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Practical Approach to Diagnosis, Prevention, and Management of Coronary No-Reflow

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ABSTRACT

Coronary no-reflow (NR) defined as inadequate myocardial perfusion despite restoration of coronary artery patency is a bane for an interventional cardiologist. It can complicate percutaneous coronary interventions especially in the setting of STEMI and dampens the potential benefits of PPCI. Broadly classified as Reperfusion NR and Interventional NR, mechanism is multifactorial. The basic underlying culprit is microvascular obstruction either secondary to distal embolization, intravascular plugging, or ischemic reperfusion injury. Coronary angiogram is an easy, readily available, and essential modality to diagnose no-reflow, but the gold standard is gadolinium-enhanced cardiovascular magnetic resonance imaging. Preventive strategies for NR should be integral part of pre-PCI planning especially in clinical scenario where NR is expected such as STEMI with delayed presentation and high thrombus burden, atherectomy, and SVG PCI. The cornerstone of treatment for NR is local vasodilators and antiplatelet therapy to ameliorate vasospasm and thromboembolism respectively, and different combinations of the two should be used in no specific order to achieve reversal of NR. NR phenomenon is associated with poor short-term and long-term prognosis and every attempt should be made to avoid or reverse it. Therapeutic hypothermia, hyperoxemic reperfusion therapy, targeted anti-inflammatory approach, and cellular approach appear proising but further research is mandatory.

Keywords: No-reflow, Coronary imaging, Therapeutic hypothermia, Pharmacological vasodilation, Antiplatelet therapy

INTRODUCTION

Coronary no-reflow (NR) is defined as inadequate myocardial perfusion despite restoration of coronary artery patency in the absence of dissection or spasm.[1] Angiographically, NR is thrombolysis in myocardial infarction (TIMI) flow Grade <3 and myocardial blush Grade (MBG) <3 manifesting as reduced or absent flow in the affected coronary vessel despite removal of primary obstruction.[2] TIMI flow Grade 0–1 is referred as NR, and TIMI flow grade as slow flow. The different terms no flow/NR/low flow/slow flow/slow reflow apparently are expressions for the same abnormality and simply referred as NR.

NR complicates nearly 50% cases of STEMI, less frequent in NSTEMI. Incidence in elective cases is <1.5% with a higher occurrence of nearly 4% in saphenous venous graft interventions.[3]

CLASSIFICATION

NR is broadly classified as reperfusion NR and interventional NR [Figure 1].

PATHOGENESIS

The mechanism of NR is multifactorial [Figure 2]. The basic underlying culprit is microvascular obstruction (MVO) secondary to distal embolization, intravascular plugging, or ischemic-reperfusion injury.[4-6]

CLINICAL PRESENTATION

Clinical scenario varies from asymptomatic state to hemodynamic compromise with life threatening arrhythmias. Reperfusion NR may be asymptomatic or present as ongoing chest pain and non-resolution of ST-segment elevation. Interventional NR classically with acute chest pain and ECG changes of ischemia which may over time. Acute ischemia presents as hemodynamic compromise prompting early initiation of strategies to reverse NR. Even in asymptomatic cases, every attempt should be made to correct NR, as it has poor outcome both short- and long-term.

PREDICTORS FOR NR

Certain clinical and angiographic factors predispose to No-reflow [Table 1].

RISK SCORES FOR NR

Wang risk score[7] based on seven clinical parameters and Yip *et al.*[8] *angiographic score* help to predict NR.

Platelet lymphocyte ratio at admission is a strong predictor of NR (Topark *et al.*) [Table 2].[9-30]

DIAGNOSIS OF NR

Electrocardiograph

Resolution of ST elevation following revascularization is highly specific (91%) for reestablishment of myocardial perfusion but less sensitive (77%).[29,30] ST resolution should be more than 70% at 60 min after PCI, anything less is a sign of NR.

Table 1: Predictors for no-reflow.

Predictors of individual susceptibility	Predictors of ischemic reperfusion injury	Angiographic predictors
• Age >65 • Female sex • Hypertension • Hyperglycemia • Smoking • Dyslipedemia • Atrial fibrillation • Renal insufficiency • Genetic- adenosine 2A receptor polymorphism (1976T>C)/ lysis resistance	• Time to treatment-delayed presentation (>6 hours) • Larger area of infarction (LAD occlusion) • Mean platelet volume • Oxidative stress • Thromboxane A2 levels • Vasoconstrictor ET-1 levels • Inflammatory markers-neutrophil count, CRP	• High thrombus burden, • Plaque composition • SVG PCI, • Long lesions (> 15 mm)

Biochemical markers

Serial measures of cardiac biomarkers, namely, troponins, creatinine kinase MB, and serum myoglobin are useful for the assessment of patency in the infarct artery.[31] They are estimated at baseline and then either 60 or 90 min after completion of reperfusion therapy. Greater increase in these markers over time from baseline indicates successful reopening of the occluded epicardial vessel, and also establishment of micro vascular tissue reperfusion.

Myocardial contrast echo

A bedside procedure to demonstrate NR where micro bubbles of an ultrasonic contrast agent is injecting intravenously. Absence of opacification of the myocardium demonstrates NR.[32,33]

Coronary angiogram

Easy, readily available, and essential modality of diagnosing NR in the catheterization laboratory.

- *TIMI flow grade* – Only TIMI 3 flow indicates successful reperfusion, a flow <3 is considered as NR.[34]
- *MBG* – MBG allows further risk stratification in patients with TIMI 3 flow, with a MBG score of 0–1 indicates NR.[35]
- *Corrected TIMI frame count* – Another method to evaluate epicardial flow. Low frame counts after PPCI indicates favorable reperfusion.[36]
- *Myocardial perfusion grade (TMPG)*-In TIMI 3 flow, TMPG is a technique to assess myocardial perfusion or "blush" on a coronary angiogram. A TMPG score of 0/1 indicates impairment of microvascular flow, whereas a TMPG grade 2/3 implies salvaged myocardium.

Intracoronary doppler

Although coronary angiogram is the most frequently done procedure for NR, it is not accurate. A measure of flow parameters and resistance parameters is a more accurate invasive technique for diagnosis of NR.

Coronary flow reserve (CFR)

A CFR value <2.0 indicates presence of MVO with nearly 80% sensitivity. NR is characterized by typical flow pattern of systolic flow reversal (retrograde) and rapid diastolic flow deceleration.

- Systolic flow reversal is due to increase in systolic myocardial stress secondary to microvasculature obstruction
- Rapid diastolic flow is due to rapid coronary filling in the unstressed volume of coronary microcirculation.[37,38]

Table 2: Risk scores for no-reflow.

MELD SCORE [Model for end-stage liver disease-XI score]	MELD-XI score = 5.11×(total bilirubin, mg/dL) +11.76× (creatinine, mg/dL) +9.44 *Bilirubin: Potent endogenous antioxidant, suppresses ROS production,*[10] *inhibits oxidative stress that contribute to no-reflow.*[11] *High bilirubin levels-* NR (Celik *et al.*[12]) *Creatinine: Marker of renal impairment. Independent marker for* NR *in STEMI patients undergoing PCI.* NR *in renal dysfunction attributed to ROS and endothelial dysfunction* • Both renal insufficiency and NR are manifestations of oxidative stress[13,14]	• Independent predictor of NR during Primary PCI • Highly predictive power for no-reflow • May be useful in early risk stratification of patients with STEMI[15,16]
R2-CHA2DS2-VAsc score [Renal function, Congestive heart failure, Hypertension, Diabetes, Age, peripheral Vascular disease, Stroke and female Sex	1 point each 2 for Stroke and Age ≥75 years 2 points for renal function (eGFR) ≤ 60 mL/min/1.73 m^2 using the MDRD formula)	• High CHA2DS2-VASc score (≥3)-independent predictor of no-reflow (80.9% sensitivity and 74.6% specificity).[19] • The R2-CHA2DS2-VASc score-relatively poor predictive value for no-reflow. Score ≥3–52.6% sensitivity and 73.1% specificity for no-reflow.[20]
Novel Biomarker: Malat1 [Metastasis-Associated Lung Adeno-Carcinoma Transcript 1] Long Non-Coding Rnas (Lnc Rnas)[21] Are Transcripts With ≥200 Nucleotides. Recognised For Their Role In Many Biological Processes (Malat1)[22] Conserved Lnc Rna, Biomarker In Lung Malignancy. Recently Identified For Its Role In Regulation Of Many Pathophysiological Processes Related To Vascular Disease	Mi RNAs namely miR-30e and miR-126[23,24] biomarkers for predicting NR in STEMI patients Elevated HPSE and EDN-1[25-27] are associated with no-reflow in STEMI	• MALAT1 regulates the expression of miR-155 • Expression of MALAT1 is significantly increased and that of miR-30e, miR-126 and miR-155 suppressed in the patients with NR
Expression of *C-reactive protein (CRP), Heparanase (HPSE) and (Endothelin-1)* EDN1 is significantly up-regulated in patients with no-reflow.[28] CRP causes microvasculature obstruction by complementary activation and neutrophil plugging and contributes to NRP. No-reflow is associated with higher values of CRP after PCI (12.10 vs. 8.13 with a $P = 0.017$)[16-18]		

Microvascular resistance index (IMR)

IMR = distal coronary pressure X mean transit time of a bolus at maximum hyperemia. It is an independent measure of microcirculatory flow

- MVO is suggested by an IMR value more than 25
- IMR value more than 40 post PCI is associated with poor prognosis
- IMR with incorporated Doppler flow velocity value more than 2.5 mmHg/cm/s is predictive of MVO.[39,40]

Angiography-derived IMR (IMR Angio)

Latest addition to the armamentarium. IMR angio can predict and IMR more than 40 units and the presence of large MVOs on cardiac magnetic resonance imaging (MRI) with good accuracy.[41]

Corflow therapy™

This new technology combines real-time microvascular assessment with the ability to administer intracoronary drugs.

- The procedure involves transient balloon occlusion of the coronary, infusion of a crystalloid at fixed incremental dose rates, and simultaneous measurement of distal and proximal pressures
- Microvascular resistance is derived from the flow and pressure quotient. The procedure is still experimental with initial encouraging results.[42]

Cardiac MRI

The gold standard[43] for NR diagnosis is gadolinium-enhanced cardiovascular magnetic resonance imaging.

- MVO appears as dark hypointense areas surrounded by hyperintense necrotic myocardium on T-weighted images in delayed gadolinium enhancement images (10–15 min),[44] or as low signal images in early (1–3 min) images[45]
- First-pass perfusion (FPP) method: FPP is another technique which is also contrast dependent. It can detect even small areas of MVO. However, it is not as specific as DGE. A perfusion defect appears as absence of contract-enhancement in the affected myocardium.[46]

Positron emission tomography (cardiac PET) and (SPECT) single-photon emission computed tomography for detection of NR have been described in experimental models, but not implemented practically.[47,48]

PREVENTION OF NR

NR is a challenging complication following PCI. Multiple therapies have been suggested, though none is 100% effective and doubtful impact on associated adverse cardiovascular outcome [Table 3].[49,50] As there are no ideal guidelines for the management of NR, first and foremost effort should be to prevent NR.

Strategies for prevention of NR should be incorporated in pre-PCI planning especially in clinical scenario where NR is expected such as STEMI with delayed presentation and high thrombus burden, atherectomy, and SVG PCI.

TREATMENT OF NR

The cornerstone of treatment for NR is local vasodilators and antiplatelet therapy to ameliorate vasospasm and thromboembolism, respectively. Intracoronary vasodilator and GP IIb/IIIa inhibitor are Class IIA recommendations for NR according to the 2021 ACC/AHA PCI guidelines.

Pharmacological vasodilatation [Table 4]

When sudden cessation of flow is seen in target artery during PCI; dissection, acute stent thrombosis, plaque prolapse, and vasospasm should be excluded ideally with imaging if the clinical scenario permits. If NR is confirmed by the presence of patent vessel, intracoronary vasodilators should be administered liberally ensuring an optimal activated clotting time and mechanical hemodynamic support if needed.

Intracoronary administration of these agents using a microcatheter or over-the-wire balloon ensure safe and effective delivery to the microcirculation with minimal adverse effects. A dedicated dual-lumen or thrombectomy catheter can also serve the purposes without losing wire position. An aspiration catheter or a pierced balloon inflated at the culprit lesion is other easily available options.

Multiple boluses of medications as mentioned above can be tried if NR persists and patient is hemodynamically stable. Different vasodilators should be tried if one does not work.

Antiplatelet therapy

The PLEIO study[51] demonstrated ticagrelor to be superior to clopidogrel in restoration of coronary microcirculation and reducing NR, also shown in a meta-analysis by Dai *et al*.[52] However, no difference was observed in sub analysis of PLATO trial, ATLANTIC trial, or REDUCE-MVI trial. Trial Platelet Inhibition to Target Reperfusion Injury[53] trial is an ongoing trial of Cardiac MRI too evaluate the efficacy of pre-procedural Cangrelor to reduce MVO and size of myocardial infarction.

Glycoprotein IIB/IIIA inhibitors

Potent antiplatelet agents appear promising for prevention and treatment of NR [Table 5]. However, none of the randomized trials have shown their benefit in NR. The latest ESC guidelines recommend them for use in NR or thrombotic complication (Class IIa, C).

In a recent study,[54] combined use of GP 2B/3A inhibitors along with aspiration and balloon inflation, in STEMI cases resulted in reduced NR.

Intracoronary fibrinolysis

Though this treatment looks promising, further strong evidence is needed for their use in NR in PPCI.

- In STEMI patients, low dose intracoronary alteplase during primary PCI did not reduce MVO in the T-TIME trial,[55] a randomized trial
- According to a meta-analysis by Alyamani *et al*.,[56] intracoronary thrombolysis was safe and effective
- In the DISSOLUTION trial.[57] manual aspiration followed by Urokinase in STEMI patients with large thrombus burden, showed greater prevalence of TIMI 3 flow, better ST-segment resolution, and favorable MACE at 6 months
- Adjunct intracoronary streptokinase improved infarct size and LVEF in STEMI patients in another small randomized study.[58]
- Intracoronary Tenecteplase dissolved thrombus and improved microvascular flow in patient with high thrombus burden in acute ST elevation MI in small series and registries.[59,60]

From these studies, the use of these agents could be beneficial in selected cases. The dose of the agent varied from 1/3rd to 1/6th of the systemic dose in these studies. Results of two on-going trials evaluating the efficacy of reduced doses of either alteplase (STRIVE trial) or Tenecteplase (RESTORE-MI) are awaited.

Thrombus aspiration

Initial results with manual thrombectomy were promising in the TAPAS study, subsequent trials were all negative results (TASTE and TOTAL trial). According to the

Table 3: Preventive strategies for no-reflow.

Reducing the time to reperfusion from the onset of symptoms is the foremost method to salvage the myocardium and reduce no-reflow	
A. Pharmacological therapy	Early use has shown to protect coronary microcirculation and reduce NR due to its anti-inflammatory role in pre-clinical studies
1. Beta-blockers (Metoprolol, Carvedilol and Nebivolol)	
2. ACE-inhibitors and ARBS	Favorable results have been observed especially with fosinopril and valsartan. Guidelines recommend early initiation of these drugs in acute MI unless contraindicated
3. Statins	High dose before PCI improved angiographic MVO in the STATIN STEMI.[49] Nearly 50% of reduction in CV events at 30 days was observed in the SECURE-PCI[50] study. Studies showed that patient who were already on statins at index event experienced lesser rates of NR
B. Procedural tips to reduce No-reflow in the Cath lab	1. Direct stenting and avoidance of high-pressure post-dilation especially in STEMI. 2. Short burr runs of <20 s; low burr speed of 140,000–150,000 rpm), and avoidance of decelerations more than 5000 rpm during atherectomy 3. Use of distal protection device (Percusurge and filter wire Ex device) have been proven to reduce no-reflow during elective SVG angioplasty 4. Deferred stenting in selected cases with high thrombus burden during which patient receives supportive treatment 5. Ischemic preconditioning pre and post though theoretically favor reduction of no-reflow, have not been proven so in randomized trials

MVO: Microvascular obstruction

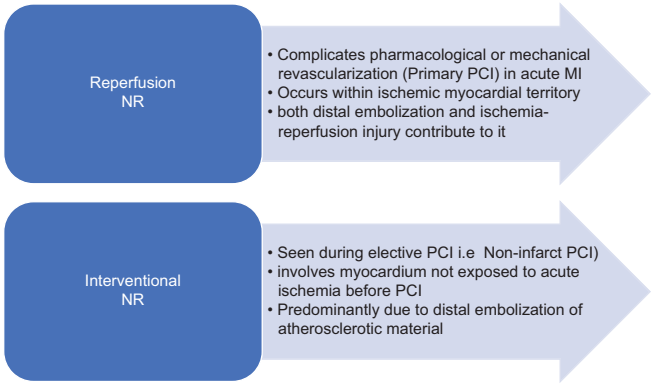

Figure 1: Classification of no-reflow (NR).

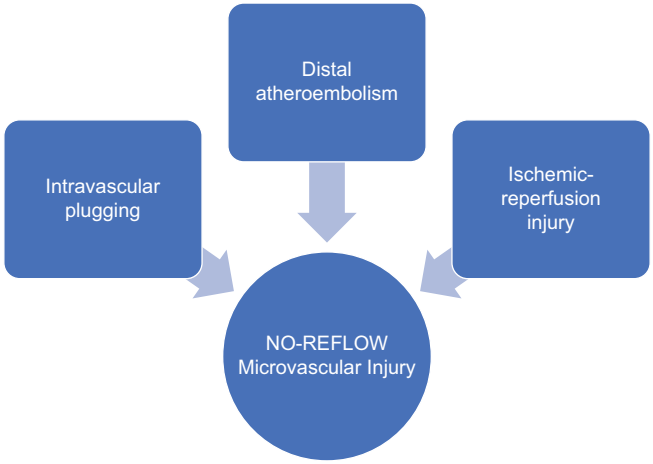

Figure 2: Pathogenesis of no-reflow.

latest guidelines,[43] routine aspiration thrombectomy in primary PCI is contraindicated. Manual aspiration thrombectomy is reasonable in primary PCI for high thrombus burden (class IIb, level of evidence C). No benefit of rheolytic thrombectomy (ANGIOJET/X-SIZER) in primary PCI.

Pressure-controlled intermittent coronary sinus occlusion (PICSO)

PICSO is a device to transiently occlude flow in the coronary sinus, which increases the cardiac venous pressure and improve microcirculatory perfusion.[61] Use of PICSO before deploying the stent in patients with IMR more than 40 showed lesser infarct extension at 6 months in the Ox AMI-PICSO trial.[62]

FUTURE INSIGHTS

Therapeutic hypothermia (TH)

It proved beneficial in reducing NR and myocardial damage in acute myocardial infarction in animal studies. However, the same benefit has not been shown in human trials. There are multiple reasons predicted to why the effective TH in animal study could not be seen in human trials-

- Methods to cool the entire body even with the most effective cooling device take too long thus prolonging the ischemic time which counteracts its benefit. Target temperature could not be reached before reperfusion

Table 4: Medications to be used for vasodilation in no-reflow.

MEDICATION	DOSE	MECHANISM OF ACTION	ADVANTAGE/ DISADVANTAGE	EVIDENCE
Adenosine	50–200 µg bolus IC 70 µg/kg/ min IV	- Dilatation of coronary microvasculature (A2 receptors mediated Smooth muscle relaxation) - Anti-inflammation - Platelet Inhibition - Ischemic preconditioning - Angiogenesis and Anti-apoptotic	Side effects-Atrioventricular blocks, Hypotension, Dyspnoea, Bronchospasm and flushing Advantage-very short half-life (<8 s)	REOPEN-AMI: MVO improved, peak Troponin levels reduced. Reduction in major CV events. Favourable LV remodelling at 1 year
Calcium channel blockers: 1. Verapamil 2. Diltiazem 3. Nicardipine	100–250 µg bolus IC 400 µg bolus IC 50–200 µg bolus IC	Block L-type calcium channels - Smooth muscle relaxation - Coronary - Reduce myocardial oxygen demand - Minimize damage mediated by oxygen free radicals	Well tolerated. Effective in the treatment of NR	Randomized trials and RECOVER-AM trial-CCB's effective in prevention and treatment of NR, doubtful effect on improvement in outcome
Epinephrine	50–200 µg bolus IC	inotropic and chronotropic properties - Alpha vasoconstriction corrects hypotension and improves coronary perfusion - Coronary vasodilation (Beta-2 receptor agonist)	Arrhythmia - MC was sinus tachycardia Occasional SVT and non-sustained VT More common with guide catheter directed therapy than local delivery of medication	According to Skelding *et al.*; both TIMI flow and TIMI frame count improved. MACCE at 30 days and 1 year improved (Darwish *et al.*)
Nitroprusside	50–200 µg bolus IC	Nitric oxide donor - Vasodilatation, - Antiplatelet - Anti-inflammatory Properties	Systemic hypotension	Inferior to CCB's and Adenosine
Nicorandil	Bolus of 2 mg IC Followed by infusion of 8 mg/h	Activation of ATP-sensitive potassium channels and nitric oxide donor - Vasodilatation - Neutrophil activation - Inhibition of ROS		No randomized trials, only small studies-proved effective in NR

Nitroglycerine (NTG): It is primarily a venodilator and minimal effect on arterial tone. Must be metabolized to nitric oxide to be effective which the microvascular arterioles are incapable to. Intracoronary NTG failed to show benefit in no-reflow

Adenosine regimen: 6 mg (One ampule or 2 mL) added to 10 cc of saline, further diluted 10-fold (add 1 cc of the solution to 10 cc saline); second dilution (again 1 cc of the solution to another 10-cc saline) to achieve final concentration of 60 µg/10 mL. To be given intracoronary injection, dose may be repeated to a maximum of 120 µg

Epinephrine regimen: 1 mg (One ampule or 1 mL) added to 10 cc saline, then diluted 10-fold (add 1 cc of solution to 10 cc saline) to achieve final concentration of 10 µg/mL. 100 µg is injected intracoronary over 5 min. Dose may be repeated up to 3 times to reach a maximum dose of 400 µg

MVO: Micro vascular obstruction, TIMI: Thrombolysis in myocardial infarction

- Systemic hypothermia had many side effects – shivering in nearly all patients and even serious atrial arrhythmias in many
- Hypothermia is effective when initiated before reperfusion, it is anticipated that in the studies conducted nearly 30% already have reperfusion and thus reperfusion injury before cooling is started.

TH appears to be a promising technique and further trials are necessary overcoming the above limitations. Results of the on-going EURO-ICE trial[63] (European Intracoronary Cooling Evaluation in Patients with ST-Elevation Myocardial Infarction), a prospective, randomized, and controlled trial evaluating the efficacy of hypothermia in humans is awaited. This is the largest study of hypothermia in humans where selective intracoronary hypothermia has been used during PPCI.

Selective Intracoronary Hypothermia

The occlusion site is first crossed with a regular guidewire and an OTW balloon inflated at the site of the occlusion.

Table 5: Glycoprotein IIB/IIIA inhibitors for the treatment of No-reflow

MEDICATION	DOSE	EVIDENCE
Abciximab	Bolus of 0.25 mg/kg iv followed by infusion of 0.125 µg/kg/min (max 10 µg/min) for 12 h	IC administration reduces NR and infarct size-CICERO trial and INFUSE-AMI No benefit in terms of death, re-infarction or heart failure-AIDA-STEMI
Eptifibatide	Bolus of 180 µg/kg, repeat 180 µg/kg bolus after 10 min, followed by infusion of 2 µg/kg/min for 18 h. If CrCl < 50 mL/min, reduce infusion by 50%	TIMI flow grading improvement in PROTECT TIMI trial
Tirofiban	25 µg/kg iv stat over 3 min, followed by infusion of 0.15 µg/kg/min for 18 h. If CrCl < 30 mL/min, reduce infusion by 50%	Prehospital intravenous infusion achieved better STR and MBG following PCI-ON TIME-2 trial

CICERO trial-(**C**omparison of Intracoronary Versus Intravenous Abciximab Administration During Emergency Reperfusion of ST-Segment Elevation Myocardial Infarction), INFUSE-AMI study: Intracoronary Abciximab and Aspiration Thrombectomy in Patients with Large Anterior Myocardial Infarction, AIDA-STEMI: Abciximab Intracoronary versus intravenous Drug Application in STEMI. MBG: Myocardial blush Grade

A pressure/temperature wire (Pressure Wire™ X; Abbott, St. Paul, MN, United States of America) is placed into the distal coronary, and the guidewire is removed. Two infusion pumps are attached to the lumen of balloon-one filled with saline at room temperature (solution A) and the other with saline 4°C (solution B).

- Solution A is infused for 7–10 min at a flow rate of 15–30 mL/min (to maintain distal coronary at 6–8°C below body temperature) – occlusion phase
- The OTW Balloon is deflated, and solution B infused for another 7–10 min-reperfusion phase. Flow rate adjusted to maintain the temperature in distal coronary 4–6°C below body temperature
- The OTW balloon is removed, and stent deployed over the Pressure Wire X
- Study in animals showed presence of temperature gradient during the occlusion phase, but not in the reperfusion phase.[64,65] The technique is being tested in humans in the EURO-ICE trial.

Hyperoxemic reperfusion (HR)

HR therapy is a treatment in which supersaturated oxygen is administered to a patient with STEMI following PCI to reduce myocardial damage. The procedure uses a device to remove arterial blood from a person, supersaturates it with oxygen and then reintroduce the highly oxygenated blood into the person's affected coronary artery after stent deployment.

- TherOx Downstream® System (TherOx Inc. of Irvine, CA) was approved in April 2019, for administration of super saturated oxygen therapy (SSO2 Therapy) following PCI to the left anterior descending coronary artery within 6 h of acute anterior wall MI
- This technique when given for 90 min after PCI documented reduction in infarct size in the AMIHOT I[66] and AMIHOT II[67] studies; however, there was increased bleeding
- In IC-HOT study,[68] the same administered for a duration of about 60 min proved safe with similar beneficial results.

Targeted anti-inflammatory approach and ***cellular approach*** for prevention and treatment of NR are presently in experimental stages. These include interventions that activate intracellular cardio protective signaling pathways directed at halting reperfusion injury. They have shown to reduce ischemic injury and improve myocardial perfusion following PCI and hold great promise. These techniques need refinement and further research is recommended before implementing them.

SIGNIFICANCE OF NR

NR phenomenon is associated with poor outcome immediately and in the long run. It underscores the benefits of PCI and is a nightmare for an interventional cardiologist. In-hospital course is complicated by life-threatening arrhythmias, heart failure and re-MI and hospitalization is prolonged. NR causes negative remodeling of the LV resulting in LV dilatation and heart failure leading to repeated hospitalizations and high 30-day mortality. Five-year survival is also low with high mortality (18.2% vs. 9.5%) in patients with NR compared to those with normal flow.

CONCLUSION

NR is an undesirable event that can complicate percutaneous coronary interventions especially in the setting of STEMI which could disheartens any interventional cardiologist. Prevention is better than cure hold true in this respect as, no available treatment is 100% effective. Different combinations of pharmacological vasodilation and antiplatelet therapy should be used in no specific order to achieve reversal of NR. Further research is mandatory to

identify techniques to treat no-reflow that could benefit the outcome in these patients.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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