

To defer, or not to defer, that is the question



Henning Kelbæk^{1*}, MD, DMSc; Dan Eik Høfsten², MD, PhD;
Thomas Engstrøm², MD, PhD, DMSc

1. Department of Cardiology, Zealand University Hospital, Roskilde, Denmark; 2. Department of Cardiology, University of Copenhagen, Copenhagen, Denmark

Acute restoration of myocardial flow during primary percutaneous coronary intervention (PCI) is pivotal to the treatment of patients with ST-segment elevation myocardial infarction (STEMI). However, reperfusion injury and reduction of nutritional flow may occur despite successful re-opening and stent implantation in the infarct-related culprit lesion, and therefore an apparently normal epicardial flow may not reflect an adequate flow at the microvascular level. Thus, infarct extension may occur without visually observed flow reduction (no-reflow) or distal embolisation, and attempts to protect the peripheral vascular bed by thrombus aspiration or distal protection to avoid these complications have not been convincing.

Sustained no-reflow is associated with the development of large myocardial infarcts and a high risk of ensuing heart failure. It occurs in a certain percentage of PCI procedures in the presence of a high thrombus or plaque burden and is induced by vasoactive substances in concert with increased platelet reactivity. Several observational reports have indicated that the risk of no-reflow and distal embolisation is diminished by deferring stent implantation, because both thrombus burden and microvascular disturbances are reduced with time after flow re-establishment. On the other hand, randomised trials have only been able to demonstrate benefit by stent deferral in certain surrogate endpoints (**Table 1**).

Table 1. Key endpoints in randomised trials of deferred stent implantation in patients with ST-segment elevation myocardial infarction.

Trial	n	No-reflow		Infarct size*		Salvage index		MVO*		LVEF		MACE	
		Def	Conv	Def	Conv	Def	Conv	Def	Conv	Def	Conv	Def	Conv
DEFER-STEMI	101	6%	29%	9%	14%	68%	56%	48%	62%			6%	6%
<i>p</i>		0.01		0.18		0.03		0.16				NS	
MIMI	140	6%	10%	61%	60%**			12%	5%**	51%	53%	0%	3%
<i>p</i>		0.43		0.64				0.05		0.70		NS	
INNOVATION	114	23%	35%	15%	19%***			43%	57%	52%	50%		
<i>p</i>		0.14		0.11				0.20		0.27			
DANAMI 3-DEFER	1,215									60%	57%	17%	18%
<i>p</i>										0.04		0.92	

*% left ventricular mass; **% area at risk; *** infarct size 16% vs. 23% and MVO 44% vs. 70% in anterior infarcts, both $p < 0.05$. Conv: conventional treatment; Def: deferred stenting; LVEF: left ventricular ejection fraction; MACE: major adverse cardiac events; MVO: microvascular obstruction

*Corresponding author: Department of Cardiology, Zealand University Hospital, Sygehusvej 10, 4000 Roskilde, Denmark.
E-mail: hkelbaek@dadlnet.dk

Notwithstanding previously published results from two French centres in favour of immediate stenting, the same centres have followed the defer concept with impressive dedication, and in this issue of EuroIntervention they focus on optimising STEMI intervention by deferring stent implantation two to 30 days after minimal manipulation of the culprit lesion to restore flow. In the Combaret et al study¹, the authors implanted a bioresorbable scaffold guided by intravascular imaging a median of four days after the index procedure in a selected group of relatively young patients, and report one reinfarction as the only major cardiac event during six months of follow-up.

Article, see page 397

In the Mester et al study², stent implantation was scheduled a median of seven days after the acute episode and, despite a considerable residual stenosis after the index PCI, the only adverse events reported were re-occlusion of the infarct-related artery in two patients not receiving glycoprotein IIb/IIIa inhibitors. Stent implantation could be waived in more than one third of these patients.

Article, see page 390

Albeit small and non-randomised, these two studies are valuable contributions to the ongoing attempt to improve invasive treatment of patients with STEMI. The concept of regaining the vasoactive and endothelial properties of the vessel by use of bioresorbable scaffolds is intriguing and can often be performed straight away, because the majority of STEMI vessels contain soft non-calcified plaque. On the other hand, care must be taken with regard to the sizing of the scaffold and in respect of the increased risk of scaffold thrombosis.

The limited number of patients in these two studies impedes any firm conclusion concerning the safety of the defer strategy, and the compilation of current experience – not least from our own DANAMI 3-DEFER trial – indicates that deferred stent implantation should not be routinely exercised in patients with STEMI³⁻⁶. However, the strategy seems safe in cases where a stable blood flow in the infarct-related artery can be restored by minimal manipulation with the supplement of efficient antithrombotic medication, and it cannot be ruled out that certain subgroups of patients with STEMI – especially those with long thrombotic lesions at the index procedure and those with non-significant lesions at the second procedure – may benefit from deferred stenting or even no stenting at all.

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Combaret N, Souteyrand G, Barber-Chamoux N, Malclès G, Amonchot A, Pereira B, Le Bivic L, Eschalier R, Trésorier R, Motreff P. Management of ST-elevation myocardial infarction in young patients by limiting implantation of durable intracoronary devices and guided by optical frequency domain imaging: “proof of concept” study. *EuroIntervention*. 2017;13:397-406.
2. Mester P, Bouvaist H, Delarche N, Bouisset F, Abdellaoui M, Petiteau PY, Dubreuil O, Boueri Z, Chettibi M, Souteyrand G, Madiot H, Belle L. At least seven days delayed stenting using minimalist immediate mechanical intervention (MIMI) in ST-segment elevation myocardial infarction: the SUPER-MIMI study. *EuroIntervention*. 2017;13:390-6.
3. Carrick D, Oldroyd KG, McEntegart M, Haig C, Petrie MC, Eteiba H, Hood S, Owens C, Watkins S, Layland J, Lindsay M, Peat E, Rae A, Behan M, Sood A, Hillis WS, Mordi I, Mahrous A, Ahmed N, Wilson R, Lasalle L, Généreux P, Ford I, Berry C. A randomized trial of deferred stenting versus immediate stenting to prevent no- or slow-reflow in acute ST-segment elevation myocardial infarction (DEFER-STEMI). *J Am Coll Cardiol*. 2014;63:2088-98.
4. Belle L, Motreff P, Mangin L, Rangé G, Marcaggi X, Marie A, Ferrier N, Dubreuil O, Zémour G, Souteyrand G, Caussin C, Amabile N, Isaz K, Dauphin R, Koning R, Robin C, Faurie B, Bonello L, Champin S, Delhay C, Cuilleret F, Mewton N, Genty C, Viallon M, Bosson JL, Croisille P; MIMI Investigators. Comparison of Immediate With Delayed Stenting Using the Minimalist Immediate Mechanical Intervention Approach in Acute ST-Segment Elevation Myocardial Infarction: The MIMI Study. *Circ Cardiovasc Interv*. 2016;9:e003388.
5. Kim JS, Lee HJ, Yu CW, Kim YM, Hong SJ, Park JH, Choi RK, Choi YJ, Park JK, Kim TH, Jang HJ, Joo HJ, Cho SA, Ro YM, Lim DS. INNOVATION Study (Impact of Immediate Stent Implantation Versus Deferred Stent Implantation on Infarct Size and Microvascular Perfusion In Patients With ST-Segment Elevation Myocardial Infarction). *Circ Cardiovasc Interv*. 2016;9:e004101.
6. Kelbæk H, Høfsten DE, Køber L, Helqvist S, Kløvgaard L, Holmvang L, Jørgensen E, Pedersen F, Saunamäki K, De Backer O, Bang LE, Kofoed KF, Lønborg J, Ahtarovski K, Vejlsstrup N, Bøtker HE, Terkelsen CJ, Christiansen EH, Ravkilde J, Tilsted HH, Villadsen AB, Aarøe J, Jensen SE, Raungaard B, Jensen LO, Clemmensen P, Grande P, Madsen JK, Torp-Pedersen C, Engstrøm T. Deferred versus conventional stent implantation in patients with ST-segment elevation myocardial infarction (DANAMI 3-DEFER): an open-label, randomized controlled trial. *Lancet*. 2016;387:2199-206.