Myocardial Preservation

2008

- Pre operative
  - Stable: maintain status quo with medication
  - Unstable: iv GTN, heparin, IABP
- Operative
- Post operative (reduce functional demands):
  - ↓Afterload
  - HR control
  - ↑ DO2 (DO2= Hb x SaO2 x CO x 1.34+PaO2 x .003)
  - ↓ O2 consumption

Non cardioplegic techniques

- Intermittent aortic cross-clamping with fibrillation
- Continuous coronary perfusion with ordinary blood
- Systemic hypothermia and elective fibrillatory arrest
- Profound hypothermic global ischaemia

Cardioplegic techniques

- Route
  - Antegrade
  - Retrograde
  - Combined
- Medium
  - Blood
  - Crystalloid
- Temperature
  - Warm
  - Cold
  - Tepid
- Timing
  - Continuous
  - Intermittent
- Solution
  - Intracellular
  - Extracellular

Intermittent aortic CCF

- Key points:
- Cardiac decompression prior to xclamping to prevent myocardial distention and myofibril disruption
- Mild hypothermia (32-34°C) increases permissible ischaemia to 15 mins and dumpens the amplitude of fibrillation

- Advantages
- Inexpensive, simple
- Comparable to plegia
- Distinguish arteries from veins easily (intramyocardial)
- Sequential construction allows evaluation of flow in each graft
- Reduced xclamp time

- Disadvantages
- Aortic trauma
- Thromboembolism (cerebral microemboli, neuropsychological disturbances, inconclusive evidence)

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Continuous coronary perfusion with ordinary blood

- Aorta is xclamped and coronaries perfused through aortic root cannula or direct coronary cannulation
- May be used for AVR with poor LV and generally in short procedures

Potential pitfalls

- Selective perfusion of LAD or Cx (direct cannulation, short LMS)
- Fibrillation should be induced electrically but maintained by hypothermia (sub-endocardial perfusion is reduced by electrical fibrillation this is hazardous in LVH)
- Excessive flow (>300 ml/min) will induce cellular damage and in longer procedures myocardial oedema will reduce compliance.

Systemic hypothermia and elective fibrillatory arrest

- systemic hypothermia (28°C),
- elective fibrillatory arrest,
- maintenance of systemic perfusion pressure at between 80 and 100 mm Hg are the key elements.
- On fibrillatory arrest, the local vessel can be isolated and myocardial revascularization performed.

Limitations

- Surgical field may be obscured by blood during revascularization
- Ventricular fibrillation is associated with increased muscular tone, which can limit the surgeon’s ability to position the heart for optimal exposure
- It is generally not applicable for intracardiac procedures.

Profound hypothermic global ischaemia

- Relies on cardiac arrest during profound hypothermia
- Generally reserved for major aortic / arch procedures.

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Cardioplegia

- Induce diastolic arrest by altering the resting potential and ionic gradients in the myocyte.
- Extracellular: Increase K in extracellular fluid prevent repolarisation
- Intracellular: block depolarisation by lowering Na.

Cardioplegic solutions

Solution	Na	K	Mg	Ca	HCO3	pH	Osm	other
Bretschneider's no. 3	12.0	10	2	5.5		5.5-7	320	
Lactated Ringer's	130	24		1.5		7.14		
Tyer's	138	25	1.5	0.5	20	7.8	275	
St. Thomas no. 2	110	16	16	1.2	10	7.8	324	
Roe's	27	20	1.5			7.6	347	
Gay/Ebert	38.5	40			10	7.8	365	
Birmingham	100	30		0.7	28	7.5	300-385	
Craver's	154	25			11		391	
Lolley's		20			4.4	7.78	350	

1950 - 1964

Bigelow WG	1950	Studied the application of hypothermia to cardiac surgery in canines
Swan H	1953	Showed that hypothermic arrest in humans provided a bloodless field for operating
Melrose DG, Bentall	1955	Introduced the concept of reversible chemical cardiac arrest in canines
Lillehei CW	1956	Detailed a method for delivering hypothermic crystalloid cardioplegia by cannulating coronary arteries
Lam CR	1957	One of the earliest known uses of the term "cardioplegia"
Gerbode F, Melrose D	1958	Used potassium citrate to induce cardiac arrest in humans
McFarland JA	1960	Challenged the safety of the Melrose technique; changed from potassium arrest to intermittent aortic occlusion or coronary artery perfusion for myocardial protection
Bretschneider H	1964	Developed a sodium-poor, calcium-free, procaine-containing solution to arrest the heart
Sondergaard KT	1964	Adopted Bretschneider’s cardioplegic solution and was one of the first to routinely use it for myocardial protection in clinical practice

1973 - 1991

Gay WA, Ebert PA	1973	Credited with revival of potassium-induced cardioplegia; demonstrated that potassium solution could arrest a canine heart for 60 minutes without cellular damage
Roe BB	1973	Demonstrated that "the modalities of cardioplegia, hypothermia, and capillary washout" provided effective myocardial protection
Tyers WA	1974	Demonstrated that an infusion of cold blood to keep the myocardial tissue below 43C provided 90 minutes of ischemia in animals
Hearse DJ	1975	Emphasized preischemic infusions to negate ischemic injuries in rats; this formula became known as St. Thomas solution no. 1
Braimbridge M	1975	One of the first to use St. Thomas solution no. 1 clinically
Effler DB	1976	Recommended simple aortic clamping at operating room tempreatures
Buckberg GD	1979	Introduced the use of blood as the vehicle for infusing potassium into coronary arteries
Akins CW	1984	Utilized technique of hypothermic fibrillatory arrest for coronary revascularization without cardioplegia
Murray C	1986	Noted that brief periods of ischemia and reperfusion enable the heart to withstand longer periods of ischemia
Lichtenstein SV, Salerno TA	1991	Reported clinically beneficial results using continuous, warm blood cardioplegia

Blood vs Crystalloid

- Can provide an oxygenated environment.
- Can provide a method for intermittent reoxygenation of the heart during arrest.
- Can limit hemodilution when large volumes of cardioplegia are used.
- Has an excellent buffering capacity.
- Has excellent osmotic properties.
- The electrolyte composition and pH are physiologic.
- Contains endogenous antioxidants and free-radical scavengers.
- Can be less complex than other solutions to prepare.

Blood vs Crystalloid (Efficacy)

- There are numerous preclinical studies as well as nonrandomized and randomized clinical trials that demonstrate that cold blood cardioplegia is an effective way to provide excellent myocardial protection.
- Many of these same studies also have suggested that cold blood cardioplegia is superior to cold crystalloid cardioplegia
- Other investigators have shown crystalloid cardioplegia to be just as cardioprotective and cost-effective, if not more so, and that crystalloid cardioplegia more reliably ensures a quiet, bloodless operative field.
- Many of the clinical trials that have compared the efficacy of blood and crystalloid cardioplegia have been single-center studies, involved a limited number of patients, focused on a specific subset of patients, and/or omitted details regarding the clinical management of the patients.

References

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Warm vs Cold

- It is not known just how long the warm heart can tolerate an ischemic event, which may occur when the infusion is interrupted,
- Obscured surgical field (continuous)
- Many prefer intermittent warm blood cardioplegia
- An O2 debt accumulates during global ischaemia, a burst of warm cardioplegia (hot shot) immediately before unclamping provides substrate resuscitation and myocardial recovery
- increased incidence of neurologic deficits reported

- Left shift of O2 dissociation curve
- ↓O2 requirements (8% per °C)
- Enzyme dysfunction
- Membrane instability
- Inefficient energy utilisation
- Disturbed osmotic homeostasis

Tepid

- Studies also have demonstrated that tepid blood cardioplegia is safe and effective.
- The majority of these studies, however, have been single-center studies and/or conducted in a relatively small cohort of patients.
- Whether tepid cardioplegia confers better protection over other current methodologies remains to be determined.

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Retrograde cardioplegia

- This approach originated with a concept developed by Pratt in 1898, who suggested that oxygenated blood could be supplied to the ischemic heart via the coronary venous system.
- Sixty years later, Lillehei and colleagues used retrograde coronary sinus perfusion to protect the heart during aortic valve surgery.

Concept

- Increased recognition that all cardioplegic techniques are dependent on
  - adequacy of distribution and
  - frequency of replenishment
- focused attention on improving distribution and minimising ischaemic time.
- Both issues were addressed to some extent with the advent of retrograde coronary sinus delivery in the early 1990s.

Retrograde vs Antegrade

- Distribution is generally good but less predictable than antegrade with incosistent RV protection
- Particularly useful for re do CABG and valve when surgery can continue during cardioplegia delivery (reducing the risk of embolization from saphenous vein grafts that could occur during antegrade perfusion during reoperative coronary artery surgery)

Under investigation

- Ischemic Preconditioning
- Adenosine
- ‘Polarised’ arrest
- Sodium-Hydrogen Exchange Inhibition
- Nitric Oxide

Ischaemic preconditioning

- Ischemic preconditioning is an adaptive biologic phenomenon in which the heart (and numerous other tissues) becomes more tolerant to a period of prolonged ischemia if first exposed to a prior episode of brief ischemia and reperfusion.
- This adaptation to ischemia was first described by Murray and colleagues and is referred to as *classic* or *early-phase preconditioning*.99
- This increased tolerance to ischemia is associated with a reduction in
  - infarct size,
  - apoptosis, and
  - reperfusion-associated arrhythmias.
- It has been demonstrated in every animal species studied and appears to persist as long as 1 to 2 hours after the ischemic preconditioning stimulus.
- It becomes ineffective when the sustained ischemic insult exceeds 3 hours. This suggests that the protection is conferred only when prolonged ischemia is followed by timely reperfusion.108

- With respect to cardiac surgery, one of the first studies indicating that preconditioning may exist in humans was conducted by Yellon and colleagues in 1993.
- In this study, the investigators reported that the release of a marker of necrosis was less in patients subjected to the preconditioning protocol.

- It is unknown whether the phenomenon of ischemic preconditioning plays any role in conferring protection when using the intermittent cross-clamp technique.
- Teoh and colleagues, however, reported that ischemic preconditioning might confer additional myocardial protection beyond that provided by intermittent cross-clamp fibrillation in patients undergoing CABG.8
- Other human studies have not shown additional protection when ischemic preconditioning was added to a myocardial protection protocol.

Adenosine

- There is considerable experimental evidence that the preischemic administration of adenosine:
  - retards the rate of ischemia-induced ATP depletion,
  - prolongs the time to onset of ischemic contracture,
  - attenuates myocardial stunning,
  - enhances post ischemic myocardial energetics
  - reduces infarct size.161
- It may play a role in mediating the infarct size–limiting effects of ischemic preconditioning.
- A transient infusion of adenosine or certain adenosine receptor agonists prior to ischemia is associated with infarct size reduction similar to that of ischemic preconditioning.

- There is preclinical and clinical evidence that adenosine is a cardioprotective agent.
- Its clinical use, however, is somewhat limited because large doses are associated with marked hypotension.
- The administration of such an agent prior to surgery could result in a reduction in the current rates of postoperative stunning and infarction and represent a significant advance in the field of myocardial protection.

Polarised arrest

- The concept of inducing arrest at a membrane potential that is close to that of the resting membrane potential, commonly termed ‘polarised’ arrest, is one that has been increasingly proposed over recent years as a means of achieving improved myocardial protection.
- Mechanisms of inducing effective polarised arrest have been demonstrated experimentally and include
  - sodium channel blockers and
  - potassium channel openers.
- Potentially, this concept could be used in blood-based solutions, which might offer the combined benefit of possible superior protection of blood-based solutions with that of polarised arrest leading to improvements in current clinically used myocardial protection strategies.
- The potential difficulties with these concepts is that many of the drugs used experimentally to induce polarised arrest (sodium-channel blockers such as lidocaine or tetrodotoxin, or potassium-channel openers such as pinacidil) have toxicity effects or other adverse side-effects that make them unsuitable for clinical use at the concentrations required to induce arrest.

Summary

- The ideal solution, technique, or delivery method has yet to be identified.
- The definition of ideal protection is no longer limited to the time that the patient is in the operating room.
- There is clearly a need to develop new therapeutic strategies to protect the heart during cardiac surgery because:
  - incidence of myocardial stunning ranges from 20 to 80%,
  - post ischemic ventricular dysfunction from 3 to 7%,
  - severe dysfunction in high-risk patients from 15 to 20%, and
  - non-Q-wave and Q-wave infarction nearly 20%,
- This need is even greater when one considers that long-term survival after heart operations is determined, in part, by adequate myocardial protection during the operation itself.