Imaging of Subendocardial Myocardial Blood Flow by Dye-Staining Cardioscopy in Patients With Coronary Artery Disease

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Summary

This study was carried out to image subendocardial myocardial blood flow (SMBF) by dye-staining cardioscopy (DSC) in patients with coronary artery disease.

In patients with epicardial coronary artery disease, SMBF plays a direct and critical role in determining the extent and severity of cardiac function and symptoms. If SMBF could be clinically imaged instantaneously, the effects of medical and interventional treatment on it can be directly evaluated. However, there are no clinically available methods for direct and real-time imaging of SMBF.

Twenty-three patients [6 with chest pain syndrome (CPS); 3 with vasospastic angina pectoris (VSA); 9 with angina pectoris due to organic coronary stenosis (AP); 5 with old myocardial infarction (OMI)] underwent DSC of the left ventricle by selective intracoronary injection of 1 mL of 2.5% Evans blue dye solution (EB). Five patients with acute myocardial infarction (AMI) underwent DSC before and after coronary stent deployment.

The endocardial surface was stained diffusely blue with EB indicating normal blood flow in patients with CPS; stained in a patchy fashion indicating patchy blood flow in patients with VSA; and stained in a patchy fashion or not stained indicating patchy or no blood flow in those with AP and OMI. Myocardial staining with EB was observed after coronary stent deployment in all patients with AMI, indicating restoration of the SMBF.

It is evident that SMBF could be imaged by DSC. This imaging modality is useful for the evaluation of therapies and accurate guidance of transendocardial therapies of the ischemic myocardium. (Int Heart J 2010; 51: 308-311)

Key words: Myocardial blood flow, Coronary artery disease, Dye-staining cardioscopy, Evans blue dye

Structurally, the left ventricular wall of the heart comprises 3 myocardial layers, namely the inner oblique, middle circular, and outer oblique myocardial layers.3 It is the inner oblique layer that is most susceptible to ischemia.3 Until recently, myocardial blood flow has been evaluated by contrast echocardiography,4,5 radionucleid imaging,6 magnetic resonance imaging,7 computed tomography,8 or electron beam computed tomography.9 However, selective evaluation of blood flow in the individual myocardial layers, especially in the inner oblique layer, namely the subendocardial myocardium, is often difficult with these imaging modalities.

A cardioscopy system using white light as the light source and obtaining color images of the heart from the inside, namely conventional cardioscopy,10 was devised by the present authors. It was applied for the differential diagnosis of myocardial and valvular diseases.11,12 This imaging modality enabled the observation of subendocardial myocardial blood flow (SMBF). However, because endocardial color was used as an indicator of SMBF, the assessment of SMBF was greatly influenced by the intensity of the light source. Therefore, a more reliable method for direct imaging of SMBF is required.

Evans blue dye (EB) was used clinically in the past to evaluate cardiac output, while more recently it is being clinically used to detect fibrin14 and damaged endothelial cells in the coronary artery15 without any side effects. Further, this dye is used to prevent coronary re-stenosis after percutaneous coronary interventions in animals and humans.16,17

As the safety of the intravascular administration of EB became evident from all these studies, intracoronary administration of this dye was performed in coronary artery disease patients to observe SMBF disturbance by cardioscopy using EB as an indicator of SMBF, namely “dye-staining cardioscopy (DSC)”.

Methods

Conventional cardioscopy system: The conventional angioscopy system was composed of a light source (CLV-A, Olympus Corporation, Tokyo), 9-F guiding balloon catheter (Clinical Supply Co, Gifu, Japan), 4.2-F fiberscope (AF 14, Olympus), and a color CCD camera (OTV-A, Olympus). Before observation, color correction was carried out by adjusting the white balance. Details of the cardioscopy system are described elsewhere.11,13
Evaluation of SMBF by dye-staining cardiscopy (DSC) in patients with coronary artery disease: DSC was carried out at Toho University Sakura Hospital and was approved by the Institutional Review Board. Twenty-three patients (15 males and 8 females; 61.6 ± 2.1 (mean ± SE) years old; chest pain syndrome (CPS) in 6, vasospastic angina (VSA) in 3, stable angina pectoris due to organic coronary artery stenoses (A) in 9, and old myocardial infarction (OMI; more than one month after the onset of acute myocardial infarction) in 5] underwent DSC. All 23 patients provided informed consent for the procedures. The patients were pretreated with oral diazepam (10 mg) before being transferred to the catheterization laboratory. After administering 50 mg of intravenous lidocaine and 5000 IU heparin, left ventriculography and coronary angiography were performed. Subsequently, a 9-F guiding balloon was introduced into the left ventricle and the balloon was inflated with CO₂. Next, a 4.2-F fiberscope was advanced through the catheter so as to position the fiberscope tip at the tip of the catheter. The balloon was gently pushed against the targeted wall segment of the left ventricle, and 50 to 100 mL of saline solution (heparin 10 IU/mL, 37°C) was injected through the catheter at 10 mL/second to displace the blood between the balloon and the ventricular luminal surface for observation. The changes in the luminal surface were recorded using a color CCD camera on a DVD recorder. The observed portion was the anteroapical segment in CPS, the wall segment which was irrigated by the artery in which spasm was evoked by intracoronary administration of acetylcholine in VSA, the wall segment irrigated by the stenotic artery in A, and the dys- or akinetic wall segment in OMI. After this, the balloon catheter was replaced by a Judkins catheter and 1 mL of 2.5% EB was injected into a coronary artery which irrigated the left ventricular wall segment under study. The balloon catheter and fiberscope were then reintroduced into the left ventricle, placing the balloon catheter tip at the same wall segment that had been previously observed, and luminal surface changes were observed again. The time required for repeated observation by DSC ranged between 10 and 15 minutes. The total amount of saline solution required to complete the observation ranged from 300 to 500 mL.

Measurement of coronary stenosis: Diameter stenosis of the coronary arteries was measured by quantitative coronary arteriography using TCS Symphony 2.02 (Mckesson Co, North Charleston, SC, USA). It was expressed as a percentage to correlate the SMBF changes to the severity of the stenosis of the irrigating coronary arteries.

Classification of subendocardial color: Subendocardial color in patients with coronary artery disease is classified into brown (nonischemic), light brown (mildly ischemic), pale (severely ischemic), and white (fibrosis).¹²,¹³

Definition of dye-staining pattern: The dye-staining pattern was classified into diffuse and patchy (blue color clearly demarcated from the surrounding portions). Diffuse staining was further classified into uniform (same depth in blue color) and nonuniform (different depth of blue color from one portion to another portion).

Evaluation of the effects of coronary stenting on SMBF: Five patients with acute myocardial infarction (AMI; 5 males; 60.3 ± 3.1 years old) underwent DSC before and after deployment of bare-metal stents (NIR in 2, Multilink in 3 patients) into the culprit coronary artery to evaluate the changes in the SMBF.

Statistical analysis: The data are expressed as the mean ± SE and were tested using the Student t test. A value of P < 0.05 was considered to be statistically significant.

RESULTS

Changes in SMBF in patients with coronary artery disease: Figure 1 shows DSC images of the left ventricle in a patient with CPS. Before the EB injection, the endocardial luminal surface was brown in color, suggesting normal blood flow. After the EB injection, the endocardial surface was stained in a patchy fashion, indicating patchy preservation of SMBF.

Staining patterns: Endocardial surface observed by DSC was diffusely stained blue in color, indicating diffuse staining of subendocardial myocardium with EB and accordingly normal SMBF in all the patients with CPS. In contrast, in patients with A and OMI due to organic coronary artery disease, patchy staining indicating patchy preservation of SMBF, diffuse but nonuniform in depth of blue color indicating differences in flow volume, and no staining indicating SMBF was absent, were frequently observed. In addition, patchy staining was also observed in patients with VSA, a functional disease (Figure 3).

Relationships between staining patterns and % stenosis of the irrigating coronary artery: It was observed that % stenoses of the irrigating coronary artery were 11.0 ± 11.1, 59.3 ± 14.3, and 88.3 ± 4.8 (mean ± SE) in the diffuse, patchy, and no staining groups, respectively. No significant difference was observed in % stenoses between the patchy and no staining...
Effects of coronary stenting on SMBF: Figure 4 shows an example of SMBF recovery induced by bare-metal stent deployment into the right coronary artery in a patient with AMI. Before stent deployment, the endocardial surface of the inferobasal wall segment of the left ventricle which was irrigated by the right coronary artery showed no change after the injection of EB into this artery. Injection of EB after stent deployment, however, caused the endocardial color to become purple (result of mixing of blue color of EB and red color of blood), indicating the mixing of EB with restored SMBF. Similar restoration of SMBF was confirmed in the remaining 4 patients.

Complications: No complications related to DSC were noted during or after the procedure.

**Discussion**

The staining pattern of the subendocardial myocardium with EB was classified as diffuse, patchy, or no staining, indicating normal SMBF, patchy preservation of SMBF, or no SMBF, respectively. Since blue is a color that is not naturally found in the human body, this EB blue color was clearly distinguishable from the other colors of the left ventricular luminal surface, namely, brown, white, yellow, and red that are observed in the various categories of heart disease.

Patchy, nonuniform, and no staining were frequently observed in patients with A and OMI due to organic coronary artery stenosis or occlusion. However, despite total occlusion of the irrigating artery, patients with OMI did not necessarily exhibit no staining, instead a few patients exhibited patchy staining. The blood supply through the antegrade collateral vessels most likely contributed to the patchy preservation of SMBF.

Generally, in VSA, the coronary circulation, including the microcirculation, is considered to be normal when vasospasm is absent, and severe myocardial ischemia occurs once vasospasm takes place. In this study, despite the apparently normal coronary arterial trees observed on angiography, patchy staining was seen in patients with this category of disease. It was reported that endocardial color is frequently light brown, indicating mild ischemia and white trabecular edges suggesting fibrosis are frequently observed in patients with VSA. The frequent and severe ischemia caused by vasospasm most likely resulted in regional endocardial and/or myocardial fibrosis, or in myocardial stunning and a resultant decrease in the vascular bed, resulting in patchy SMBF in this category of coronary ar-
tery disease.18"
There were no obvious differences in % stenosis of the irrigating coronary artery between the patchy staining and no staining groups. It is likely that antegrade collaterals, microvessel disease, and myocardial fibrosis obscured the difference. Cardioscope-guided endomyocardial biopsy may provide much information on these underlying changes.19 However, this diagnostic method was not employed in this study.

Endocardial surface was stained blue in color following successful coronary stenting, indicating restoration of SMBF in patients with AMI. Therefore, this imaging modality can be used to evaluate interventional therapies for coronary artery disease.

The contribution of the collateral circulation was not investigated in this study. By selective administration of EB into the other coronary artery, the contribution of the collateral vessels in maintaining the SMBF in the diseased regions of the myocardium can be more precisely evaluated.

EB was clinically used to measure cardiac output in the past. This dye is now being used clinically to detect vascular endothelial damage and fibrin.14,15 The usefulness of EB for regression of atherosclerosis and prevention of coronary re-stenosis has been demonstrated.16,17 Therefore, this dye can be used clinically not only to evaluate SMBF but also to achieve pin-point guidance of transendocardial angiogenic and myogenic therapies20-25 and intracardiac surgery such as laser myocardial revascularization.20

Conclusions: SMBF was evaluated by DSC using EB as an indicator of myocardial blood flow in patients with coronary artery disease. SMBF pattern was classified as diffuse, patchy, and no flow. Patchy and no flow were observed in patients with A and OMI. Patchy flow was also observed in patients with VSA. In patients who had undergone successful coronary stenting, restoration of SMBF was clearly demonstrated by DSC. The results indicate the clinical feasibility of this imaging modality to evaluate SMBF and accordingly to evaluate and guide medical, interventional, and surgical procedures for treating coronary artery disease.

References

4. Zipes DP, Libby P, Bonow RO, Braunwald E. Relative merits of coronary re-stenosis has been demonstrated.16,17 Therefore, this dye can be used clinically not only to evaluate SMBF but also to achieve pin-point guidance of transendocardial angiogenic and myogenic therapies20-25 and intracardiac surgery such as laser myocardial revascularization.20

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References