Safety and Feasibility of Regional Myocardial Hypothermia during Acute Myocardial Infarction

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Background

• Despite therapeutic advances, there is still a need to further improve the treatment outcomes of patients with acute myocardial infarction (Lancet 2003;361:13-20).

• Mild systemic hypothermia has been shown to reduce myocardial infarct size in animal studies (Am J Physiol Heart Circ Physiol 2002;282:H1584-H1591).

• Systemic hypothermia has been shown to be feasible, safe, and possibly effective in reducing myocardial infarct size in patients (JACC 2002;40:1928-34).
Potential Mechanisms

- Energy preservation from decreased cellular metabolism and myocardial oxygen demand
- Pre-conditioning effect
- Prevention of reperfusion injury?
- Protection of microcirculation?
Potential Benefits of Regional versus Systemic Hypothermia

• Regional myocardial hypothermia during AMI may be more effective in myocardial salvage compared with systemic hypothermia with less side-effects.

• Regional myocardial hypothermia in conjunction with cardioprotective agents during AMI may salvage more myocardium at risk compared with conventional reperfusion therapy.
Options for Regional Hypothermia

- Intraventricular (cooling of the arterial blood)
- Peri-cardial/epicardial
- Coronary sinus
- Intra-coronary
Objective

- To examine whether regional myocardial hypothermia by intra-coronary infusion of cold solutions during acute coronary intervention is feasible and safe during acute myocardial infarction.
Methods

- *In vivo* open-chest study without an infarction
- *In vivo* open-chest study with an infarction
- *In vivo* closed-chest study with an infarction
- Infusions of saline, lactated ringer’s, and autologous blood using a proprietary infusion system during balloon inflation
In Vivo Open-Chest Pig Model

Intramyocardial thermistors, both at the ischemic areas and non-ischemic area; body temperature with a rectal thermistor
In Vivo Results

- No hemodynamic consequences
- No arrhythmia
0.018 balloon with Ringers Lactate @ 25 ml/min

Balloon Inflation/Infusion
Consolidated Temperature Data

Infusion Rate, ml/min

Tissue Temperature Drop, °C

RT

Linear (RT)

Linear (15)
0.018 balloon with Ringers Lactate @ 24 ml/min with controlled re-warming.
Ringers @ 25 ml/min (intra-arterial temp (needle stick))
Conclusions

• It is safe and feasible to achieve regional myocardial hypothermia by intracoronary infusion of cooled solution.
• Myocardial temperature can be controlled by altering the infusion pressure and volume.
• The rate of tissue cooling and rewarming can be controlled.
• Intra-arterial temperature can be used as a surrogate marker for tissue temperature.
Future Directions

- Efficacy of regional myocardial hypothermia on myocardial salvage during AMI
- Cooled blood versus other solutions
- Mechanisms of the benefit
- Other routes of regional myocardial hypothermia
- Relative efficacy of regional versus systemic hypothermia on myocardial salvage
- *Infusion of cardioprotective agents during regional myocardial hypothermia*