SURGERY

Protecting the heart during myocardial revascularisation

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Much effort has been expended assessing the relative merits of percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery. Much less energy has been directed towards understanding the potential of these two interventions for causing additional myocardial damage during the procedure and the means to avoid this injury.

This review examines the impact of myocardial injury in elective PCI and CABG, principles of myocardial protection, and their efficacy in current coronary revascularisation. The objective of every coronary revascularisation should be a technically perfect result without producing myocardial damage. A patent graft that perfuses an area of myocardium with numerous pockets of myocyte necrosis serves no useful purpose.

Myocardial damage induced by PCI

Most of the clinical research studies on percutaneous coronary intervention (PCI) have focused on angiographic and clinical outcomes. Cardiomyocyte necrosis associated with impaired flow to side branches or occlusion after coronary stenting does occur, but has received little attention. Atherosclerotic debris can plug the downstream coronary microcirculation and ischaemia-reperfusion injury may occur after revascularisation of occluded vessels. Creatinine kinase myocardial band (CK-MB) and troponin T levels, and electrocardiogram (ECG) evidence of infarction have been used as markers for post-procedure cardiomyocyte necrosis. CK-MB elevation, which occurs in approximately 25% of patients, and troponin T release, which occurs in up to 50% of patients,[1] have been shown to be predictors of poor late outcome.[2,3]

Magnetic resonance imaging (MRI) has been used to assess myocardial damage. In a recent study, Selvanayagam and co-workers[4] correlated post-PCI troponin elevations with the volume of myocardial tissue destruction using delayed-enhancement MRI. This was a low-risk group of 50 patients in whom a single- or double-vessel PCI was planned with a mean left ventricular (LV) ejection fraction of 67 ± 11%. Some 28% of the patients had evidence of procedure-related myocardial necrosis resulting in a loss of 5.0 ± 4.8% of total ventricular mass (**table 1**). There was no statistically significant adverse effect on global LV function. Myocardial injury occurred in one or both of two distinct sites:

1. An area of the apical myocardium apparently related to embolisation of solid matter during left anterior descending (LAD) coronary artery balloon dilatation plus stenting.
2. The mid-ventricular myocardium adjacent to the new stent.

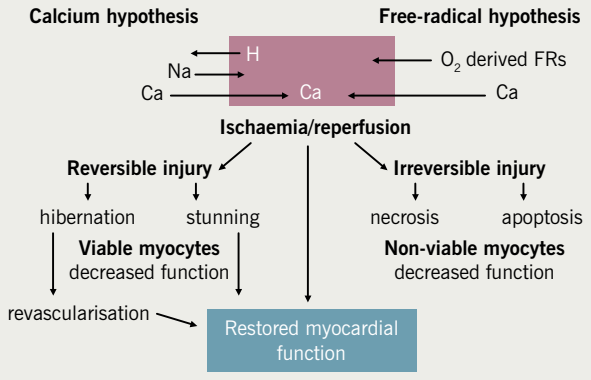
In an attempt to minimise PCI-induced myocyte damage, mechanical devices including balloons distal to a central aspiration device, and a polyurethane filter bag contained on a radio-opaque loop to trap embolic debris, have been introduced. In a randomised trial of 500 patients,[5] the device entrapped embolic debris in 73% of cases, but there was no information about any reduction in cardiomyocyte necrosis. This may be because these devices do not eliminate side branch occlusion and have no effect on PCI-induced endothelial dysfunction.

Table 1. Delayed-enhancement magnetic resonance imaging (MRI): percutaneous coronary injury (PCI) and coronary artery bypass surgery (CABG) compared.[10] Note the contrast in loss of left ventricular (LV) mass between the two groups in these patients with well-preserved LV function

PCI (N=50)	CABG (N=30)
Single + double PCI	2.9 ± 0.8 grafts per patient
Mean EF= 67 ± 11%	Mean EF = 67 ± 8%
28% myonecrosis	36% myonecrosis
Loss of 5% LV mass	Loss of 2% LV mass

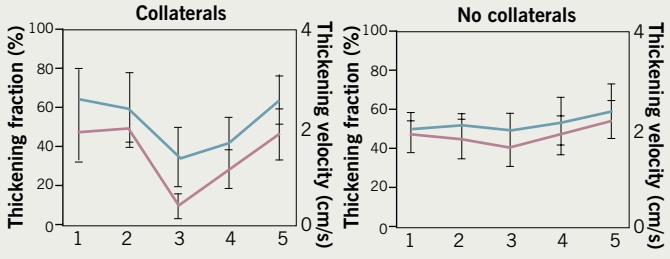
Key: PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft; EF = ejection fraction; LV = left ventricular

Figure 1. Ischaemia-reperfusion injury and the calcium and free-radical hypotheses. After the aortic cross-clamp is removed, the myocardial cell may function normally, be stunned, or become dysfunctional due to either necrosis or apoptosis



Key: FRs = free radicals

Figure 2. Results of occluding the left anterior descending (LAD) artery on anterior wall thickening during beating heart surgery. Note the rapid resolution of this injury



Key:
1= baseline
2= stabilisation
3= occlusion
4= 2 minutes post snare release
5= 10 minutes post snare release

Thickening fraction
Thickening velocity

Myocardial damage induced by surgery

The objective of every operation should be a technically perfect result without producing myocardial damage. From the practical viewpoint the prerequisites for optimal protection are uniform and adequate distribution of a protective agent, excellent visualisation of the operative field, a simple technique that does not distract the surgeon, and optimal protection of the brain and kidneys. The consequences of inadequate myocardial protection range from low cardiac output states leading to multi-organ failure, increased mortality and prolonged hospital stay; to subtle degrees of damage causing delayed myocardial fibrosis. In patients with pre-operative impaired LV function, the margins of functional reserve are narrow. Recently much debate has occurred about the relative merits of on-pump and off-pump surgery and whether the avoidance of a period of extracorporeal perfusion is beneficial to the myocardium. This debate remains unresolved, but in expert hands equivalent results can be obtained by both techniques.

Myocardial stunning and cardiomyocyte necrosis associated with ischaemia/reperfusion injury results from the attenuation or cessation of coronary blood flow, such that oxygen delivery to the myocardium is insufficient to meet basal myocardial requirements to preserve cellular membrane stability and viability. Recovery involves the resumption of normal oxidative metabolism and the restoration of myocardial energy reserves, the reversal of ischaemia-induced swelling and loss of membrane ion gradients, and repair of damaged cell organelles, such as the mitochondria and the sarcoplasmic reticulum (**figure 1**). There are two major hypotheses; increases in intracellular calcium and the accumulation of reactive oxygen species (ROS) causing the sarcolemmal peroxidation of the cell phospholipid layer, leading to the loss of cellular integrity and facilitating calcium entry. After the aortic cross-clamp is removed, the cardiomyocyte may function normally, be stunned, or become dysfunctional from either necrosis or apoptosis.

Post-operative myocardial stunning

There is plenty of clinical evidence to indicate that all patients undergoing coronary artery bypass graft (CABG) experience varying degrees of myocardial stunning. This is defined as a form of post-ischaemic dysfunction where there is normal myocardial perfusion, preserved contractile reserve, and delayed but full recovery of function. This occasionally requires inotropic support, which after hours or days resolves and leaves behind no objective evidence of myocardial infarction.[6] However, there are significant disadvantages to the use of inotropes.

Experimental studies have shown clearly that increasing doses of catecholamines will cause cardiomyocyte necrosis as the myocardial oxygen consumption exceeds the heart's capacity to increase coronary blood flow. There is recent evidence that therapeutic levels of inotropic support in the post-ischaemic heart increases intracellular calcium and subsequent apoptosis resulting in cell death.[7] This is probably critical in the post coronary artery surgical patient if there are areas of the heart that have not been adequately revascularised.

In a study comparing PCI and CABG outcomes, there was a greater incidence of CK-MB leak from CABG patients than PCI patients.[8] However, when the criterion for significant myocardial injury was changed to 10-times normal, there was no difference and the CABG patients had a significant, but small, increase in three-year survival. In the Arterial Revascularisation Therapies Study (ARTS) there was a direct relationship between CK-MB and long-term outcomes.[9] At one year the worst adverse outcomes as defined by the incidence of major adverse clinical events (MACE) occurred in patients with CK-MB levels greater than five-times normal. In a more recent study from the UK using troponin levels and delayed-enhancement MRI, Selvanayagam and co-workers[10] reported a 36% incidence of myocyte necrosis and a 2% loss of LV mass.

The principles of myocardial protection

The basic principles of myocardial protection are:

- rapid cardiac arrest, since the myocardial oxygen stores are depleted within six seconds as oxidative metabolism switches from aerobic to anaerobic metabolism
- hypothermia to decrease myocardial oxygen consumption and prevent the depletion of high energy phosphate
- the avoidance of myocardial oedema.

Most surgeons use blood cardioplegia to provide additional substrate oxygen, improved buffering and anti-oxidants; and they employ a combination of antegrade and retrograde delivery systems. Despite numerous reports, there have been no definitive prospective studies that narrow the techniques enough to allow universal adoption of one particular technique.

The avoidance of cardiopulmonary bypass by the use of off-pump techniques has not resulted in a clear benefit in terms of reduced mortality or reduced incidence of peri-operative infarction. However, most observers have reported a significant reduction in troponin T release. Although there is enormous enthusiasm for off-pump coronary artery surgery in some quarters, the overall uptake has been about 20% across the board. Using high-fidelity LV pressure recordings combined with 2-D echo recordings from peri-operative transoesophageal echocardiography, we have shown remarkable tolerance of the myocardium to occlusion of the LAD artery for periods of up to 15 minutes (**figure 2**). In the presence of collaterals from a dominant right coronary artery, there is very little change in myocardial contractility as revealed by analysis of anterior wall thickening. In the absence of collaterals, normal wall thickening is restored within 10 minutes.[11]

It has been known for some time that short bursts of ischaemia followed by reperfusion protect the myocardium against subsequent longer ischaemic insults, as evidenced by reduction of cardiac troponin T release. This phenomenon, called ischaemic pre-conditioning, can protect the human heart from ischaemic injury during coronary bypass surgery but is not practised routinely because repeated clamping of the aorta is likely to induce cerebral emboli.[12] Pharmacological pre-conditioning may also confer benefit but this remains unproven.

Conclusion

Over the last 50 years in coronary artery surgery, intra-operative myocardial damage from inadequate protection has decreased progressively, despite the demographic changes that have brought older and sicker patients forward for myocardial revascularisation. Nevertheless, both CABG and PCI are associated with a small but definite incidence of myocardial injury. Myocardial protection strategies are less developed in PCI and the need for repeat revascularisation procedures is more frequent than after surgery. We must rise to the challenge by finding ways and means of providing adequate revascularisation while inducing the least amount of cardiomyocyte injury for our patients

Conflict of interest

None declared.

Key messages

- Heart muscle may be damaged during revascularisation
- Both percutaneous intervention and surgery can result in damage
- New methods are being developed to minimise myocardial cell injury

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