

Reperfusion Injury Prevention, A Volume-Controlled Reperfusion Method in Acute Coronary Artery Occlusion

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Research status of reperfusion injury protection :

- Prevention of Reperfusion Injury in STEMI No-reflow/slow-reflow Thrombectomy Deferred stenting Potent anti-thrombotic tx Stunning Potent microvasodilator Spontaneous resolution Coronary occlusion **Reperfusion Arrhythmia** Treatable Lethal Reperfusion Injury Ischemic postconditioning Remote ischemic postconditioning Pharmacological conditioning (Cyclosporin A, adenosine, etc)
- Ischemic post-conditioning procedures in animal experiments and clinical proof of concept trial can reduce ischemia-reperfusion injury
- Post-conditioning and gradual adaptation have not shown consistent protection of cardiac function in large clinical randomized trials, such as POST, DANAMI-3 IPOST.
- Reperfusion injury acts on all ischemic areas under the occlusion section, including myocardial cells and coronary endothelial cells in the injured area.
- Endothelial cells are more tolerant to ischemia, but more sensitive to reperfusion injury.
- Non myocardial cells and microvascular injury may be the key link in the protection of reperfusion injury.



Derek J. Hausenloy et al, Ischaemic conditioning and targeting reperfusion injury: A 30 years voyage of discovery Basic Res Cardiol, (2016) 111:70

• Gerd Heusch and Bernard J. Gersh, The pathophysiology of acute myocardial infarction and strategies of protection beyond reperfusion: a continual challenge. European Heart Journal (2017) 38, 774278



Lesion:

PPCI procedure has been perfected day by day, difficult to observe iPost protective effect without considering the lesion site. We prefer proximal part of dominant blood vessel



Start-up time:

Thrombus aspiration widely used since 2008, might delayed the start of iPost procedure, attenuate protect effect on reperfusion injury



Operation method:

During balloon inflate/ deflate circle, uncontrolled blood perfusion which may cause reperfusion injury signal stimulation.



Blocking site:

The balloon dilated site is usually not on lesion, may be proximal to the target lesion.

and the forward blood flow cannot be completely blocked during the procedure.



Criminal vessels:

iPost assume that the target lesion is a localized/segmental lesion, cannot understand the patency of the distal vessel.

Problems with classic post-conditioning operations



Our ideas

Clinical experience:

iPost procedure might have inherent defects which affect protective effect of reperfusion injury.

Literature Review:

The end point of the clinical study focused too much on myocardial infarction size, ignored the effects on infarctrelated blood vessels, endothelial function, and microvascular embolism. Proposed assumption: Reperfusion injury of coronary endothelial system is key issue during the PPCI

New method:

Designed "Volume-Controlled Revascularization method" based on optimized iPost and gradual reperfusion



"Volume Controlled Revascularization "in STEMI PPCI (VCR)





Case presentation, case 1

- 54 y/o male, chest pain 6 hours
- intravenous thrombolysis 4 hours ago (Recombinant human pro-urokinase, rhPro-UK, 20mg iv st, 30mg iv drop at 1mg/min)
- No history of hypertension, diabetes or smoking
- On arrival his heart rate was 80 bpm, blood pressure was 130/80 mmHg. No heart murmurs or rales in auscultation.
- Tnl 0.08ng/ml (0-0.5ng/ml)



ECG Serie



On Ambulance

Pre-thrombolysis

1 hour after thrombolysis





Angiography indicated total occlusion in proximal RCA, TIMI 0





- RA route, 6FJR 4, 3.0-15mm NC balloon standby
- Heart rate drop to 40-50bpm, blood pressure drop to 70/50mmHg while BMW wire manipulation
- NC balloon inflated at proximal RCA, heat rate and blood pressure gradually back to stable

Reperfusion injury happens while workhorse wire manipulation





- RF route, 6FJR4,
- BMW2 to RCA distal



- Aspiration catheter was positioned 10-15mm advanced of NC balloon
- Keep 3.0NC balloon inflation at 8atm to block forward blood flow



- Angiography via aspiration catheter to confirm distal part patency
- Keep 3.0NC balloon at 8atm,
- Intra-aspiration catheter infusion of mixture solution (artery blood 10ml +heparin NS 10ml)
- 20ml/min for 5 mins







- Balloon deflated, perform angiography when hemodynamic status was stable.
- Two overlapping drug-eluting stents were deployed from mid to proximal RCA. 3.5-23mm, 3.0-15mm
- 3.5-4.0NC balloon post dilation









After catheterization

Transient arrythmia

Self converting sinus rhythm

- Patient was safe transferred to ICU with blood pressure 124 /70 mmHg, heart rate 60 BPM, both lungs were free of rales.
- Elevated ST-segment resolute to base level .
- Echocardiography on day 1: Lower left ventricular posterior wall motion; LVED was 55 mm; EF58%; minor regurgitation in mitral, tricuspid and aortic valve area; a small amount of pericardial effusion. Echocardiography on day 7 maintained stable.
- BNP was 115.3 ng / ml (0-100 ng / ml) after catheterization and was 200ng/ml on discharge. Peak Troponin I level was
 over 50ng/ml (0-0.034) on day 1 and dropped two-fold after 24 hours.
- No arrythmia or severe discomfort was documented.



CASE 2





- Acute inferior STEMI,
- Total occlusion in proximal RCA, in-stent occlusion
- Active balloon occlusion and trans micro-catheter reperfusion within one 7F guiding catheter





- 7FJR 4.0 GC , Workhorse wire to RCA distal,
- 3.5*16 GRIP[™] 8atm block forward blood flow actively



- APT 130mm microcatheter was advanced 20mm distal to GRIP[™] balloon.
- Trans microcatheter angiography indicate distal part patency





- Keep 3.5NC balloon at 8atm,
- Intra-microcatheter infusion of mixture solution (artery blood 10ml +heparin NS 10ml)
- 20ml/min for 3 mins
- Difficult to maintain infusion of 20ml/min, because limited diameter of 1.9F micaocatheter.



- Angiography show in-stent stenosis in Mid-RCA, blood flow TIMI III
- Note balloon inflate/deflate location was proximal to target lesion



Dilation with GRIP[™] 3.5*16 at 10atm for 30s





Blood flow TIMI III

- 3.5*30mm DCB @12atm, 60s. Residual stenosis<30%, TIMI III,
- stable hemodynamic data during procudure
- 1.9F microcatheter cannot provide sufficient perfusion volume (>20ml/min)
- Other microcatheter (such as 2.8F) not covered by current insurance policy





- CASE 3
- 57 yls male, acute inferior & anterior STEMI 4 hours
- LAD proximal subtotal occlusion, TIMI 0-1; RCA proximal total occlusion, TIMI 0. Supine shortness of breath, blood pressure 130/80mmHg
- Dural guiding catheter technique via RA & RF route, inserted blockage balloon and aspiration catheter via separate guiding catheter respectively, active forward blood flow blockage and distal part perfusion were performed.
- 5 rounds of intra-aspiration catheter infusion, instant blood flow TIMI III, patient was in stable condition during and after procedure.





- Diffuse lesion in LAD, proximal tutorial and calcification.
- Firebird stent 2.5*29mm, 3.0*23mm from mid to proximal LAD
- TIMI III and collateral circulation from apex and septal branch to RCA



- RA route JR 4 GC
- Wire to distal RCA
- 3.5 NC balloon inflated @ 8atm block forward blood flow

- Aspiration catheter was positioned 15mm advanced of NC balloon
- Keep 3.5NC balloon inflation at 8atm to block forward blood flow
- Angiography via aspiration catheter to confirm distal part patency









- Keep 3.5NC balloon at 8atm,
- Intra-aspiration catheter infusion of mixture solution (artery blood 10ml +heparin NS 10ml)
- 20ml/min for 5 mins

 Firebird 4.0*29mm stent deployed @ 12 atm • TIMI III blood flow with poor local expansion at target lesion





- Post dilation with 4.0 NC @ 12-14 atm, fully expansion with TIMI III blood flow
- Heart rate & blood pressure maintain stable, Bp: 105/80mmHg



Classic iPost is still in continuous improvement

Protection target switched for ischemia reperfusion

The criteria of termination of protective operation



Classic iPost is still in continuous improvement:

Start-up time,

flow management,

cycle times and operation duration,

start-up and termination criteria



Protection target change for ischemia reperfusion:

From maintaining mitochondrial integrity of AAR cardiomyocytes and controlling mPTP opening, to protection against reperfusion injury of non-cardiomyocytes, such as vascular endothelial cells.



The standard of termination of protective operation:

Fixed number of iPost cycles?

or according to stable blood flow or hemodynamic status?



Reduce ischemia-reperfusion injury and improve the effect of perfusion therapy

To establish a reperfusion injury protection strategy with adequate restoration of coronary blood flow and reduction of microvascular obstruction(MVO) as the primary endpoint

Research goals for "VCR"





THANKS

谢谢您的关注