The Impella to Balloon (ITB) Strategy Limits Infarct Size and Improves Survival in Acute Myocardial Infarction Complicated by Cardiogenic Shock: A Bench to Bedside Study

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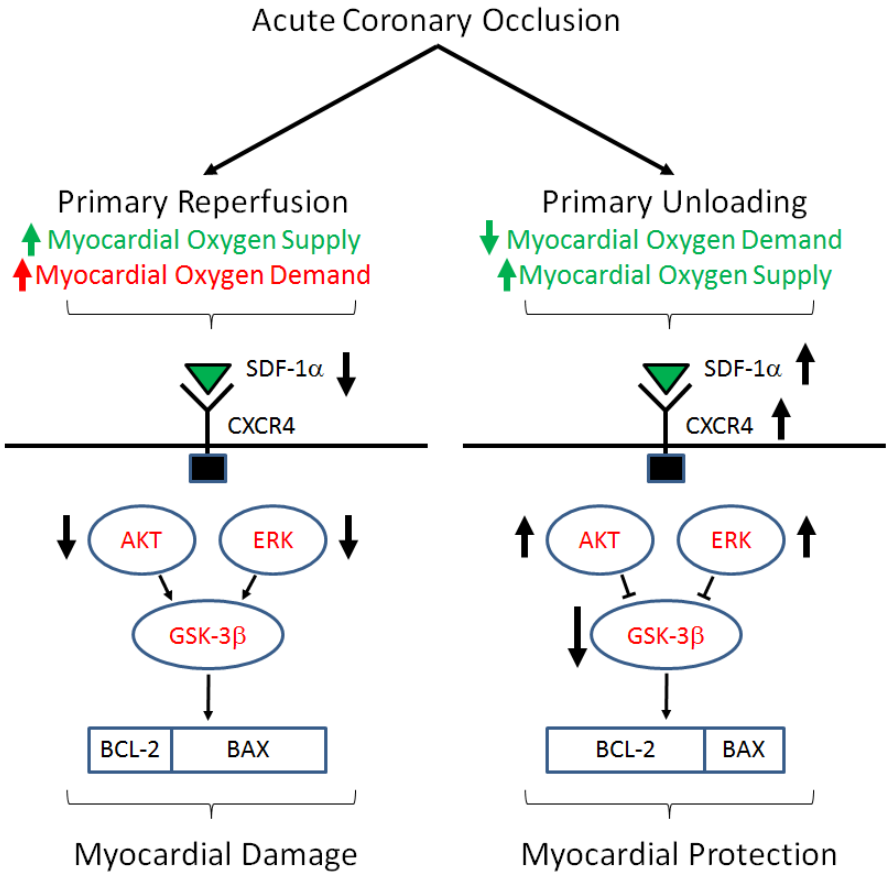


Background

Multiple attempts to limit ischemia-reperfusion injury (IRI) in acute myocardial infarction (AMI) have failed to show clear benefit. We reported that first unloading the left ventricle (LV) then reperfusing the coronary vessel reduces infarct size. However whether the benefit of mechanical unloading requires pre-reperfusion unloading remains unknown.

Mechanical Conditioning in AMI

Primary LV unloading activates a cardio-protective program that involves kinases such as Akt, ERK, and GSK3b, thereby limiting myocardial damage compared to primary reperfusion alone.

(Kapur NK et al. JACC HF 2015)

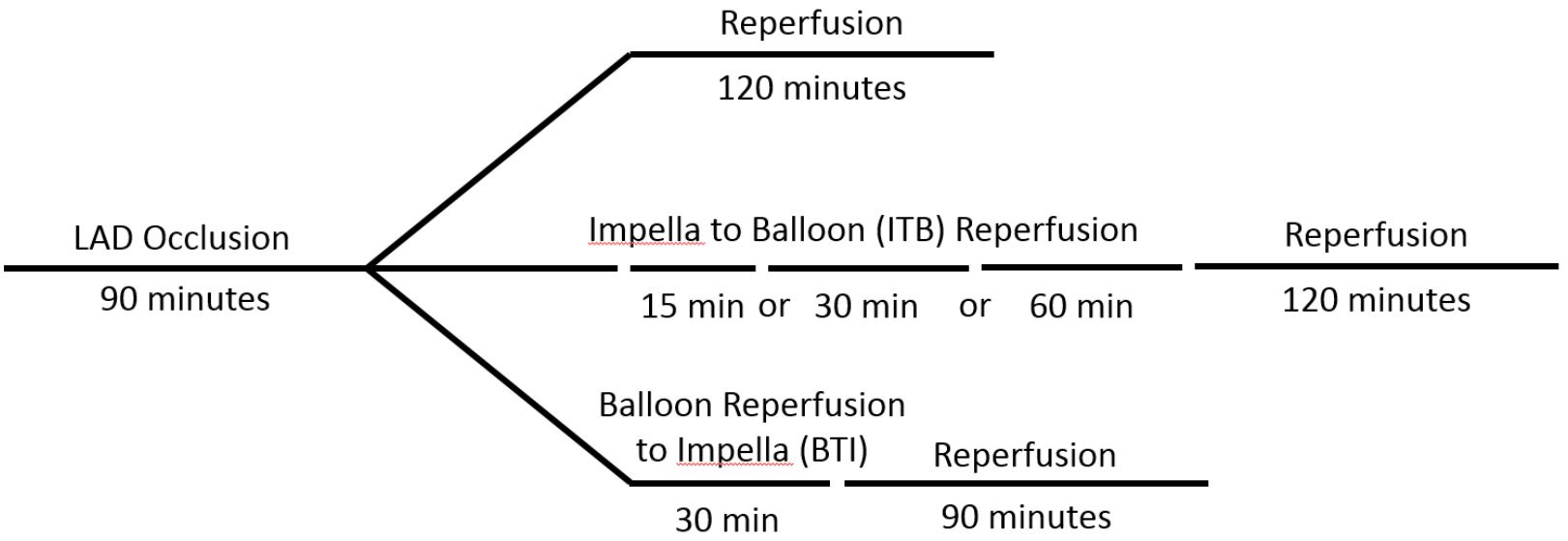
The Kinetics of Primary Unloading in AMI

Hypothesis

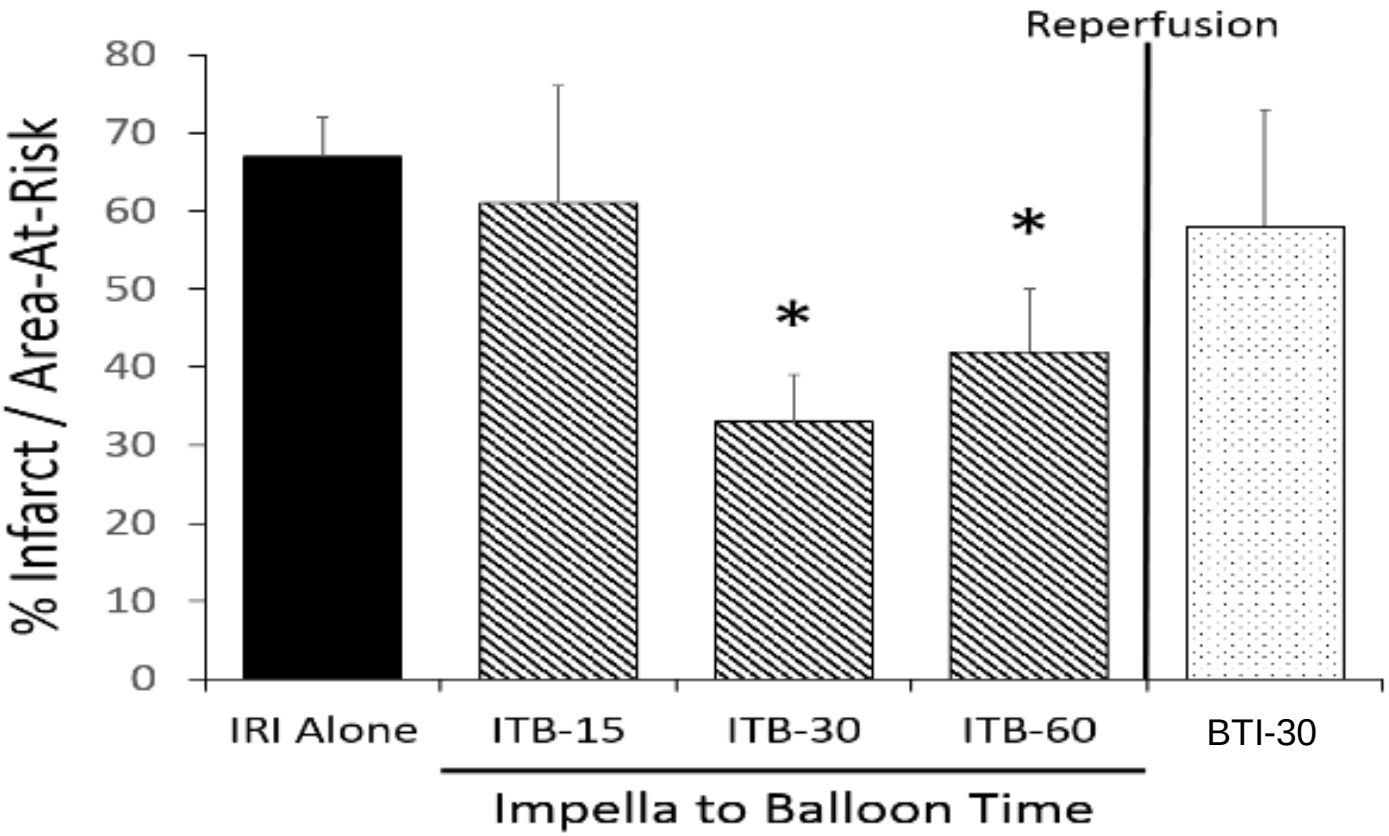
We explored the kinetics of LV unloading with an axial flow catheter (Impella) in relation to balloon reperfusion as a strategy to reduce infarct size and improve survival in the setting of an acute myocardial infarction.

Methods (Preclinical)

We first employed a swine model of AMI. After 90 minutes of LAD occlusion, adult, male swine (n=4.group) were randomized to either: 1) 120 minutes of reperfusion alone (IRI), 2) 15, 30, or 60 minutes of LV unloading before 120 minutes of coronary reperfusion (Impella to Balloon Group; ITB-15; ITB-30; ITB-60) or 3) 30 minutes of coronary reperfusion followed by LV unloading and an additional 120 minutes of reperfusion (Balloon to Impella Group; BTI). Infarct size, myocardial kinase activity, and mitochondrial integrity were quantified.



The Kinetics of Primary Unloading in AMI



Results (1)

Compared to IRI alone, infarct size was reduced in the ITB-30 and ITB-60 groups, but not in the ITB-15 or BTI groups.

Mitochondrial Integrity in AMI

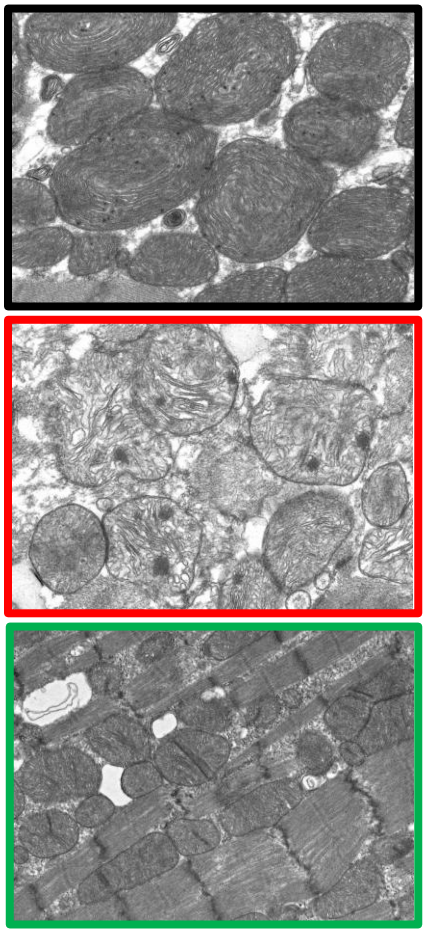
Results (2)

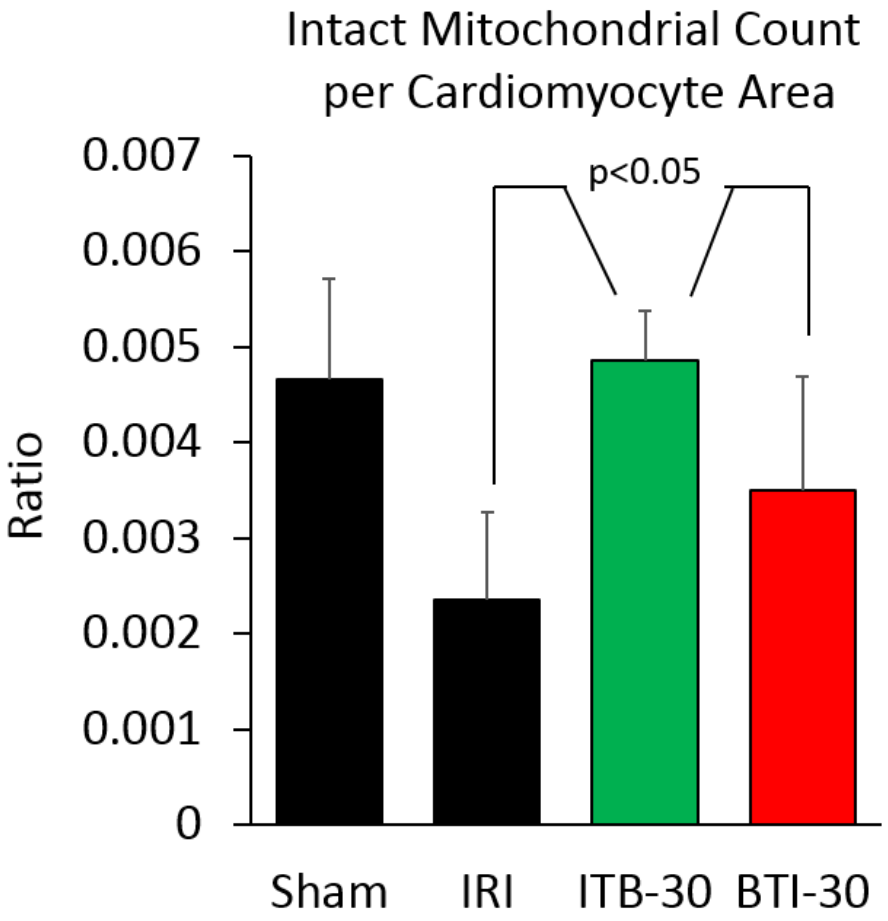
Mitochondria integrity was improved and numbers per cardiomyocyte increased within the infarct zone in the ITB-30 group, compared to the IRI or BTI groups.

Sham – No IRI

BTI-30

ITB-30

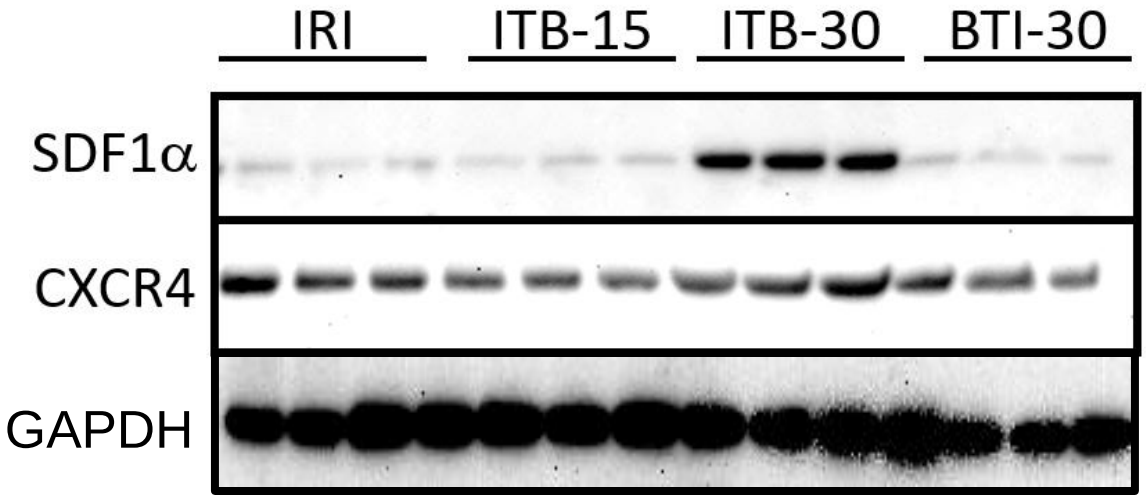


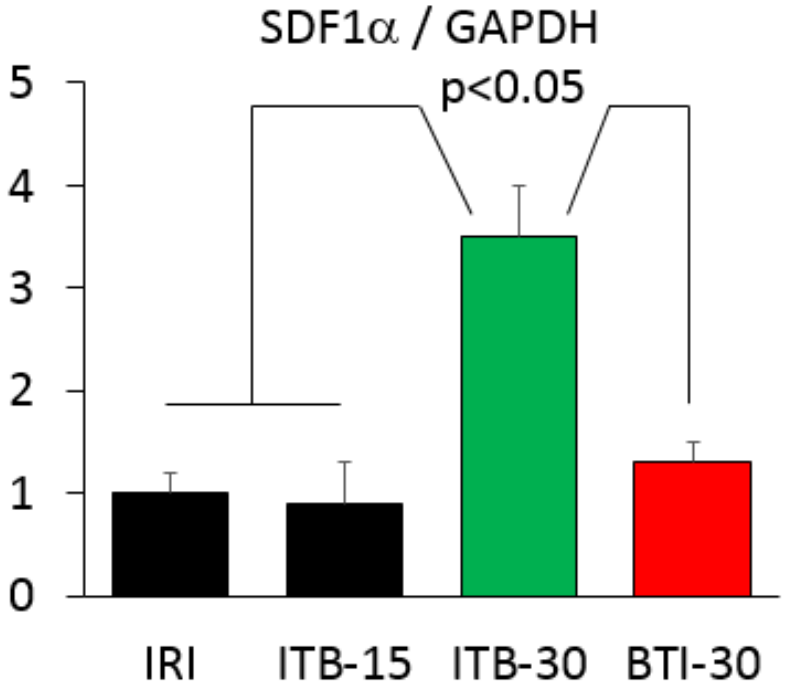


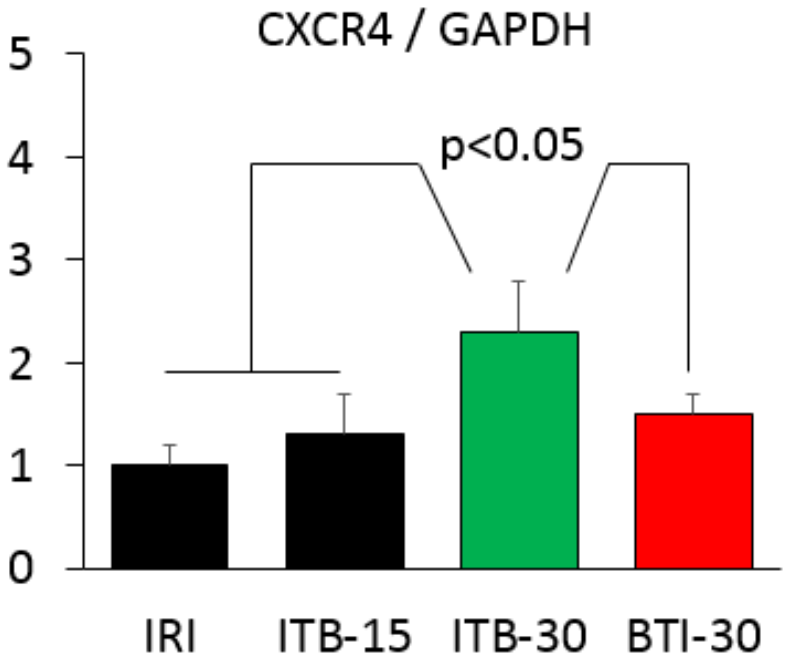
ITB vs BTI Signaling: SDF1a/CXCR4

Results (3)

Figure 3. Levels of phosphorylated kinases, Akt and GSK3b, and the ligand-receptor, SDF1a and CXCR4, were increased within the infarct zone in the ITB-30 group, not the ITB-15 or BTI groups.



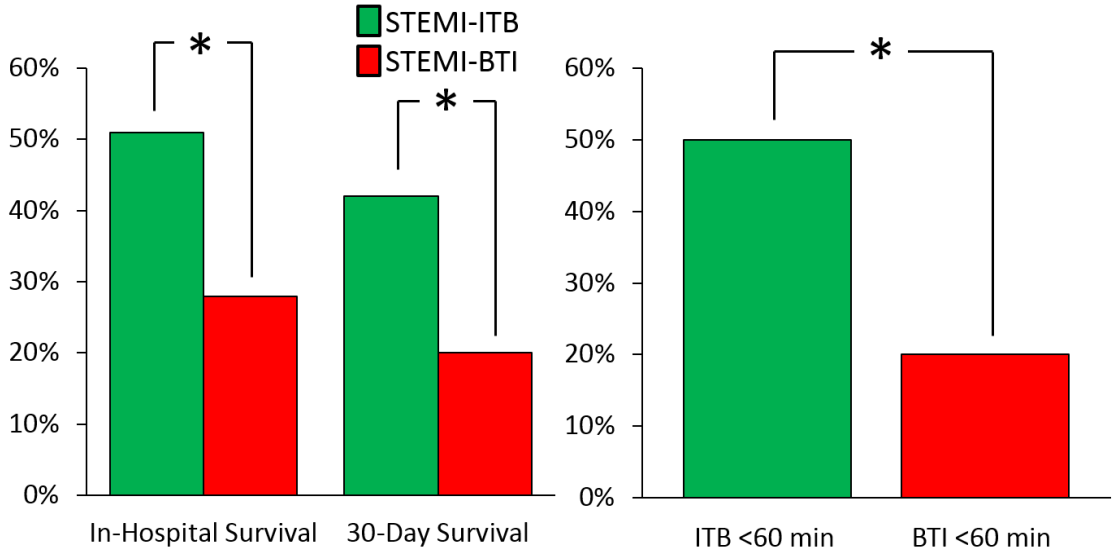




Insights from Clinical Practice: cVAD Registry

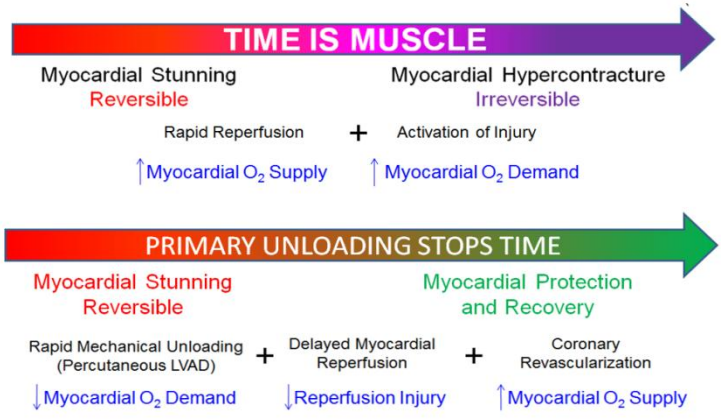
Results (4)

In the cVAD registry, in-hospital (51% vs 28%, p=0.02) and 30-day survival (42% vs 20%, p=0.03) were higher in the STEMI-ITB than the STEMI-BTI group. A STEMI-ITB time of less than 60 minutes (n=38) was associated with higher in-hospital survival than a STEMI-BTI time of less than 60 minutes (n=40) (50% vs 25%, p=0.02).



Conclusions

Primary LV unloading for 30 minutes before, not after, coronary reperfusion reduces infarct size, increased cardioprotective signaling, and improved mitochondrial integrity. These preclinical findings are supported by improved survival among patients treated with an axial flow catheter before, not after reperfusion. Prospective studies are required to explore the utility of primary unloading in AMI.



Primary Unloading vs Primary Reperfusion

By targeting myocardial oxygen demand, primary LV unloading attenuates ongoing ischemic injury and allows for activation of a protection program that protects the myocardium and allows for myocardial recovery.