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Long-Term Benefit of Postconditioning

Hélène Thibault, Christophe Piot, Patrick Staat, Laurence Bontemps, Catherine Sportouch, Gilles Rioufol, Thien Tri Cung, Eric Bonnefoy, Denis Angoulvant, Jean-François Aupetit, Gérard Finet, Xavier André-Fouët, Jean Christophe Macia, Franck Raczka, Rolland Rossi, Rolland Itti, Gilbert Kirkorian, Geneviève Derumeaux and Michel Ovize

Circulation. 2008;117:1037-1044

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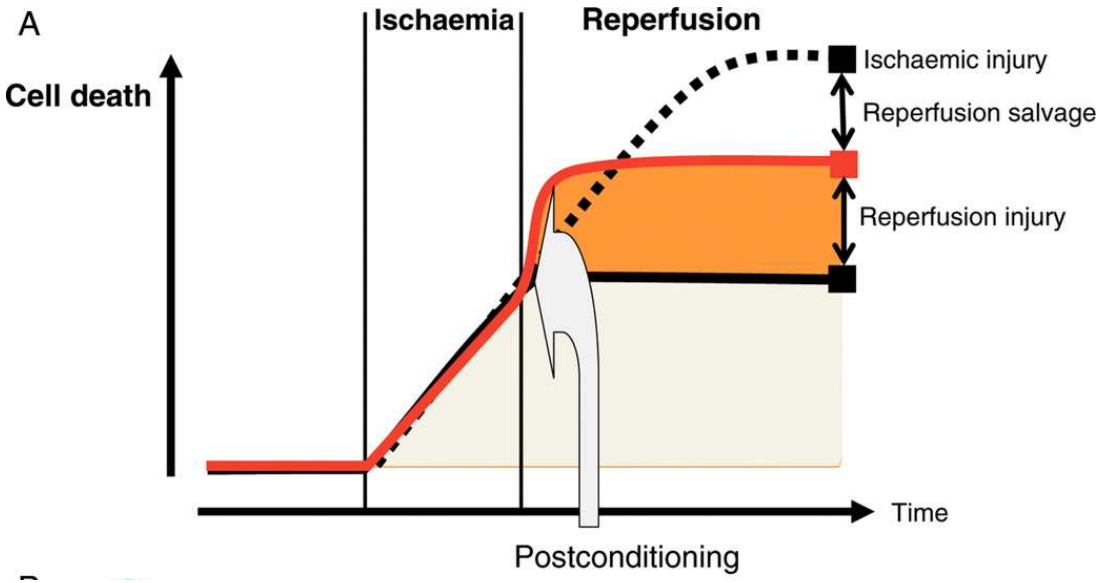
Reperfusion-Injury



The concept of lethal reperfusion injury.

Ovize et al. *Cardiovascular Research Dis 2010*

Preconditioning

Ischemic Preconditioning

*… is a process by which a brief ischemic insult confers protection against **subsequent** ischemic episode of similar or greater magnitude*

e.g. 4 transient (5 minutes) periods of coronary artery occlusion alternately with 5 minutes of reperfusion

Pagelet al. *Anesthesia Service* 2011

Postconditioning

Ischemic Postconditioning

*… is a process by which a brief ischemic insult confers protection against **previous** ischemic episodes of similar or greater magnitude*

e.g. 4 transient (5 minutes) periods of coronary artery occlusion alternately with 5 minutes of reperfusion

Pagelet al. *Anesthesia Service* 2008

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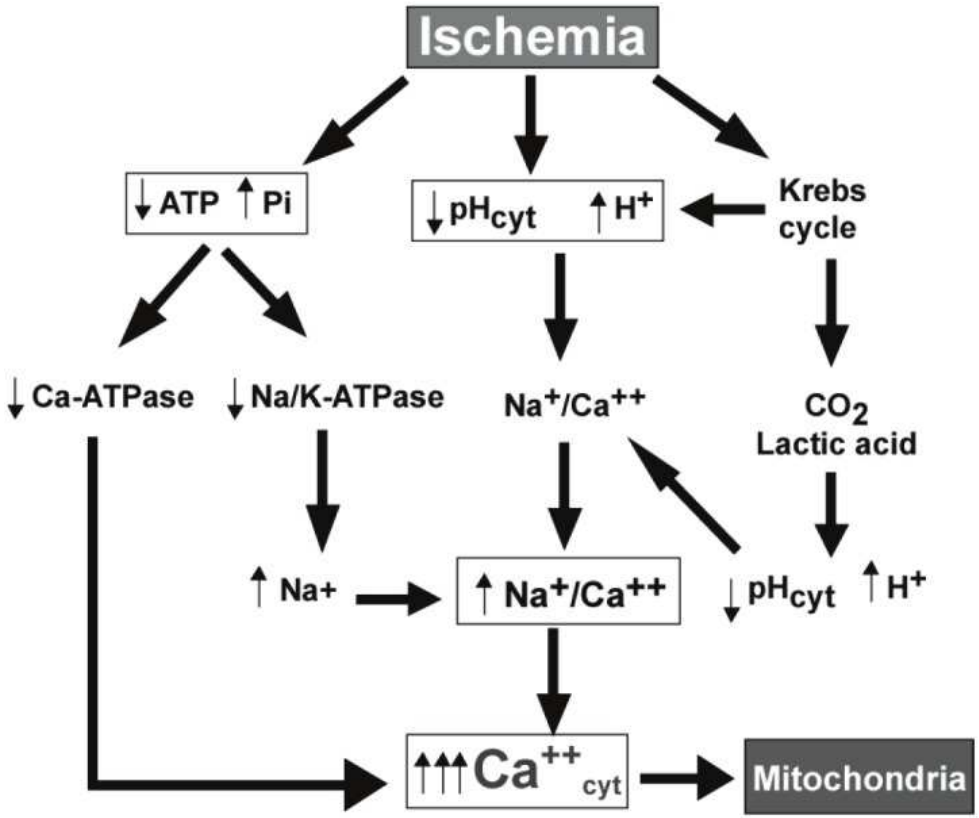
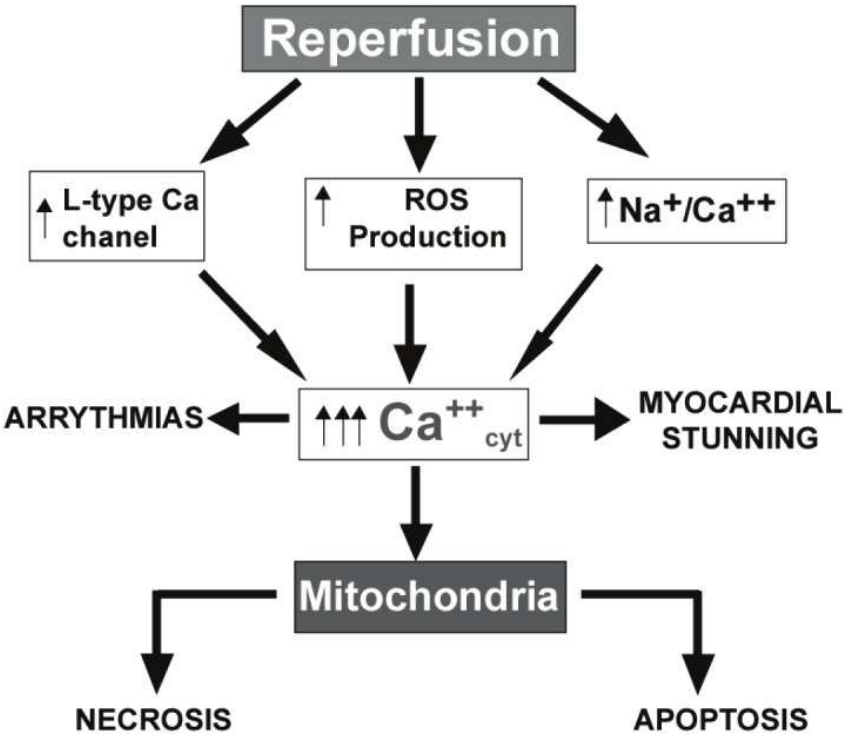
Postconditioning





Bopass et al. *Am J Cardiovasc Dis 2012*

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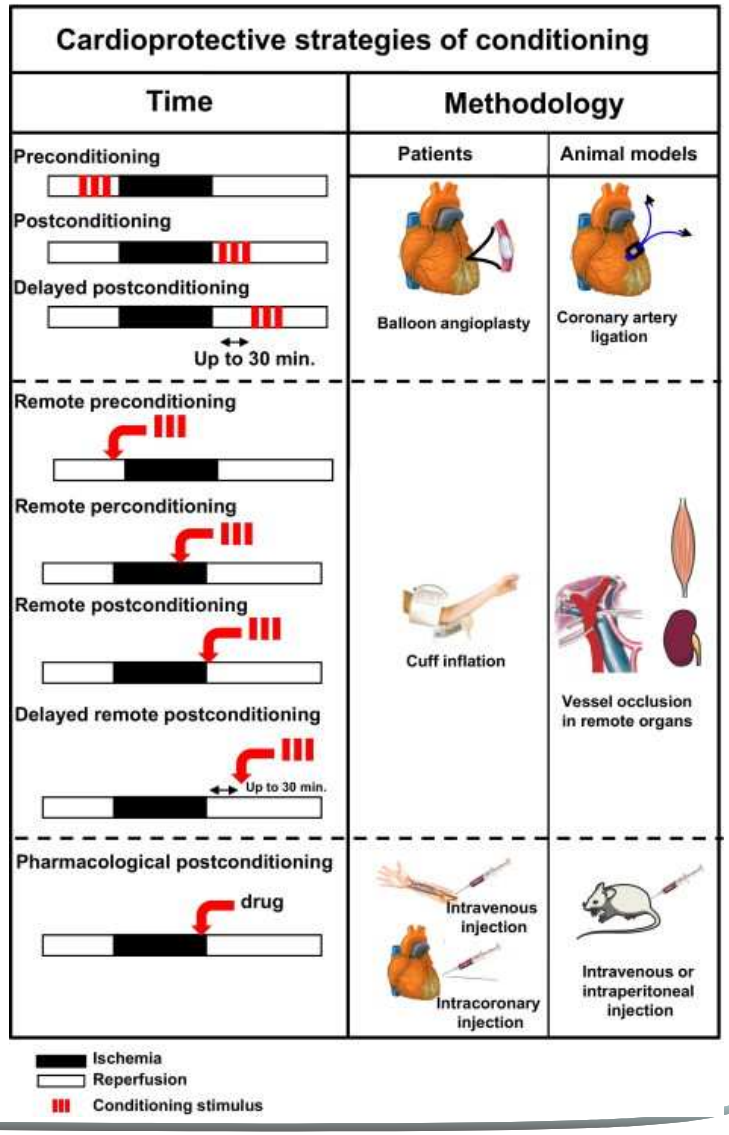
Ischemia Treatment



Lemaire et al.. *Trands in Cardiovascular Medicin 2012*

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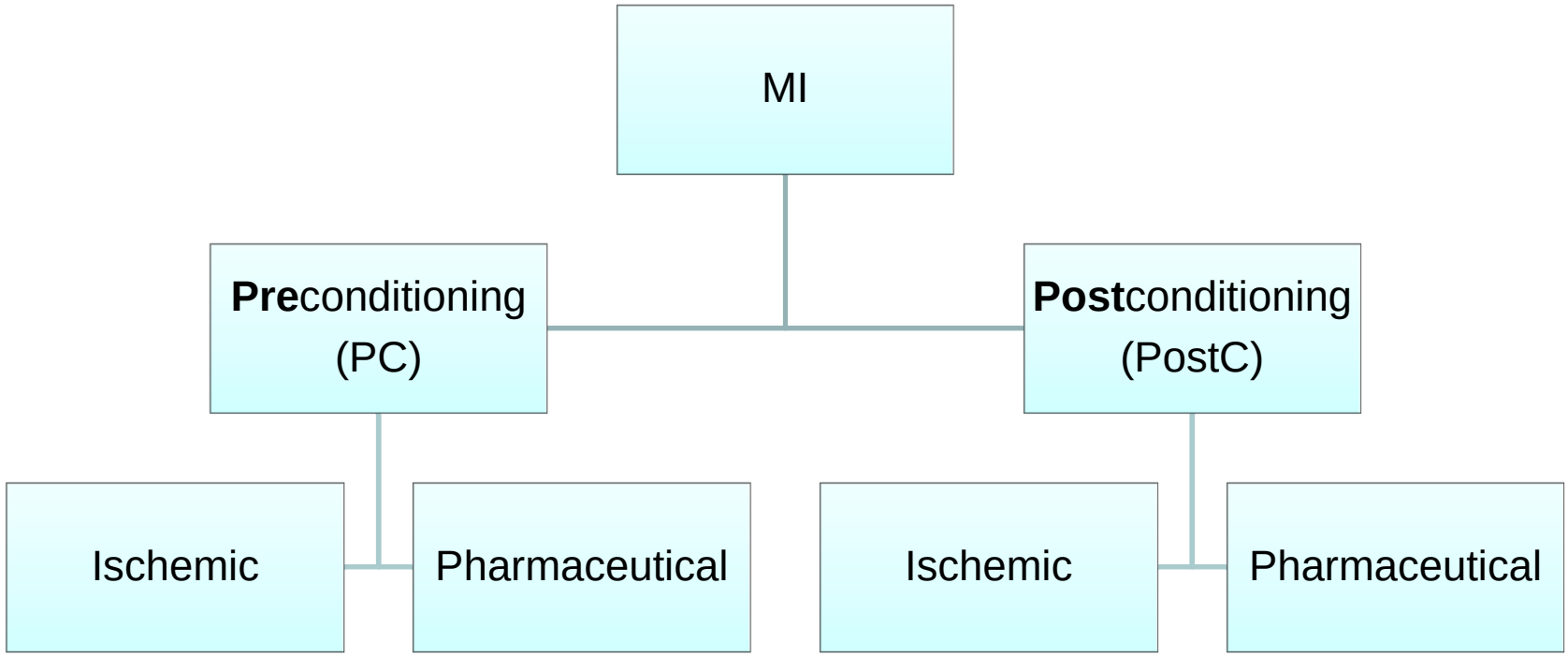
Ischemia Treatment



Pharmacologic postconditioning

Administration immediately before or during early reperfusion mimicked the beneficial action of IPC

- Adenosin
- Bradykinin
- Opioids
- Insulin
- Growth Factors
- Statins
- Volatile anesthetics

Pagelet al. *Anesthesia Service* 2008

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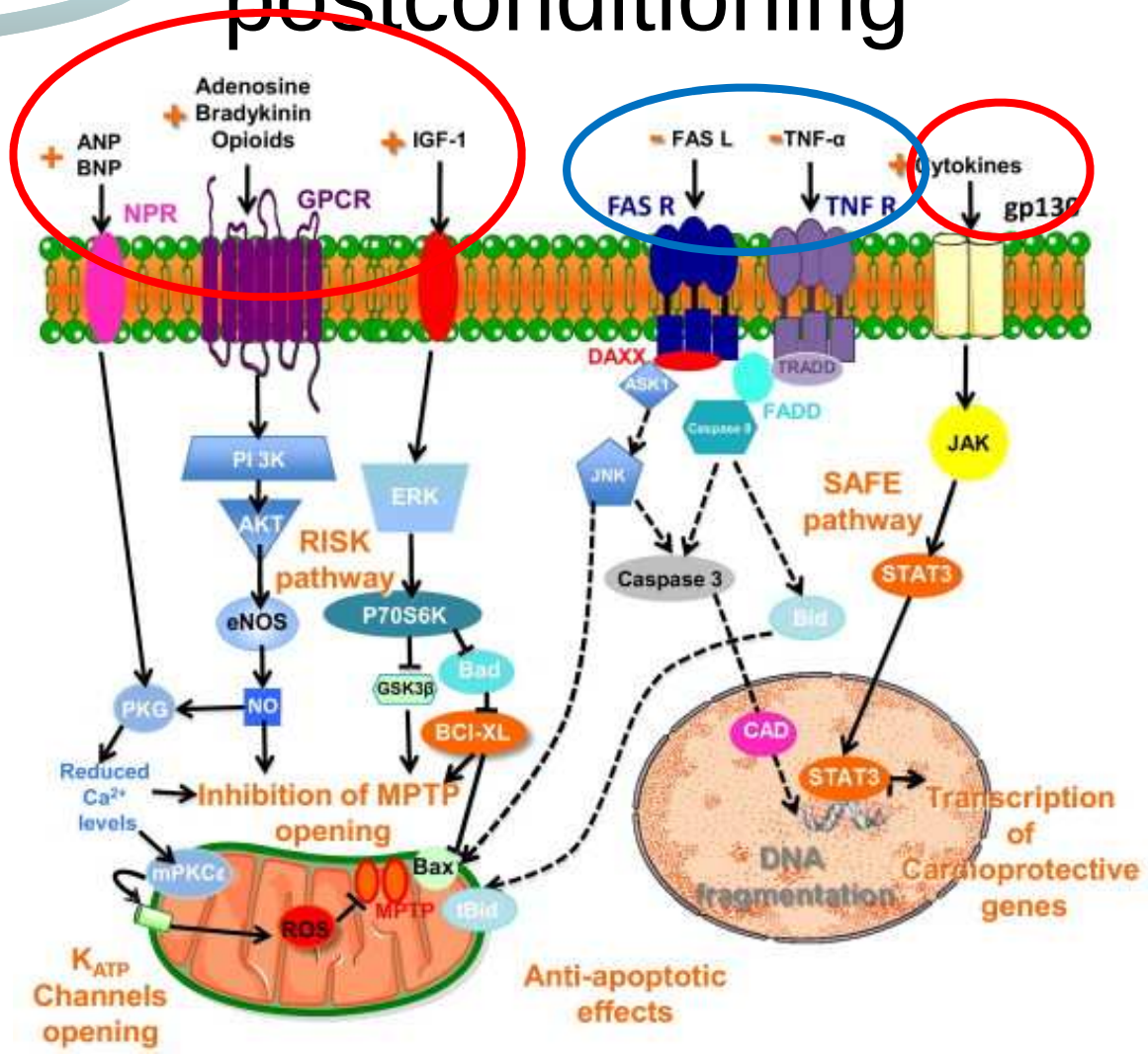
Pharmacologic postconditioning

RISK = reperfusion injury salvage
SAFE = survivor activating factor enhancement



Lemaire et al.. *Trands in Cardiovascular Medicin 2012*

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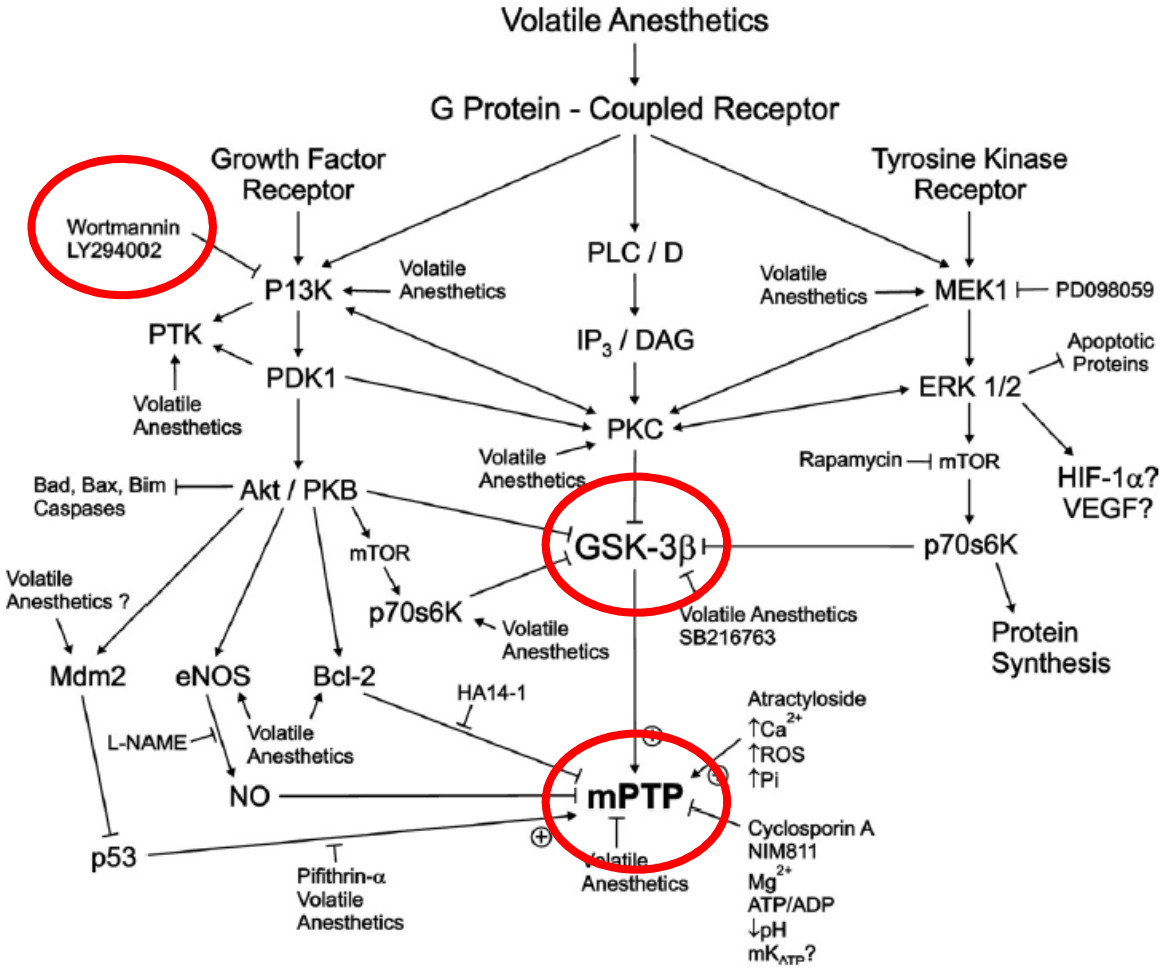
Volatile Anesthetics

Isoflur



Pagelet al. *Anesthesia Service* 2008

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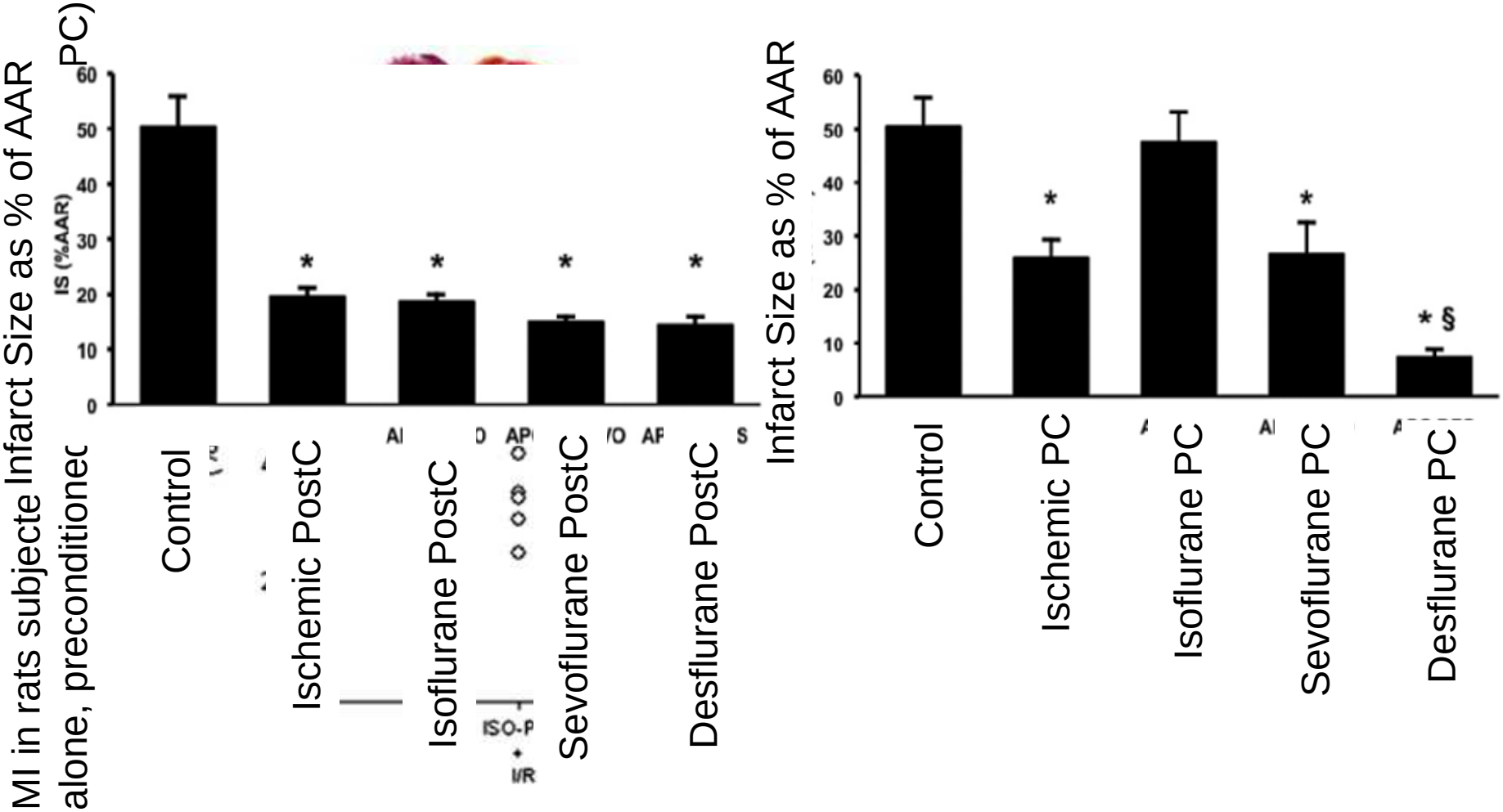
Volatile Anesthetics



Chen et al. *Shock* 2008.; Redel et al. Exp Bio Med. 2009.

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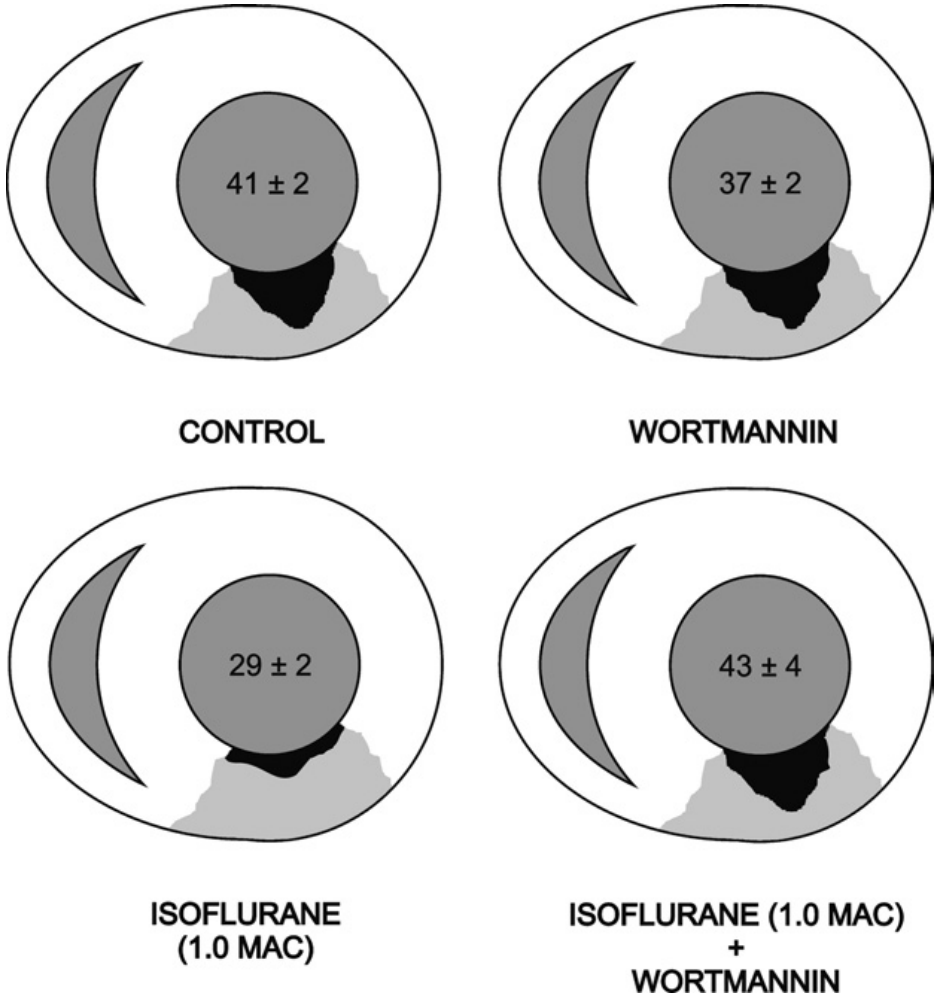
Volatile Anesthetics

Illustration of rabbit myocardium subjected to a 60-minute CAO an reperfusion (Wortmannin is a selective Pi3K antagonist



Pagelet al. *Anesthesia Service* 2008

Ischemic PostC

first discribed in the 1980s by *Buckberg* and associates

myocardial reperfusion conditions reduce the extent of injury resulting from restoration of coronary blood flow

Buckberg et al. *J Thorac Cardivasc Surg* 1986

Ischemic PostC

Zhao et al. 2003

- proposed that a series of short (30 sec) episodes of coronary artery occlusion intersepersed with 30-sec periods of reperfusion before final resoration of coronary artery blood flow possessed protective effects

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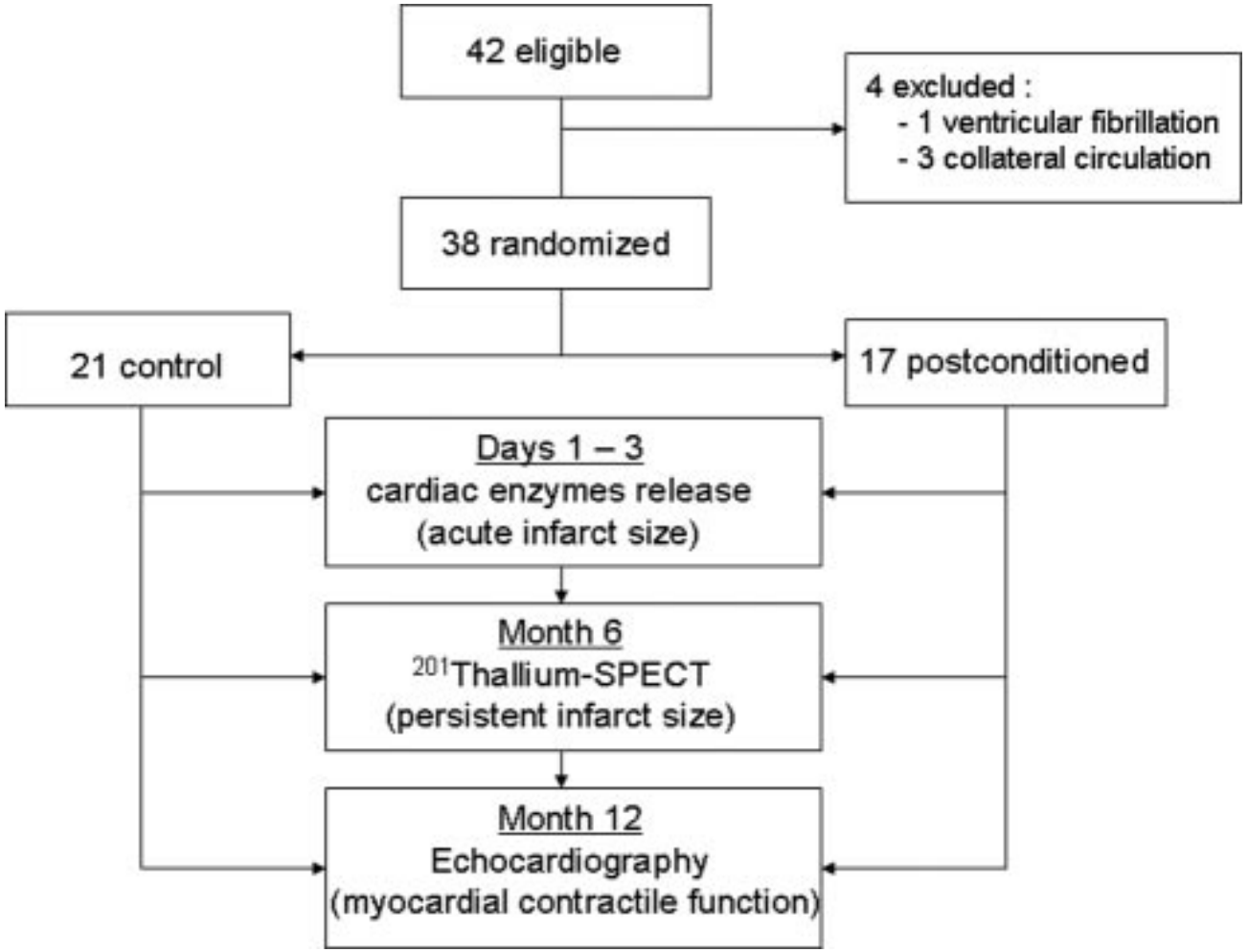
Study Design



Thibault et al. *Circulation*. 2008

Study Design

performed during the first 8 minutes of reperfusion. In the postconditioned group, within 1 minute of reflow after the direct stenting, the angioplasty balloon was reinflated 4 times for 1 minute, with low-pressure (4 to 6 atm) inflations, each separated by 1 minute of reflow.[16] After minute 8 of reperfusion, the PCI procedure was completed according to the physician's judgment with respect to

Thibault et al. *Circulation*. 2008

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Table 1. Baseline Characteristics

	Control Group (n=21)	Postconditioned Group (n=17)	*P*
Age, y	56±13	56±12	0.97
Male sex, %	78	76	0.64
Body mass index, kg/m^2	26±5	27±4	0.47
Hypertension, %	35	29	0.54
Smokers, %	65	65	0.63
Dyslipidemia, %	49	52	0.37
Diabetes, %	10	12	0.61
History of coronary artery disease, %	9	0	0.30
Admission blood glucose levels, μmol/L	8.4±2.3	8.8±2.8	0.65
Admission hemodynamics			
Heart rate, bpm	73±13	72±12	0.67
Systolic blood pressure, mm Hg	133±23	136±20	0.62
Diastolic blood pressure, mm Hg	84±13	83±12	0.87
Admission ST-segment elevation			
Contiguous leads with >1-mm ST shift, n	4.0±1.8	3.9±0.8	0.80
Maximum ST shift, mm	4.2±2.3	4.2±2.0	1.00
LV and coronary angiography			
Single-/multiple-vessel coronary artery disease, %	86/14	82/18	0.56
Culprit artery (left anterior descending), %	52	56	0.47
LV ejection fraction, %	46±5	44±8	0.51
Abnormally contracting segments, %	39±14	40±8	0.60
Ischemia time, min	297±104	283±82	0.35
Stenting of culprit lesion	100	100	1.00
Treatment before angioplasty, %			
Intravenous nitrates	48	50	0.57
Morphine	48	56	0.43
Treatment at time of angioplasty, %			
Heparin	91	100	0.30
Antiaggregants	100	100	1.00
Treatment at discharge, %			
β-Blockers	83	94	0.56
Angiotensin-converting enzyme inhibitors	88	89	0.60
Statins	94	89	0.42
Antiaggregants	100	100	1.00
Long-acting nitrates	12	11	0.65
Diuretics	33	6	0.07

Data are presented as percentage or as mean±SD. Patients' characteristics and treatment at hospital admission and discharge are presented.

Thibault et al. *Circulation*. 2008

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Results

Table 2. Infarct Size and LV Function

	Control Group (n=21)	Postconditioned Group (n=17)	*P*
Cardiac enzyme infarct size (at days 1 to 3)			
CK release (AUC $\times 10^4$)	37.9±19.5	22.7±9.3*	0.01
TnI release (AUC $\times 10^4$)	24.6±20.6	13.0±7.0*	0.02
SPECT infarct size (at 6 months)			
Perfusion defect index (%)	19.5±13.3	11.8±10.3*	0.04
LV function by echocardiography (at 12 months)			
LV ejection fraction, %	49±13	56±8*	0.04
Wall motion score index	1.6±0.4	1.4±0.4*	0.04
Strain rate, s^{-1}	0.6±0.4	1.2±0.8*	0.0002

Data are presented as mean±SD. AUC indicates area under the curve. Infarct size was assessed early (cardiac enzyme release) and at 6 months by SPECT imaging. LV function was evaluated at 12 months by echocardiography.

*$P<0.05$ vs control.

Thibault et al. *Circulation*. 2008

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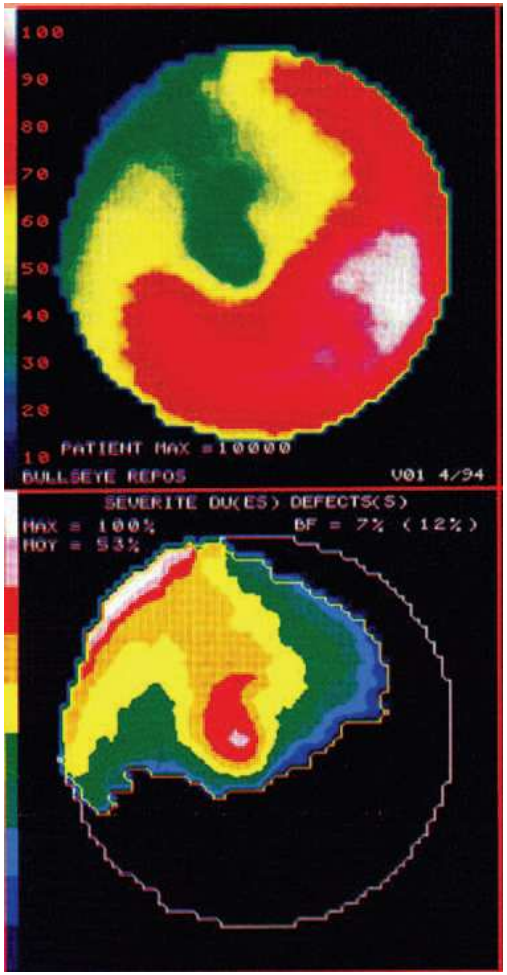
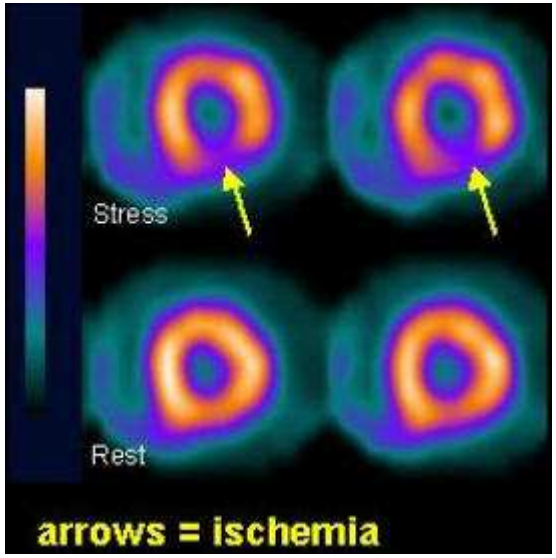
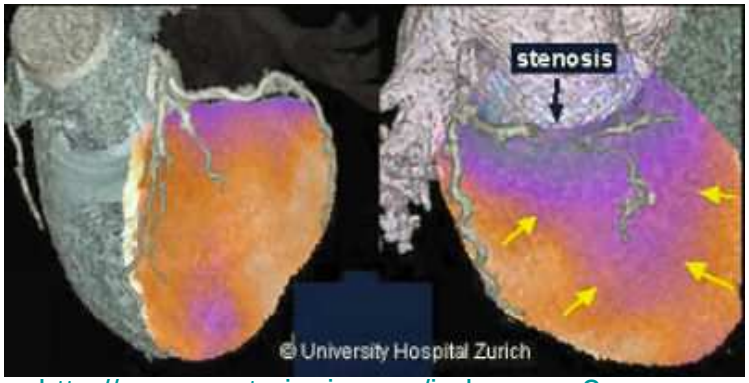
SPECT







http://www.auntminnie.com/index.aspx?sec=sup_n&sub=mol&pag=dis&ItemID=71235

Thibault et al. *Circulation*. 2008

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Discussion

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Reduction of infarct size measured in SPECT as well as a reduction of surrogate prameters (TnI, CK)

Improved functional recovery at 1 year after AMI (7% improvement in LV ejection fraction)

Better clinical outcome?

Risk of repeated in,- and deflation of the balloon

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Discussion

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Questions I think that still have to be answered:

Does this procedure improve patients outcome?

First principle: Do not harm!

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Thank you for your attention