The role of the percutaneous coronary intervention in acute coronary syndrome

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Abstract

Most cases of acute coronary syndromes are caused by coronary thrombosis on top of an atherosclerotic plaque. Besides intensive antithrombotic therapy, dilatation of the culprit lesion has now been standard of care. Sealing and stenting of the culprit lesion may prevent recurrent coronary thromboses, but also carries a risk of thromboembolic and atheroembolic complications. Furthermore, percutaneous coronary intervention after acute coronary syndrome needs even more intense antithrombotic therapy, which may further increase the risk of bleeding in general and the need for transfusion in particular, which is associated with increased risk of early and late mortality. Yet, percutaneous coronary intervention is necessary in many patients and in most of them it leads to a definitive solution of a coronary plaque rupture that lead to the acute coronary syndrome.

Key words: acute coronary syndrome, angina, complications, percutaneous coronary intervention.

The history of percutaneous coronary intervention

Ischemic heart disease is the major cause of mortality and one of the major causes of morbidity in the Western world. Current treatment consists of medical therapy and, in selected cases, of revascularisation of occluded or narrowed coronary arteries. Coronary bypass surgery was first applied in the early sixties by René Favoloro in Cleveland and significantly contributed to quality and quantity of life in patients with symptomatic ischemic heart disease. In 1977 Andreas Grüntzig introduced percutaneous transluminal coronary angioplasty, which technique postponed or even avoided coronary surgery in many symptomatic patients. Nowadays, percutaneous coronary intervention (PCI) largely outnumbers coronary artery bypass surgery in the Western world.

Possible benefit of revascularisation in acute myocardial ischemia

Early angiographic observations in the seventies have shown that most cases of acute myocardial ischemia are caused by coronary atherosclerosis. In transmural myocardial infarction (ST segment elevation on the presenting ECG) an occlusion of a major epicardial coronary artery was observed in most cases [1]. Since the introduction of intracoronary thrombolytic therapy for acute myocardial infarction it became clear that the nature of this occlusion is thrombotic [2]. It became also apparent that after lytic therapy

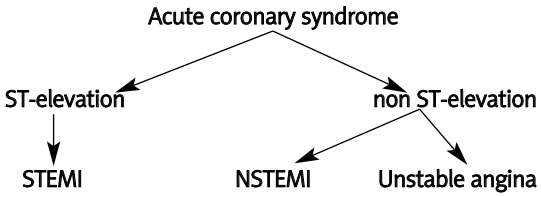

Figure 1. Current nomenclature of acute coronary syndromes depending on the presenting ECG and occurrence of subsequent myocardial necrosis

STEMI – ST-elevation myocardial infarction, NSTEMI – non-ST-elevation myocardial infarction

many coronary stenoses that had produced acute occlusion probably not have been very severe to start with [3]. From these observations the hypothesis emanated, that coronary thrombosis is an acute phenomenon and may occur on not very tight coronary stenoses. From histopathology it became clear that rupture of a lipid laden coronary plaque may initiate acute coronary thrombosis [4]. Three types of coronary thrombosis in acute coronary syndromes have been distinguished: occlusive, non-occlusive and dispersive coronary thrombosis. Occlusive coronary thrombosis usually causes ST-segment elevation myocardial infarction with Q-wave formation. Non-occlusive thrombosis is most seen in non-ST-segment elevation acute coronary syndromes, and may (non-ST elevation myocardial infartcion or NSTEMI) or may not lead to myocardial necrosis (unstable angina). Dispersive thrombosis has been observed downstream of a ruptured atherosclerotic plaque in patients with sudden cardiac death, apparently resulting in malignant electric instability.

The current nomenclature of the syndrome of acute myocardial ischemia (acute coronary syndrome) is based on the presenting ECG (Figure 1) and the occurrence of subsequent myocardial necrosis. If myocardial markers are found in the plasma, myocardial infarction is diagnosed. If not, unstable angina is the final diagnosis. Intervening with revascularisation may influence he course of the acute coronary syndrome by mitigating or even aborting myocardial necrosis [5].

Percutaneous coronary intervention in ST-elevation myocardial infarction

Reperfusion therapy for ST-elevation acute coronary syndromes aims at early and complete recanalization of the infarct-related artery in order to salvage myocardium and improve both early and late clinical outcomes. The benefit rises exponentially the earlier therapy is initiated. The highest number of lives saved is within the first hour after symptom onset: *the golden hour*. The exponential form of the curve relating mortality to time-to-reperfusion has major implications for the timing of treatment. The impact of delay in time-to-treatment lessens as the duration of ischemia lengthens. Consequently, reducing delays will have a much more positive return in patients presenting early for those presenting late. These considerations have provided a strong incentive for the initiation of very early reperfusion therapy.

Thrombolytic therapy has become the gold standard of reperfusion therapy since the 80s. Although thrombolytic therapy for acute myocardial infarction is very widely applicable, it is only successful in restoring full early patency in about 50% of patients and has a low, but significant risk of severe side effects. Primary angioplasty carried out as an alternative to thrombolysis circumvents the cost and risk of thrombolytic therapy and might restore patency in nearly 90% of cases. Outcome of randomised trials of primary angioplasty vs. thrombolytic therapy in acute myocardial infarction are convincingly in favour of angioplasty [6]. As primary thrombolysis has improved (bolus lytic therapy with bolus and subcutaneous low-molecular weight heparin), also primary angioplasty has become even more effective using routine coronary stenting [7]. However, pre-angioplasty administration of drugs (thrombolytics, glycoprotein receptor IIb/IIIa antagonists or both) has not been successful in improving the results of primary angioplasty [8, 9]. This approach is currently called "facilitated angioplasty" is meant to speed up reperfusion and indeed is associated with better pre-angioplasty coronary patency, but it increases bleeding. An interesting new development in improving the results of primary angioplasty is thrombosuction prior to balloon inflation. This may result in better reperfusion [10] and improved survival [11], but this venue has to be established in more trials.

As primary angioplasty proves to be a valuable and more effective alternative to thrombolysis, acute angioplasty is expensive, needs a costly infrastructure and, therefore, is not widely applicable. Transport to a tertiary center for primary angioplasty, however, seems feasible and safe. Although it delays time to treatment with a further 60 min, it tends to save lives and strokes and significantly reduces reinfarction [12]. Yet, the mechanism of improved outcome with primary angioplasty is not fully clear. Post-angioplasty patency figures are usually given in the 90 to 95% range. However, in GUSTO IIb, the largest study of primary angioplasty vs. lytic therapy, core lab read TIMI-3 flow in the angioplasty patients did not exceed 75%. This comes close to the figures in the studies combing half-dose lytic with abciximab, which in 2 megatrials did not result in better survival [13]. Therefore, there may be other

mechanisms operative in the benefit of primary angioplasty. These may include less reocclusion [14], or the knowledge of the coronary anatomy, by which high-risk patients in the need for urgent coronary surgery, can be identified early.

As pointed out earlier, timing of reperfusion therapy is important. Also with percutaneous intervention mortality deteriorates as symptom-to-balloon time increases [15]. Intervention later than 12 h is not thought to be useful, although myocardial salvage beyond 12 h has been proven by scintigraphy [16]. But opening occluded infarct arteries beyond 72 h has not shown clinically beneficial in the large OAT (Open Artery Trial) study [17].

Percutaneous coronary intervention in non-ST-elevation myocardial infarction

Unlike in STEMI acute total coronary occlusion is not common in non-STEMI. Therefore, reperfusion therapy with thrombolysis is not appropriate and may even be harmful [18]. Yet, myocardial ischemia is the key element in non-ST-elevation myocardial infarction and should be treated with anti-ischemic therapy consisting of nitroglycerin and β-blockade. Early coronary intervention in this syndrome is feasible as found out already in the mid 80s [19]. It usually relieves myocardial ischemia and is a good prognosticator. However, randomized trials comparing an early invasive strategy to a conservative or a more selective approach did not show a mortality benefit on the short [20] and long term [21]. The reason for this may be that the benefit of early intervention may be balanced by possible harm (see below). Current medical therapy of non-STEMI besides anti-ischemic drugs includes aspirin, clopidogrel, (low molecular) heparin, statins and ACE-inhibitors. Each of these medical interventions on its own has shown efficacy in acute myocardial ischemia. Therefore, it is difficult to show a mortality benefit over this broad-based medical background. Finally, myocardial infarction may be less with an early intervention, but myocardial infarction is a cumbersome endpoint in the randomized clinical trials in this syndrome. It is both an entry criterion and an endpoint at the same time, and it can be considered as a complication of the treatment (periprocedural during and after an intervention, or spontaneous by not performing an intervention). Such an endpoint is difficult to adjudicate, since the above trials are open by design.

Timing of percutaneous intervention in non-ST-elevation myocardial infarction is also a matter of debate. Early intervention may prevent further infarction, but also may be harmful given the thrombotic milieu of the culprit lesion. Medical passivation of coronary plaques may be beneficial, but will take time during which recurrent infarction may occur. So far there is only one relatively small randomized trial comparing very early (< 6 h after admission) vs. late (> 3 days) intervention, which showed a significant benefit of early treatment in the prevention of recurrent infarction [22].

Complications of percutaneous coronary intervention

Complications of percutaneous coronary intervention can be either cardiac or vascular. Cardiac consequences are cardiac death and myocardial infarction, whereas vascular complications mainly consist of spontaneous bleeding and of bleeding at the vascular access site.

Myocardial infarction and death

Both in STEMI and non-STEMI coronary plaque rupture is a pivotal process. Intervention in a recently ruptured plaque may be harmful by causing athero-embolic and thromboembolic phenomena resulting in extending or recurrent myocardial infarction. Although meant to improve myocardial perfusion and stabilizing the ruptured plaque percutaneous intervention may lead to (re)infarction, which can amount to 1-2% in STEMI [6] and up to 5% in non-STE acute coronary syndrome [23].

Bleeding

In general the hemostatic system seems to play an important role in bleeding complications. In elective PCI severe bleeding may be seen in up to 5% of cases depending on definition. Intervention in unstable coronary disease may have more vascular complications. Since non-STEMI should be treated with at least 3 antithrombotic agents (aspirin, clopidogrel and heparin), bleeding is more common than in elective intervention.

Age is strong risk factor for bleeding as well as renal dysfunction [24]. Blood transfusions in this syndrome do not seem to improve outcome. On the contrary, death and myocardial infarction triple after transfusion [24].

Conclusions

Although not everywhere available, early percutaneous coronary intervention has gained an important place in the early management of acute coronary syndromes. Usually it offers prompt relief of myocardial ischemia and probably inhibits propagation of ongoing myocardial infarction. In ST-elevation myocardial infarction emergent intervention reduces early and late mortality, whereas in non-ST elevation acute coronary syndrome myocardial (re)infarction but not long-term mortality is effectively diminished with early coronary intervention. Percutaneous intervention is

associated with an inherent bleeding risk, which may result in increased mortality. Excess bleeding complications are probably due to the widespread use of strong antiplatelet and anticoagulant medication used in the syndrome.

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