Coronary microcirculation in acute myocardial ischaemia: From non-invasive to invasive absolute flow assessment

Microcirculation coronaire après un syndrome coronarien aigu : de l’évaluation non invasive à la mesure invasive du flux absolu coronaire en pratique clinique

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Summary Although substantial progress has been made in recent decades in reducing mortality and performing optimal revascularization in patients with myocardial infarction, ischaemic heart disease, including acute coronary syndrome, remains the leading cause of mortality worldwide. One of the remaining challenges is to better detect, prevent and treat extended myocardial damage despite angiographically optimal revascularization. Several indices are available in clinical practice to evaluate myocardial damage, infarct size and potential myocardial recovery. These indices are divided into two categories: non-invasive, generally performed after revascularization; and invasive, performed during the revascularization procedure. They

\textit{Abbreviations:} ACS, acute coronary syndrome; CFR, coronary flow reserve; CMR, cardiac magnetic resonance; FFR, fractional flow reserve; IMR, index of microvascular resistance; MACE, major adverse cardiac events; MCE, myocardial contrast echocardiography; MVO, microvascular obstruction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; PET, positron emission tomography; STEMI, ST-segment elevation myocardial infarction; STR, ST-segment elevation resolution; TIMI, Thrombolysis In Myocardial Infarction.

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allow the clinician to detect patients at risk and may help us to tailor the medical therapy and discharge strategy according to myocardial damage. Because of the number of indices, it is difficult to properly evaluate new therapeutics or to adopt one index that will provide sufficient data to better evaluate and understand the part of the coronary vasculature that is not seen — the microcirculation or so-called “black box”. The aim of this review is to describe the non-invasive and invasive indices used to describe the microcirculation and their ability to predict clinical impact, and current dedicated therapeutics that may help to reduce microvascular damage and improve clinical outcomes.

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**MOTS CLÉS**
Syndrome coronarien aigu ; Dommage myocardique ; Microcirculation coronaire

**Résumé** Malgré les progrès substantiels en cardiologie qui ont permis de réduire la mortalité cardiovasculaire ces dernières décennies, la cardiopathie ischémique incluant le syndrome coronarien aigu demeure la cause la plus importante de mortalité dans le monde. Un des défis actuels est de mieux prévenir, de détecter et de traiter les dommages myocardiques malgré une revascularisation angiographiquement optimale. Plusieurs indices sont actuellement disponibles en pratique clinique afin de détecter l’évolution vers une nécrose myocardique étendue. Ces indices peuvent être non invasifs, généralement réalisés après la procédure de revascularisation, ou invasifs, réalisés pendant la même procédure, après revascularisation. Ces indices permettent aux cliniciens de détecter les patients à risque afin d’adapter précoce- cement la stratégie médicale en terme de médication et de retour au domicile. Devant le nombre important d’indices, il est difficile d’évaluer les traitements et les stratégies thérapeu- tiques qui permettraient de réduire ces dommages myocardiques et microcirculatoires post revascularisation d’un syndrome coronarien aigu. L’objectif de cette revue est de décrire les principes de ces indices non invasifs et invasifs permettant d’évaluer l’atteinte microcirculatoire et myocardique post-infarctus du myocarde, leurs implications cliniques ainsi que les thérapeutiques actuellement employées et en cours d’évaluation.

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**Background**

Despite advances in recent decades in the treatment of acute coronary syndromes (ACS) [1], most progress has been in the field of epicardial coronary artery revascularization. The coronary tree can be divided into two main compartments, which regulate blood flow into the myocardium. The macrocirculation, which is composed of epicardial vessels, mainly assures conductance, whereas the microcirculation, composed of small vessels, mainly assures resistance (Fig. 1). While the macrocirculation is seen with coronary angiography, it represents only 5–10% of the overall coronary vasculature. The most important part of the coronary tree — the microcirculation — is not seen and is therefore poorly assessed during and after an ACS [2]. Even in the early phase of an ACS, with state-of-the-art therapeutics, although interventional cardiologists can treat acute epicardial artery occlusion effectively, myocardial damage can remain high, as a result of microcirculation impairment [3].

In this review, we describe the non-invasive and invasive techniques for evaluating the coronary microcirculation, the prognosis of microcirculation impairment after an ACS, the therapeutic targets and perspectives for the treatment of the microcirculation, which may represent the next research challenge in improving prognosis after an ACS.

**Non-invasive evaluation of the microcirculation**

**Electrocardiography**

In the thrombolytic era, several studies demonstrated that in patients with ST-segment elevation myocardial infarction (STEMI), rapid ST-segment elevation resolution (STR) after fibrinolysis strongly suggested effective reperfusion of the occluded infarct-related artery [4]. In contrast, persistent ST-segment elevation (Fig. 1A) or incomplete STR after treatment was frequently associated with fibrinolysis failure to save the myocardial area at risk of necrosis, suggesting a failure to restore epicardial coronary blood flow. Nevertheless, when primary percutaneous coronary interventions (PCI) were commonly performed to treat STEMI, it became clear that a lack of rapid STR did not necessarily indicate failure to recanalize the artery, but rather the inability to restore myocardial perfusion caused by microvascular obstruction, which has also been correlated with worse clinical outcome [5].

Several electrocardiogram variables have been investigated in the diagnosis of microvascular obstruction. These variables have been evaluated as markers of infarct size, impaired myocardial salvage, reperfusion injury and
Figure 1. Non-invasive tools to assess microvascular obstruction. (A) ST-segment resolution is a useful tool of coronary microvascular obstruction after myocardial infarction; black arrows show absence of ST-segment resolution after artery recanalization. (D) Single-photon emission computed tomography shows absent tracer uptake (white arrow, scintigraphic no-reflow phenomenon) compared with normal uptake (left position). (C) Myocardial contrast echocardiography shows lack of intramyocardial contrast opacification (indicated by white arrow). (B) Cardiac magnetic resonance; on late gadolinium enhancement, areas of microvascular obstruction are seen as hypoenhancement (so-called “dark zones”) within an avidly enhancing site of myocardial infarction.

prognosis. Nijveldt et al. prospectively included 180 patients with STEMI to assess STR, residual ST-segment elevation and number of Q waves, using the 12-lead electrocardiograms acquired on admission and 1 hour after successful PCI. Residual ST-segment elevation was the only independent predictor of microvascular injury (odds ratio 19.1, 95% confidence interval 2.4–154; \(P=0.005\)) in multivariable analysis. STR was not associated with LV function, infarct size, transmurality indexes or microvascular injury in multivariable analysis [6]. More recently, Rommel et al. analyzed the electrocardiograms of 572 consecutive patients with STEMI regarding the presence or absence of distortion of the terminal portion of the QRS complex (so-called grade 3 ischaemia). In their study, the presence of grade 3 ischaemia was significantly associated with infarct size, impaired myocardial salvage and reperfusion injury in a reperfused STEMI population, as assessed by cardiac magnetic resonance (CMR). Moreover, grade 3 ischaemia was independently associated with major adverse cardiac events (MACE) [7].

Echocardiography

Myocardial contrast echocardiography (MCE) is a bedside technique that can be used to assess microvascular perfusion (Fig. 1C). Echocardiographic contrast agents are microbubbles of inert gases of sizes and rheology similar to those of red blood cells, and can be administered intravenously. As the microbubbles stay within the vascular space, the intensity of the echocardiographic signals reflects the concentration of the microbubbles in the vascular space; they flow freely within patent microcirculation, while lack of intramyocardial contrast opacification is caused by microvascular obstruction (MVO). Myocardial uptake of microbubbles is delayed or absent in areas of “no reflow” and MVO, and the myocardium appears devoid of acoustic signal, which can be delineated. Real-time MCE clearly shows the absence of myocardial perfusion a few hours after primary PCI. MCE can detect the relevant percentage of patients (25–33%) with a no-reflow phenomenon after ACS [8,9], similar to CMR, but at a lower cost, and it can be performed easily at the bedside in a coronary care unit. Indeed, MCE has been shown to predict recovery after acute myocardial infarction [9]. However, the widespread use of MCE has been hampered by the long learning curve for image acquisition and reporting, uncertain reproducibility, concerns over microbubble contrast safety, and issues regarding reimbursement in countries such as the USA. Moreover, MCE has some limitations, such as operator dependency, moderate spatial resolution, incomplete left ventricular coverage and semiquantitative assessment of MVO.

CMR

CMR is a great tool for assessing MVO; it allows multislice imaging with high tissue contrast and high spatial resolution, enabling accurate quantification and localization of MVO and the infarct size relative to the entire left ventricle. When myocardial perfusion is strongly altered by MVO, contrast agent wash-in and concentrations are severely impaired. At first-pass perfusion, contrast “wash-in” causes a homogenous signal increase in both normal and infarcted myocardium, but not in areas of MVO, resulting in a lack of gadolinium enhancement during the first pass. Ten to 15 min later, lack of gadolinium enhancement within a necrotic region is identified by late gadolinium hyperenhancement (Fig. 1B). First-pass MVO is more sensitive than late MVO, as the latter underestimates the extent of MVO. In addition, CMR-defined MVO has been well correlated with MCE, angiographic and invasive indices used for the assessment of
MVO [10]. Recent meta-analyses raised the hypothesis that CMR-based variables of irreversible myocardial ischaemic damage, such as infarct size or MVO, may be useful for improving risk stratification of patients with STEMI in the short term (< 24 months) [11]. Indeed, in a recent study, Symons et al. demonstrated that early postinfarction CMR-based MVO was a strong independent predictor of MACE in patients with reperfused STEMI at long-term follow-up. Remarkably, MVO extent ≥2.6% of the left ventricle was the strongest independent predictor of death and heart failure hospitalization, over-riding the prognostic performance of traditional outcome predictors, and leading to better long-term risk stratification [12].

Nuclear imaging

Both single-photon emission computed tomography [13] and positron emission tomography (PET) [14] have demonstrated that the no-reflow phenomenon in humans can be detected by nuclear imaging, the former by Schofer et al. using intracoronary thallium-201 and technitium-99m microalbumin aggregates. Similarly, Kondo et al. showed that single-photon emission computed tomography was useful in the detection of scintigraphic no-reflow; their findings suggested that scintigraphic no-reflow phenomenon can occur in a subgroup of patients without angiographic no-reflow phenomenon, that the myocardial damage depends on the severity of microvascular damage and that prolonged ischaemia time may increase the likelihood of “microvascular no-reflow phenomenon” (Fig. 1D) [15]. Using PET, further work in animal studies showed that acute inflammation and MVO may coexist early after acute myocardial infarction, and that they could be detected by increased 2-[18F]-fluoro-2-deoxy-D-glucose uptake on PET and no reflow on delayed enhancement computed tomography, respectively [16]. Moreover, PET scanning, with its ability to measure myocardial blood flow in absolute terms, and hence assess myocardial flow reserve, has allowed assessment of coronary microvascular function, detection of subclinical coronary artery disease, improved characterization of disease burden and identification of balanced myocardial ischaemia. However, PET scanning is still underutilized in clinical practice, and its clinical use is limited to sites with PET scans and cyclotrons or generators.

Invasive evaluation of the microcirculation

Invasive evaluation of the microcirculation is of particular interest because these techniques can be performed during the revascularization procedure. Indeed, immediate results could change therapeutic management at the early phase. The potential of these techniques is summarized in Table 1.

Coronary angiography

Contrast medium progression speed into the coronary artery is preserved in the absence of subocclusive coronary stenosis (<90%) and in the absence of microcirculation damage. Therefore, after successful revascularization of an epicardial coronary stenosis, contrast medium progression impairment could reflect microcirculation damage. From the Thrombolysis In Myocardial Infarction (TIMI) study group, two indices were described: TIMI flow grade 0–3 is a semi-quantitative variable that ranges from no contrast medium progression (0) to normal progression (3); TIMI frame count is a quantitative index calculating the number of frames between two landmarks proximal and distal to the interro- gated coronary artery. Compared with TIMI grade flow, which is immediate and subjective, TIMI frame count is objective and gives better accuracy [17]. In patients with ACS with preserved TIMI grade flow after revascularization, microcirculation can also be evaluated with myocardial blush, which corresponds to a densitometric method, assessing maximum intensity of contrast medium in the microcirculation. In practice, coronary microvascular obstruction is defined as TIMI grade flow ≤3 with myocardial blush stagnation (grade 0 or 1) [18]. Nevertheless, angiographic methods of assessing the microcirculation may have reproducibility inaccuracy. Furthermore, no large studies have compared the diagnostic accuracy of angiographic techniques with the intracoronary physiological techniques described below. Despite limitations related to these techniques, they are cost free, easy to perform, available and associated with clinical outcome. Thus, TIMI grade flow ≤2 has been associated with an increased risk of 5-year mortality [19], and myocardial blush grade 0–1 has been associated with increased mortality at 16-month follow-up [20].

Fractional flow reserve

Fractional flow reserve (FFR) is defined as the ratio of maximal myocardial blood flow in the presence of steno- sis divided by the theoretically normal maximal myocardial blood flow. Therefore, it can uniquely quantify the epicardial obstruction that is limiting hyperaemic flow, and predicts to what extent it is correctable by revascularization. However, FFR depends on the microcirculation, which represents the flow reserve. Similar stenoses can have different FFR values according to risk factor accumulation, underlying the microcirculation impairment, in stable coronary artery disease [21]. As described above, FFR is not an index for measuring the microcirculation, but FFR values integrate the microcirculation compartment. Therefore, significant FFR values induce myocardial ischaemia, with microcirculation hypoperfusion caused by epicardial coronary stenosis. In patients with STEMI, FFR in the culprit vessel is not recommended. In the COMPARE-ACUTE trial, patients with STEMI were randomized to revascularization of the culprit lesion only or to complete revascularization guided by FFR in non-culprit lesions, with the latter demonstrating clinical benefit [22]. In patients with non-STEMI (NSTEMI), FFR was used in the FAMOUS-NSTEMI trial, showing similar clinical outcome between revascularization guided by visual estimation of FFR or by angiography, and less revascularization in the FFR-guided group [23]. Similarly, in patients with NSTEMI, the PRIME-FFR study demonstrated the safety of FFR use to defer lesions, with non-significant lesions interrogated with FFR [24]. These studies suggest that in patients with ACS, complete revascularization guided by FFR reduces myocardial ischaemia and improves microcirculation perfusion, and therefore could benefit patient
Table 1  Non-invasive tests to assess the microcirculation after acute coronary syndrome, with pros and cons.

<table>
<thead>
<tr>
<th>Test</th>
<th>Pros</th>
<th>Cons</th>
<th>Studies</th>
<th>Summary of results</th>
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<tbody>
<tr>
<td>Angiographic evaluation: TIMI grade flow and myocardial blush FFR</td>
<td>Cost free; easy to perform</td>
<td>Reproducibility; subjective evaluation</td>
<td>Ndrepepa et al., 2010 [19]; Henriques et al., 2003 [20] COMPAIR-ACUTE, Smits et al., 2017 [22]; FAMOUS-NSTEMI, Layland et al., 2014 [23]; PRIME-FFR, Van Belle et al., 2017 [24]</td>
<td>Increased risk of 5-year mortality with TIMI grade flow ≤2; increased mortality with myocardial blush grade 0–1 after 16 months of follow-up in patients with STEMI with multivessel disease, the addition of FFR-guided complete revascularization of non-culprit lesions in the acute setting resulted in a lower risk of clinical events compared with medical therapy; in patients with NSTEMI, higher rate of revascularization guided with angiography compared with FFR; revascularization reclassification rate of 38% with FFR and safe deferral under medical therapy alone, in patients with ACS Diastolic deceleration time &lt;600 ms associated with higher in-hospital mortality after MI</td>
</tr>
<tr>
<td>CFR</td>
<td>Assessment of both macro- and microcirculation</td>
<td>High variability; depends on resting condition; not specific for microcirculation</td>
<td>Yamamuro et al., 2002 [25]</td>
<td></td>
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<tr>
<td>IMR</td>
<td>Objective; assessment of microcirculation compartment</td>
<td>Some variability</td>
<td>Fearon et al., 2013 [26]; Murai et al., 2017 [28]</td>
<td>IMR &gt; 40 after revascularization is an independent predictor of mortality and rehospitalization for congestive heart failure; in patients with NSTEMI, IMR &gt; 23 is an independent predictor of MACE at 4 years</td>
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</tbody>
</table>

ACS: acute coronary syndrome; CFR: coronary flow reserve; FFR: fractional flow reserve; IMR: index of microvascular resistance; MACE: major adverse cardiac events; MI: myocardial infarction; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction; TIMI: Thrombolysis In Myocardial Infarction.

outcome, with safe deferral of NSTEMI lesions with non-significant FFR.

Coronary flow reserve

Coronary flow reserve (CFR) is defined as the ratio between maximum and rest myocardial blood flow. This technique interrogates the overall coronary circulation, with a number of limitations to the assessment of the microcirculation (Fig. 2). First, this technique includes measurement of two different states: resting and hyperaemic. However, during ACS, the resting condition is highly questionable. Second, CFR evaluates both compartments without distinction. Third, CFR has high measurement variability. Although CFR assesses the microcirculation poorly, the coronary flow velocity pattern for microcirculation impairment is defined as a diastolic deceleration time <600 ms, and the presence of systolic flow reversal after revascularization has been associated with higher in-hospital mortality in patients with ACS [25].

Index of microvascular resistance

Index of microvascular resistance (IMR) measures the resistance to myocardial flow, specifically related to the coronary microcirculation compartment. IMR is defined as the ratio of distal coronary pressure ($P_d$) and the thermodilution-derived mean transit time during maximal hyperaemia, measured with a pressure/temperature wire (Fig. 3). IMR is an objective index dedicated to the coronary microcirculation, with some degree of variability resulting from the manual injection of an intracoronary bolus of saline at room temperature. Several studies correlated clinical outcome after ACS with high IMR values. In patients with STEMI, an IMR > 40 was correlated with a significant increase in rehospitalization for heart failure and mortality rate [26]. Furthermore, in

Figure 2. Illustration representing the arterial coronary circulation, and different invasive techniques for evaluating the coronary tree. CFR: coronary flow reserve; FFR: fractional flow reserve; IMR: index of microvascular resistance.
Coronary microcirculation evaluation after acute coronary syndrome

Figure 3. (A) Coronary flow reserve (CFR) tracing example. (B) Index of microvascular resistance (IMR) tracing example.

Patients with STEMI, IMR was shown to be a useful tool for predicting viability compared with PET, with a good area under the receiver operating curve of the IMR for predicting left ventricular function recovery [27]. In patients with NSTEMI, a recent study compared FFR, CFR and IMR in 83 patients, and looked at MACE rates at long-term follow-up. Results showed no difference in MACE rates with FFR, higher MACE rates with low CFR values and higher MACE rates with higher IMR values. IMR was the best index to predict MACE, with an optimal cut-off value of 23 [28].
Echavarria-Pinto et al. showed that FFR, CFR and IMR measured in stable patients had poor correlation with each other, and determined at least five different patterns in stable coronary artery disease, by mixing FFR, CFR and IMR results [29]. In this study, the association of low CFR with high IMR was linked to higher MACE rates. Nevertheless, multiplying indices together might confuse the cardiological community, in terms of understanding and performing microcirculation evaluation in patients with ACS.

Coronary thermodilution

Recently, a novel index based on thermodilution background was introduced to determine, during the same measurement, maximal absolute coronary flow (L/min), minimal resistance (Wood units) and FFR without hyperaemic agent. This technique uses a pressure/temperature wire and an infusion microcatheter (Rayflow; Hexacath, Rueil-Malmaison, France). The wire is advanced distally in the vessel while the infusion catheter is advanced in the proximal part of the vessel. The infusion catheter is connected to an infusion pump to continuously infuse saline solution at a fixed rate (called Qi) at room temperature through side holes. The mixture between blood and saline reaches a steady state called T in few seconds. Thereafter, the pressure/temperature wire is pulled back at the side-hole level to measure the temperature of saline at the exit of the infusion catheter, called Ti. Flow (Q) is calculated as the ratio between Ti and T multiplied by Qi and a constant of 1.08. The pressure/temperature wire gives simultaneously pressure and temperature. As pressure equals flow multiplied by resistance, we are therefore able to determine microvascular resistance as the ratio between distal pressure (Pd) and coronary flow (Q). This technique has already been evaluated in vivo and in vitro, and showed accurate measurements [30,31]. Human studies determined that saline continuous infusion at room temperature induces maximal hyperaemia compared with adenosine. Therefore, the technique becomes simpler to perform, and makes it possible to obtain FFR during the same measurement [32]. Finally, as shown in the example provided in Fig. 4 during the same measurement, flow in L/min, resistance in Wood units and FFR can be obtained simultaneously. FFR is defined as the ratio between maximal coronary flow and theoretical maximal coronary flow without stenosis; therefore, by setting FFR as 1, we obtain the theoretical ‘‘normal’’ flow and resistance. As a result, we obtain the value of FFR, which corresponds to the haemodynamic impact of epicardial stenosis, absolute coronary flow in L/min and resistance in Wood units. The differences compared with previous indices are objective measurement with good reproducibility, absolute values instead of index or ratios and comprehensive and understandable values (flow in L/min and resistance in Wood units).

‘‘BASIC’’ therapeutic targets to treat microcirculation impairment after ACS

Numerous efforts have been made to optimize the treatment strategy to prevent microcirculation impairment during ACS.

Beta-blockers

Some beta-blockers are able to protect the microcirculation and reduce infarct size. For instance, prehospital intravenous metoprolol in patients with anterior STEMI (Killip class II or less) has been shown to reduce infarct size, increase left ventricular ejection fraction and reduce the need for implantable cardioverter-defibrillator implantation, with fewer admissions for heart failure after 2 years [33].

Antiplatelet drugs

Among antiplatelet drugs, prehospital abciximab with half-dose reteplase significantly reduced infarct size, but did not have clinical benefit in terms of mortality at 1 year [34]. On the other hand, the On-TIME-Z trial showed that routine prehospital initiation of tirofiban might improve STR and clinical outcome after PCI [35]. Indeed, the latest European STEMI guidelines recommend glycoprotein IIb/IIIa inhibitors in case of no-reflow phenomenon at the acute phase. Nevertheless, prehospital use is no longer recommended [36].

Adenosine

Adenosine used in myocardial infarction might have some benefit in terms of preventing extensive microcirculation injury. Intravenous adenosine, given before reperfusion therapy, was suggested to reduce infarct size compared with placebo in the AMISTAD randomized clinical trial [37]. Similarly, the larger AMISTAD II trial demonstrated infarct size reduction in the adenosine group compared with the placebo group, but without significant benefit in terms of clinical outcome [38]. When looking at the post hoc analysis of the AMISTAD II trial, in the subgroup with successful reperfusion within 3 h, the adjunct of adenosine infusion enhanced early and late survival, and reduced the composite clinical endpoint of death or congestive heart failure at 6 months [39]. In addition, during reperfusion, the addition of intracoronary adenosine after thrombectomy, through the thrombectomy catheter, showed a significant improvement in STR, with better 1-year left ventricular remodelling and reduction in clinical events compared with saline and nitroprusside [40,41].

Statins

Based on STR, TIMI frame count and myocardial blush, Kim et al. showed that a high dose of atorvastatin may produce an optimal result in patients with STEMI undergoing PCI by improving microvascular myocardial perfusion, without significant clinical improvement [42].

Ischaemic conditioning therapeutics

Reducing body temperature to reduce ischaemic conditioning has been proposed as a promising therapeutic strategy. The COOL-MI study investigated the effect of hypothermia at the early phase of STEMI. This study demonstrated the potential to cool patients with an anterior STEMI to 33.6 °C at the time of coronary guidewire crossing, with a numerical 7.1% absolute and 30% relative reduction in infarct size.
assessed by magnetic resonance imaging, although this was not statistically significant [3].

Calcium inhibitors, cyclosporine and other drugs

Finally, intracoronary calcium inhibitors are probably the most evaluated and effective drugs available for the prevention and treatment of no-reflow phenomenon. In a meta-analysis by Su et al., including seven trials involving 539 patients with intracoronary verapamil administration at a dosage of 200 μg to 2 mg, the authors showed a significant decrease in no-reflow incidence, a better TIMI grade and frame count, and a reduction in MACE, 2 months after PCI (relative risk 0.56, 95% confidence interval 0.33—0.95) [43]. Administration of cyclosporine at the time of reperfusion was associated with a smaller infarct size, the underlying mechanism thought to be inhibition of the opening transition pores of mitochondrial permeability, which could attenuate lethal myocardial injury [44]. Other drugs, such as atrial natriuretic peptide and exenatide, also showed a beneficial effect in terms of infarct size, without a significant difference in clinical improvement [45,46].

Discussion and perspectives

Proper, early coronary microcirculation evaluation is essential to guide therapeutics in patients with ACS. Recent guidelines recommended a length of stay of 48–72 h after admission (IIa, A) for STEMI in patients aged <70 years and with ejection fraction >45% after successful reperfusion [36]. This short length of stay is hardly compatible with patients discharged with full optimal medical therapy in clinical practice. Therefore, it seems important to evaluate our patients according to the extent of myocardial infarction postreperfusion therapy, in order to plan and adapt the medical therapy and tailor the discharge delay.

One of the difficulties with microcirculation assessment is the multiplication of invasive and non-invasive indices, and the lack of a gold standard. In addition, the clinical benefit of dedicated drugs on top of regular optimal medical therapy prescribed after ACS is missing, and is a drawback of microcirculation assessment for most cardiologists. The ideal index of coronary microcirculation in patients with ACS should be objective, accurate and available at the acute phase without side effects or extra cost. Such an index does not yet exist. In this review, we described non-invasive and invasive indices, the pros and cons of each index, as well as their predictability in terms of infarct size and/or clinical outcome.

A recent index allows us to simplify invasive microcirculation evaluation with the thermodilution principle, to obtain absolute coronary flow and microvascular resistance. This novel technique could facilitate easier evaluation in experimental models to explore microcirculation after ACS and test therapeutics. Therefore, the common use of objective and quantifiable indices could ease evaluation and guide potential dedicated therapeutics in the future.

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Disclosure of interest

The authors declare that they have no competing interest.

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