## Cardioplegia Temperature; How low do you go?

A Systemic Literature Review Mélissa Goulet, Perfusion Student, BScN, RN October 2017 Vancouver





"I can't believe I'm sitting through another cardioplegia presentation. Haven't we been talking about this for decades already?! Maybe I should use this time to go pee instead."

- Your own thought 2 minutes ago...

... Probably



### **QUICK OVERVIEW**

#### Introduction

How did we get Here?

#### Methodology

Study Eligibility Data Extraction Search Results Results

Study Characteristics Reported Outcomes

#### Discussion

Risk of Bias Assessment Strengths and Limitations Final Thoughts



### Introduction

A Touch of History



### Dur Past

1955

1952 Induced ventricular fibrillation Manual injection of a mixture of high dose potassium and blood in aortic root

1962 Intermittent aortic clamping

1950

1950-1958 Systemic cooling to stop the heart 1954 First recorded uses of CPB

1958 Aortic root perfusion with blood 1976 Concept of continuous cold crystalloid cardioplegia

1964 Bretschneider cold crystalloid cardioplegia

Buckberg 4:1 blood cardioplegia 1997 Toronto's Warm Heart Investigators

Our Present

1975 Braimbridge: St-Tomas solution

1978

Warm terminal reperfusion; Buckberg

2006 Enriched blood cardioplegia 2017

1986 Warm induction and cold maintenance; Buckberg



### Methodology

Study eligibility Data extraction Search results





### **Study selection**

- » Searches launched in:
- PubMed
- ◊ Medline
- ◊ Google scholar

» Filtered results with Cochrane randomization tool



#### **Inclusion & Exclusion Criterions**

#### Included

- Randomized control trials
- Isolated CABG under CPB
- At least two temperatures are compared
- Intermittent and/or continuous administration



#### **Inclusion & Exclusion Criterions**

#### Excluded

- Emergency surgery
  - Aged < 18 years
- Beating heart surgery
  - Valve surgery
- Crystalloid cardioplegia
  - Terminal Hot-Shot
    - Non-randomized/ retrospective studies



### **Keywords: Targeted Population**

- » CABG
- » Cardiac surgery
- » CPB
- » Thoracic surgery





### **Keywords: Intervention**

- » Cardioplegia temperature
- » Heart surgery
- » Cold cardioplegia induction
- » Cardioplegic solution
- » Cardioplegia
- » Chilled perfusate
- » Warm perfusate
- » Asystole
- » Potassium cardioplegic solutions
- » Heart arrest
- » Induced heart arrest



### **Keywords: Comparators**

- » Cold cardioplegia
- » Warm cardioplegia
- » Tepid cardioplegia
- » Normothermic cardioplegia
- » Euthermic cardioplegia
- » Warm cardioplegia induction
- » Method of myocardial protection
- » Induced heart arrest
- » Induced asystole





### **Keywords: Outcome**

- » CK-MB
- » Troponins
- » Lactates
- » Myocardial Infarctions
- » Length of stay
- » IABP
- » Inotropes



### Initial Records obtained (n= 2280)

Studies comparing two cardioplegia temperatures (n=130)

Records screened for eligibility (n=130)



- Pediatric (n=3)
- Language (n=3)
- Crystalloid vs. blood cardioplegia (n=45)
- Hot-Shots (n=25)
- Valves (n-12)
- Not randomized/meta-analysis (n=28)

#### Records included ( $\underline{n=14}$ )



### Results

Study Characteristics Reported Outcomes



### **Study Characteristics**









#### The "in between"

30	40	40	40
40	52	72	130
200	200	204	1374



#### Together, 14 studies represent







#### **Route of administration**

- All authors gave via **aortic root**
- 2 gave maintenance doses via **coronary sinus**
- 2 gave maintenance doses via new vein grafts

100% reporting rate



#### **Rate of administration**

- Induction: 200-300 mL/min (8 authors)
- Maintenance: 125-300mL (4 authors)
  - > Interval times ranging from 10 25 minutes

57% & 28% reporting rate





**Induction amounts** 

4 authors reported their induction amounts:

- ➢ 10 mL/Kg
- ≻ 300 mL
- ≻ 500 mL
- ≻ 1000 mL

28% reporting rate







What's in a Name? Definitions of Temperatures



Only 2 authors used the term "tepid"





What's in a Name? Definitions of Temperatures



"Warm/ Normothermic"

	Numb	er of parti	cipants	Cardio	plegia temp (°C)	perature	Cardioplegia method				Systemic perfusion temperature (°C)		
	Group A	Group	Care	Group	Group B	C		Group A	Group B	Group A	Group B	Group C	
Christakis et al.	103	101	-	6-10	37	-	-	4:1 dilution	- 4:1 dilution	28-30	35-37	-	
(1992)							-	Aortic root and vein grafts delivery	<ul> <li>Aortic root and vein grafts delivery</li> </ul>				
							-	1L high K induction	<ul> <li>1L high K induction</li> </ul>				
							-	200 – 300mL after each distal anastomoses	<ul> <li>followed by 50- 200mL/min</li> </ul>				
							-	interval unknown	continuously				
					1				- if the heart does not arrest – converted to cold cardioplegia				
Pelletier et al.	100	100	-	10*	33*	-	-	4:1 dilution	-	33-34	33-34	-	
(1994)12							-	Aortic root delivery					
							-	Initial dose 300mL: press in the aortic root	ures not exceeding 250mmHg				
							-	Intervals 12-15 minute be	tween anastomoses				
							-	Maintenance dose 300mI					
$(1995)^{17}$	11	10	-	28	37	-	-	7:1 dilution	-	-	-	-	
(1555)							-	aortic root induction with both groups	warm cardioplegia (37°C) in				
							-	retrograde maintenance					
							-	induction rate 200mL/min	1				
							-	maintenance rate 125mL/ pressure	min not exceeding 40mmHg				
Engelmen et al.	37	50	43	8-10	32	37	-	4:1 dilution		20	32	37	
(1990)*							-	Aortic root and coronary	sinus delivery				
							-	Cardioplegia was given c visualization –interrupted	ontinuously except when it impaired distal anastomosis for no more than 10 minutes				
Landymore et al.	20	20	-	8	37	-	-	4:1 dilution of high K	-	37	37		
(1990)							-	10cc/kg induction					
							-	Intervals of 10 minutes					

\* cardioplegia temperature measured by mean septal temperature

	Numb	er of parti	cipants	Cardiop	(°C)	perature	Cardioplegia method				temperature (°C)		
Author	Group A	Group B	Group C	Group A	Group B	Group C	Group A	Group B	Group C	Group A	Group B	Group C	
<u>Chello</u> et al. (1997) <sup>15</sup>	20	20	-	5	37	-	<ul> <li>4:1 St-Thomas I solution</li> <li>Rate of 200-300 mL/min</li> <li>Indcution with high pota</li> </ul>	ı ı ıssium	-	25-28	37	-	
							<ul> <li>Maintenance with low p</li> <li>Intervals 18 minutes (rational structure)</li> </ul>	otassium nge 12-18)					
Christakis et al. (1997) <sup>18</sup>	682	692	-	5-8	37	-	<ul> <li>4:1 dilution Fremes solution</li> </ul>	<ul> <li>4:1 dilution of Fremes solution</li> </ul>	-	30	34	-	
							<ul> <li>Aortic root and vein grafts delivery</li> </ul>	<ul> <li>Aortic root and vein grafts delivery</li> </ul>					
							<ul> <li>Rate 200-300mL/min</li> <li>15-20 minutes intervals</li> </ul>	<ul> <li>Rate 200-300mL/min</li> <li>continuous</li> <li>10 -15 min intervals if interrupted</li> </ul>					
								<ul> <li>catch-up doses of high K if interval greater then 5 minutes</li> </ul>					
Fiore et al. (1998) <sup>9</sup>	27	25	-	4	29	-	- 4:1 dilution		-	32	32	-	
							<ul> <li>Rate of 200-400mL/min at aortic root</li> </ul>	to maintain 70 mmHg pressure					
Fremes et al.	384	378	-	5-8	37	-	<ul> <li>Interval 20 minutes</li> <li>4:1 dilution of Fremes s</li> </ul>	alution	-	25-30	33-37	-	
(2000)19							<ul> <li>Aortic root delivery</li> </ul>	Sidion					
Bical et al. (2001) <sup>13</sup>	15	15	-	4	37		<ul> <li>Rate 250mL/min</li> <li>Initial dose of 500mL</li> <li>Intervals of 15-18 minutervals</li> </ul>	es		33	33	-	
<u>Chello</u> et al. (2003) <sup>16</sup>	20	20	-	5	37		<ul> <li>4:1dilution of St-Thoma</li> <li>Rate of 200-300 mL/min</li> <li>Indcution with high pota</li> <li>Maintenance with low p</li> </ul>	s I 1 Issium otassium	-	25-28	37	-	

of participants Group Group B C 100 -	Cardioplegia te (°C) Group Group A B 4 33-34	o Group C	- 4:1 d - aortic - Rate	Group A ilution - c root delivery -	Cardioplegia method Group B Mini-plegia high K aortic root delivery	Group C	Syste tem Group A 32-34	emic perfi perature ( Group B 32-34	usion °C) Group C -
Group Group B C 100 -	Group Group A B 4 33-34	Group C	- 4:1 d - aortic - Rate	Group A ilution - c root delivery - of 200mL (min -	Group B Mini-plegia high K aortic root delivery	Group C	Group A 32-34	Group B 32-34	Group C
100 -	4 33-34	, -	<ul> <li>4:1 d</li> <li>aortic</li> <li>Rate</li> </ul>	ilution - c root delivery -	Mini- <u>plegia</u> high K aortic root delivery	-	32-34	32-34	-
			- Interv	vals 20-25 minutes	Rate 300mL/min induction with continuous maintenance at 150 mL/min Intervals 20-25 minutes				
20 -	0-4 37	-	<ul> <li>Bloodratio</li> <li>plegis</li> <li>Aorti</li> <li>20 m</li> <li>Topic</li> <li>slush</li> </ul>	d cardioplegia – – unknown with sol and high K ic root delivery – inute intervals – cal cooling with	Blood cardioplegia – ratio unknown with plegisol and high K Aortic root delivery 20 minute intervals	-	35	35	-
36 -	4-6 37	-	<ul> <li>4:1 d</li> <li>Aorti</li> <li>interv</li> <li>induc 300m</li> <li>main 150m</li> <li>interv</li> </ul>	ilution - ic root delivery vals 15-20 minute - totion rate 200- nL/min - tenance rate - nL/min vals 15-20 minutes -	Blood cardioplegia with added potassium and magnesium Aortic root delivery intervals 15-20 minute induction rate 200- 300mL/min maintenance rate 150mL/min intervals 15-20 minutes	-	32-34	37	-
	20 -	20 - 0-4 37 36 - 4-6 37	20 - 0-4 37 - 36 - 4-6 37 -	20 - 0-4 37 Bloo ratio plegi - Aorti - 20 m - Topi slush 36 - 4-6 37 4:1 d - Aorti - inter - induc 300n - main 150n - inter	20 - 0.4 37 - Blood cardioplegia – ratio unknown with plegisol and high K - Aortic root delivery - 20 minute intervals - Topical cooling with slush 36 - 4-6 37 - 4:1 dilution - Aortic root delivery intervals 15-20 minute - induction rate 200- 300mL/min - maintenance rate 150mL/min - intervals 15-20 minutes -	<ul> <li>- Intervals 20-25 minutes</li> <li>- 0-4 37 - Blood cardioplegia – ratio unknown with plegisol and high K</li> <li>- Aortic root delivery - Aortic root delivery</li> <li>- 20 minute intervals</li> <li>- Topical cooling with slush</li> <li>- Aortic root delivery</li> <li>- 4:1 dilution</li> <li>- Aortic root delivery</li> <li>- intervals 15-20 minute</li> </ul>	<ul> <li>- 0-4 37 - Blood cardioplegia - ratio unknown with plegisol and high K</li> <li>- Aortic root delivery - Aortic root delivery</li> <li>- 20 minute intervals</li> <li>- 36 - 4-6 37 - 4:1 dilution</li> <li>- Aortic root delivery</li> <li>- intervals 15-20 minute</li> <li>- induction rate 200- 300mL/min</li> <li>- maintenance rate</li> <li>- 150mL/min</li> <li>- intervals 15-20 minutes</li> <li>- maintenance rate</li> <li>- 150mL/min</li> <li>- intervals 15-20 minutes</li> </ul>	<ul> <li>- 0-4 37 - Blood cardioplegia - ratio unknown with plegisol and high K</li> <li>- Aortic root delivery - Aortic root delivery</li> <li>- 20 minute intervals</li> <li>- 20 minute intervals</li> <li>- 20 minute intervals</li> <li>- 20 minute intervals</li> <li>- 35</li> </ul>	<ul> <li>- Intervals 20-25 minutes</li> <li>- 0-4 37 - Blood cardioplegia - ratio unknown with plegisol and high K</li> <li>- Aortic root delivery - Aortic root delivery</li> <li>- 20 minute intervals</li> <li>- 70pical cooling with slush</li> <li>- 4-6 37 - 4.4:1 dilution</li> <li>- Aortic root delivery</li> <li>- intervals 15-20 minute</li> <li>- induction rate 200- 300mL/min</li> <li>- maintenance rate</li> <li>- intervals 15-20 minutes</li> <li>- maintenance rate</li> <li>- intervals 15-20 minutes</li> <li>- maintenance rate</li> <li>- intervals 15-20 minutes</li> </ul>

CK-MB Troponins Lactates Myocardial Infarctions

Length of stay IABP Inotropes



11/14 studies reported CK-MB levels

#### No Difference

- Higher Enzymes
   Warm p < 0.005</li>
- Higher Enzymes Cold p < 0.05</li>



5/14 studies reported troponin levels

Troponin

#### No Difference

Higher Enzymes
 Warm

Higher Enzymes Cold p < 0.05</li>

Lactates

No Difference

Higher Levels Warm p < 0.01</p>

Higher Levels Cold

3/14 studies reported lactate levels

**Myocardial Infarctions** 



None Occured

No Difference

Higher Incidence Cold p < 0.025</p>

8/14 studies reported rates of MI

Length of Stay



3/14 studies reported LOS

- No Difference
- Shorter LOS Cold
- Shorter LOS Warm



**IABP** 



6/14 studies reported the use of IABP

Not UsedNo Difference



7/14 studies reported inotrope use

 No Difference
 Higher Needs Cold p <0.05</li>



### Discussion

Risk of Bias Assessment Strengths and limitations Final thoughts





#### **Risk of Bias Assessment**

» A bias is a systematic error, or deviation from the truth, in results or inferences.

» Biases can lead to underestimation or overestimation of the true intervention effect.

Cochrane Handbook (5.1)



Study	Sequence generation	Allocation concealment	nt	Performance blinding	Intervention	Detection Blinding	Attrition	Reporting	Summary
Christakis et al. (1992)7	Low	Low		Low	High	Unclear	Low	Low	Low
Pelletier et al. (1994) <sup>12</sup>	Low	Low		High	High	Unclear	Low	Low	Low
Rainio et al. (1995) <sup>17</sup>	Unclear	Unclear		Unclear	Low	Unclear	Low	Low	Unclear
Engelmen et al. (1996) <sup>8</sup>	Low	Unclear		Unclear	High	Low	Low	Low	Low
Landymore et al. (1996) <sup>20</sup>	High	High		High	Low	Unclear	Low	Low	High
Chello et al. (1997) <sup>15</sup>	Low	Unclear		Unclear	High	Unclear	Low	Low	Unclear
Christakis et al. (1997) <sup>18</sup>	Low	Low		High	High	Hig <mark>h</mark>	Low	Unclear	High
Fiore et al. (1998)9	Unclear	Unclear		High	Low	Low	Low	Low	Low
Fremes et al. (2000) <sup>19</sup>	Low	Low		High	High	Hig <mark>h</mark>	High	High	High
Bical et al. (2001) <sup>13</sup>	Unclear	Unclear		Unclear	Unclear	Unclear	Low	Low	Unclear
Chello et al. (2003) <sup>16</sup>	Low	Unclear		Unclear	High	Unclear	Low	Low	Unclear
Franke et al. (2003) <sup>10</sup>	Low	Unclear		High	Low	Unclear	Low	Low	Low
Cakir et al. (2013) <sup>14</sup>	Unclear	Unclear		High	Unclear	High	Low	Low	Unclear
Kuhn et al. (2015) <sup>11</sup>	Low	Low		High	High	Low	Low	Low	Low

#### **Strengths & Limitations**

#### **Strengths**

- Strict inclusion and exclusion criterions
- Multiple databases
- The selected outcomes are easy to measure and integrate to clinical practice





### **Strengths & Limitations**

#### **Limitations**

- Single reviewer
- Limited to English and French publications
- Plethora of different cardioplegia methods and compositions
- Inconsistent outcome reporting
- Various definitions of temperatures
- Mostly small patient samples



## Alright. Where does that leave us?

**Based on currently** available prospective randomized data for CABG patients using blood based cardioplegia ... ... All roads lead to Rome





#### **Future Direction in Research**

- » Assessment of <u>3 study</u> groups:
- » Warm induction, cold maintenance
- » Cold induction, cold maintenance
- » Warm induction, warm maintenance

» Same systemic temperature

» Same cardioplegia composition and administration method

# Thank you for your attention! So? How low do you go?

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