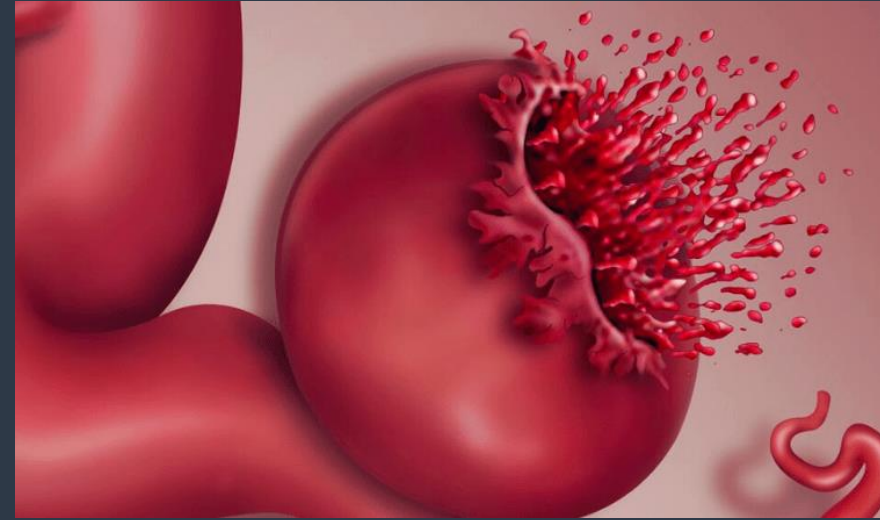
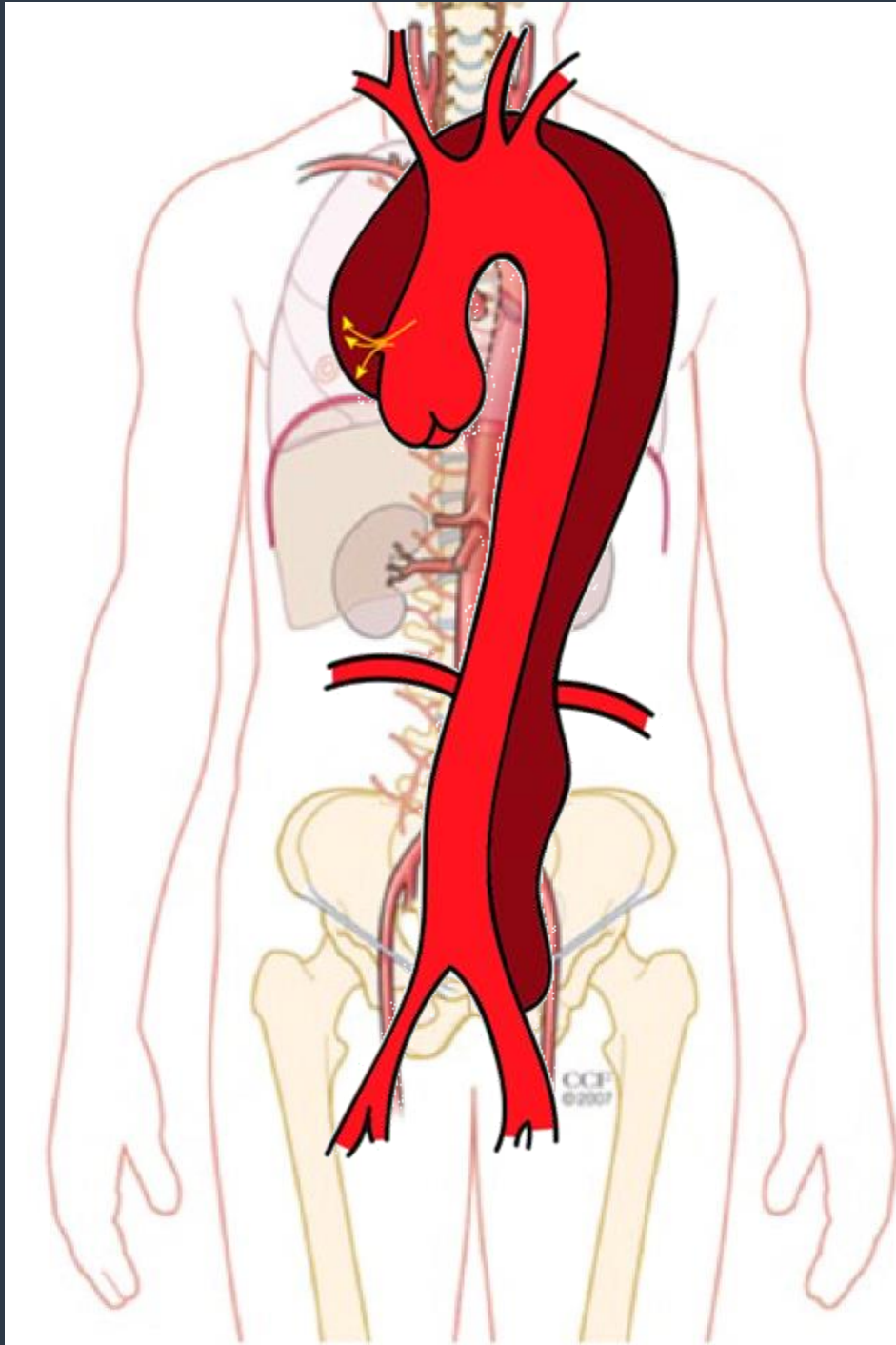


# Temperature Strategy for Acute Type A Aortic Dissection

한양 대학교 병원  
심장 혈관 흉부외과  
김완기



# Surgical Repair



## Ant. Approach (sternotomy)

- Arch surgery
  - Hemi-arch (ascending aorta replacement)
  - Partial arch
  - Total arch
- Root surgery
  - Root replacement with aortic valve (Bentall)
  - Valve sparing root reimplantation (VSRR)

## Lat. Approach (thoracotomy)

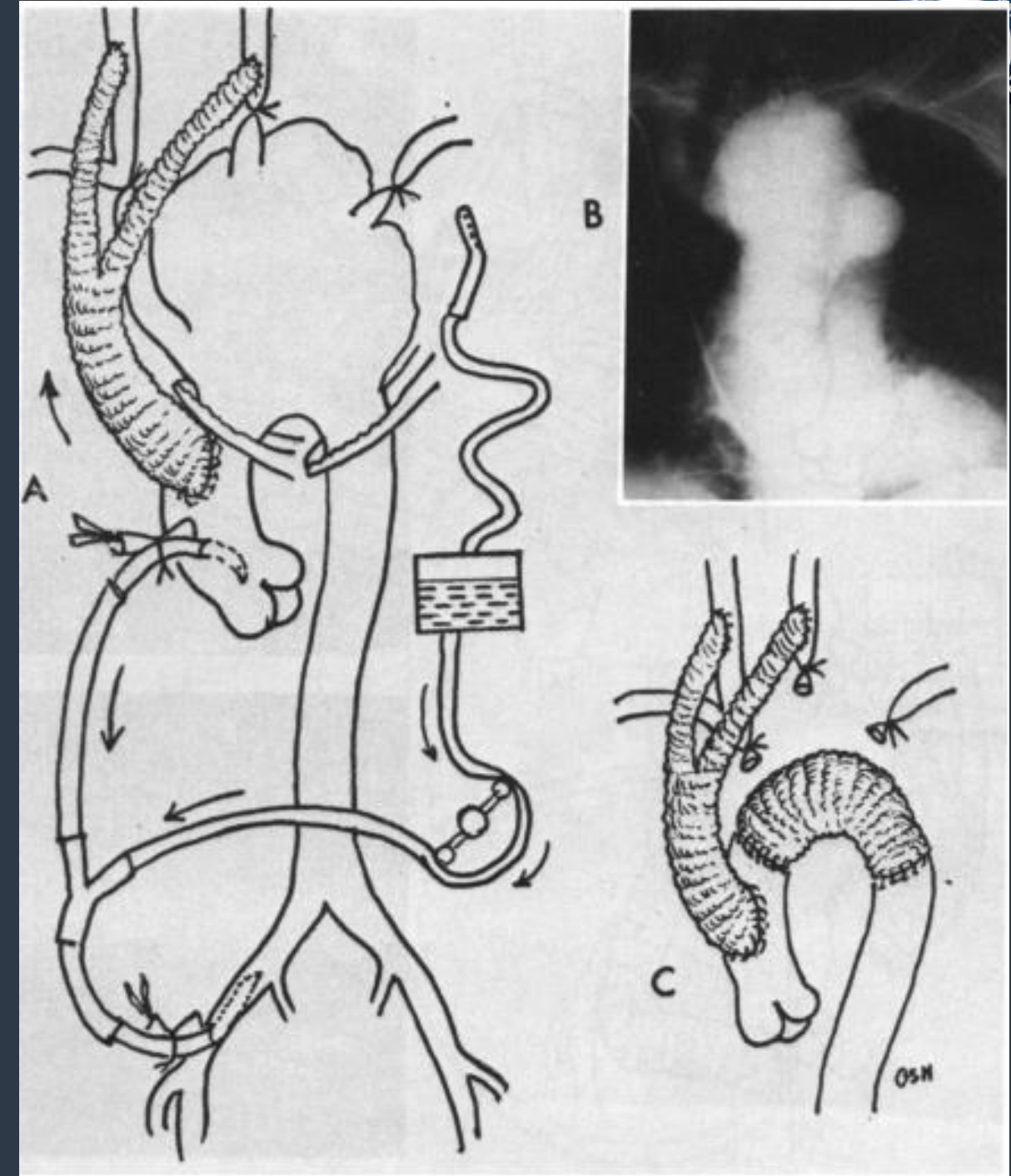
- Descending thoracic aorta replacement
- Thoracoabdominal aorta replacement
  - Crawford extent I to V



*Denton A. Cooley  
Cardiovascular  
Surgical Society*

# Milestones in the Treatment of Aortic Aneurysm

Denton A. Cooley, MD, and the Texas Heart Institute

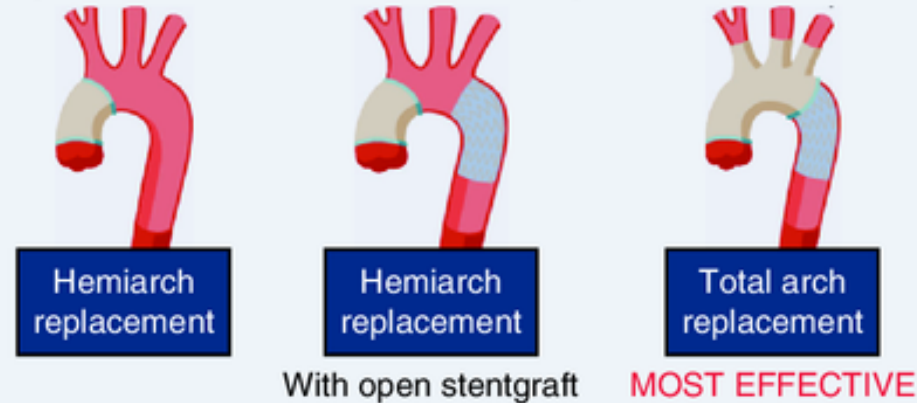
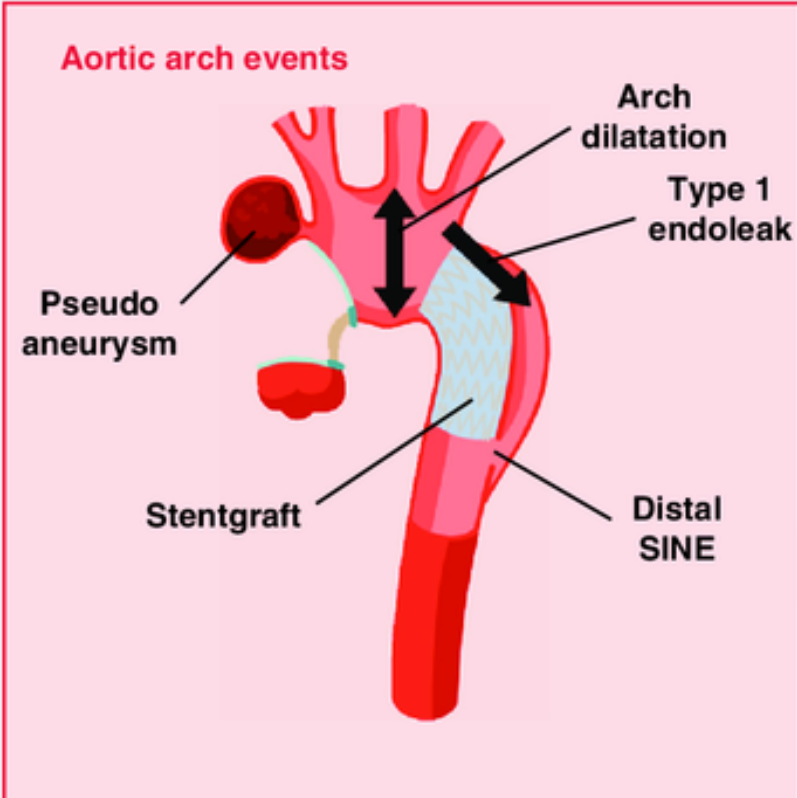


# The Role of Total Arch Replacement

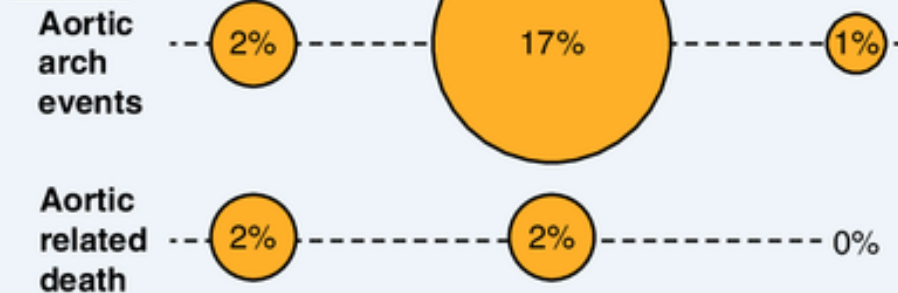
Which procedure is preferred for acute aortic dissection DeBakey type 1?

**Methods:**

Comparing the rate of aortic arch events among three different procedures.



**Results:**



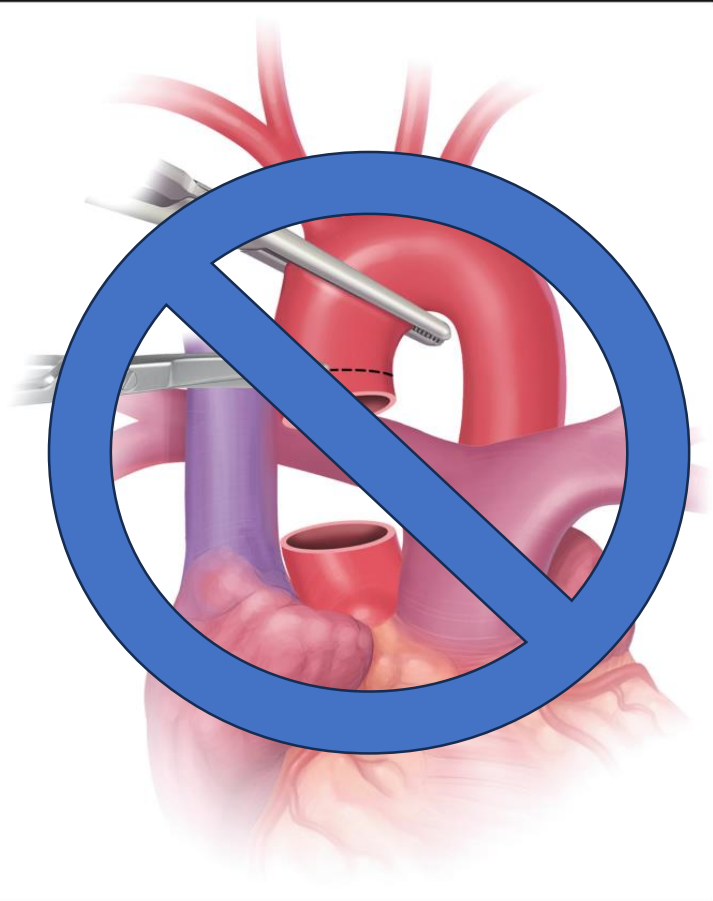
The rate of aortic arch events was the lowest after total arch replacement, while the highest after hemiarch replacement with open stentgraft.

Total arch replacement was the most effective and preferable, especially in young patients without perioperative risks. Benefits of open stentgraft with hemiarch replacement were not detected.

SINE: stentgraft induced new entry

## SOCIETAL STATEMENT

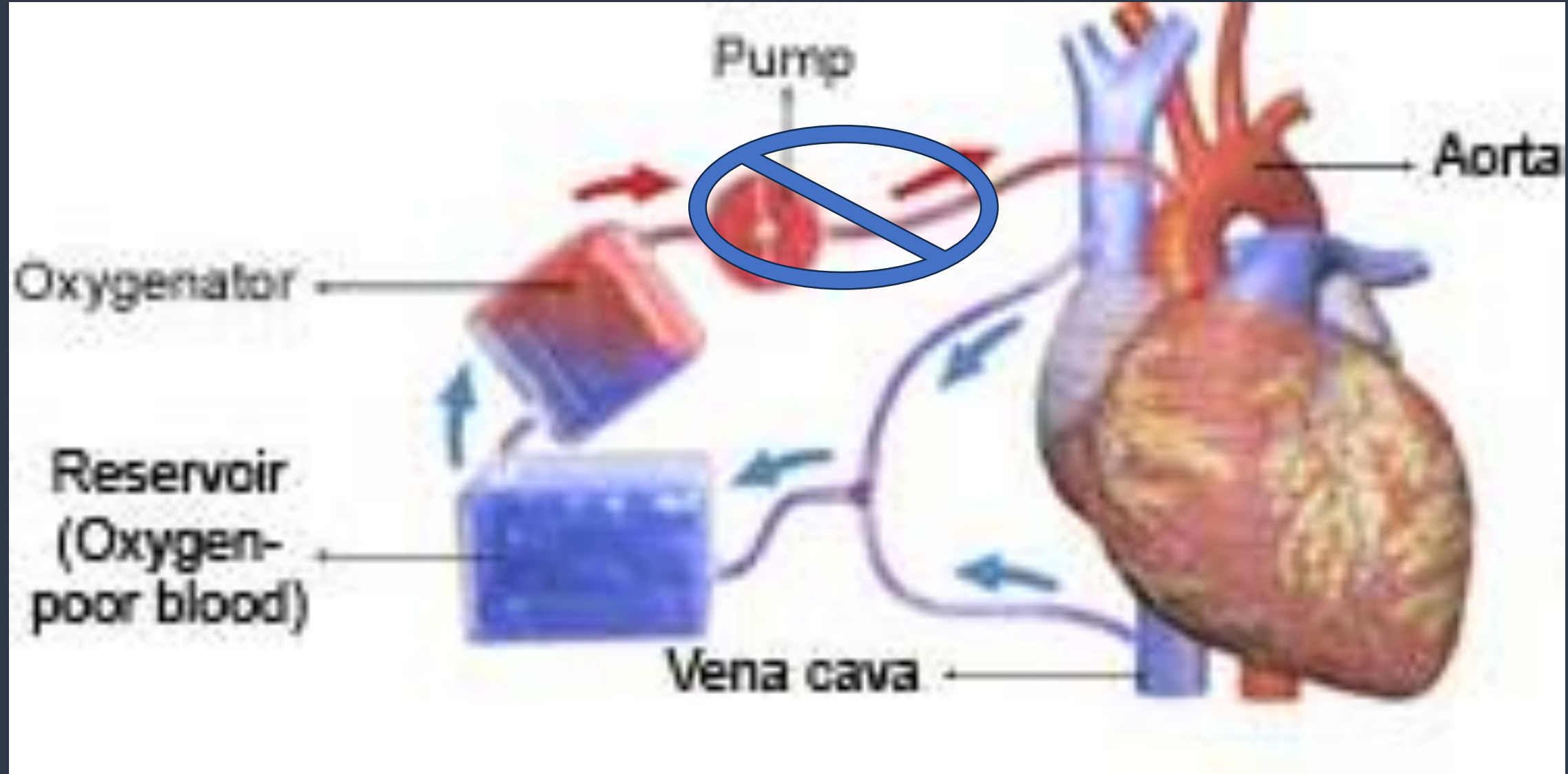
# 2022 Aortic Disease Guideline-at-a-Glance



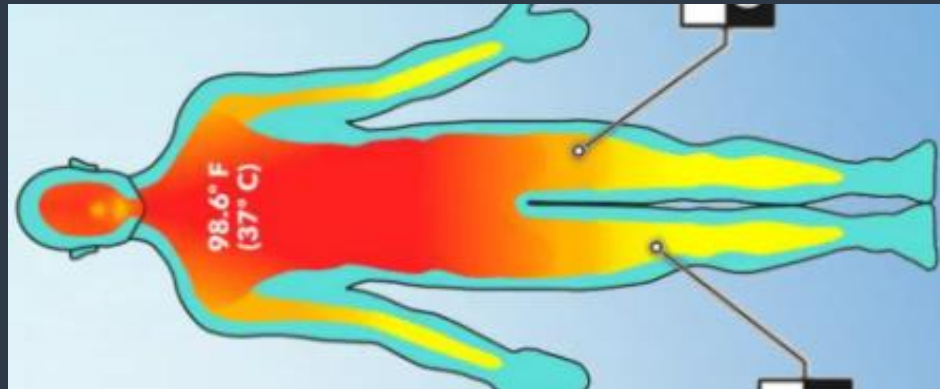
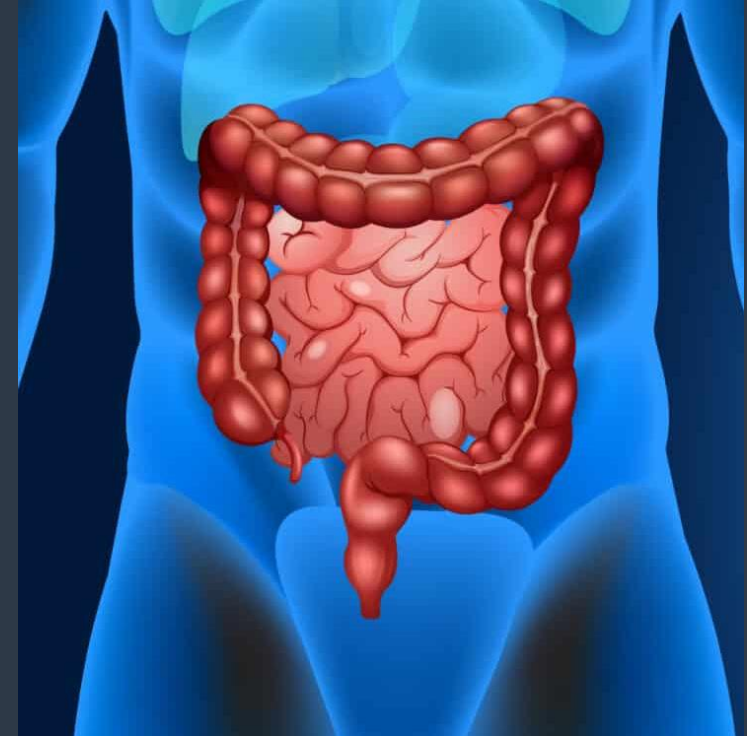
8. Patients with acute type A aortic dissection, if clinically stable, should be considered for transfer to a high-volume aortic center to improve survival. The operative repair of type A aortic dissection should entail at least an **open distal anastomosis** rather than just a simple supracoronary interposition graft.



# Stop the Organ Perfusion



# Lower the Temperature

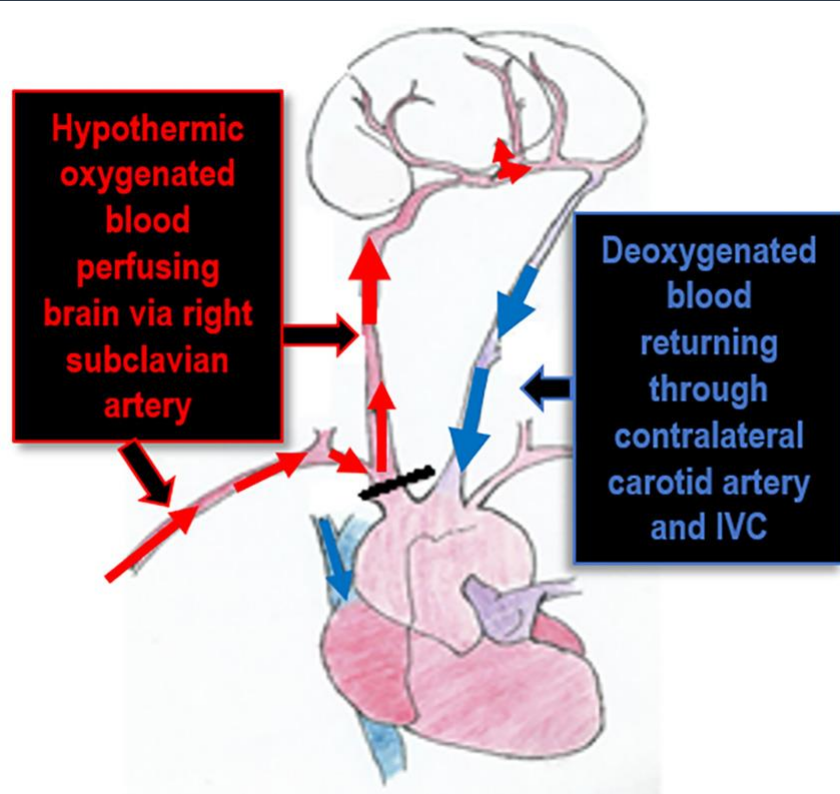




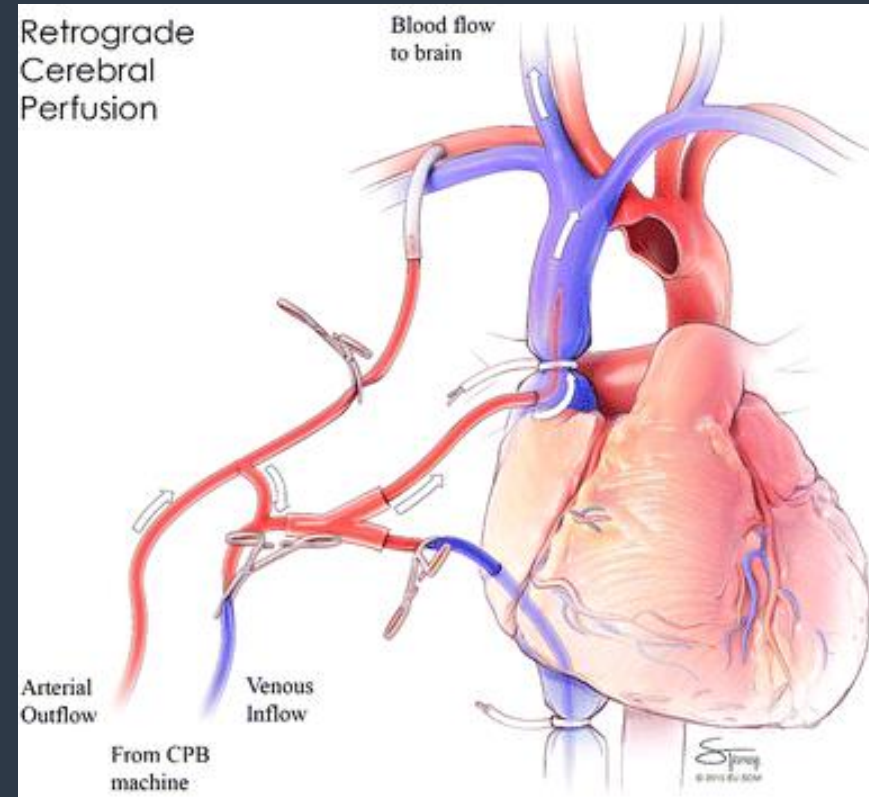


# Ways To Protect Brain

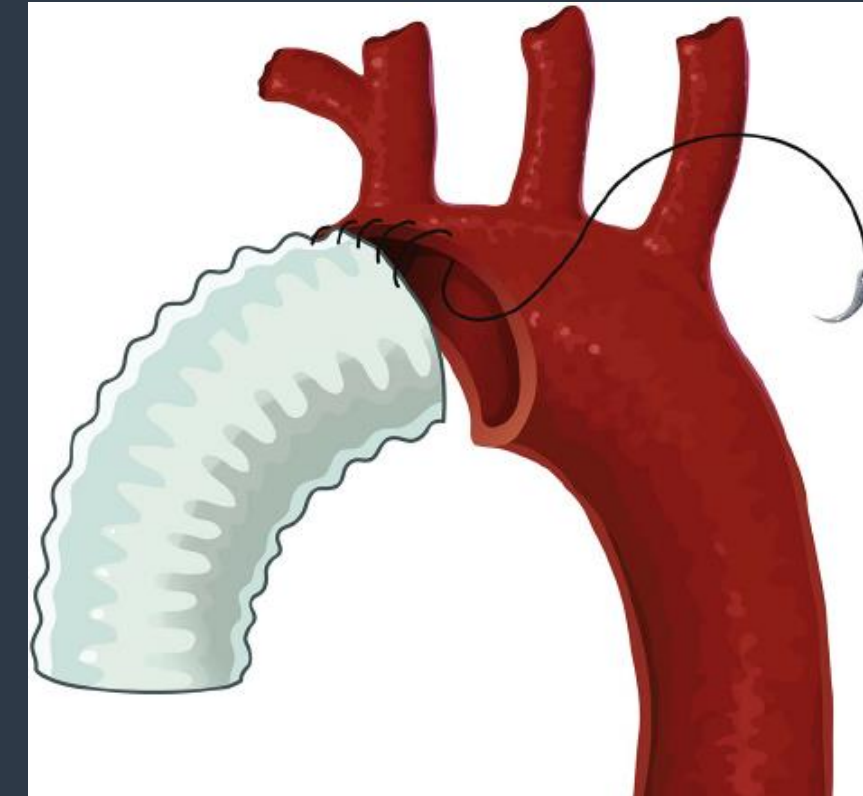
## Selective perfusion



## Retrograde perfusion



## No perfusion



## Optimal temperature management in aortic arch operations

Michael O. Kayatta<sup>1</sup> · Edward P. Chen<sup>1</sup>

**Table 1** Comparison of temperature management strategies (modified from Englum et al. [121])

Study	Years	No. of patients	Systemic temperature	Cerebral temperature	Cerebral perfusion	TND (%)	PND (%)	Mortality (%)
<b>Deep and profound hypothermia</b>								
Svensson et al. [89]	1999–2003	1336	ECI/<20 °C	ECI/<20 °C	SACP or RCP	NR	6.1	8.3
Gega et al. [29]	1996–2005	394	16–20 °C	16–20 °C	None	NR	4.8	6.3
Etz et al. [122]	1998–2004	680	10 °C	12–15 °C	None or SACP	NR	NR	5.9
Lima et al. [123]	2005–2010	245	ECI/14 °C	ECI/12 °C	SACP or RCP	NR	4.1	2.9
<b>Moderate hypothermia</b>								
Bachet et al. [124]	1984–1999	171	25–28 °C	6–12 °C	SACP	NR	NR	16.9
Di Eusano et al. [65]	1995–2002	588	22–26 °C	20 °C	SACP	5.6	3.8	8.7
Okita et al. [113]	2002–2012	438	20–23 °C	23 °C	SACP	8.7	5.3	9.7
<b>Mild hypothermia</b>								
Zierer et al. [81]	2000–2011	1002	26–34 °C	28–30 °C	SACP	4	3	5
Urbanski et al. [98]	2005–2009	347	28–34 °C	28 °C	SACP	2.3	0.9	0.9
Suzuki et al. [125]	2008–2012	105	30–32 °C	25–28 °C	SACP	3	3	1
<b>Comparisons</b>								
Di Eusano et al. [126]	1995–2001	128	ECI/16 °C	ECI/16 °C	None	7.1	12.5	13.3
		161	22–26 °C	22–26 °C	SACP	8.7	7.6	9.9
Kamiya et al. [11]	1999–2005	125	20–24.9 °C	15 °C	SACP	14.1	10.9	8.6
		252	25–28 °C	15 °C	SACP	9.7	9.7	10.8
Pacini et al. [115]	1996–2005	116	<25 °C	<25 °C	SACP	8.6	1.7	13.8
		189	≥25 °C	≥25 °C	SACP	7.9	3.1	12.7
Milewski et al. [127]	1997–2008	682	ECI/18 °C	ECI/12 °C	RCP	3.7	2.8	2.8
		94	21–26 °C	21–26 °C	SACP	5.3	3.2	3.2
Misfield et al. [128]	2003–2009	220	22 °C	22 °C	None	12.7	14.1	11.4
		51	24 °C	24 °C	RCP	17.6	15.7	7.8
		242	24 °C	24 °C	uSACP	17.9	10.6	7.3
		123	24 °C	24 °C	bSACP	14.9	8.3	14.0
Leshnower et al. [116]	2004–2011	233	22–26 °C	16 °C	SACP	6.3	7.2	7.2
		277	27–34 °C	16 °C	SACP	4.3	2.5	5.1

ECI electrocerebral inactivity, NR not recorded





자고로 수술은 말이야...

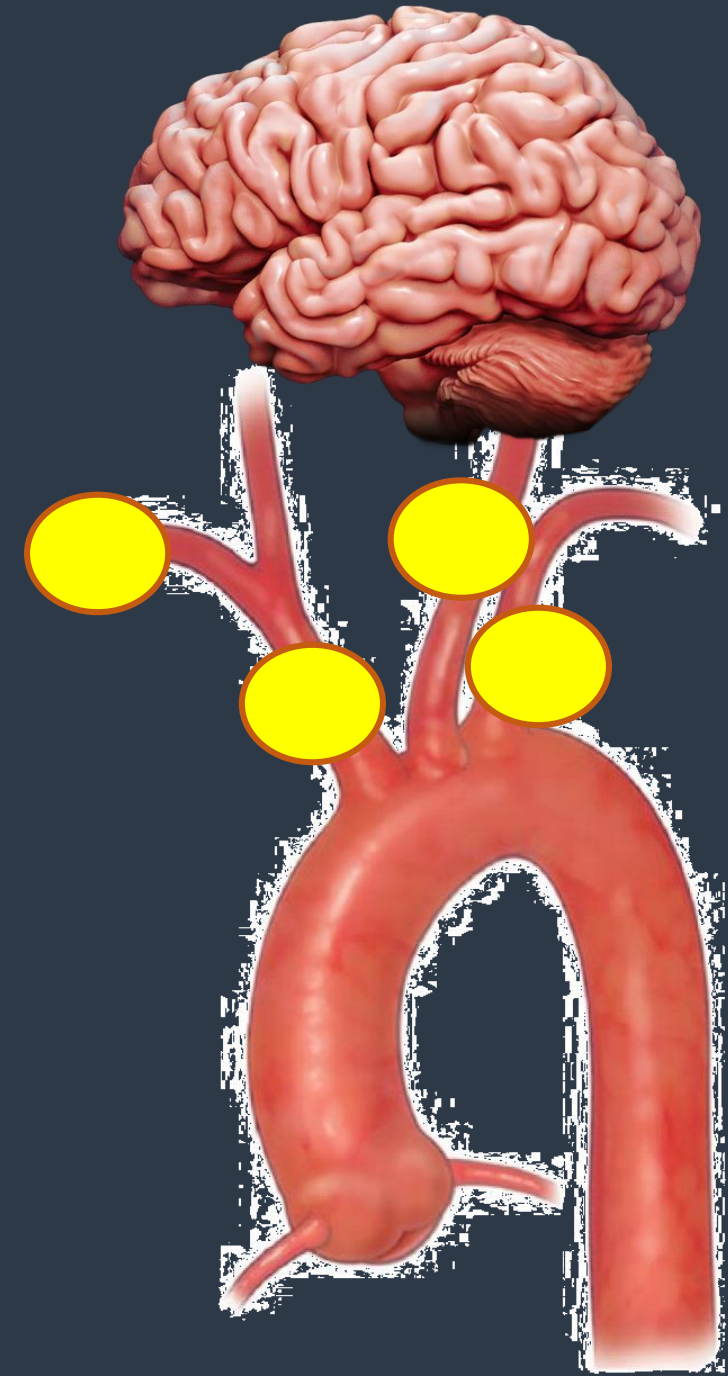
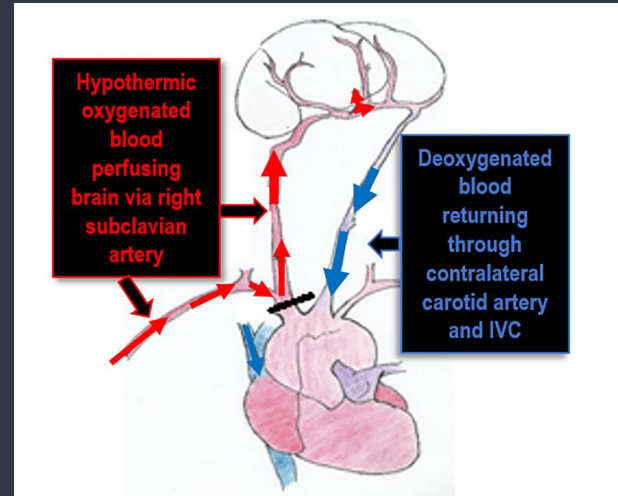


# Evidence!!



# Selective Cerebral Perfusions

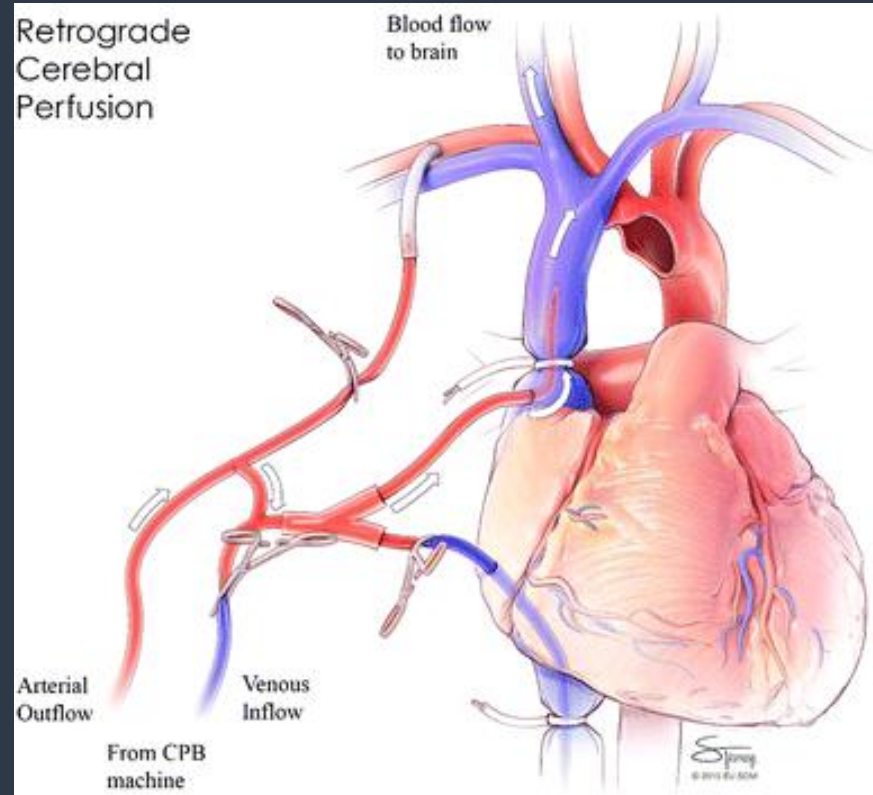
- Unilateral perfusion
  - Innominate artery
  - Axillary
- Bilateral perfusion
  - LCCA
  - LSCA
- No need for hypothermia



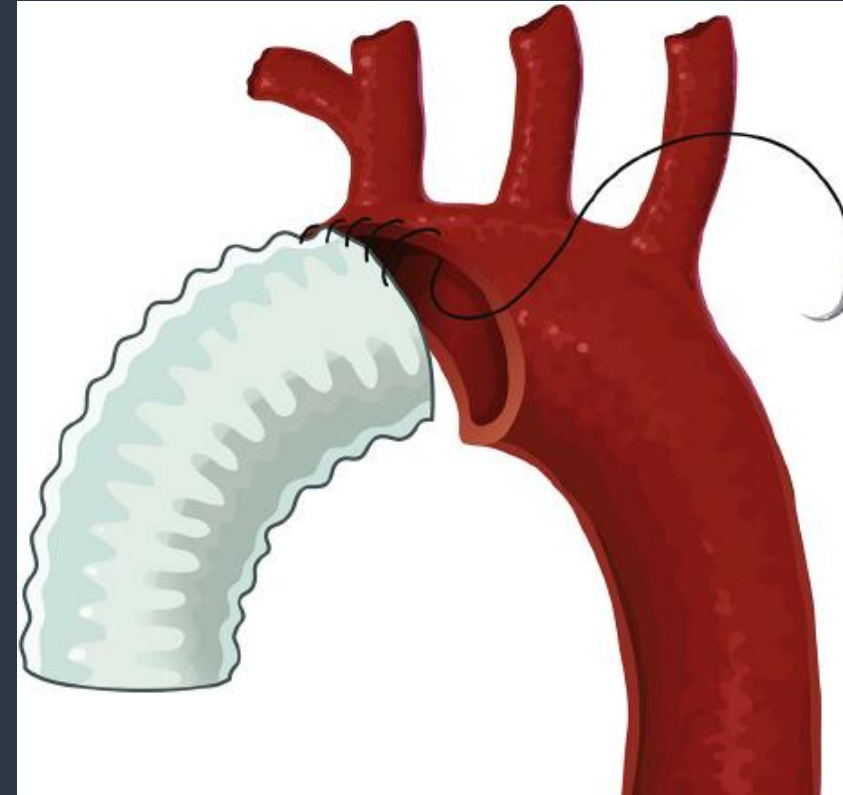


# Hypothermia Required

## Retrograde perfusion



## No perfusion



# Effect of Hypothermia on Cerebral Blood Flow and Metabolism in the Pig

Marek P. Ehrlich, MD, Jock N. McCullough, MD, Ning Zhang, MD,  
Donald J. Weisz, PhD, Tatu Juvonen, MD, Carol A. Bodian, DrPH, and  
Randall B. Griepp, MD

Departments of Cardiothoracic Surgery, Neurosurgery, and Biomathematics, Mount Sinai Medical Center, New York, New York

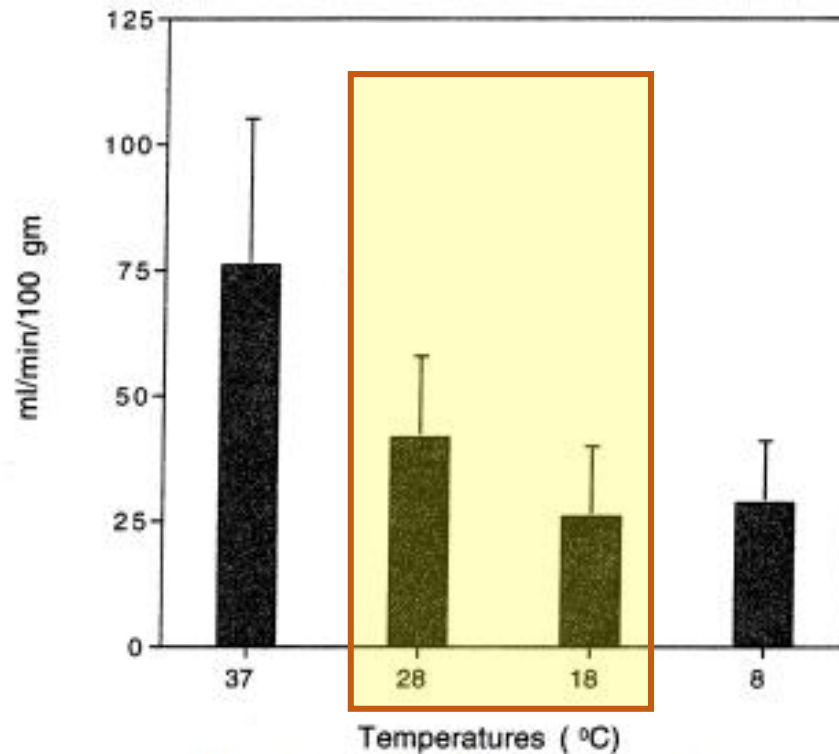
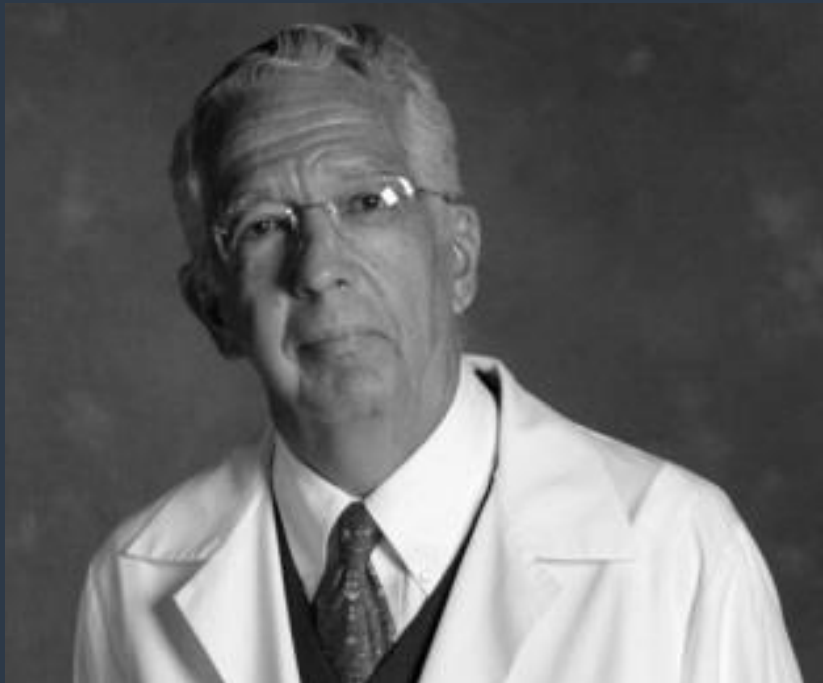


Fig 1. Cerebral blood flow (CBF) on cardiopulmonary bypass, measured in all 12 pigs as described in the text. Data are from Table 2. When the percentage of base line CBF is calculated for each pig at each temperature, for the two groups of pigs combined mean percentage of base line CBF (95% confidence limits) is 62% (42%, 83%) of base line at 28°C; 36% (26%, 46%) of base line at 18°C; and 43% (30%, 55%) of base line at 8°C.

CBF/CMRO<sub>2</sub>

If the ratio of cerebral blood flow to cerebral oxygen metabolism at base line is considered ideal, representing

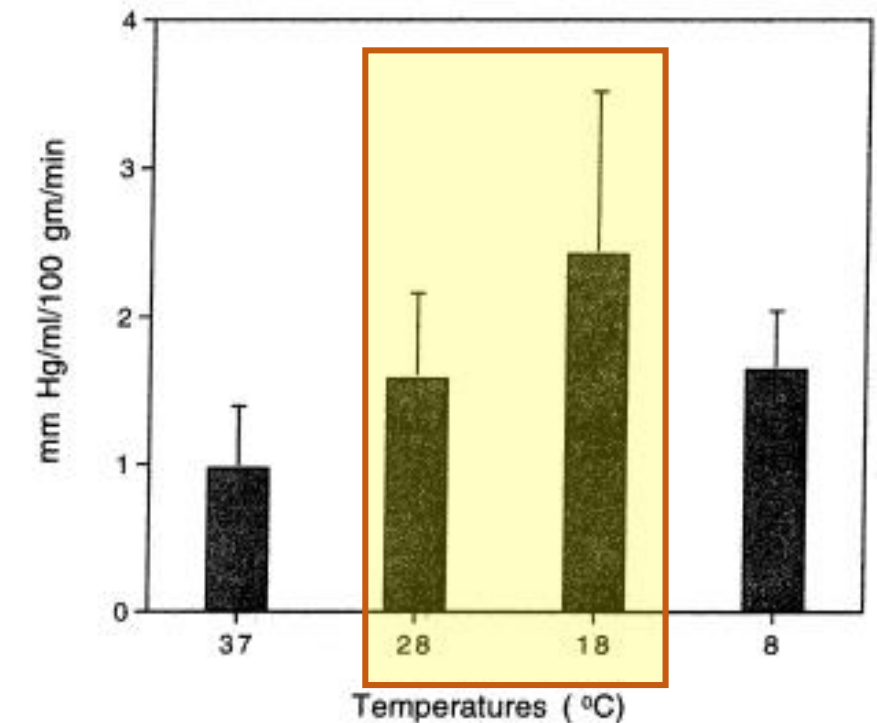


Fig 2. Cerebral vascular resistance (CVR) on cardiopulmonary bypass measured in all 12 pigs as described in the text. Data are from Table 2.

# Effect of Hypothermia on Cerebral Blood Flow and Metabolism in the Pig

Marek P. Ehrlich, MD, Jock N. McCullough, MD, Ning Zhang, MD, Donald J. Weisz, PhD, Tatu Juvonen, MD, Carol A. Bodian, DrPH, and Randall B. Griepp, MD

Departments of Cardiothoracic Surgery, Neurosurgery, and Biomathematics, Mount Sinai Medical Center, 1

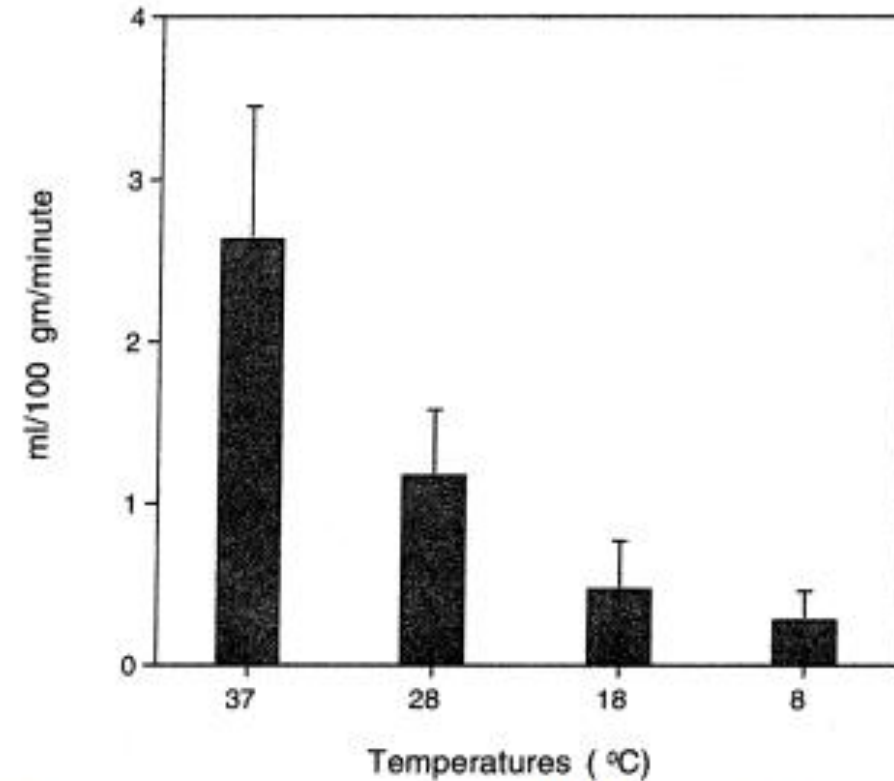
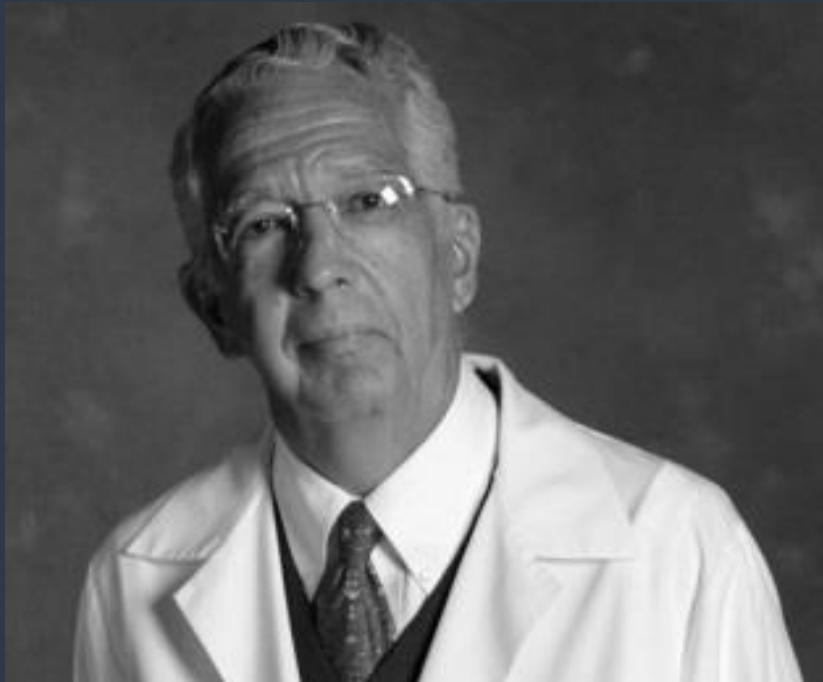


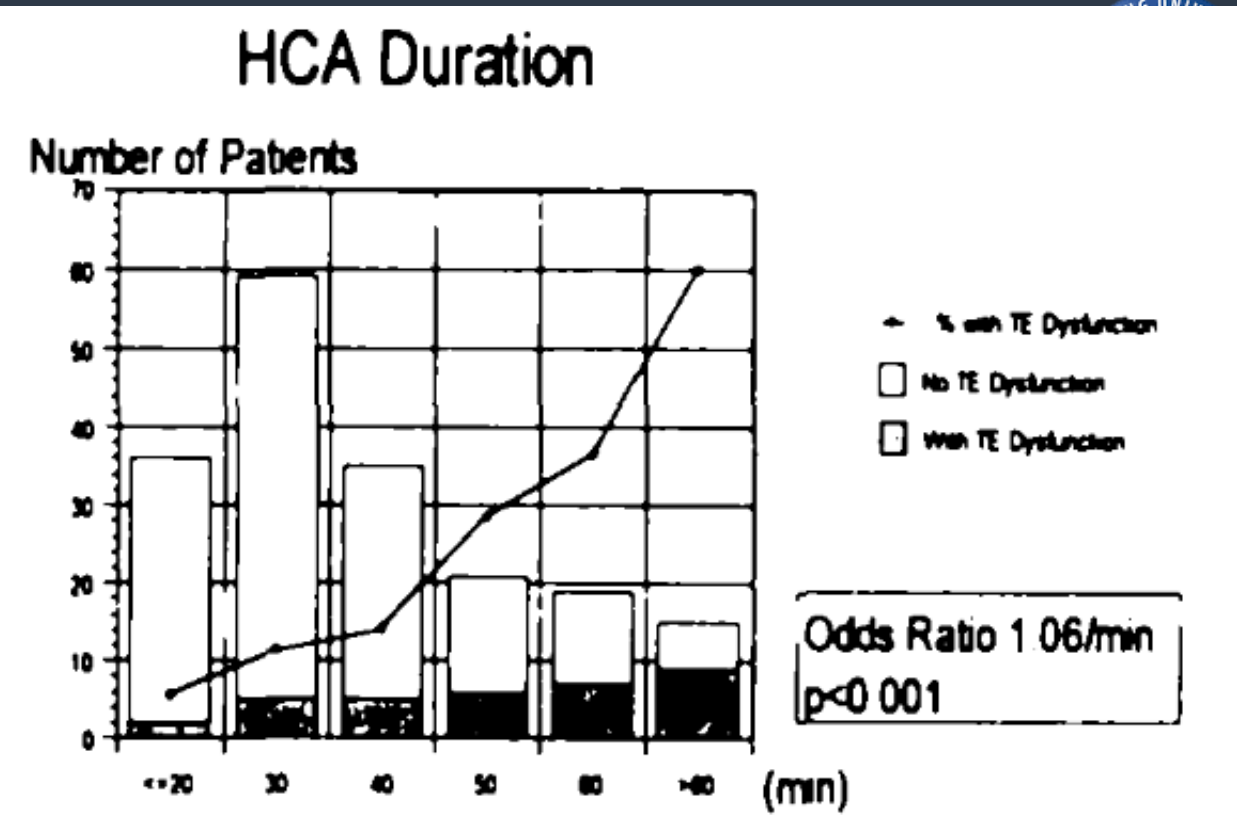
Fig 3. **Cerebral oxygen consumption (CMRO<sub>2</sub>)** on cardiopulmonary bypass measured in all 12 pigs as described in the text. Data are from Table 3. When the percentage of base line CMRO<sub>2</sub> is calculated for each pig at each temperature, for the two groups of pigs combined mean percentage of base line CMRO<sub>2</sub> (95% confidence limits) is 50% (35%, 65%) of base line at 28°C; 19% (13%, 25%) of base line at 18°C; and 11% (6%, 16%) of base line at 8°C.



# Hypothermic Circulatory Arrest and Other Methods of Cerebral Protection During Operations on the Thoracic Aorta

M. Arisan Ergin, M.D., Ph.D., Eva B. Griepp, M.D., Steven L. Lansman, M.D., Ph.D., Jan D. Galla, M.D., Michael Levy, M.D., and Randall B. Griepp, M.D.

Department of Cardiothoracic Surgery, Mount Sinai Medical Center, New York, New York

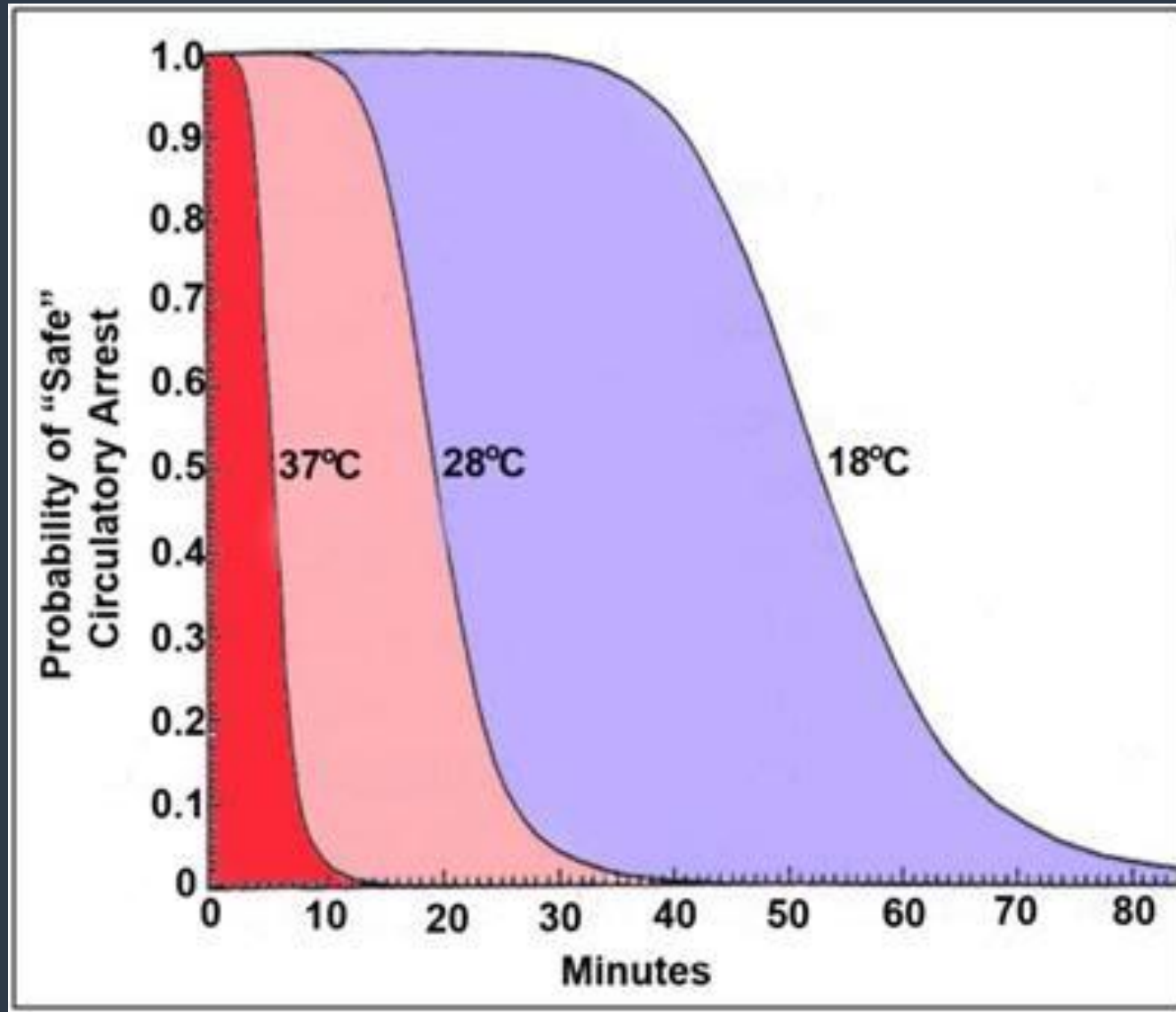


**TABLE 2**  
**Outcomes in Comparative Clinical Experience of Hypothermic Circulatory Arrest\***

	1985–1992 <sup>15</sup> (n = 200) Standard Application	1992–1994 (n = 83) Modified Application	p
HCA time (min)	35.8 ± 16.5	31.7 ± 14.1	NS
Mortality	30 (15%)	4 (4.8%)	< 0.02
Temporary dysfunction	36 (19%)	21 (25.3%)	NS
Permanent (global)	5 (2.6%)	1 (1.2%)	NS
Stroke (perm.)	13 (6.9%)	6 (7.2%)	NS
Stroke (trans.)	9 (4.8%)	0	< 0.04

\*Chi-square. NS = not significant.

# Temperature and Safety Margin



**Table 3** Calculated safe intervals for interruption of brain perfusion at various temperatures

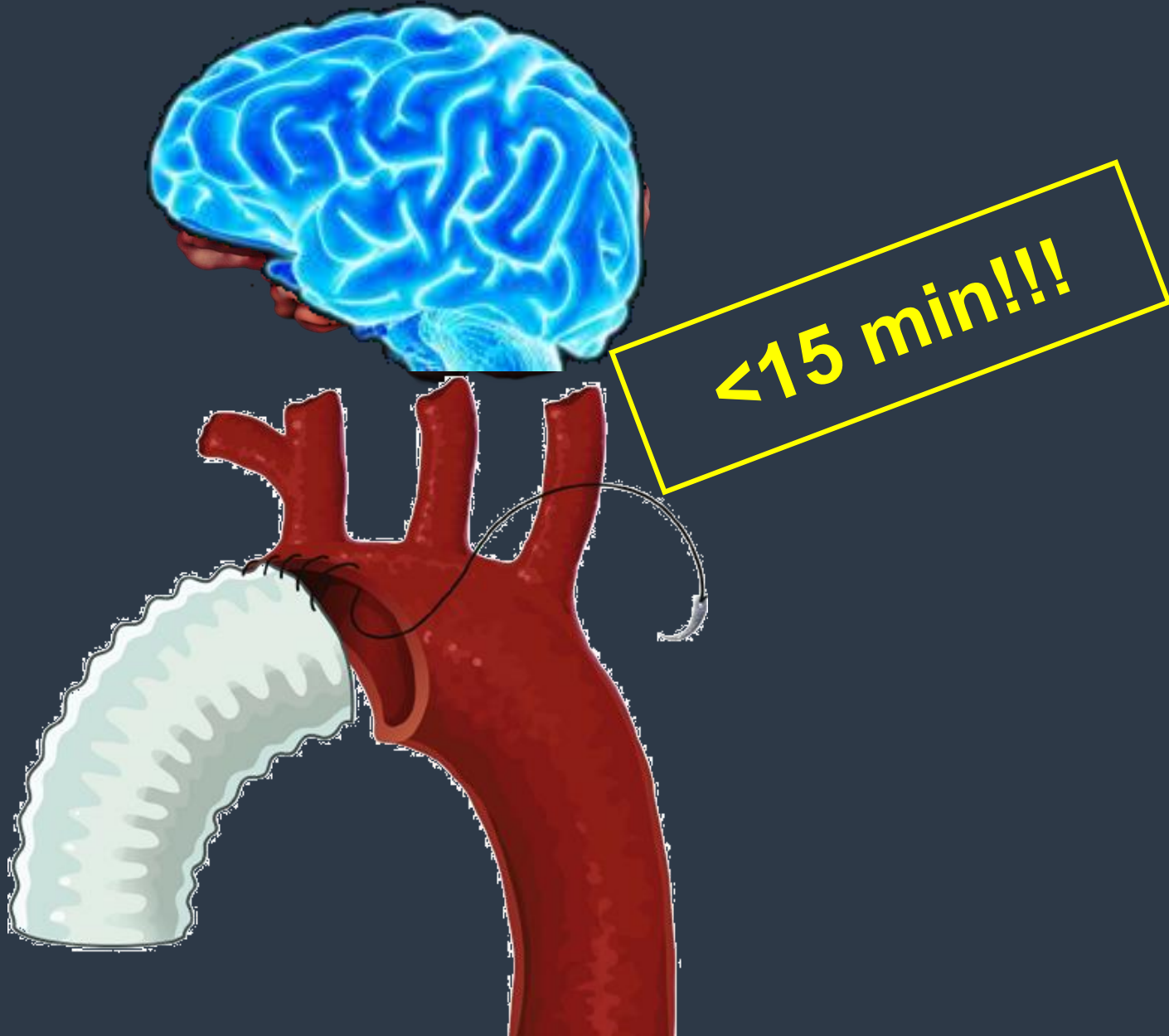
Temperature (°C)	Cerebral metabolic rate (% of baseline)	Calculated safe duration of HCA (min)
37	100	5
30	56 [52–60]	9 [8–10]
25	37 [33–24]	14 [12-15]
20	24 [21–29]	21 [17–24]
15	16 [13–20]	31 [25–38]
10	11 [8–14]	45 [36–62]

Data are means with 95% confidence intervals (CI).

J Thorac Dis. 2017 May;9(Suppl 6):S508-S520.

J Thorac Cardiovasc Surg 2013;145:S56-8.

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J Thorac Dis. 2017 May;9(Suppl 6):S508-S520.

J Thorac Cardiovasc Surg 2013;145:S56-8.



## Vascular Medicine

# Cerebral Protection During Surgery for Acute Aortic Dissection Type A

## Results of the German Registry for Acute Aortic Dissection Type A (GERAADA)

Tobias Krüger, MD\*; Ernst Weigang, MD\*; Isabell Hoffmann; Maria Blettner, PhD;  
Hermann Aebert, MD; on behalf of the GERAADA Investigators

**Background**—Cerebral protection during surgery for acute aortic dissection type A relies on hypothermic circulatory arrest, either alone or in conjunction with cerebral perfusion.

### Methods and Results

centers in  
underwent  
Unilateral  
in 34 patients  
interventions  
overall) and  
cardiopulmonary

**Arrest time < 30 min: TCA is enough**

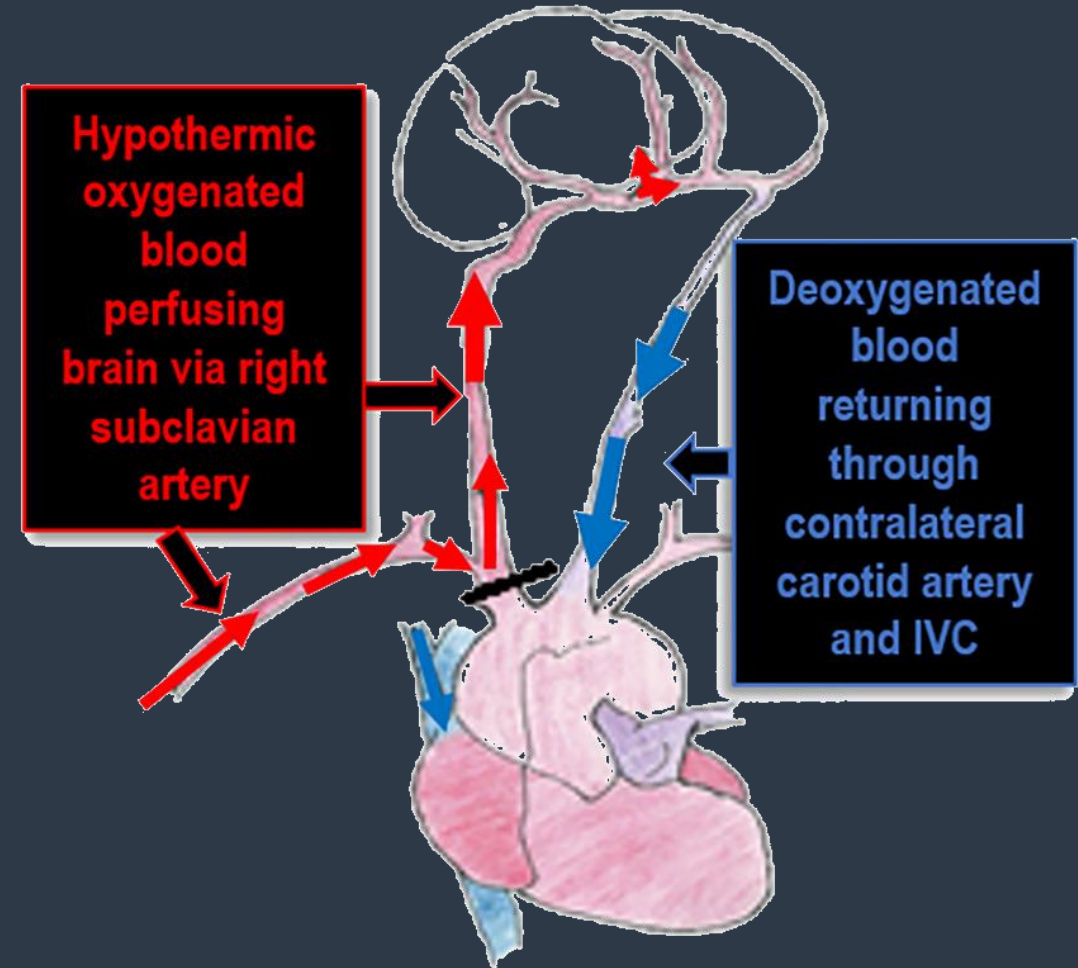
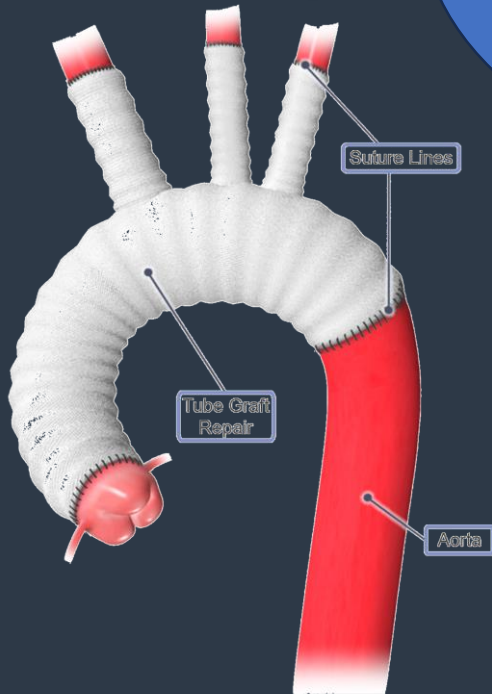
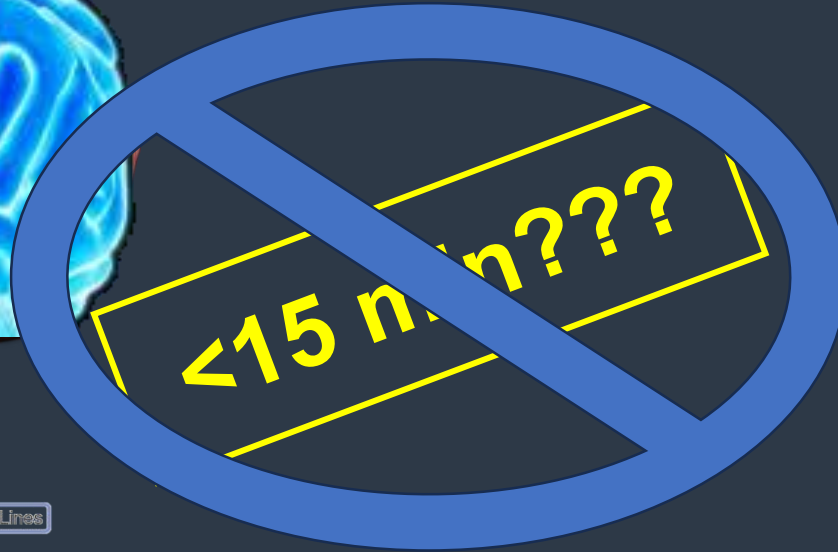
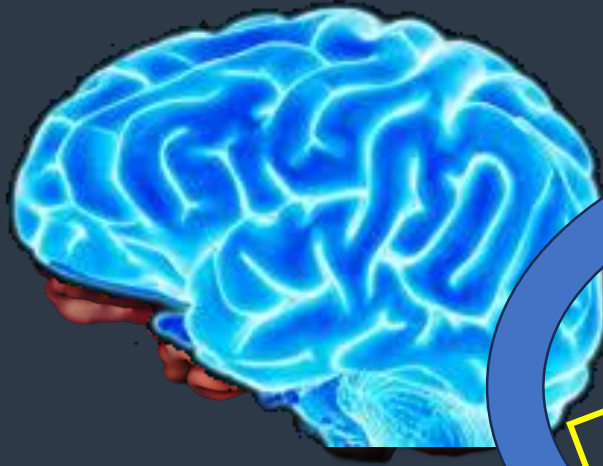
**Arrest time ≥ 30 min: ACP is needed**

mortality rate of 19.4% and a mortality-corrected permanent neurological dysfunction rate of 11.5%, whereas the rates were 13.9% and 10.0%, respectively, for unilateral ACP and 15.9% and 11.0%, respectively, for bilateral ACP. In contrast with the ACP groups, there was a profound increase in mortality when systemic circulatory arrest times exceeded 30 minutes in the hypothermic circulatory arrest group ( $P<0.001$ ). Mortality-corrected permanent neurological dysfunction correlated significantly with perfusion pressure in the ACP groups.

**Conclusions**—This study reflects current surgical practice for acute aortic dissection type A in Central Europe. For arrest times less than 30 minutes, hypothermic circulatory arrest and ACP lead to similar results. For longer arrest periods, ACP with sufficient pressure is advisable. Outcomes with unilateral and bilateral ACP were equivalent. (*Circulation*. 2011;124:434-443.)

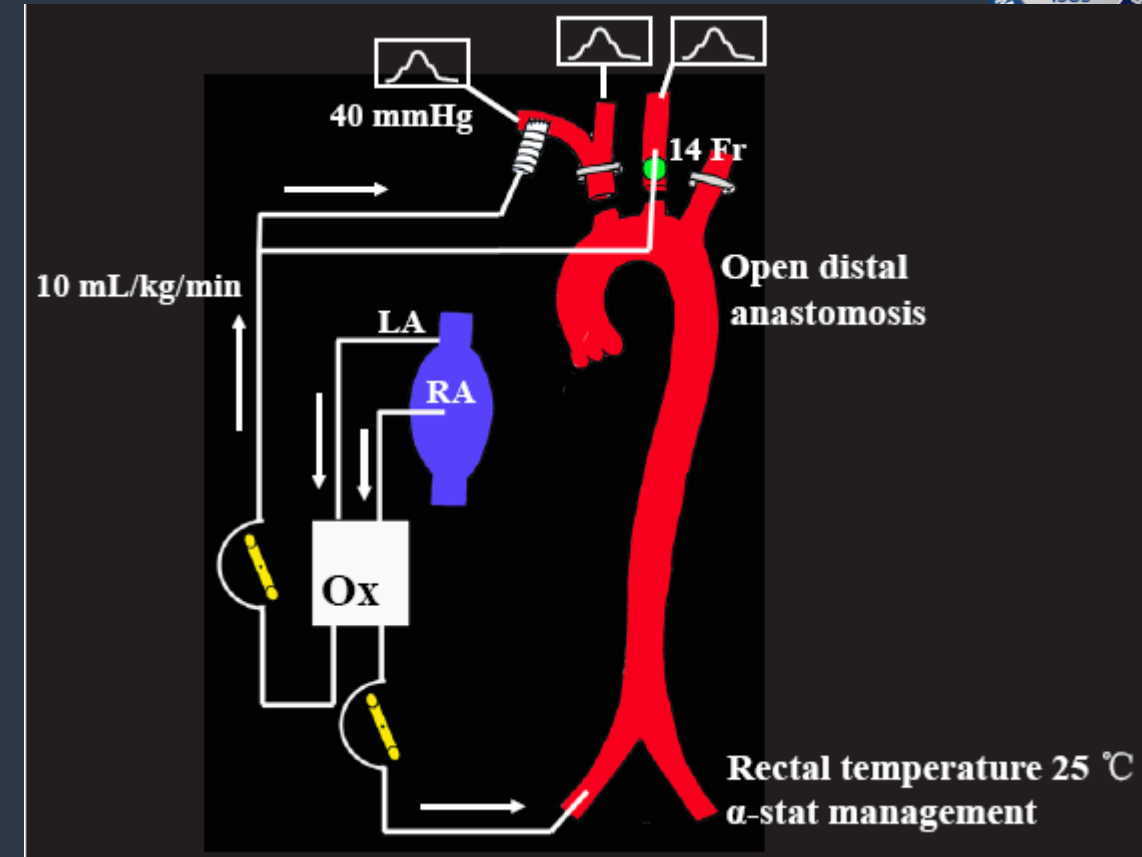
cardiac surgery  
A, 355 (22.8%)  
fusion was used:  
ograde perfusion  
arrest and arch  
nortality (15.9%  
e values for the  
lted in a 30-day

# Temperature and Safety Margin



# Arch Vessel Perfusion

- Selective antegrade perfusion
  - Innominate artery
  - LCCA
- 22°C
- 600 ml/min



> J Cardiovasc Surg (Torino). 1989 May-Jun;30(3):402-6.

## Surgical treatment of aneurysms of the transverse aortic arch

T Kazui<sup>1</sup>, N Inoue, S Komatsu

Affiliations + expand

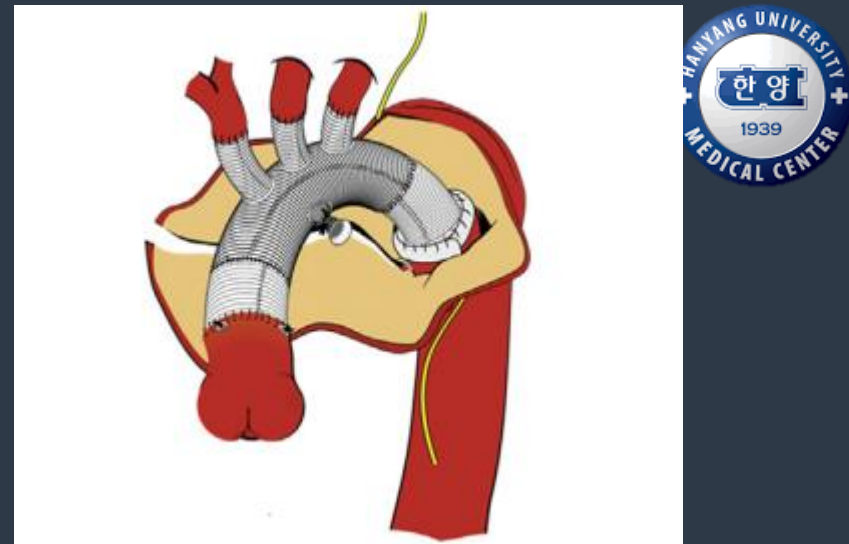
PMID: 2745527



# Total arch replacement using a 4-branched graft with antegrade cerebral perfusion



Kenji Minatoya, MD, PhD,<sup>a</sup> Yosuke Inoue, MD,<sup>a</sup> Hiroaki Sasaki, MD, PhD,<sup>a</sup> Hiroshi Tanaka, MD, PhD,<sup>a</sup> Yoshimasa Seike, MD,<sup>a</sup> Tatsuya Oda, MD,<sup>a</sup> Atsushi Omura, MD, PhD,<sup>a</sup> Yutaka Iba, MD, PhD,<sup>b</sup> Hitoshi Ogino, MD, PhD,<sup>c</sup> and Junjiro Kobayashi, MD, PhD<sup>a</sup>



**TABLE 3. Postoperative variables**

Variable	Value
In-hospital mortality	
In-hospital mortality in all cases	5.1 (52/1005)
In-hospital death in cases without shock	4.4 (42/955)
In-hospital death in cases with shock	16.7 (10/60)
In-hospital death in cases with age <80 y	3.9 (34/853)
In-hospital death in cases with age ≥80 y	11.8 (18/152)
Early complication	
Prolonged ventilation >72 h	14.8 (149/1005)
Transient neurological dysfunction	6.4 (64/1005)
Permanent neurological dysfunction	3.6 (36/1005)

Values are presented as % (n/N).

**TABLE 8. Subgroup univariate analysis of risk factors in octogenarians and nonagenarians for in hospital death**

Variable	Hospital survivor (n = 134)	In-hospital death (n = 18)	<i>P</i> value
Temperature			
≥25°C	56 (41.8)	6 (33.3)	.61
≥28°C	21 (15.6)	1 (5.6)	.47

# Moderate hypothermia during aortic arch surgery is associated with reduced risk of early mortality

January Y. Tsai, MD,<sup>a</sup> Wei Pan, MD,<sup>a,c</sup> Scott A. LeMaire, MD,<sup>b,d</sup> Paul Pisklak, MD,<sup>a</sup> Vei-Vei Lee, MS,<sup>e</sup> Arthur W. Bracey, MD,<sup>f</sup> MacArthur A. Elayda, MD, PhD,<sup>e</sup> Ourania Preventza, MD,<sup>b,d</sup> Matt D. Price, MS,<sup>b,d</sup> Charles D. Collard, MD,<sup>a,c</sup> and Joseph S. Coselli, MD<sup>b,d</sup>

**Conclusions:** Moderate hypothermia with ACP is associated with lower in-hospital and 30-day mortality, shorter cardiopulmonary bypass time, and fewer neurologic sequelae than deep hypothermia in patients who undergo aortic arch surgery with ACP. (J Thorac Cardiovasc Surg 2013;146:662-7)

**TABLE 2. Postoperative outcomes in patients (N = 221) undergoing aortic arch repair with DHCA or MHCA with antegrade cerebral perfusion**

Postoperative outcome	DHCA (n = 78)	MHCA (n = 143)	P	OR	95% CI
30-d mortality, %	9	2	.02	4.7	1.2-18.6
In-hospital death, %	8	1	.005	9.3	1.1-81.6
Stroke, %	8	3	.09	3.4	0.9-12.6
Postoperative MI, %	1	1	.6	0.5	0.3-7.6
Bleeding necessitating reoperation, %	3	7	.27	0.4	0.1-2.0
Hospital stay, d	16 ± 12	14 ± 12	.39	—	—
Postoperative serum creatinine level, mg/dL	1.31 ± 0.64	1.43 ± 0.95	.30	—	—
Preoperative-postoperative change in serum creatinine, mg/dL	0.06 ± 0.60	0.15 ± 0.72	.38	—	—
Postoperative AKI by AKIN criteria, %	17	19	.89	1.0	0.4-2.0
Postoperative AKI by RIFLE criteria, %	12	12	.94	1.0	0.4-2.4
Postoperative dialysis, %	3	2	.84	0.8	0.1-5.9

RIFLE, Risk, Injury, Failure, Loss, and End-stage kidney diseases; DHCA, deep hypothermic circulatory arrest; MHCA, moderate hypothermic circulatory arrest; OR, odds ratio; CI, confidence interval; MI, myocardial infarction; AKI, acute kidney injury; AKIN, acute kidney injury network.

# A meta-analysis of deep hypothermic circulatory arrest versus moderate hypothermic circulatory arrest with selective antegrade cerebral perfusion

## Neurologic damage

			A+SACP			Odds Ratio	
			ts	Total	Weight	M-H, Random, 95% CI	Year
Kazui	1	10	0	11	1.0%	3.63 [0.13, 99.85]	1989
Di Eusanio	16	128	11	161	17.5%	1.95 [0.87, 4.36]	2003
Tan	4	19	1	13	2.1%	3.20 [0.31, 32.53]	2003
Müller	0	12	3	30	1.2%	0.31 [0.02, 6.55]	2004
Harrington	2	22	0	20	1.2%	5.00 [0.23, 110.71]	2004
Sundt	20	220	4	74	9.3%	1.75 [0.58, 5.30]	2008
Halkos	3	66	8	205	6.2%	1.17 [0.30, 4.55]	2009
Misfeld	31	220	33	365	41.8%	1.65 [0.98, 2.78]	2012
Wiedemann	27	116	11	91	19.6%	2.21 [1.03, 4.73]	2012
<b>Total (95% CI)</b>		<b>813</b>		<b>970</b>	<b>100.0%</b>	<b>1.80 [1.28, 2.52]</b>	

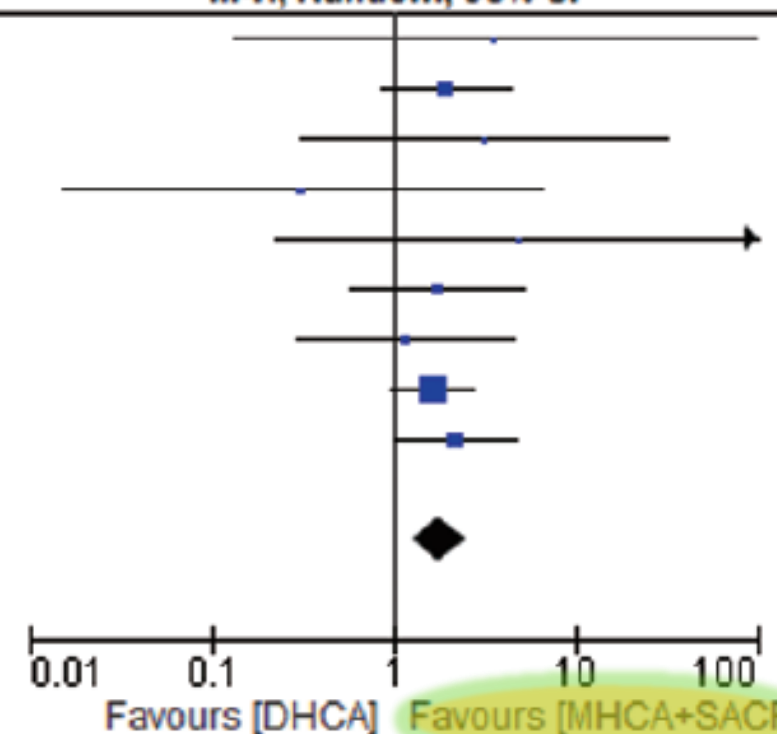
Total events

104

71

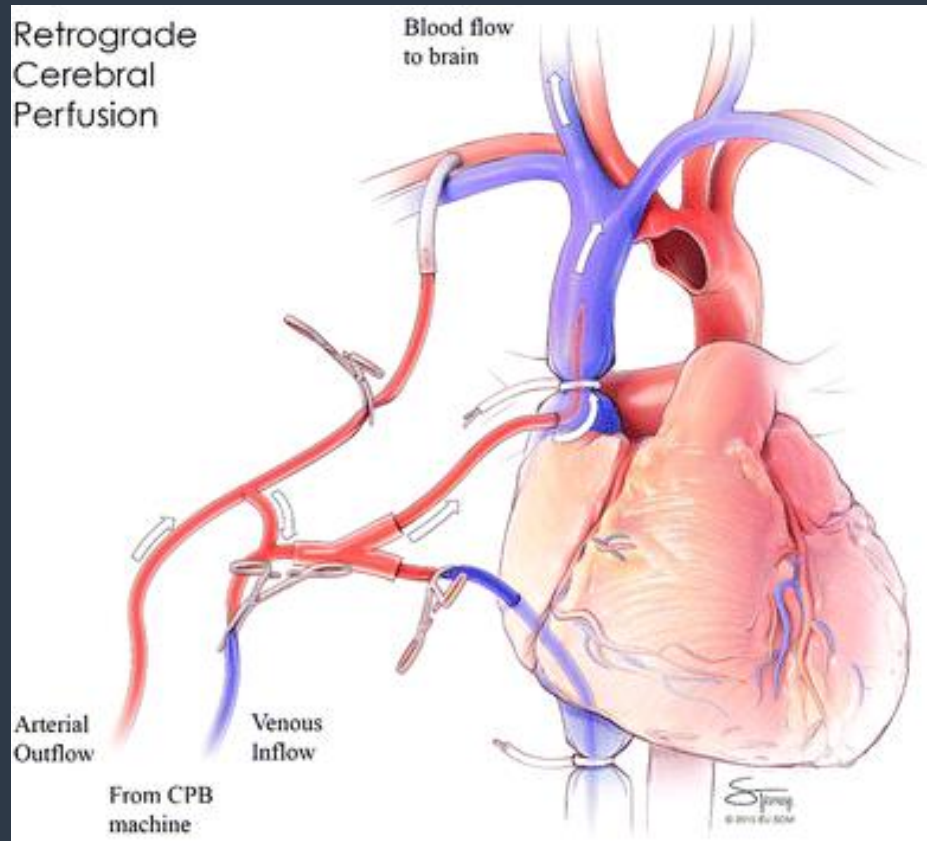
Heterogeneity:  $\tau^2 = 0.00$ ;  $\chi^2 = 2.90$ ,  $df = 8$  ( $P = 0.94$ );  $I^2 = 0\%$ Test for overall effect:  $Z = 3.40$  ( $P = 0.0007$ )

Odds Ratio  
M-H, Random, 95% CI





# Retrograde Perfusion



RCP via cerebral capillaries :  
microspheres recovered from brain

0.01 cc

Non-brain capillary perfusion 9.19 cc

Veno-arterial shunts 0.8 cc

Veno-venous shunts

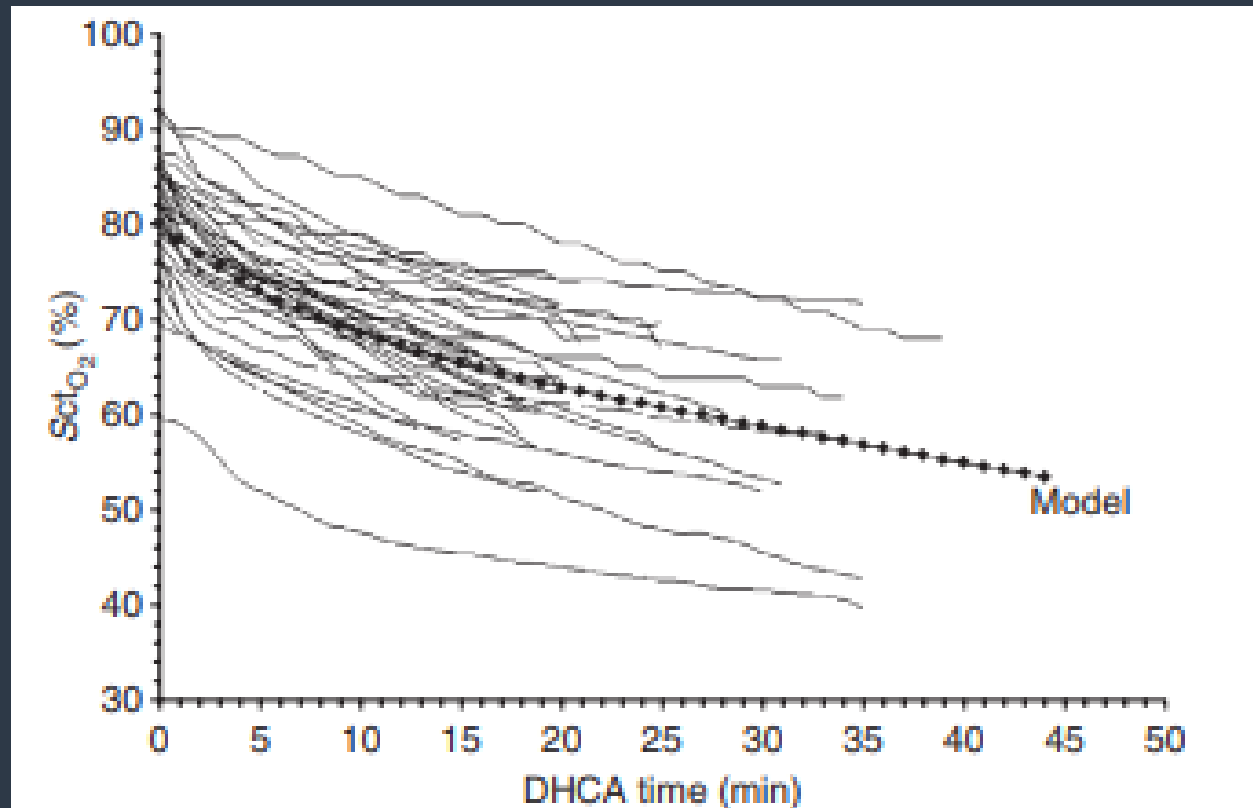
10 cc  
Aortic Arch  
recovery

SVC input  
100 cc

90 cc  
IVC (RA)  
recovery

# Retrograde Perfusion

- Deep hypothermic circulatory arrest
- $\text{ScT}_{\text{O}_2} [t] \frac{1}{4} 81.42(11.53 \pm 0.37t) (120.88 \exp(-20.17t))$



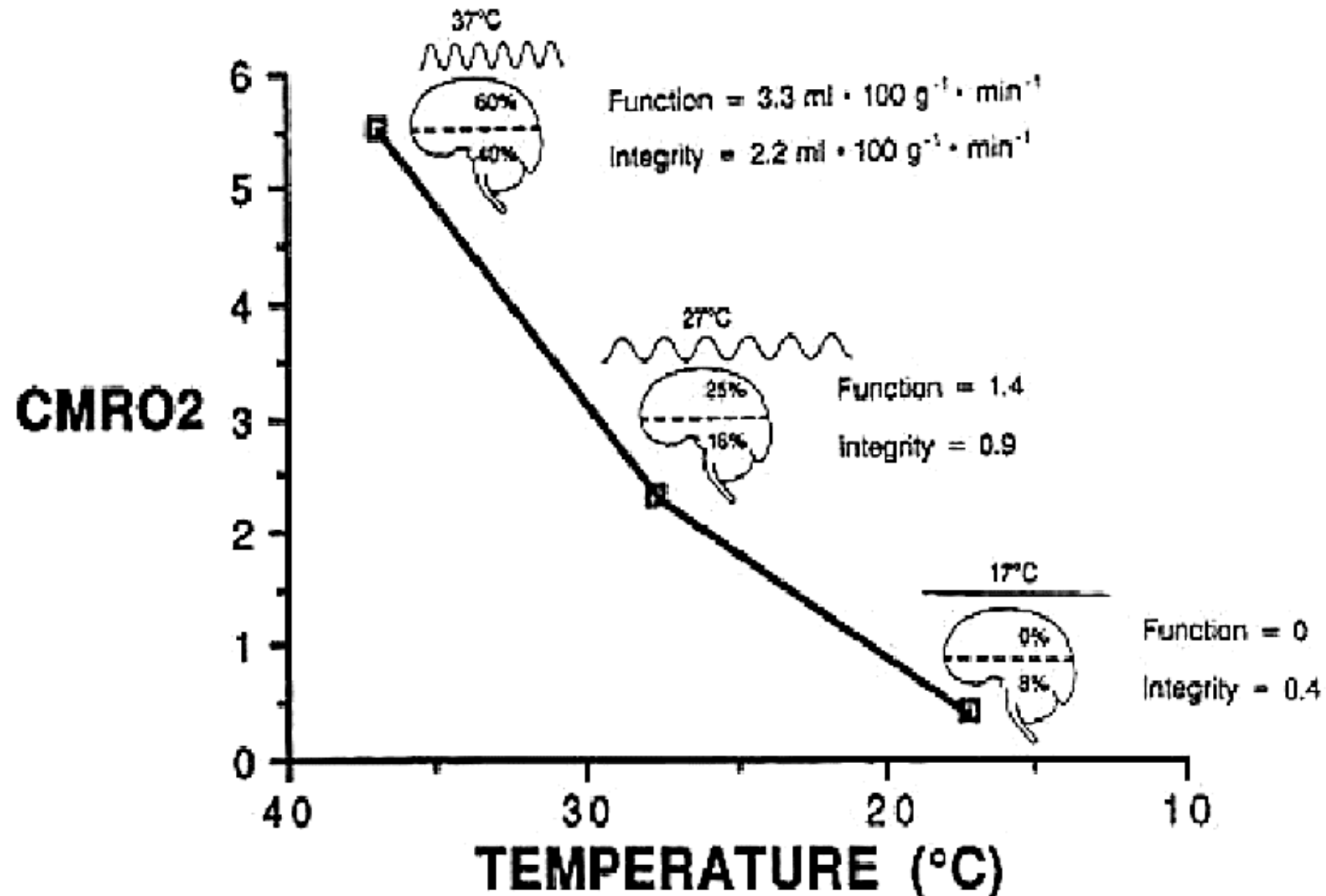
*British Journal of Anaesthesia* **104** (1): 59–66 (2010)  
doi:10.1093/bja/aep335 Advance Access publication November 20, 2009

BJA

## Mathematical model for describing cerebral oxygen desaturation in patients undergoing deep hypothermic circulatory arrest

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# Retrograde Perfusion





# Deep Hypothermia With Retrograde Cerebral Perfusion Versus Moderate Hypothermia With Antegrade Cerebral Perfusion for Arch Surgery



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*Table 4. Neurologic Outcomes After Hemiarch Replacement Using Deep Hypothermic Circulatory Arrest With Retrograde Cerebral Perfusion or Moderate Hypothermic Circulatory Arrest With Antegrade Cerebral Perfusion*

Variable <sup>a</sup>	DHCA+RCP (n = 11)	MHCA+ACP (n = 9)	p Value
Composite of stroke, TIA, MRI DWI lesions	5 (45)	9 (100)	0.01 <sup>b</sup>
Stroke	1 (9)	1 (11)	0.28
Transient neurologic dysfunction	0	2 (22)	0.19
TIA	0	0	1
S-100 level, ng/mL			
Postoperative day 1	123 ± 66	132 ± 58	0.77
Postoperative day 3	62 ± 38	67 ± 46	0.79
Postoperative day 7	53 ± 34	49 ± 24	0.66
Patients with MRI DWI lesions	5 (45)	9 (100)	0.01 <sup>b</sup>
Number of DWI lesions	1.2 ± 2.1	4 ± 3.5	0.01 <sup>b</sup>
Volume of DWI lesions, cm <sup>3</sup>	0.54 ± 0.72	1.29 ± 3.01	0.63

<sup>a</sup> Data are presented as mean ± SD or as number (%). <sup>b</sup> Statistically significant (p < 0.05).

DHCA+RCP = deep hypothermic circulatory arrest with retrograde cerebral perfusion; DWI = diffusion-weighted imaging; MHCA+ACP = moderate hypothermic circulatory arrest with antegrade cerebral perfusion; MRI = magnetic resonance imaging; TIA = transient ischemic attack.

# Retrograde Cerebral Perfusion Is Effective for Prolonged Circulatory Arrest in Arch Aneurysm Repair



Christopher Lau, MD,\* Mario Gaudino, MD,\* Erin Mills Iannacone, MD, Ivancarmine Gambardella, MD, Monica Munjal, MS, Lucas B. Ohmes, MD, Benjamin C. Degner, MD, and Leonard N. Girardi, MD

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## Favorable late survival after aortic surgery under straight deep hypothermic circulatory arrest

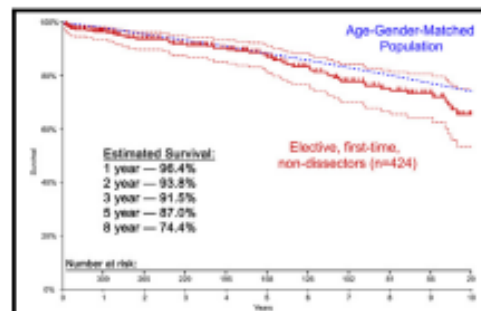


Anneke Damberg, MD,<sup>a</sup> Davide Carino, MD,<sup>a</sup> Paris Charilaou, MD,<sup>a</sup> Sven Peterss, MD,<sup>a,b</sup> Maryann Tranquilli, RN,<sup>a</sup> Bulat A. Ziganshin, MD, PhD,<sup>a,c</sup> John A. Rizzo, PhD,<sup>a,d,e</sup> and John A. Eleftheriades, MD<sup>a</sup>

### ABSTRACT

**Background:** Surgical and cerebral protection strategies in aortic arch surgery remain under debate. Perioperative results using deep hypothermic circulatory arrest (DHCA) have been associated with favorable short-term mortality and stroke rates. The present study focuses on late survival in patients undergoing aortic surgery using DHCA.

**Methods:** A total of 613 patients (mean age, 63.7 years) underwent aortic surgery between January 2003 and December 2015 using DHCA, with 77.3% undergoing hemiarch replacement and 20.4% undergoing arch replacement, with a mean DHCA duration of  $29.7 \pm 8.5$  minutes (range, 10-62 minutes). We examined follow-up extending up to a mean of  $3.8 \pm 3.4$  years (range, 0-14.1 years).






Survival of elective, first-time nondissection cases compared with the reference population (n = 424).



## ORIGINAL RESEARCH ARTICLE

## Cognitive Effects of Body Temperature During Hypothermic Circulatory Arrest Trial (GOT ICE): A Randomized Clinical Trial Comparing Outcomes After Aortic Arch Surgery

G. Chad Hughes, MD , Edward P. Chen, MD , Jeffrev N. Browndvke, PhD .Wilson Y.  
Gaca, MD  
Michael L  
Mathew, I

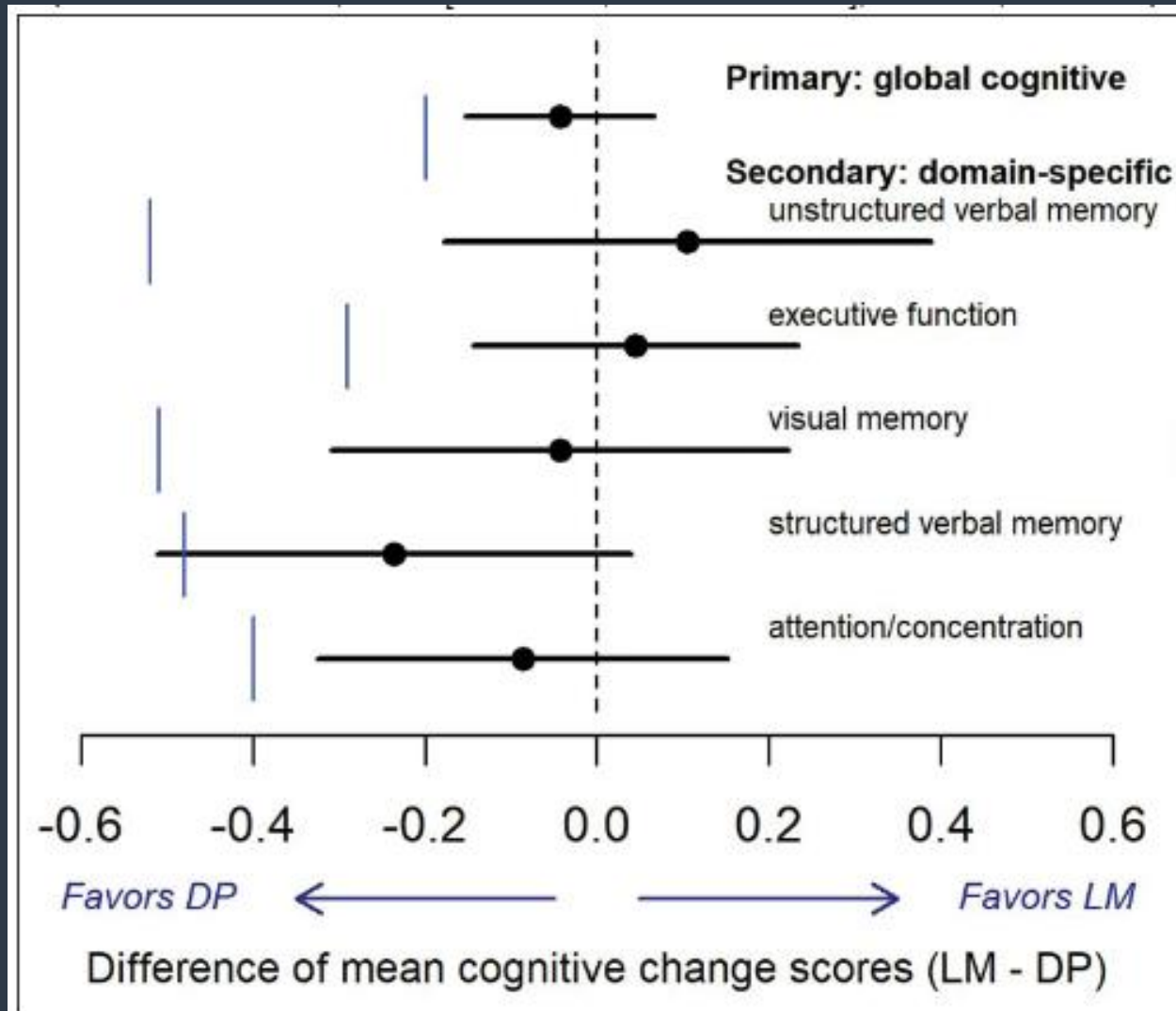
**Methods:** This was a randomized single-blind trial (GOT ICE [Cognitive Effects of Body Temperature During Hypothermic Circulatory Arrest]) of patients undergoing arch surgery with HCA plus antegrade cerebral perfusion at 4 US referral aortic centers (August 2016–December 2021). Patients were randomized to 1 of 3 hypothermia groups: DP, deep ( $\leq 20.0$  °C); LM, low-moderate (20.1–24.0 °C); and HM, high-moderate (24.1–28.0 °C). The primary outcome was composite global cognitive change score between baseline and 4 weeks postoperatively. Analysis followed the intention-to-treat principle to evaluate if: (1) LM noninferior to DP on global cognitive change score; (2) DP superior to HM. The secondary outcomes were domain-specific cognitive change scores, neuroimaging findings, quality of life, and adverse events.



## ORIGINAL RESEARCH ARTICLE

# Cognitive Effects of Body Temperature During Hypothermic Circulatory Arrest Trial (GOT ICE): A Randomized Clinical Trial Comparing Outcomes After Aortic Arch Surgery

G. Chad Hughes, MD , Edward P. Chen, MD , Jeffrey N. Browndyke, PhD , Wilson Y. Szeto, MD, J. Michael DiMaio, MD , William T. Brinkman, MD, Jeffrey G. Gaca, MD, James A. Blumenthal, PhD , Jorn A. Karhausen, MD, Tiffany Bisanar, RN, Michael L. James, MD , David Yanez, PhD , Yi-Ju Li, PhD , and Joseph P. Mathew, MD, MHSc, MBA 





ORIGINAL RESEARCH ARTICLE

Cognitive Effects of Body Temperature During Hypothermic Circulatory Arrest Trial (GOT ICE): A Randomized Clinical Trial Comparing Outcomes After Aortic Arch Surgery

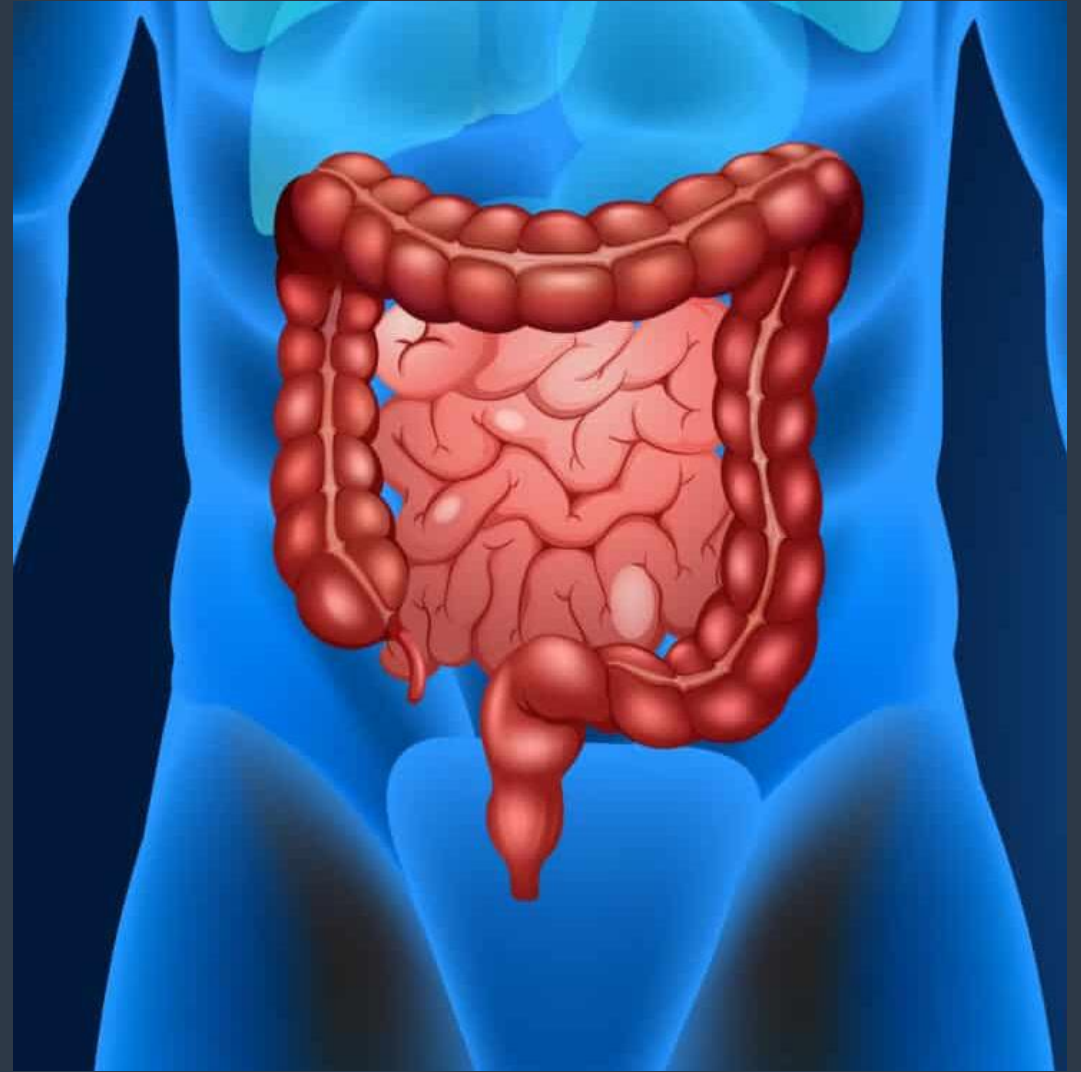
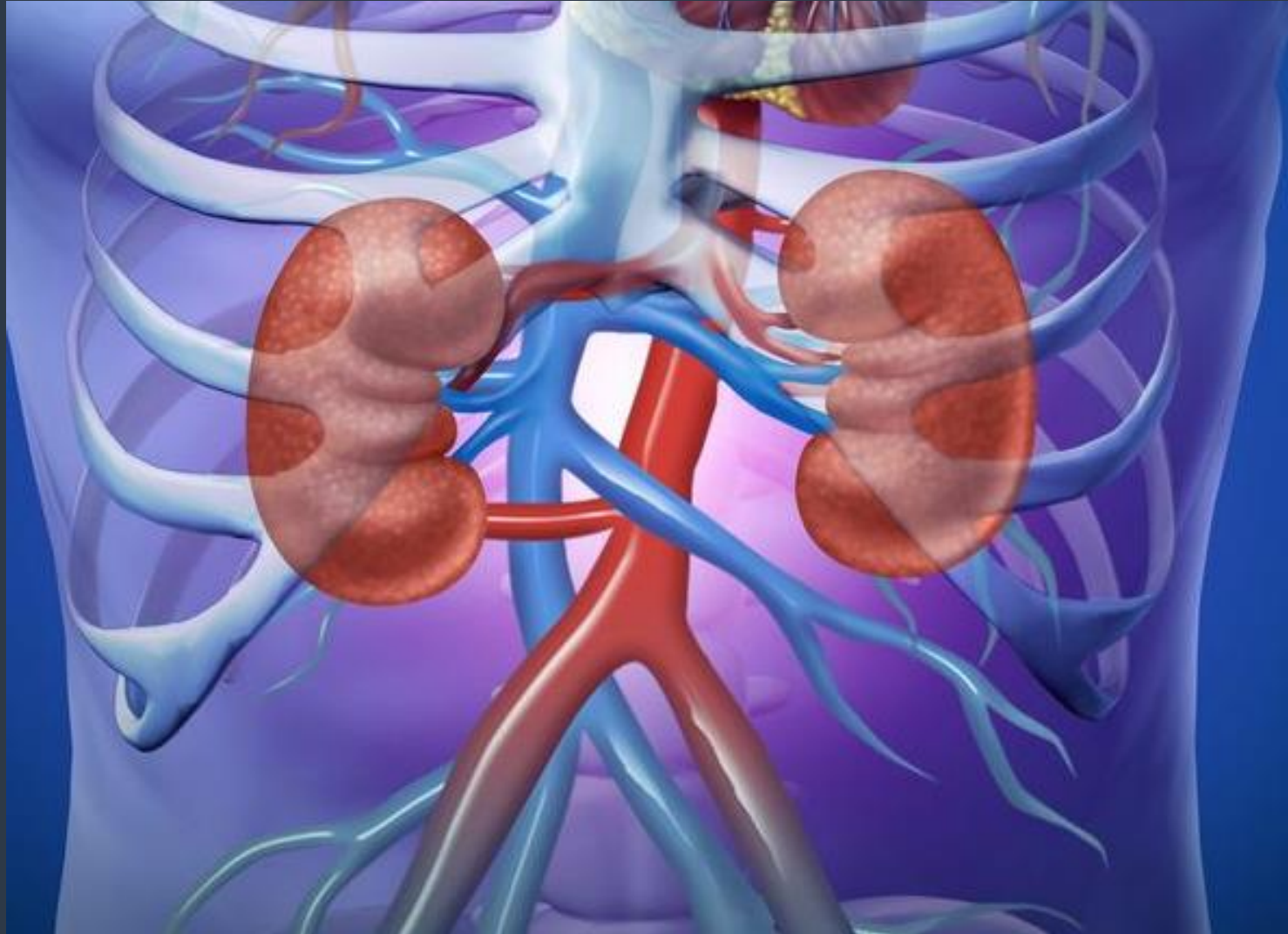
G. Chad Hughes, MD , Edward P. Chen, MD , Wilson Y. Szeto, MD, J. Michael DiMaio, MD , Gaca, MD, James A. Blumenthal, PhD , Jorn A. Michael L. James, MD , David Yanez, PhD , Mathew, MD, MHSc, MBAk

CES-D indicates Center for Epidemiologic Studies Depression Scale; DASI, Duke Activity Status Index; Health, Health score from short form 36; MA, Cognitive Difficulties Scale; NIHSS, National Institutes of Health Stroke Scale; OARS-IADL, Duke Older American Resources and Services Procedures–Instrumental Activities of Daily Living; SA, Social Anxiety Scale; SCL-90, Hopkins Symptom Checklist; SOCSUP, Perceived Social Support Scale; STAI, State Trait Anxiety Inventory; and WA, Work Activity Scale.

Change scores	DP vs HM			LM vs DP		
	Mean diff*	97.5% CI	P value†	Mean diff*	97.5% CI	P value†
NIHSS	0.12	(−0.05 to 0.29)	0.15	−0.11	(−0.25 to 0.03)	0.11
OARS-IADL	0.58	(−0.87 to 2.03)	0.43	−0.77	(−2.18 to 0.64)	0.28
CES-D	−1.23	(−3.89 to 1.42)	0.36	−1.00	(−3.49 to 1.50)	0.43
DASI	0.10	(−5.27 to 5.47)	0.97	3.47	(−1.84 to 8.79)	0.20
STAI	−1.71	(−4.98 to 1.56)	0.30	−0.07	(−2.88 to 2.73)	0.96
Health	−0.12	(−0.46 to 0.22)	0.50	−0.30	(−0.65 to 0.05)	0.09
MA	3.25	(−1.61 to 8.11)	0.19	−0.91	(−5.28 to 3.45)	0.68
SA	0.04	(−1.06 to 1.14)	0.94	−0.41	(−1.58 to 0.76)	0.49
SOCSUP	−3.47	(−7.40 to 0.45)	0.08	1.43	(−2.82 to 5.68)	0.51
SCL-90	−0.59	(−1.81 to 0.62)	0.34	−0.49	(−1.69 to 0.72)	0.42
WA	0.41	(−0.90 to 1.71)	0.54	−0.76	(−2.01 to 0.48)	0.23
Postoperative delirium	27 (29.7%)	33 (35.9%)	0.37	33 (38.4%)	27 (29.7%)	0.22

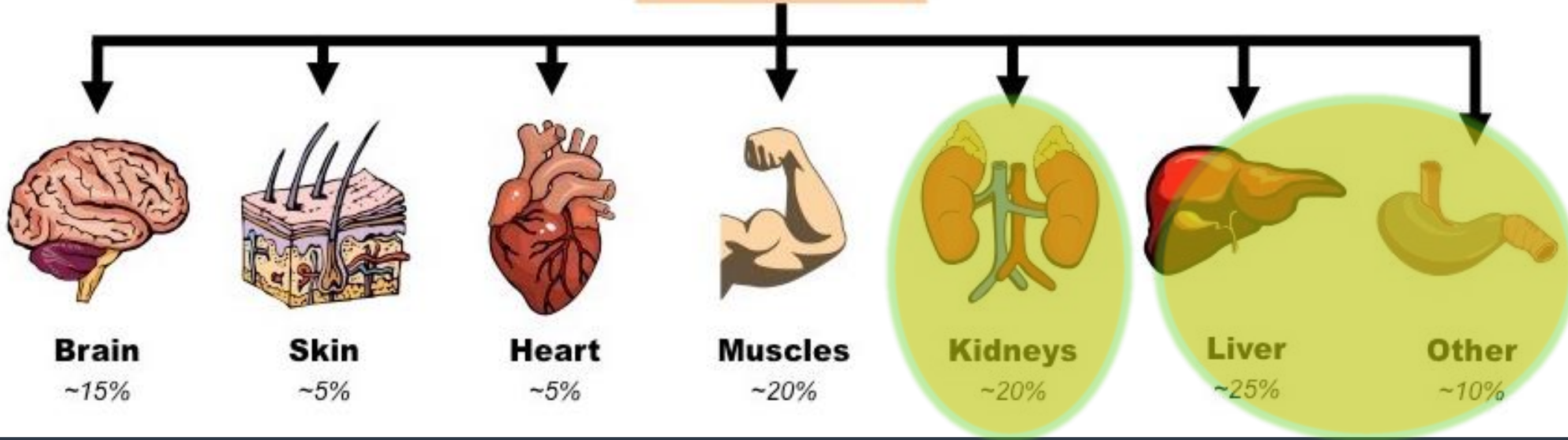
'우리가 좋아하는 걸 하자'  
'우리가 잘하는 걸 하자'





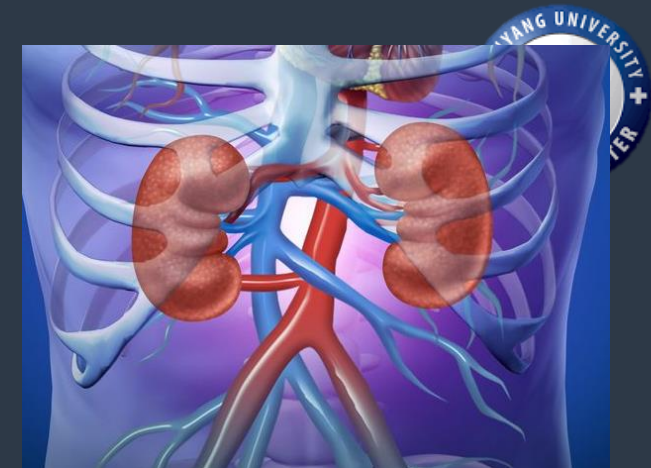
## Cardiac Output

$\sim 5 \text{ L / min}$





*Hypoxic signaling: some organs are more equal than others.* Focus on  
“Differential HIF and NOS responses to acute anemia: defining organ-specific  
hemoglobin thresholds for tissue hypoxia”



damage (2). For example, it seems likely that hemodilution during surgery performed in combination with cardiopulmonary bypass promotes renal hypoxia, and thus the development of acute kidney injury. Evidence for this includes the observations that whole body oxygen delivery during cardiopulmonary bypass, which is largely determined by the degree of hemodilution, is a major determinant of the risk of postoperative acute kidney injury (1). Furthermore, the kidney appears to be more sensitive than other organs (e.g., heart and intestines) to the ability of acute anemia to induce tissue hypoxia (7, 10).

In their paper in the current issue, Tsui and colleagues compare the HIF signalling responses to graded anemia of the kidney and liver with that of the brain. They used a transgenic mouse in which firefly luciferase acts as a reporter for HIF-1 $\alpha$  bioavailability (9). They showed that in the kidney, unlike the brain, activation of HIF-1 $\alpha$  by anemia is independent of nNOS. This seems to make adaptive sense, in that HIF signalling in the kidney may be more finely tuned to respond to hypoxia than in other tissues, where an ability to respond to additional stimuli might provide some adaptive advantage.

(5). Consequently, in order for the kidney to mount an appropriate response to anemia, through synthesis and release of erythropoietin, cortical tissue  $PO_2$  must fall in response to anemia. Indeed, it seems that the kidney has evolved multiple mechanisms that enhance its susceptibility to tissue hypoxia in anemia. These likely include the relative insensitivity of renal vascular tone to hypoxia and the ability of anemia to enhance the diffusional shunting of oxygen from arteries to veins (2, 6).

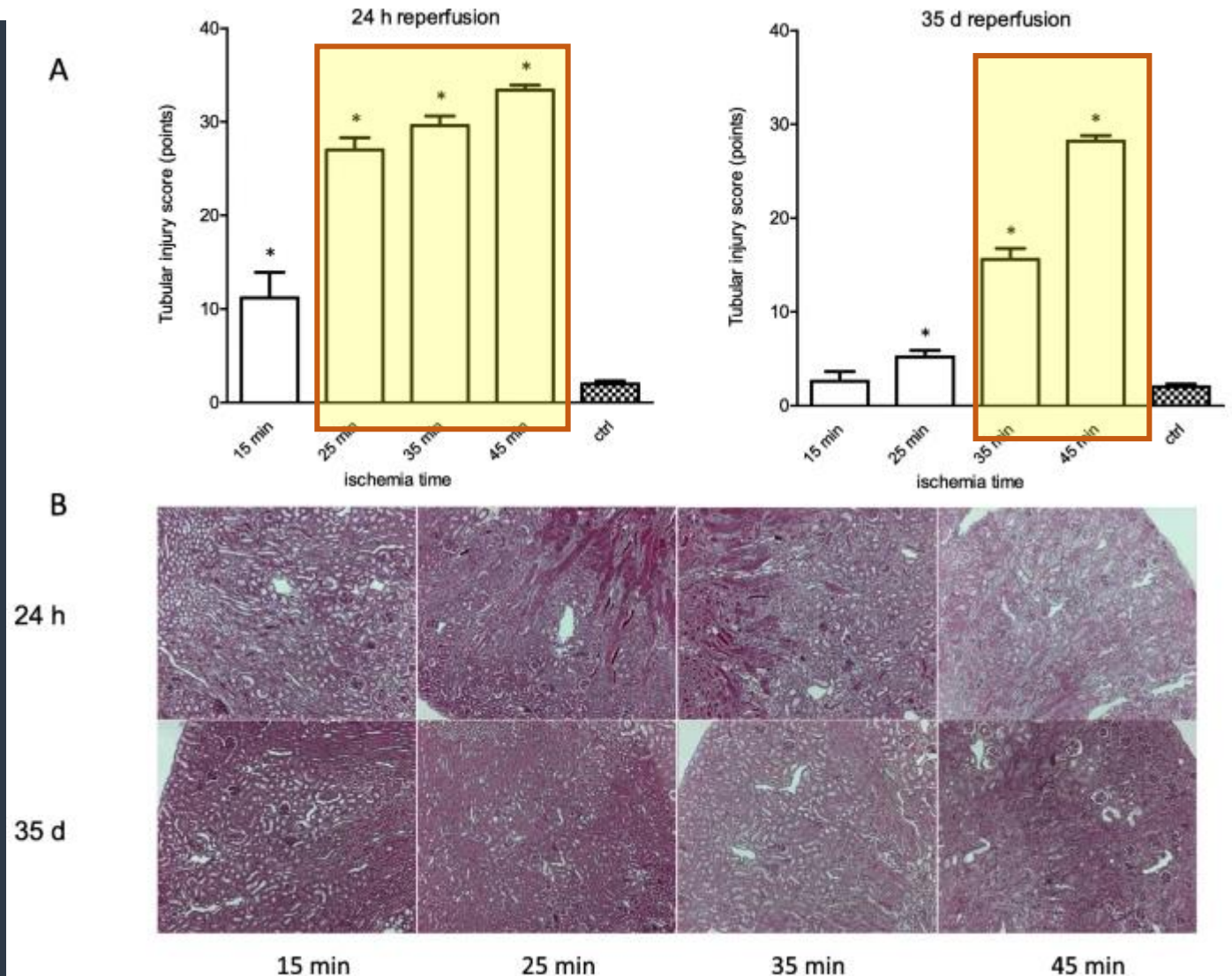
Given that the response of tissue  $PO_2$  to anemia differs in the kidney relative to other organs, one might also expect to find differences in the cellular signalling cascades mediating the cellular responses to hypoxia. In this issue of *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, Tsui and colleagues (9) provide strong evidence that this is the case. [제목 없음]ious study, they demonstrated a critical role of neuronal nitric oxide (NO) synthase (nNOS) in





# "Point of no return" in unilateral renal ischemia reperfusion injury in mice

Alexander Holderied<sup>1\*</sup>, Franziska Kraft<sup>2</sup>, Julian Aurelio Marschner<sup>2</sup>, Marc Weidenbusch<sup>2</sup> and Hans-Joachim Anders<sup>2</sup>



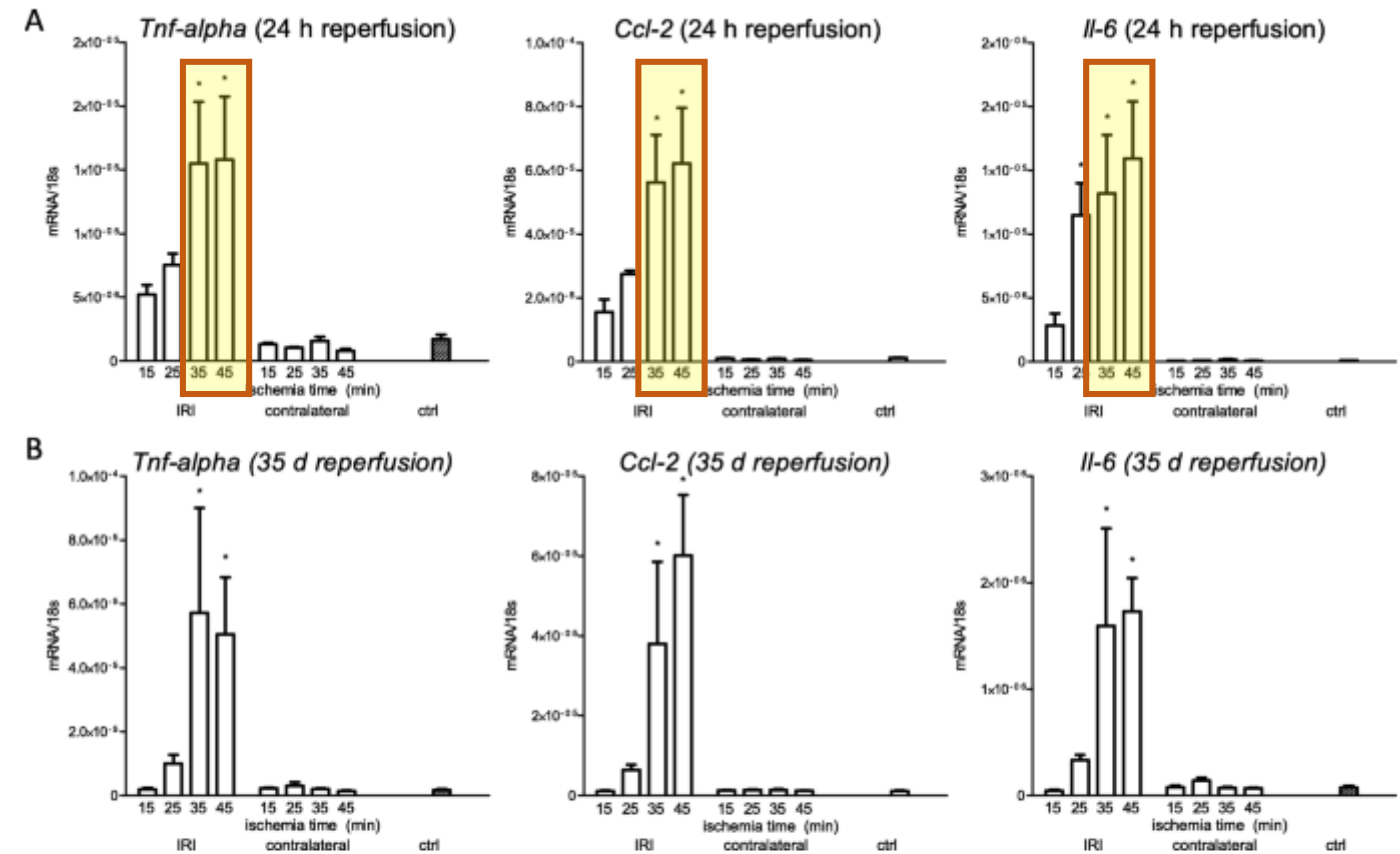


# "Point of no return" in unilateral renal ischemia reperfusion injury in mice

Alexander Holderied<sup>1\*</sup>, Franziska Kraft<sup>2</sup>, Julian Aurelio Marschner<sup>2</sup>, Marc W. Hans-Joachim Anders<sup>2</sup>

**Normothermia  
<30 min!!!**

**Fig. 3**



Gene expression of inflammation markers after ischemia for 15, 25, 35 and 45 min and reperfusion for 24 h and 5 weeks. **a**: 24 h after ischemic injury gene expression of *Tnf- $\alpha$* , *Ccl-2* and *Il-6* were significantly upregulated following ischemia for 35 and 45 min. *Il-6* additionally revealed significant gene expression after ischemia for 25 min. **b**: 5 weeks after the ischemic injury the expression of *Tnf- $\alpha$* , *Ccl-2* and *Il-6* was significantly upregulated only after ischemia for 35 min and 45 min. Displayed are means with s.e.m. \* $P < 0.05$  versus control



## DSC, as a new method to verify the exact warm and cold ischemic injury during small bowel surgery

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### ABSTRACT

The fact that **small bowel is extremely sensitive** to ischemia/reperfusion injury had encouraged us to compare the influences of warm and cold ischemia on the intestinal structural changes by differential scanning calorimetry (DSC) method. Warm and cold ischemia groups were established on Wistar rats with 1, 3 and 6 h ischemic times. Intestinal biopsies were collected after laparotomy and at the end of the ischemia periods. DSC measurement was performed on mucosa, on muscular layer and on the total intestinal wall. Our DSC data confirmed that longer warm ischemia period caused more severe damage in the structure of mucosa and muscular layers. According to the results of transition temperature and calorimetric enthalpy suggest that these changes reduced by cold ischemic procedure in University of Wisconsin solution. However, the thermal destruction of each layers following cold preservation injury revealed significant differences compared to normal bowel structure.

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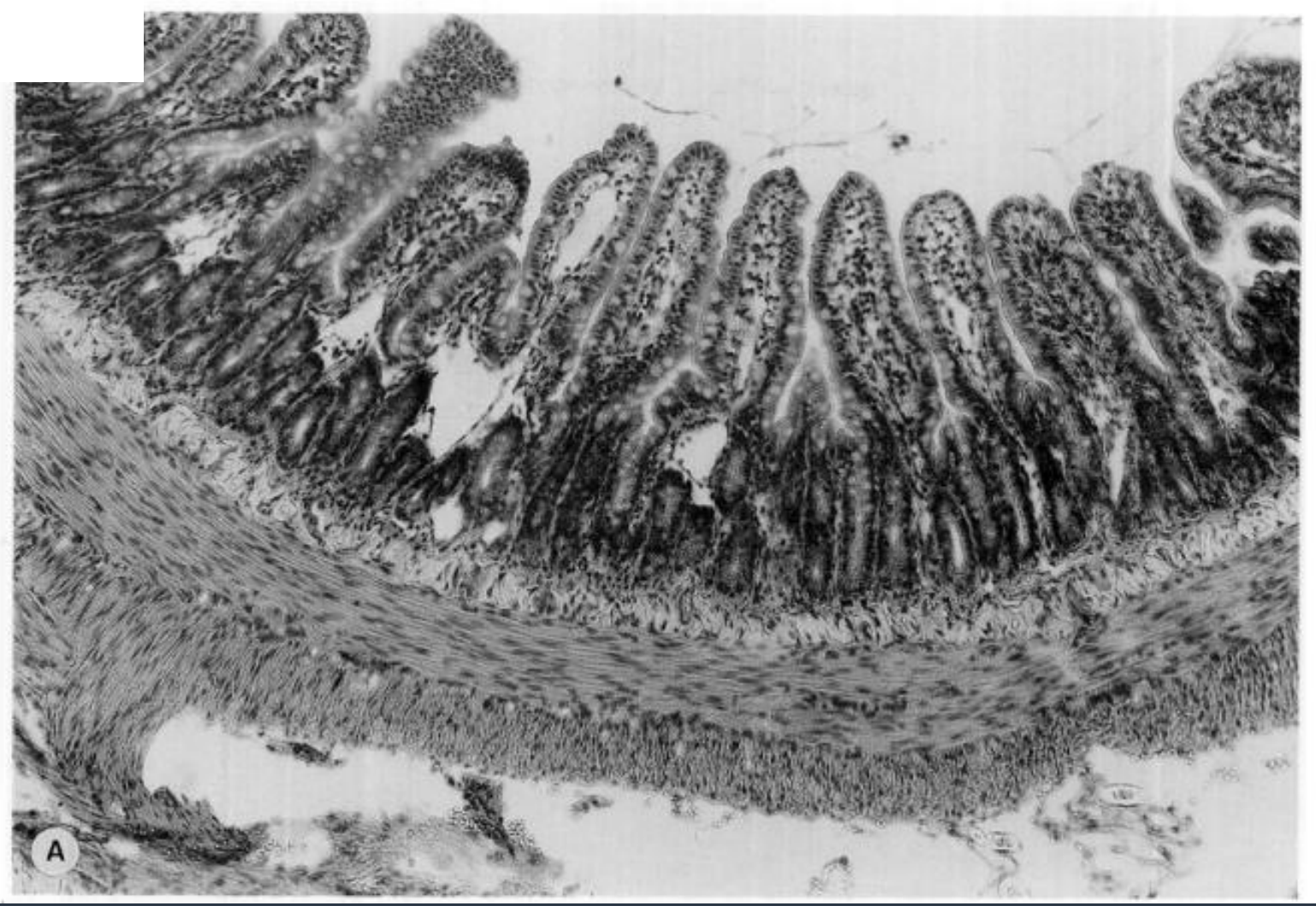
# The Time Sequence of Injury and Recovery Following Transient Reversible Intestinal Ischemia

RAPHAEL UDASSIN, M.D., AMOS VROMEN, M.D., AND YUVAL HASKEL, M.D.

*Department of Pediatric Surgery, Hadassah University Hospital, Mount Scopus, Jerusalem, Israel*

Submitted for publication October 13, 1992

**Intestinal mucosal damage** and regeneration were examined in rats following transient ischemia produced by the occlusion of the superior mesenteric artery for 30 min. Animal groups were assigned for harvesting of small bowel specimens at 10, 17, and 30 min and 1, 2, 3, 4, 6, 12, and 24 hr post-relief of ischemia. Severe damage to the villi was evident already at 10 min postischemia. Thereafter a very rapid restitutional process was observed with restoration of villi epithelium in 47.6% of the examined animals at 60 min, 75% at 4 hr, and 100% at 12 hr. This rapid sequence of events should be taken into consideration when designing experimental ischemic bowel animal models and possible therapeutic modalities. © 1994 Academic Press, Inc.





# The Time Sequence of Injury and Recovery Following Transient Reversible Intestinal Ischemia

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TABLE 1

Percentage of Intestinal Specimens Harvested at Different Postischemic Times at Each Pathological Grade\*

Postischemic times: Number of animals:	10 min	17 min	30 min	60 min	2 hr	3 hr	4 hr	6 hr	12 hr	24 hr
A	8.3	9.1	19.2	47.6	62.5	60.0	75.0	77.8	100	94.1
B	66.6	63.6	57.7	47.6	37.5	40.0	12.5	22.8	0	5.9
C	16.6	18.2	15.4	4.8	0	0	12.5	0	0	0
D	8.3	9.1	7.7	0	0	0	0	0	0	0

\* Pathological grading: (A) normal architecture, (B) epithelial denudation of the tips of the villi with some inflammation, (C) destruction of half of the villi's height, (D) total destruction of the villi.

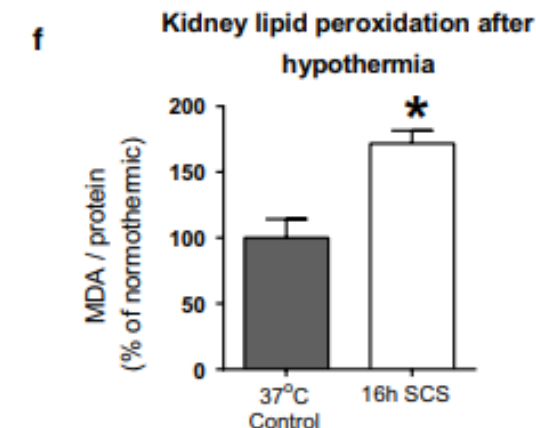
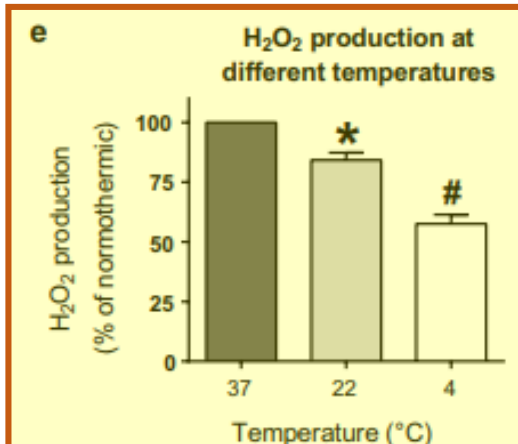
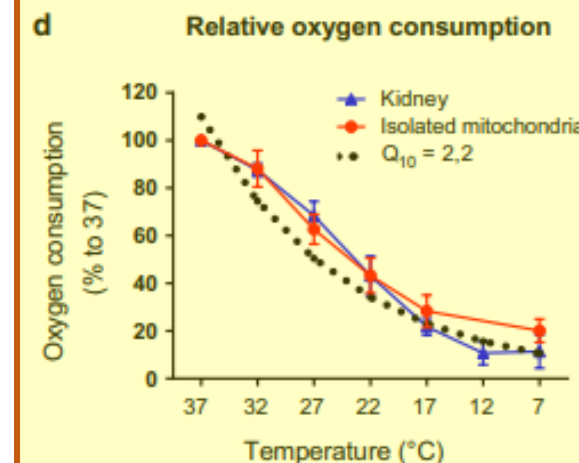
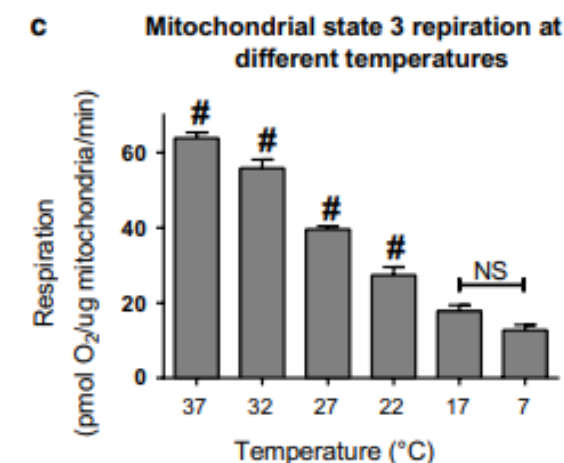
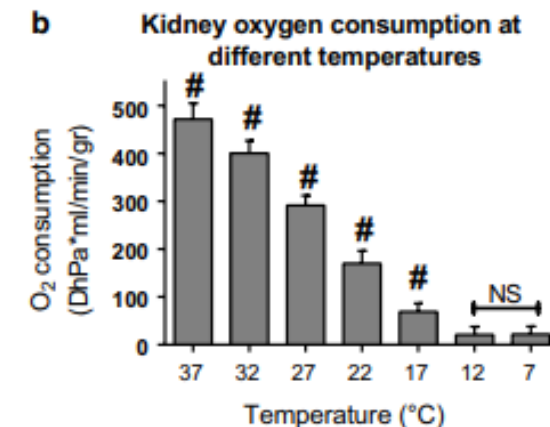
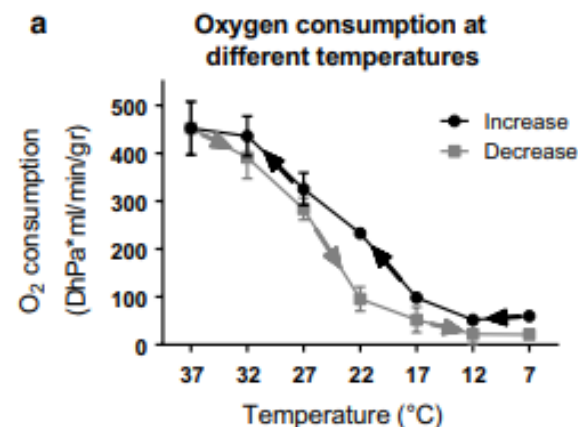
RESEARCH

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# Renal temperature reduction progressively favors mitochondrial ROS production over respiration in hypothermic kidney preservation

Koen D. W. Hendriks<sup>1,2†</sup> , Isabel M. A. Brüggewirth<sup>3†</sup>, Hanno Maassen<sup>2</sup>, Albert Gerding<sup>4</sup>, Barbara Bakker<sup>5</sup>, Robert J. Porte<sup>3</sup>, Robert H. Henning<sup>1</sup> and Henri G. D. Leuvenink<sup>2</sup>





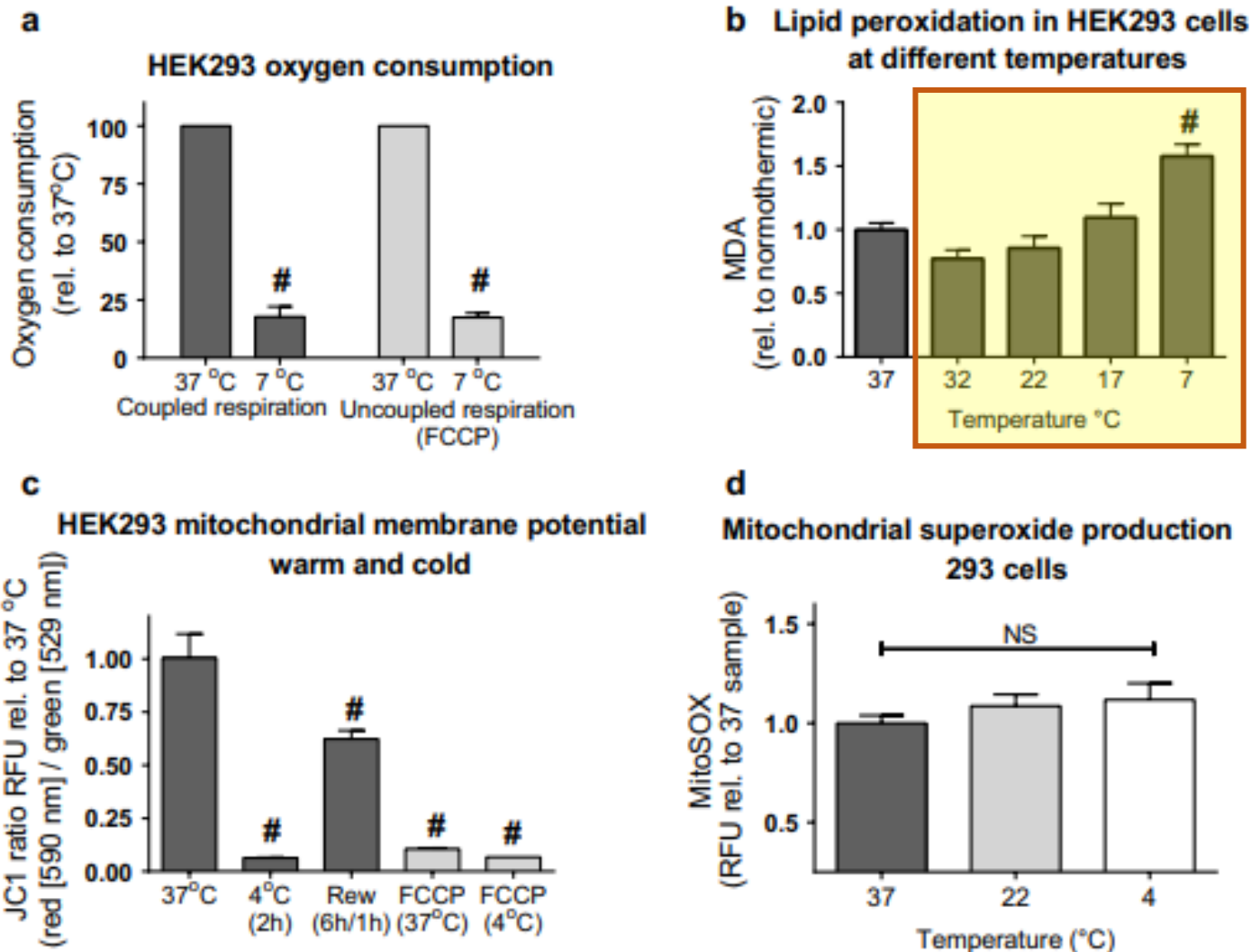
RESEARCH

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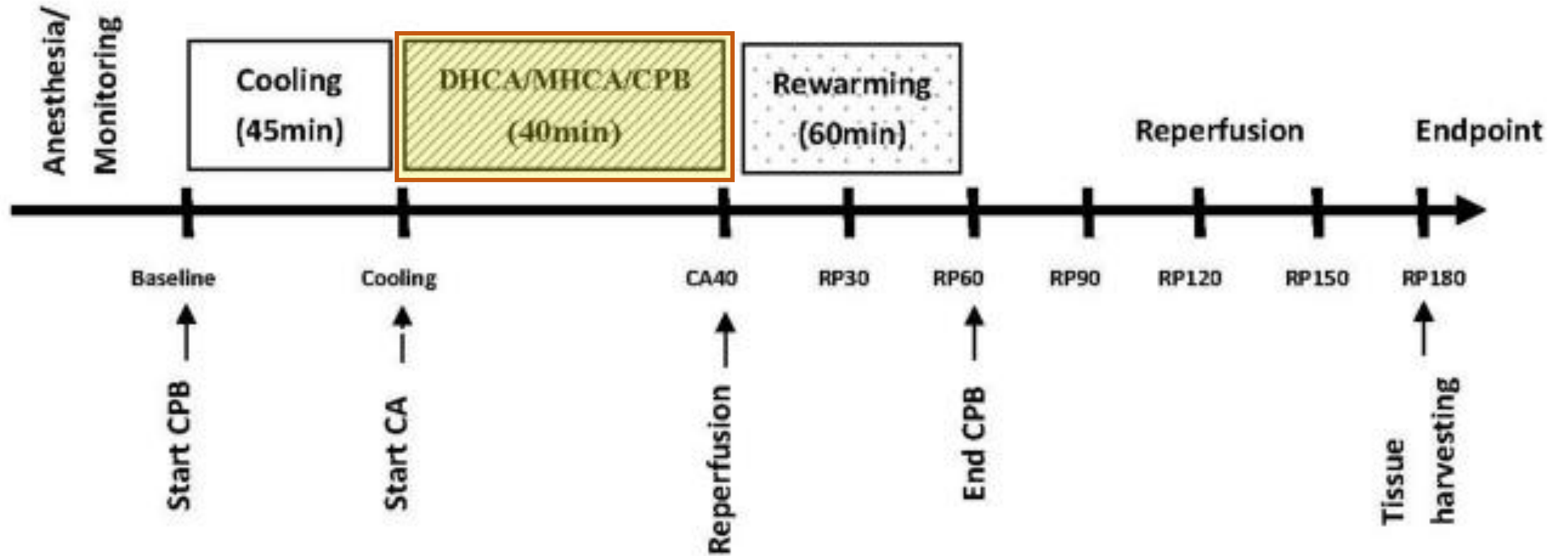
# Renal temperature reduction progressively favors mitochondrial ROS production over respiration in hypothermic kidney preservation

Koen D. W. Hendriks<sup>1,2\*†</sup>, Isabel M. A. Brüggewirth<sup>3†</sup>, Hanno Maassen<sup>2</sup>, Albert Gerding<sup>4</sup>, Barbara Bakker<sup>5</sup>, Robert J. Porte<sup>3</sup>, Robert H. Henning<sup>1</sup> and Henri G. D. Leuvenink<sup>2</sup>



RESEARCH ARTICLE

# Moderate Hypothermia Provides Better Protection of the Intestinal Barrier than Deep Hypothermia during Circulatory Arrest in a Diabetic Model: A Microdialysis Study



**Fig 1. Experimental protocol.** CA40, circulatory arrest for 40 min; RP30, reperfusion for 30 min; RP60, reperfusion for 60 min; RP 90, reperfusion for 90 min; RP 120, reperfusion for 120 min; RP 150, reperfusion for 150 min; and RP 180, reperfusion for 180 min.

doi:10.1371/journal.pone.0163684.g001

RESEARCH ARTICLE

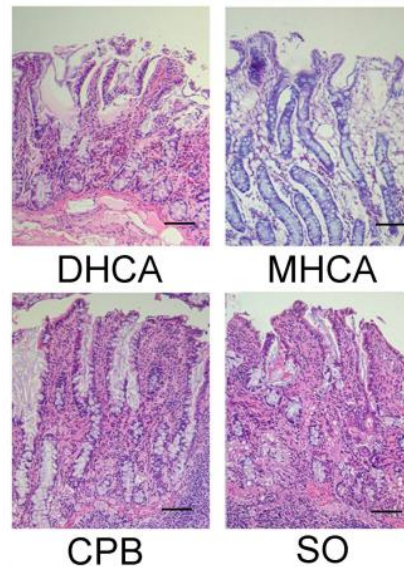
# Moderate Hypothermia Provides Better Protection of the Intestinal Barrier than Deep Hypothermia during Circulatory Arrest in a Piglet Model: A Microdialysis Study

Mengya Liang<sup>1</sup>\*, Kangni Feng<sup>1</sup>\*, Xiao Yang<sup>2</sup>\*, Guangxian Chen<sup>1</sup>, Zhixian Tang<sup>1</sup>, Weibin Lin<sup>1</sup>, Jian Rong<sup>3</sup>, Zhongkai Wu<sup>1</sup>\*

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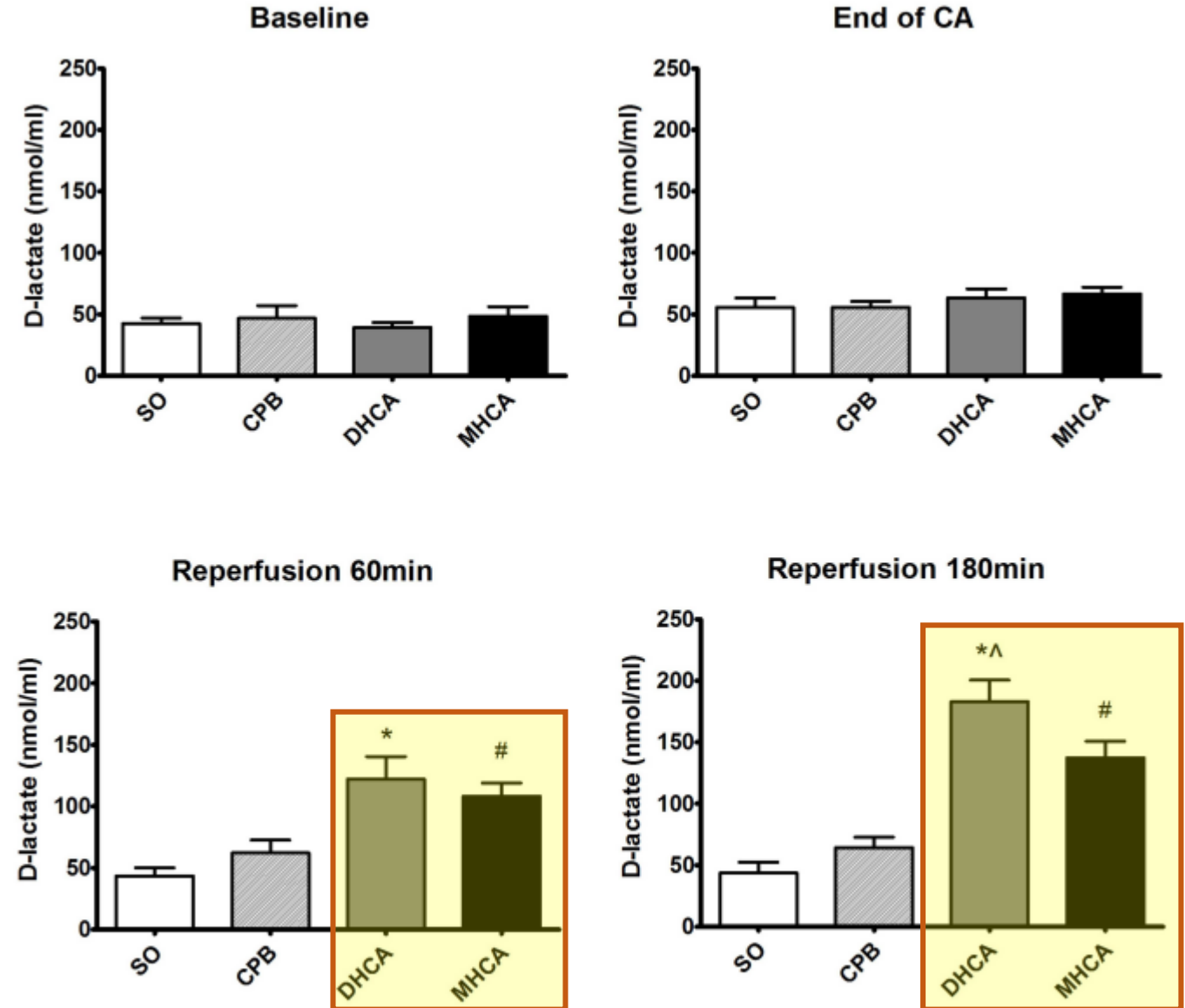
\* These authors contributed equally to this work.

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**Fig 2. Hematoxylin-eosin staining of the intestinal tissue.** The mucosal villi and glands were normal in the intestinal epithelia of the SO and CPB groups. Marked edema of the mucosal villi, increased gaps between the epithelial cells and inflammatory cell infiltration were observed in the MHCA and DHCA groups. Magnification: 100 folds; the scale bars indicate 100  $\mu$ m.

doi:10.1371/journal.pone.0163684.g002



**Fig 3. Serum D-lactate levels at 180 min of reperfusion.** SO, sham operation group; CPB, cardiopulmonary bypass group; DHCA, deep hypothermic circulatory arrest group; MHCA, moderate hypothermic circulatory arrest group. Mean  $\pm$  SD.  $n = 5$ . \* $P < 0.001$  DHCA vs. CPB ( $t = 7.330$  at 60 min of reperfusion and  $t = 15.32$  at 180 min of reperfusion); # $P < 0.001$  MHCA vs. CPB ( $t = 6.898$  at 60 min of reperfusion and  $t = 9.415$  at 180 min of reperfusion); and ^ $P < 0.05$  DHCA vs. MHCA ( $t = 5.515$  at 180 min of reperfusion).

doi:10.1371/journal.pone.0163684.g003





# Evolving Selective Cerebral Perfusion for Aortic Arch Replacement: High Flow Rate With Moderate Hypothermic Circulatory Arrest

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Table 4. Operative Variables

Variables	Group A	Group B	Group C	p Value
Cardiopulmonary bypass (min)	195 ± 41	197 ± 54	194 ± 50	0.97
Circulatory arrest (min)	67 ± 16	55 ± 12	51 ± 9	<0.0001
SCP (min)	133 ± 41	126 ± 28	131 ± 30	0.69
SCP flow (mL · kg <sup>-1</sup> · min <sup>-1</sup> )	9.1 ± 1.8	10.9 ± 3.3	19.0 ± 4.2	<0.001
Cooling (min)	27 ± 7	31 ± 10	36 ± 2	<0.001
Rewarming (min)	162 ± 38	147 ± 50	108 ± 42	<0.0001
Lowest blood temperature (°C)	16.0 ± 3.2	21.6 ± 2.7	25.9 ± 1.3	<0.0001
Transfusion (mL)	2430 ± 2270	3200 ± 2600	3160 ± 3300	0.39
Platelet transfusion (%)	45.9	63.6	33.3	0.028
Blood temperature at ICU admission (°C)	35.6 ± 0.8	36.1 ± 0.7	36.3 ± 0.7	0.0006
Lactate at ICU admission (mmol/L)	3.4 ± 1.7	2.7 ± 1.0	2.7 ± 1.1	0.026

ICU = intensive care unit; SCP = selective cerebral perfusion.

# Does moderate hypothermia really carry less bleeding risk than deep hypothermia for circulatory arrest? A propensity-matched comparison in hemiarch replacement

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## ABSTRACT

**Background:** Moderate (MHCA) versus deep (DHCA) hypothermic circulatory arrest in aortic arch surgery has been purported to reduce coagulation bleeding complications, although there are limited data supporting this. This study aimed to compare bleeding-related events after aortic replacement with MHCA versus DHCA.

**Methods:** Patients who underwent hemiarch replacement at a single institution from July 2005 to August 2014 were stratified into DHCA and MHCA (minimum systemic temperature  $\leq 20^{\circ}\text{C}$  and  $>20^{\circ}\text{C}$ , respectively) and then, 1:1 propensity matching was performed to adjust for baseline differences.

**Results:** During the study period, 571 patients underwent hemiarch replacement: 401 (70.2%) with DHCA and 170 (29.8%) with MHCA. After propensity matching, 155 patients remained in each group. There were no significant differences between matched groups with regard to the proportion transfused with packed red blood cells, plasma, platelet concentrates, or cryoprecipitate on the operative day, the need for reoperation for bleeding, or postoperative hematologic laboratory values. For patients who received plasma, the median transfusion volume was statistically significantly lower in the DHCA group (6 vs 5 units,  $P = .01$ ). MHCA also resulted in a slightly lower median volume of blood returned via cell saver (500 vs 472 mL,  $P < .05$ ) and lower 12-hour postoperative chest tube output (440 vs 350,  $P < .01$ ). Thirty-day mortality and morbidity did not differ significantly between groups.

**Conclusions:** MHCA compared with DHCA during hemiarch replacement slightly reduce perioperative blood-loss and plasma transfusion volume, although these differences do not translate into reduced reoperation for bleeding or postoperative mortality and morbidity. (J Thorac Cardiovasc Surg 2016;152:1559-69)

TABLE 3. Primary bleeding-related outcomes after propensity matching

Variable	Total (n = 310)	DHCA (n = 155)	MHCA (n = 155)	P value
Intraoperative PRBC				
Number of patients transfused (%)	208 (67.1%)	103 (66.5%)	105 (67.7%)	.90
Median (IQR) units among patients transfused	3 (2, 5)	3 (2, 5)	3 (2, 5)	.65
Intraoperative plasma				
Number of patients transfused (%)	281 (90.6%)	138 (89.0%)	143 (92.3%)	.44
Median (IQR) units among patients transfused	6 (4, 8)	6 (4, 9)	5 (4, 8)	.01
Intraoperative platelets				
Number of patients transfused (%)	271 (87.4%)	133 (85.8%)	138 (89.0%)	.49
Median (IQR) units among patients transfused	2 (2, 3)	2 (2, 3)	2 (2, 3)	.12
Intraoperative cryoprecipitate				
Number of patients transfused (%)	126 (40.6%)	57 (36.8%)	69 (44.5%)	.20
Median (IQR) units among patients transfused	1 (1, 1.75)	1 (1, 1)	1 (1, 2)	<.01
Cell saver, mL	500 (250, 718)	500 (250, 738)	472 (250, 700)	<.01
Intraoperative rFVIIa	86 (27.7%)	34 (21.9%)	52 (33.5%)	.03
Postoperative rFVIIa	13 (4.1%)	8 (5.2%)	5 (3.2%)	.57
12-h chest tube output, mL	400 (250, 699)	440 (300, 735)	360 (230, 633)	<.01
Reoperation for bleeding	10 (3.2%)	5 (3.2%)	5 (3.2%)	.99
Postoperative laboratory values				
Hemoglobin, g/dL	9.9 (9.3, 10.6)	9.9 (9.2, 10.6)	10.0 (9.4, 10.6)	.52
Platelets, $10^9/\text{L}$	145 (123, 172)	140 (120, 169)	147 (127, 173)	.09
INR	1.1 (0.9, 1.2)	1.1 (1.0, 1.2)	1.1 (0.9, 1.2)	.02
Partial thromboplastin time, s	28.5 (26.0, 32.2)	28.5 (25.8, 33.9)	28.6 (26.3, 31.4)	.51

Continuous variables are reported as median value (Q1, Q3). DHCA, Deep hypothermic circulatory arrest; MHCA, moderate hypothermic circulatory arrest; PRBCs, packed red blood cells; IQR, interquartile range; rFVIIa, recombinant activated factor VII; INR, international normalized ratio.

# Then, How long in MHCA?

## Distal Aortic Repair

Hypothermic arrest was obtained at tympanic and rectal temperatures less than **23°C** and less than 30°C, respectively, and then the ascending aorta and aortic arch were opened and assessed. If the entry tear in the hemiarch was excisable or a partial arch aortic replacement was needed, the inside and outside of the distal aorta were reinforced with Teflon felt. We do not use surgical adjuncts inside the distal false lumen to avoid the risk of distal organ embolization. When excision of the entry tear in the hemiarch or partial arch replacement was impossible, TAR proceeded using a tetra-furcated branched graft and the elephant trunk technique with another 18- or 20-mm Dacron graft. Our method of protecting the brain shifted from retrograde to antegrade cerebral perfusion during 2002. The details of brain protection during TAR have been reported.<sup>12-14</sup> Open distal anastomosis proceeded using a 4-0 polypropylene suture with external Teflon felt reinforcement. Another 7- to 10-cm-long graft with a diameter of 18 or 20 mm was applied to the descending aorta during the elephant trunk technique. Teflon felt outside the adventitia was fixed by three 4-0 polypropylene sutures and reapproximation using running sutures. After completion of the distal anastomosis, lower-body circulation was reinstituted through 1 branch of the tetra-furcated graft, the patient was warmed, and the graft was anastomosed to the proximal aortic stump. Blood flow to the heart was then restored, and the left subclavian, left cervical, and innominate arteries of the aortic arch were sequentially reconstructed.

**TABLE 2. Intraoperative data**

Variable	Overall n = 197	TAR n = 88	Non-TAR n = 109	P value*
Entry site				
Aortic root sinotubular junction	9 (4.6)	4 (4.5)	5 (5.2)	.77
Ascending	85 (43.1)	17 (19.3)	68 (62.4)	<.01
Ascending aortic arch	53 (26.9)	26 (29.5)	27 (24.8)	.45
Distal arch	27 (13.7)	27 (30.7)	0	<.01
Unknown	23 (11.7)	14 (15.9)	9 (8.3)	.15
CPB duration	212 ± 83	244 ± 88	187 ± 71	<.01
Cardiac ischemic time	119 ± 46	135 ± 50	107 ± 39	<.01
Antegrade cerebral perfusion	147 (74.6)	86 (97.7)	61 (56.0)	<.01
Antegrade cerebral perfusion duration	92.8 ± 52.4	<b>124.0 ± 42.5</b>	48.1 ± 26.6	<.01



# SUMMARY

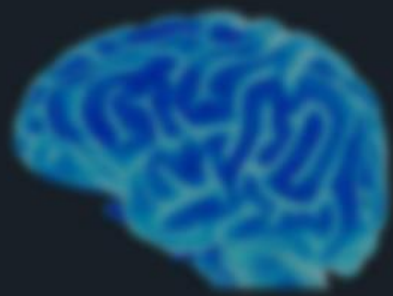
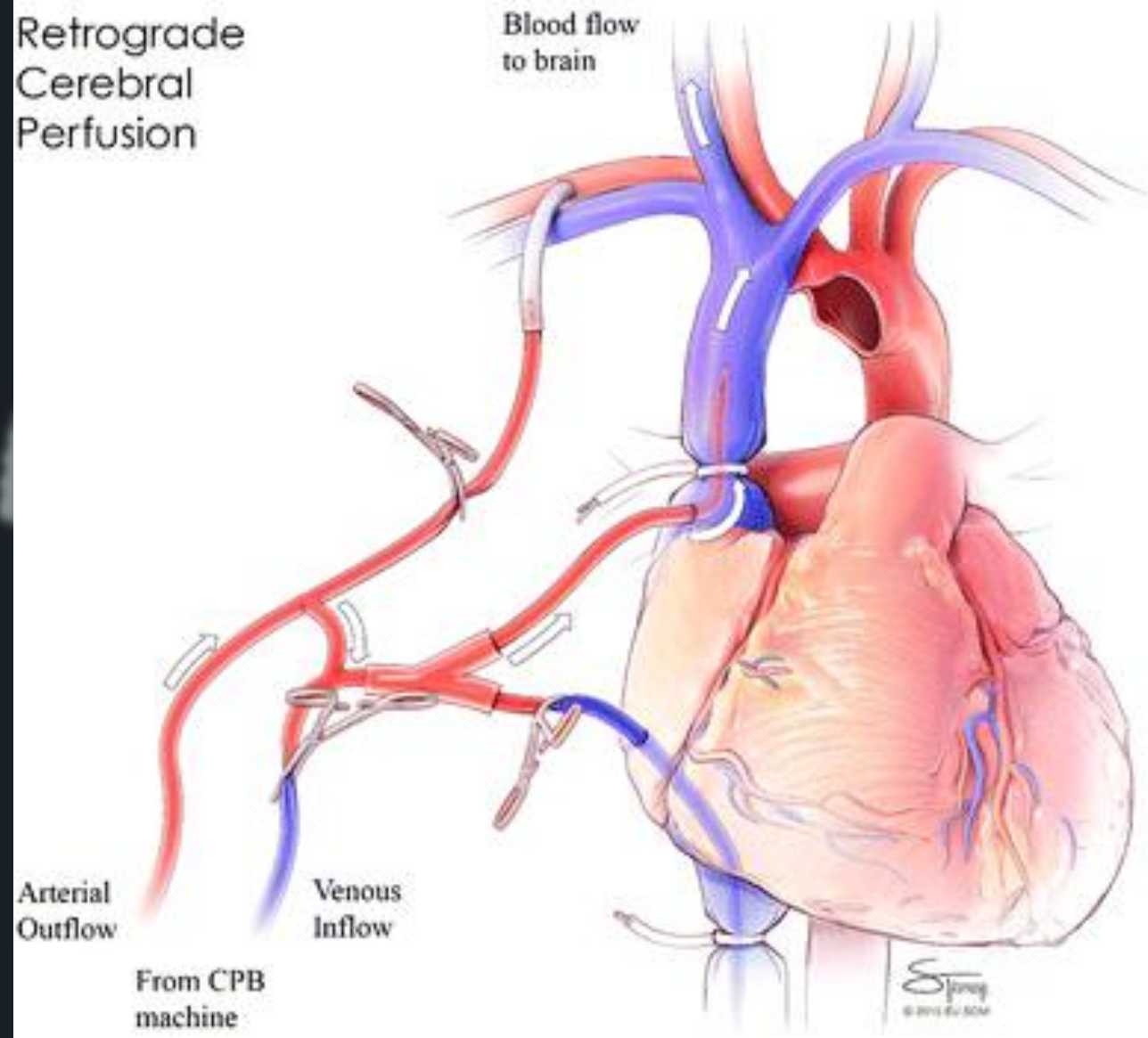


Table 1 Calculated safe intervals for interruption of brain perfusion at various temperatures

Temperature (°C)	Cerebral rate (%)
37	5

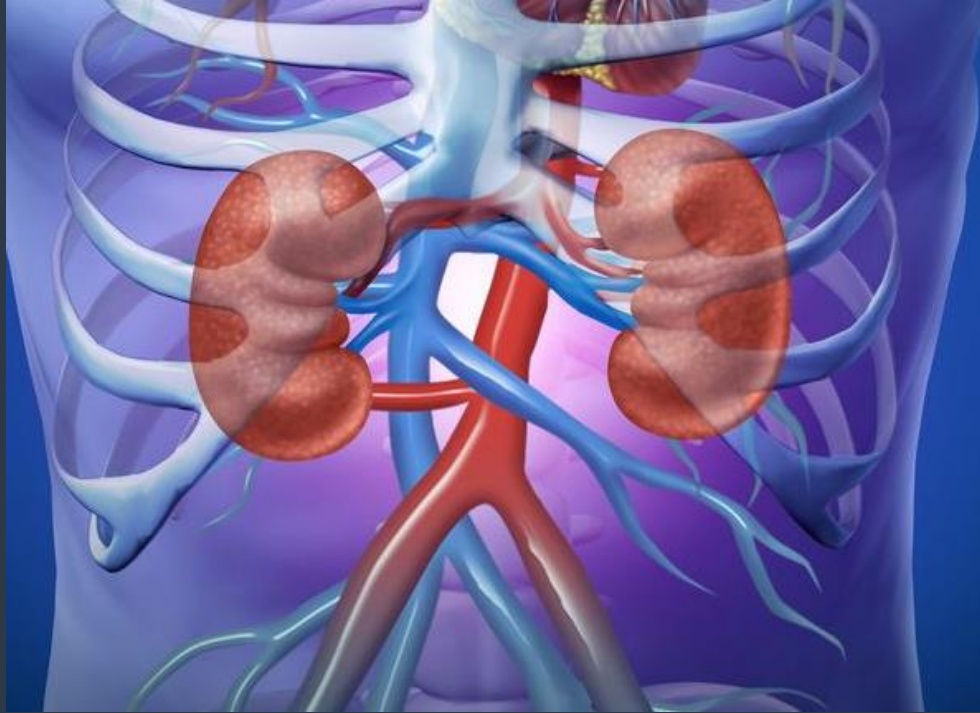
## Retrograde Cerebral Perfusion



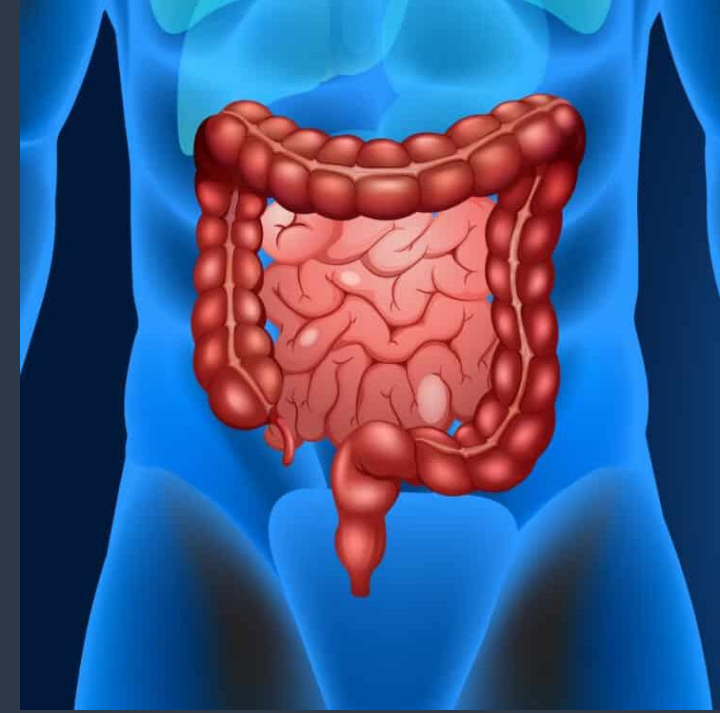
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# Summary



**Normothermia  
<30 min!!!**



**Moderate Hypothermia  
<100 min!!!**



