complete revascularization, we can expect more flow and diameter increments in triplevessel disease in comparison with doublevessel disease. S. M. Seyedian *et.al* (36) study aimed to test whether the CSD increases after CABG and whether TTE can be used as a suitable noninvasive method for the detection of diameter changes in the recovery period or afterward. There is also an assumption that the coronary flow and perfusion improves after CABG. In conclusion, our results suggest that the TTE determined CSD can be a potential surrogate marker for myocardial perfusion clopidogrel after CABG. Further studies are warranted to assess the predictive value of the CSD for the patency of grafts after CABG.

Myocardial perfusion reserve (MPR) is defined as the maximal possible increase in myocardial blood flow (MBF) above baseline conditions. Global MBF can be measured non-invasively by means of coronary sinus flow velocity encoded cine (VENC) cardiovascular magnetic resonance (CMR). Shomanova Z *et.al* (43) aimed to explore the relationship between global MBF/MPR and the extent and severity of coronary artery disease (CAD) in patients referred for CAD workup by adenosine-stress CMR.

The use of coronary sinus flow velocity encoded cine (VENC) cardiovascular magnetic resonance (CMR) sequences for non-invasive quantification of global myocardial blood flow (MBF) has proved to be a promising technique and was validated in clinical and experimental settings, respectively (48-52). The ratio between hyperaemic-to-rest MBF was defined as MPR and shown to be impaired in some cardiac diseases of non-ischaemic/ischaemic origin (50;53; 53-55).

The study of Shomanova Z *et.al* (43) aimed at evaluating the relationship of non-invasively quantified global MPR by coronary sinus flow CMR (at rest and under peak adenosine-stress) to the anatomical and functional extent of atherosclerotic lesions in patients with suspected obstructive CAD. The major findings of this study can be summarized as follows (44); In the study population, global MPR was significantly reduced when compared to a younger control group with a low CAD pre-test probability (45); A significant decrease in global MPR was found in patients with a high CAD burden (Syntax >22) when compared to patients without obstructive CAD (Syntax =0) (46); Global MPR impairment was primarily related to the presence of proximal epicardial lesions and/or presence of multi-vessel disease, but not to the occurrence of limited regional stress-induced ischaemia (47); The diagnostic yield of stress CMR for the diagnosis of CAD (>50% stenosis) increased substantially (from 65% to 88%) when global

MPR assessment was considered in addition to stress perfusion imaging. Hence, the performance of global MPR measurements—in addition to conventional first-pass stress perfusion imaging—may help to identify those patients with severe proximal epicardial stenoses and/or multi-vessel disease and thereby (i) extend the diagnostic information that is obtained by conventional stress perfusion imaging and (ii) support clinical decision-making (e.g. whether or not to perform invasive coronary angiography after diagnostic CMR testing).

Coronary sinus flow derived global MPR by CMR is impaired in patients with hypertrophic and dilated cardiomyopathy, after cardiac transplantation and in the presence of chronic heart failure with a reduced LVEF—most probably secondary to a diffuse involvement of the coronary microvasculature (50;51; 53-55). Conversely, due to large variability in atherosclerotic CAD burden with a non-neglectable impairment of both epicardial haemodynamics and microcirculatory response to hyperaemic stimuli, the interpretation of changes in global MPR is more challenging in case of CAD and published data are relatively scarce (56;57; 61-64).

The current findings of a decreased global MPR in patients with suspected obstructive CAD compared to younger, healthy controls are in line with the only two studies that were so far published on this issue: The first study of Shomanova Z *et al.* (43) found an inverse association between MPR and the cardiovascular risk factor burden, while the second one related MPR to the presence of 1- or 2-vessel disease and heart failure symptoms (56; 61). Interestingly, earlier PET studies showed an inverse relationship between global MPR and age, particularly in those patients aged >70yrs (65). However, considering the detailed results in Shomanova Z *et al.* (43) study group ( $n = 58$ ) with large differences in the presence of epicardial CAD, the major findings primarily reflect the extent and severity of epicardial CAD (47). Of course, the additional microvascular effects since cannot be excluded (i) microvascular disease is often present in patients with advanced epicardial CAD and (ii) microvascular dysfunction can even occur without advanced epicardial CAD. However, since global MPR values did not differ between those patients with completely smooth coronaries compared to those patients with non-obstructive (<50%) lesions, microvascular effects are believed to play only a minor role (if at all).

Furthermore, most of the available non-invasive data regarding the disruption of normal coronary physiology in CAD come from PET and SPECT studies (57). Global MPR is primarily reduced in patients with a high anatomical burden of obstructive CAD (Syntax >22), Ziadi *et al.* (59) found MPR to be an independent predictor for three-vessel CAD by Rubidium-82 PET. Similarly, the SPECT study by Ben BF *et al.* (66) showed an association between global MPR and CAD extent, defined as the number of obstructed vessels, with a significant difference between patients with and without three-vessel disease (66). Moreover, a 'normal' MPR was shown to have a high

negative predictive value for excluding high risk CAD on angiography (58). A high correlation and agreement between CMR and PET studies was already demonstrated for both global MBF and MPR—with only MBF being slightly underestimated by CMR due to anatomical factors (the coronary sinus drains most of but not the whole myocardium) (48;51). Therefore, some differences in reported MPR values are likely due to the differences in CAD severity between studies (e.g. MPR in the present study in Syntax >22: 1.7 vs. in three-vessel disease by Ziadi *et al.* (59) and by Ben BF *et al.* (66)).

Interestingly, in spite of being lower in positive compared to negative adenosine-stress perfusion subgroups, global MPR was not significantly related to the presence of induced perfusion defects, however, associated with the CAD extent/SYNTAX score according to current available definitions (60). Previous nuclear studies showed a marked decrease in regional peak MBF and 'regional' MPR in territories with flow-limiting stenoses as defined by invasive fractional flow reserve, compared to preserved values in normal territories. This phenomenon is nicely visualized as a regional perfusion defect (66;67). However, if 'global' MPR is looked at, the data from Shomanova Z *et al.* (43) suggest that in those patients without proximal epicardial stenosis or without three-vessel disease (representing 84% of our study population) compensatory mechanisms like increased regional flow in non-stenosed segments contribute to a maintained normal global MPR (63). Therefore, a reduced global MPR in a patient with positive stress perfusion could serve as a supplementary parameter of CAD severity—in addition to the number of segments with perfusion deficits. Above all, estimates of ischaemic burden by functional imaging are the major factor in revascularization decisions and a simple addition of global MPR based on coronary sinus flow measurements to a standard adenosine-stress perfusion CMR may enable a higher diagnostic yield and an improved characterization of CAD/ischaemia extent, particularly in multi-vessel disease.

In patients with obstructive CAD defined by anatomical criteria (>50% luminal narrowing according to SYNTAX score), has been showed that only the presence of ischaemia (shown by stress perfusion CMR) is associated with a decrease in global MPR. This finding is in accordance with current stable angina guidelines that underline the importance of knowledge about coronary function besides anatomy when evaluating CAD patients (44;45;68).

The assessment of changes in pre- and post-operative left ventricular - LV systolic indices and function after coronary artery bypass grafting - CABG is limited, perhaps due to the lack of routine echocardiography after CABG. A study of [Ryan J. Koene](#) (69) is the largest to assess pre- and post-operative echocardiograms in a population including both normal and reduced pre-operative LV function. While prior studies have similarly found an improvement in LV systolic function in patients with pre-operative LV systolic dysfunction, to our knowledge, this is the first study to show a decrease in left ventricular ejection frac-



tion - LVEF with CABG in patients with normal baseline LV systolic function. While the magnitude of decrease in LVEF was small (mean 3% reduction), which may not have any clinical significance, the change in EF ranged from -33% to 15%, meaning that some patients had a clinically significant decline in EF. A decrease in LV systolic function with CABG surgery may result from intraoperative global ischemia or myocardial stunning, or from early post-operative graft failure. These results warrant confirmation in prospective studies with unselected patients.

Few studies have compared pre- and post-operative cardiac imaging after CABG. In patients with preserved pre-operative systolic function, Diller *et al.* (69) prospectively followed 32 patients at 5 days, 6 weeks, and 18 months after CABG, demonstrating an improvement in LV diastolic function. In contrast to [Ryan J. Koene's](#) study, this small study (69) did not find a significant reduction in LV systolic function immediately after CABG. In patients with reduced LV function, several smaller studies have shown improvement in LV function with CABG in patients with baseline LV systolic dysfunction. The STICH trial (70) was the only prospective, randomized, controlled trial to specifically investigate the role of CABG in patients with severe LV systolic dysfunction (EF  $\leq 35\%$ ). A post hoc subgroup analysis of this trial showed a significant improvement in LV size and function in the subgroup of patients with higher baseline LV end-systolic dimensions (70). Similarly, the results of [Ryan J. Koene's](#) study show EF improvement to be associated with greater baseline LV dimensions. Our study is also in agreement with these studies in demonstrating an improvement in LVEF in the subgroup of patients with pre-operative LV systolic dysfunction.

In patients undergoing CABG, pre-operative LVEF appears to be an important determinant of change in LV function following surgery. In [Ryan J. Koene](#) study, patients with pre-operative LVEF  $< 50\%$  had an improvement in LV systolic function whereas those with normal pre-operative LVEF had a decline in LV systolic function. The other LV indices that changed after CABG were LVID, which decreased, and LAD, which increased. This study really broadens the existing knowledge on peri-operative changes in LV systolic function in patients undergoing CABG, to include a population with both normal and depressed pre-operative LV systolic function.

## Conclusion

We can conclude that this issue requires further research. Therefore, our team continues to obtain material on this issue, and we are also conducting practical research, the results of which we will present to you in the following articles.

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