Myocardial Blush Grade: An Interventional Method for Assessing Myocardial Perfusion

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Myocardial perfusion is affected by many factors including patient's blood pressure (mainly diastolic), small coronary vascular bed, myocardial tissue (including myofibers, extracellular matrix and accidental constituents such as inflammatory cells and edema) and left ventricular diastolic pressure. Coronary angiography portrays only a silhouette of the epicardial coronary arterial lumen. Several non-invasive tests have been used to assess myocardial perfusion including radionuclide scans, positron emission tomography, myocardial contrast echocardiography, and stress/dobutamine echocardiography.

During recent years several invasive techniques have emerged for the assessment of coronary blood flow and myocardial perfusion, including intravascular coronary Doppler wire for coronary flow (velocity) reserve, and intravascular pressure wire for fractional flow reserve measurement. TIMI flow is a simple method for assessing coronary flow either qualitatively or by counting frames needed for the dye to advance from the coronary artery orifice to its distal end. It was first used to identify patients with small coronary disease [1] and later on to identify angiographic and clinical outcome of thrombolytic agents in the TIMI studies (Thrombolysis In Myocardial Infarction) [2]. Successful restoration of flow in the infarct-related artery was considered by TIMI investigators to be an ultimate goal of reperfusion, but substantial evidence has grown over the years showing that distortion of microvasculature and myocardial perfusion often present despite epicardial artery patency. This might be the result of a combination of distal embolization and reperfusion injury with cellular and extracellular edema, neutrophil accumulation and release of detrimental oxygen free radicals. The "no-reflow" phenomenon – namely, diminished or absent blood flow in an open coronary artery (during myocardial infarction or percutaneous angioplasty) – attracted attention to tissue perfusion (or "blush") by coronary blood and contrast medium.

Myocardial blush

Myocardial blush was first defined by Arnoud van't Hof et al. [3]. It is a qualitative visual assessment of the amount of contrast medium filling a territory supplied by an epicardial coronary artery. It is graded as Myocardial Blush Grade: 0 = no myocardial blush or contrast density, 1 = minimal myocardial blush or contrast density, 2 = myocardial blush or contrast density which exists to lesser extent and its clearance is diminished compared to non-infarct-related coronary artery, and 3 = normal myocardial blush or contrast density comparable with that obtained during angiography of a contralateral or ipsilateral non-infarct-related coronary artery.

Myocardial blush grade is a valuable tool for assessing coronary microvasculature and myocardial perfusion in patients undergoing coronary angiography and angioplasty

When myocardial blush persists ("staining"), it suggests leakage of the contrast medium into the extravascular space or impaired venous clearance and is graded 0. Assessing MBG should follow a strict protocol. This involves choosing the best projection that demonstrates the territory supplied by a given coronary artery without superimposition of adjacent myocardium, applying intracoronary nitroglycerin (100–200 μg), injecting 5–10 ml contrast media, and documenting a run long enough to allow visualization of the territory of interest until the venous phase of the contrast passage is evident.

Clinical significance of MBG in specific clinical subsets

MBG in patients with unstable angina pectoris was found to inversely correlate with post-procedural elevation of troponin-I and P; improved blush grade was associated with lower troponin elevation [4].

MBG = myocardial blush grade

MBG predicted mortality (odds ratio 2.6, $P = 0.01$) after primary angioplasty for acute ST-segment elevation myocardial infarction, independently of other variables [3]; the higher the MBG, the lower the infarct size and the better the left ventricular ejection fraction. Patients with blush grades 3, 2 and 0–1 had mean ejection fraction of 50%, 46% and 39%, respectively ($P < 0.0001$). After a mean follow-up of 1.9 ± 1.7 years, mortality rates of patients with MBG 3, 2 and 0–1 were 3%, 6% and 23%, respectively ($P < 0.0001$). Furthermore, they identified a large group (67%) of patients who had TIMI 3 flow and MBG of 0 or 1 that was related to poor ST-segment resolution and a larger area of infarction. Moreover, the incidence of adverse outcomes was 30% with blush grades 0–1 and 11% with TIMI flow 0–2. These findings implied that MBG reflects microcirculation integrity and tissue perfusion better than TIMI flow. Similar findings were reported in other studies of primary angioplasty for acute STEMI [5-7].

The predictive value of MBG in patients with acute myocardial infarction and signs of congestive heart failure undergoing percutaneous coronary intervention was recently investigated [8]. Killip class was linearly associated with MBG rate, angiographic success, and 1 year mortality rate. MBG 0–1 was an independent predictor of 1 year mortality in patients with advanced Killip class (> 1) at presentation. MBG was also a predictor (independent of TIMI) of both in-hospital and long-term mortality in patients with AMI admitted with cardiogenic shock who underwent primary angioplasty [9,10].

Reduced myocardial blush grade identifies patients at higher risk who need more aggressive treatment both during the procedure to improve myocardial perfusion and later for secondary prevention

Interestingly, it was found that MBG after AMI improved in 40% of patients during the first 30 days [11]. Such an improvement correlated with better ejection fraction and smaller infarct size, and probably reflects distal microvasculature thrombi lysis, cellular edema absorption, and improvement in endothelial function and arteriole tone. This phenomenon should conceivably allow a window for therapeutic measures.

MBG and ST-segment resolution during AMI

Integrated ST resolution is a known marker of reperfusion during MI, and is considered more powerful than TIMI in predicting the outcome of primary angioplasty [12]. While ST resolution is related to myocardial perfusion and cell membrane integrity (that affects electrocardiography), MBG reflects myocardial perfusion and microvascular patency. Moreover, MBG is based on an image taken at one time (immediately after PCI), while ST resolution incorporates dynamic and evolving changes after reperfusion. This explains why in some studies the two parameters correlated well [13,14] while in others [15-17] they did not. In fact, Haager at al. [17] found that combining ST resolution increased the power of MBG in predicting mortality ($P = 0.029$). The two parameters should therefore be considered complimentary.

MBG and adjuvant therapies for distal embolization during PCI

In patients undergoing PCI, distal embolization correlates with infarct size, ejection fraction, ST resolution and long-term mortality [18]. Identifying poor MBG in such patients should therefore allow a window of opportunity for administration of adjuvant therapies to improve microvascular perfusion and clinical outcome.

Pharmacological therapies

The value of nitroprusside was compared to nitroglycerin in 45 patients with no-reflow phenomenon by assessing MBG [19]; improvement was achieved in 48.8% of patients treated with nitroprusside vs. 28.8% of those treated with nitroglycerin ($P = 0.008$), with a tendency for improvement in TIMI 3 flow (93.33% vs. 84.44%, $P = 0.221$). MBG was also used to assess the benefit of IIb-IIIa inhibitors. In the CADILLAC study [7] abciximab had no incremental benefit on MBG. In the ON-TIME study [20], pre-procedural tirofiban improved TIMI and MBG compared to early tirofiban but did not improve post-PCI outcome. Nevertheless, pre-PCI MBG 2–3 was a relatively strong predictor of post-PCI angiographic outcome.

Mechanical modalities

MBG has been used in many trials examining protection devices for native coronary arteries [21-25]. In most of these studies MBG was used as an immediate indicator of salvaged myocardium, with no long-term follow-up. In the X-TRACT trial a protection device was used during an elective procedure of a diseased saphenous vein graft or thrombotic native coronary arteries [26]. MBG 0–1 was found to be an important prognostic predictor of complications for 6 months even among patients who achieved TIMI 3 epicardial flow after angioplasty. The incidence of combined death or any MI during 6 months of follow-up was 42.5% in patients with MBG 0–1 and 17.3% in those with MBG 3 ($P < 0.05$). In patients with TIMI 3, the incidence of combined death or any MI was 28.3% for MBG 0–1 and 16.6% for MBG 3 ($P < 0.05$).

Limitations and perspectives

An inherent technical problem in measuring myocardial blush should be noted. The customary way to measure myocardial blush is by viewing the territory of a coronary artery in profile. This view includes a large three-dimensional myocardial mass condensed into a two-dimensional view. Reduced myocardial blush in only a part of this muscle is usually underestimated. As mentioned, the

STEMI = ST-segment elevation myocardial infarction
AMI = acute myocardial infarction

PCI = percutaneous coronary intervention

operator should wait for the venous phase to appear for appropriate MBG assessment. Part of the discrepancy between the clinical value of the method and the scarcity of its use may be due to the additional (albeit short) time needed for viewing the venous phase, as well as low awareness of MBG value.

There is also a need to develop methods for automatic quantification of myocardial blush, methods of automatic measurement of blush in a large myocardial area, and measuring MBG in successive frames in order to get distribution and clearance curves on the time axis.

Conclusions

MBG is an independent predictor of mortality and a valuable tool for assessing coronary microvasculature and myocardial perfusion in patients with AMI and in other patients undergoing PCI. Reduced MBG identifies patients at higher risk who need more aggressive treatment both during the procedure to improve myocardial perfusion and later for secondary prevention.

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