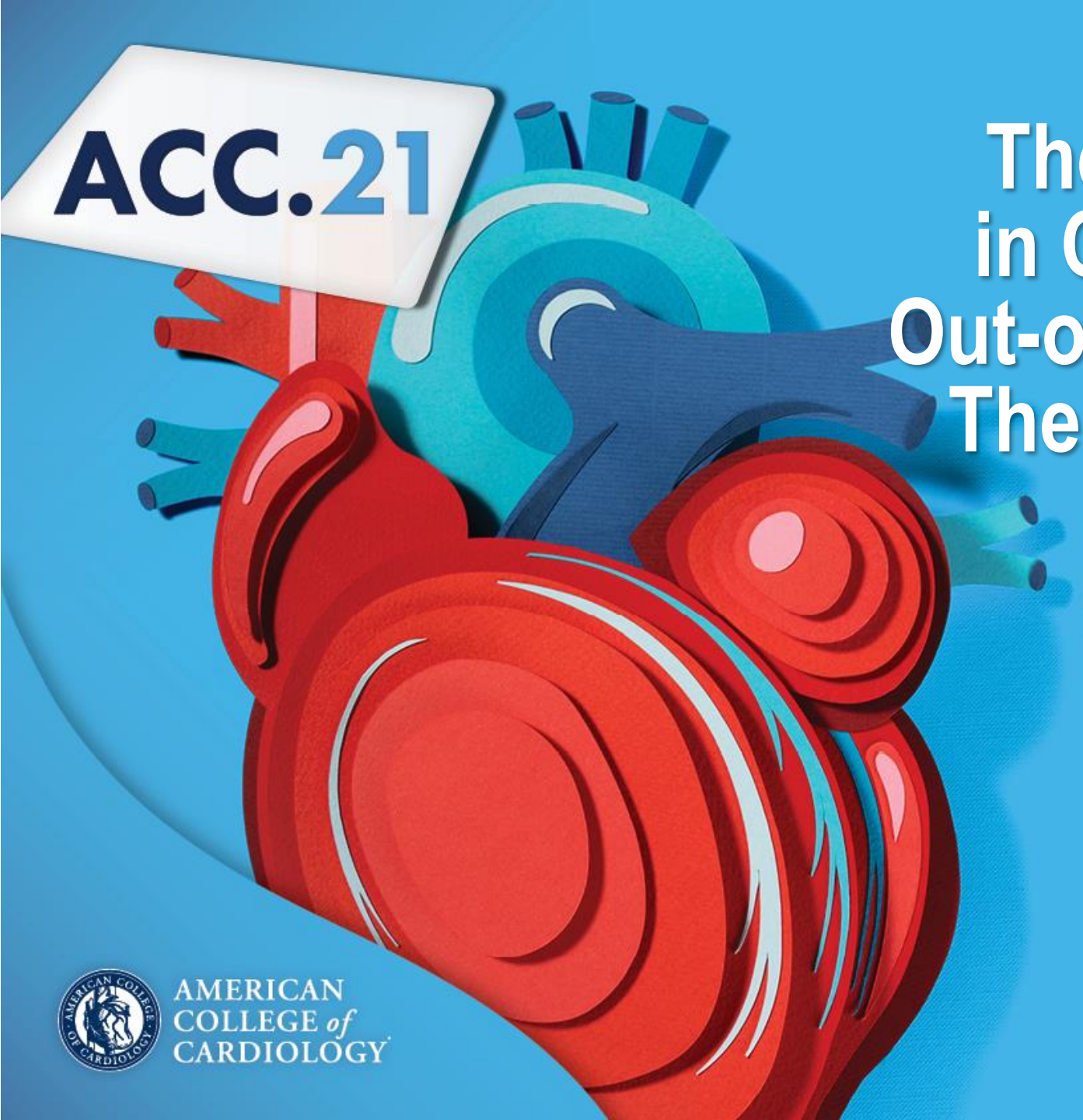


Moderate vs Mild Therapeutic Hypothermia in Comatose Survivors of Out-of-Hospital Cardiac Arrest The CAPITAL-CHILL TRIAL

Michel Le May MD

University of Ottawa Heart Institute,
Ottawa, Ontario,
Canada.

@michelrlemay

AMERICAN COLLEGE of CARDIOLOGY

CAPITAL-CHILL TRIAL

Investigators:

Michel Le May, M.D.[1], Christina Osborne, B.Sc. [1], Juan Russo, M.D.[1], Derek So, M.D.[1], Aun Yeong Chong, M.D.[1], Alexander Dick, M.D.[1], Michael Froeschl, M.D.[1], Christopher Glover, M.D.[1], Benjamin Hibbert, M.D.[1], Jean-François Marquis, M.D.[1], Sophie De roock, M.D [1], Marino Labinaz, M.D.[1], Jordan Bernick, M.Sc.[1], Shawn Marshall, M.D.[2], Ronnen Maze, M.D.[1] , George Wells, Ph.D.[1]

Affiliations:

[1] University of Ottawa Heart Institute, Ottawa, Ontario, Canada

[2] University of Ottawa, The Ottawa Hospital, Ottawa, Ontario, Canada

ClinicalTrials.gov, NCT02011568

Background

- Comatose survivors of OHCA continue to experience high rates of death and severe neurologic injury
- Current guidelines recommend TTM ranging from 32°C to 36°C for 24 hrs
- Optimal target temperature remains unclear.
- Studies have suggested that moderate therapeutic hypothermia (28°C and 32°C) could improve clinical outcomes[1]

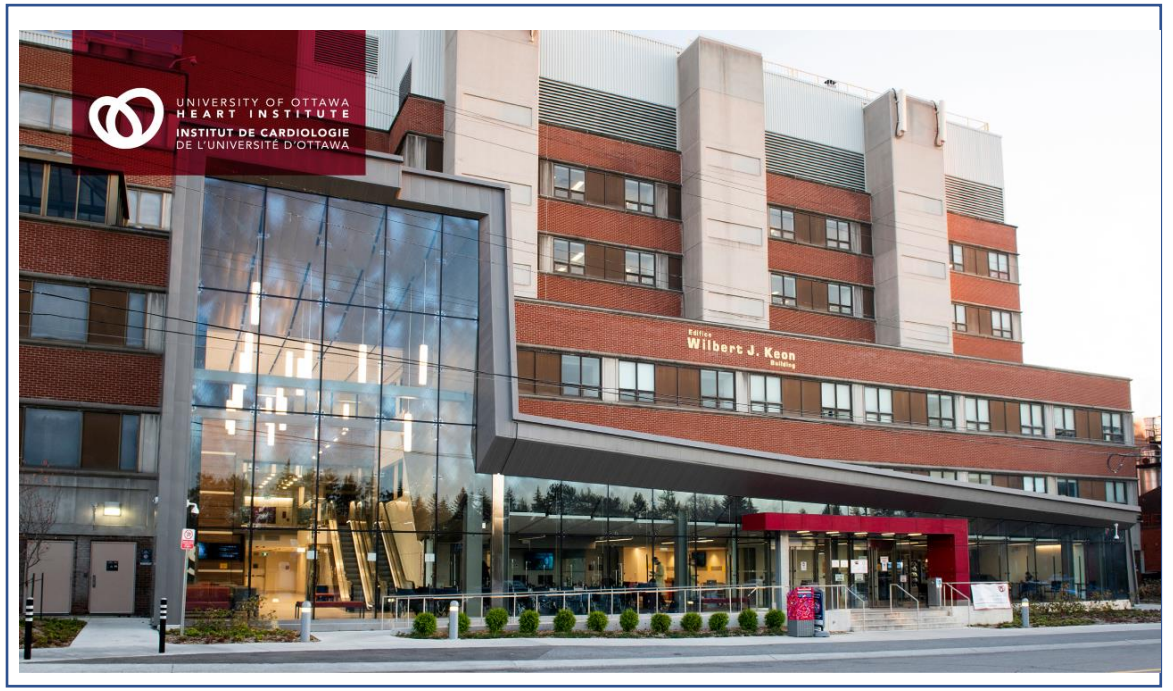
[1]Lopez-de-Sa E, Circulation 2012;126(24):2826-2833.

Objective

CAPITAL CHILL trial was designed to assess whether moderate hypothermia (target temperature of 31°C), as compared with mild hypothermia (target temperature of 34°C), improves clinical outcomes in comatose survivors of out-of-hospital cardiac arrest.

CAPITAL- CHILL

- Pts randomized between August 2013 and March 2020
- Investigator-driven, single-center, prospective, randomized, double blind trial
- Funded by the University of Ottawa Heart Institute Cardiac Arrest Program



The University of Ottawa Heart Institute

Target Temperature Intervention

Target Temp. 31 ℃

72 Hour Time Period		
24 Hours	48 Hours	
Target Temp. Period	Rewarming Period	Maintenance Period
24 hours at target temperature	24 hours	Normothermia Remaining time - approx. 24 hours

Target Temp Reached 31ºC

Rewarming Begins

37ºC Reached

Process Complete

Target Temp. 34 ℃

60 Hour Time Period		
24 Hours	36 Hours	
Target Temp. Period	Rewarming Period	Maintenance Period
24 hours at target temperature	12 hours	Normothermia Remaining time - approx. 24 hours

Target Temp Reached 34ºC

Rewarming Begins

37ºC Reached

Process Complete

Inclusion Criteria

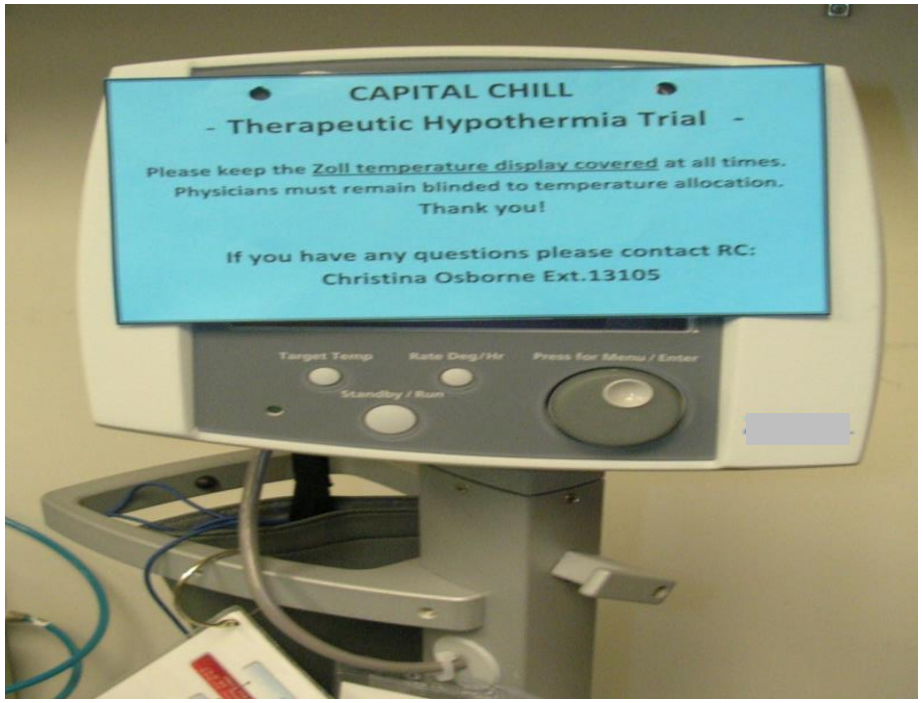
- Out-of-hospital cardiac arrest
- 18 years of age or older
- Unconscious (Glasgow Coma Score of ≤ 8}
- Irrespective of initial rhythm at the time of the cardiac arrest
- Presumed cardiac cause for the arrest

Exclusion Criteria

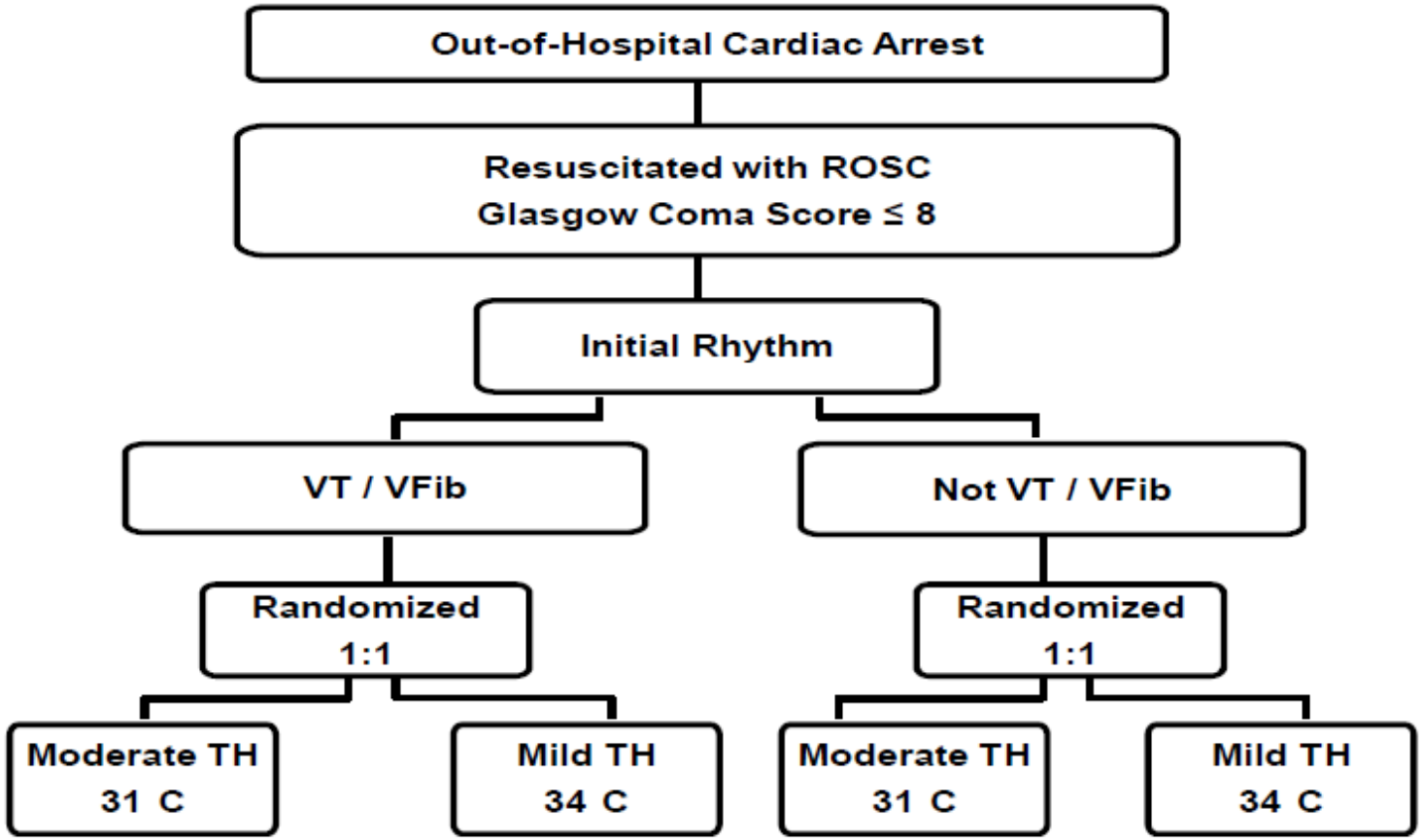
- Known inability to perform activities of daily living
- Known Intracranial bleed
- Severe coagulopathy with clinical evidence of major bleeding
- Coma not attributable to the cardiac arrest,
- Life expectancy of less than one year
- Endovascular cooling device not available

Methods

- Endovascular cooling device used
- Early coronary angiography
- Double blind:
  - Shields over monitors to hide temperature readings
  - Only Nurses aware of temperature assignment and responsible for managing the cooling catheter
  - Separate charting of temperatures



Study Design



Primary Outcome

All cause mortality or poor neurological outcome at 180 days

Neurologic outcome was assessed using the Disability Ratings Scale (DRS), an ordinal scale that evaluates functional dependence[1]

DRS ranges from 0 (no disability) to 29 (extreme vegetative)

Poor neurologic outcome was taken as a DRS score of >5

[1]Gouvier WD, et al. Arch Phys Med Rehabil 1987;68(2):94-97.

Key Secondary Outcomes

- Mortality
- DRS
- Modified Rankin Score
- Stroke
- Seizure
- Stent thrombosis
- Bleeding
- Pneumonia
- Renal replacement therapy
- LOS in the unit
- LOS in the hospital

Sample size

- Expected rate of the primary outcome of 50% in the 34ºC group based on available studies.[1-3]
- Sample size of 340 pts required to detect a 30% relative risk reduction with 80% power and a type I error of 5%.[1,2]
- Sample size increased to 360 pts (180 per group) to account for a potential crossover rate of 3%. Minimal loss to follow-up was expected.

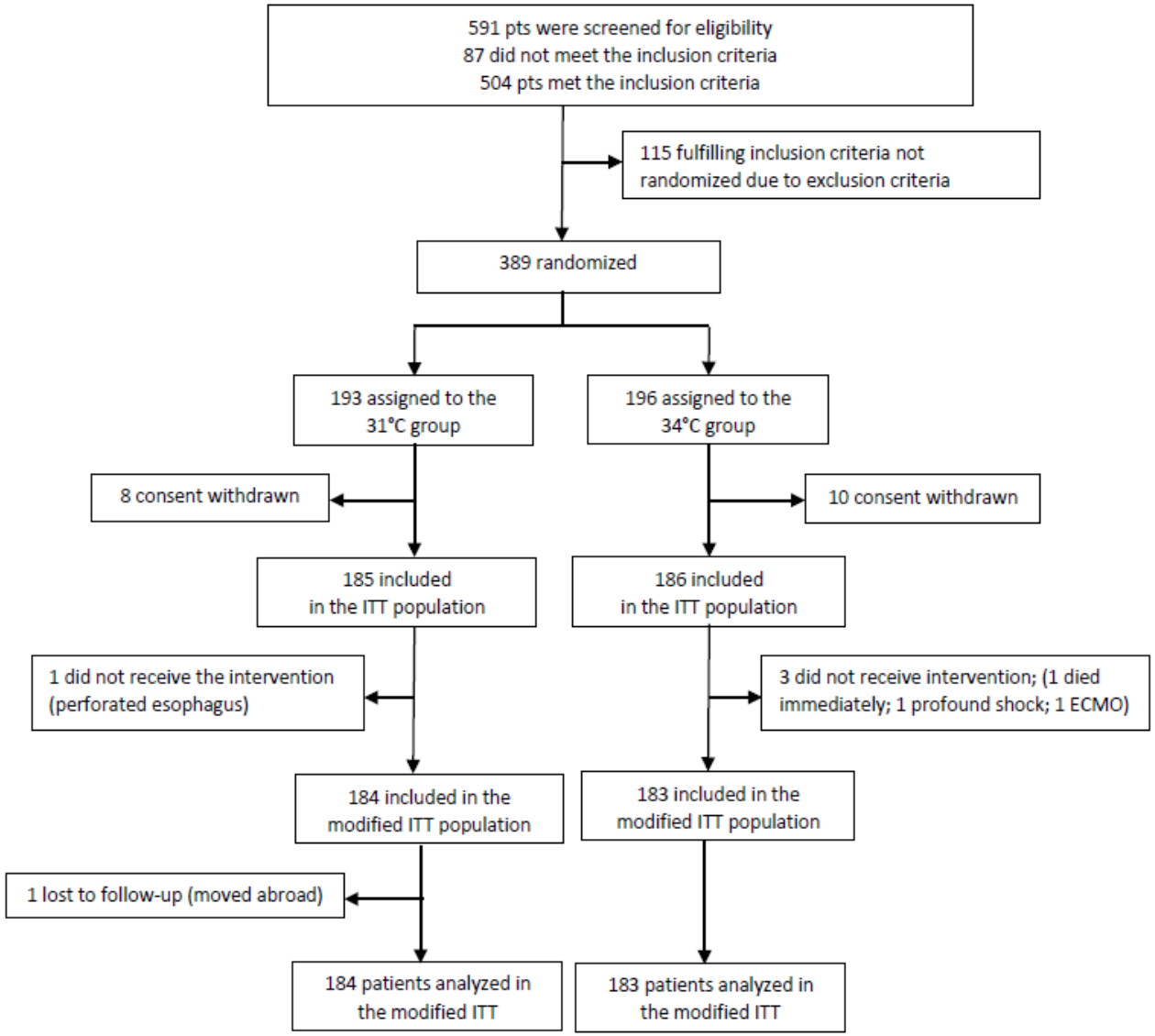
[1] NEJM 2002;346(8):549-556.
[2] Bernard SA, et al. NEJM 2002;346(8):557-563
[3] Mooney MR, et al. Circulation 2011;124(2):206-214.

Adjudication Committee

Blinded members adjudicated on

- Primary outcome
- Stroke
- Stent thrombosis
- Seizure

Patient Flow Diagram



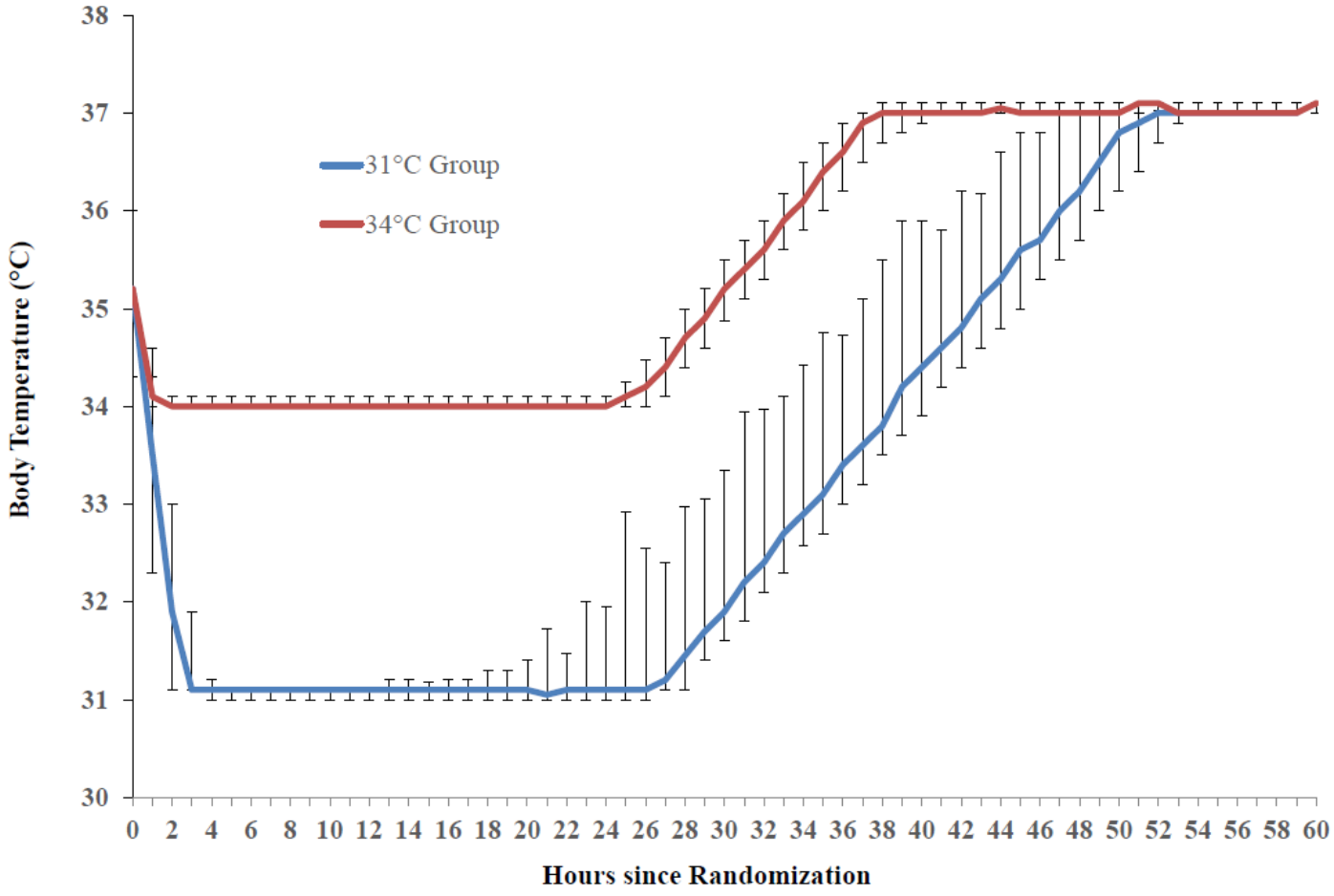
Baseline Characteristics

	31ºC Group (N=184)	34ºC Group (N=183)
Age, mean ± SD, y	61 ± 14	62. ± 13
Male sex	83%	80%
Bystander witnessed	85%	83%
Bystander-performed CPR	69%	68%
Shockable Rhythm	86%	86%
Lactates, mmol/L	4.6 ± 3.4	4.4 ± 3.8
Inotropes/ Pressor agents	43%	42%
STEMI	35%	40%
GCS, median (IQR)	3 (3-3)	3 (3-3)
Arrest to ROSC, min, median, (IQR)	23 (15-35)	20 (14-31)
Arrest to randomization, min, median, (IQR)	228 (167-313)	204 (146-297)

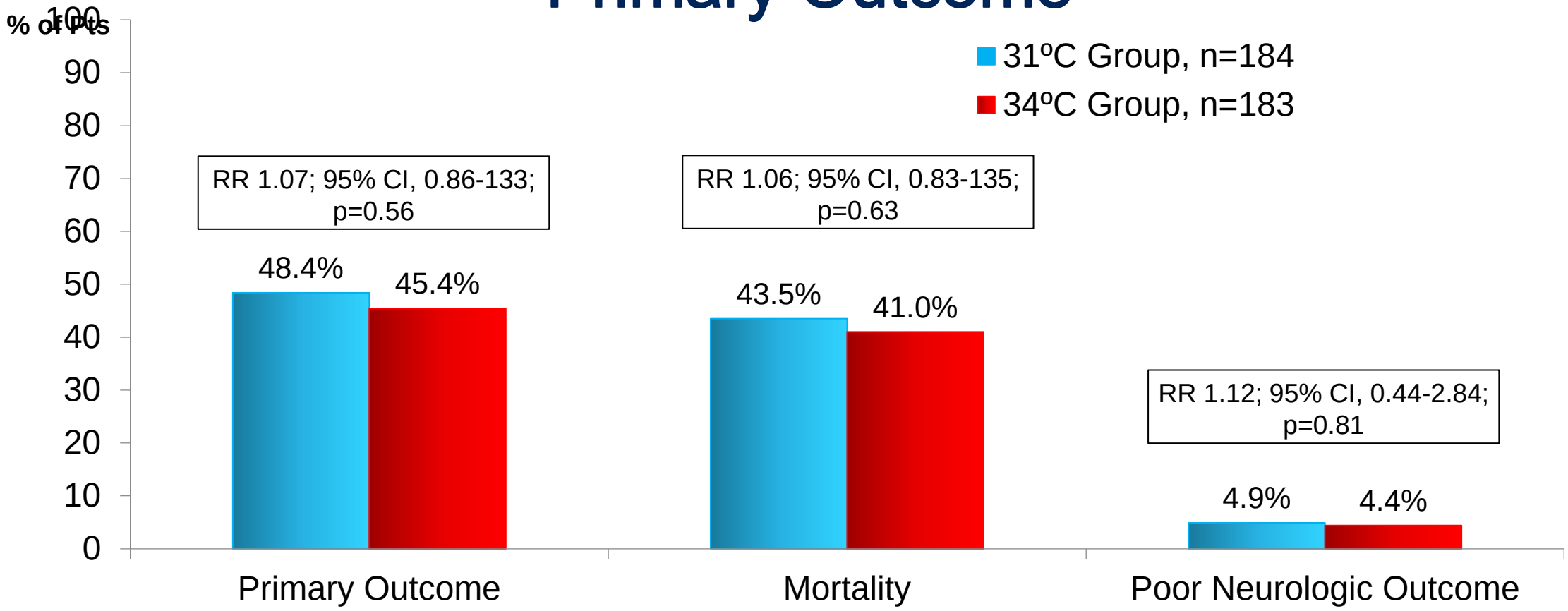
Interventions

	31°C Group (N=184)	34°C Group (N=183)
Coronary angiography	97%	97%
PCI performed	57%	59%
Stenting performed	52%	53%
Intra-aortic balloon pump	6%	11%
Arrival at cardiac center to balloon inflation—median (IQR), min	73 (46-107)	60 (43-104)
Contrast Volume, ml	203 ± 100	192 ± 100

Median Temperatures and IQRs

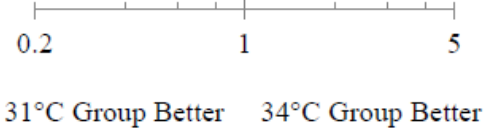


Death or Poor Neurologic Outcome at 180 days
Primary Outcome

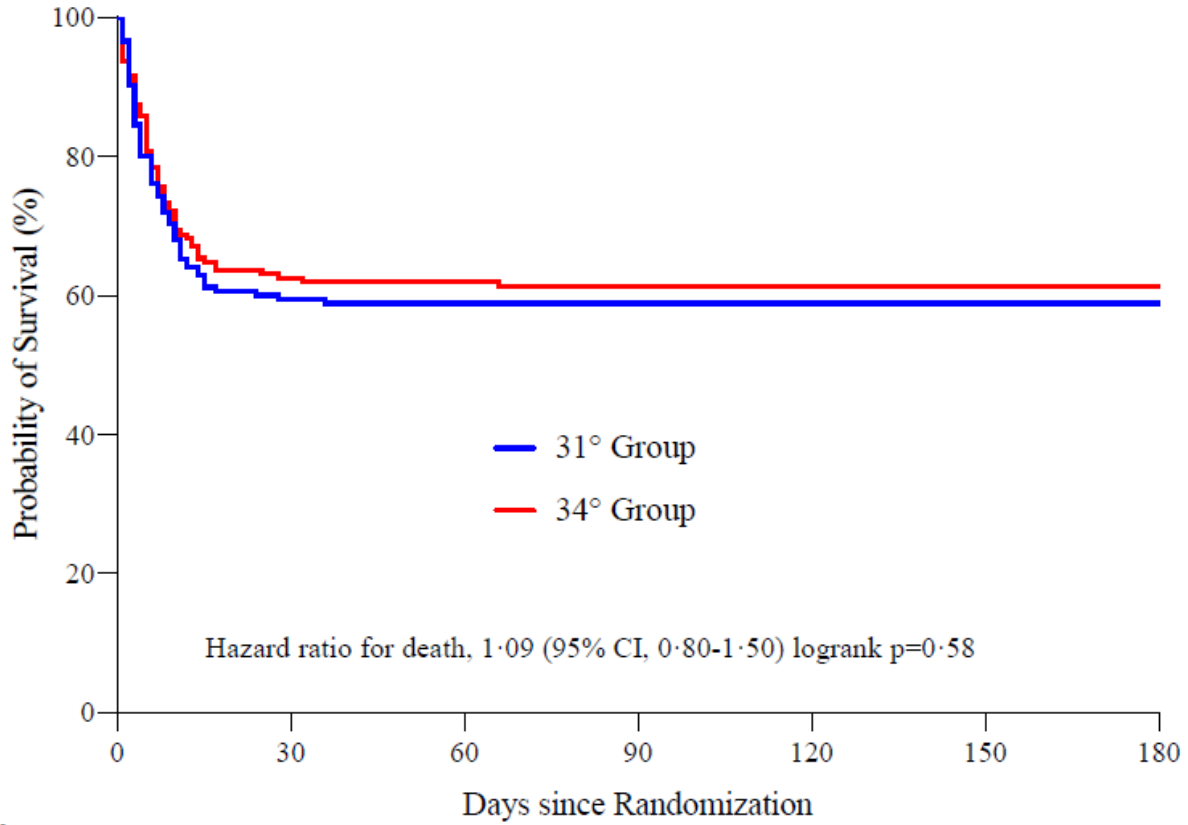


Subgroup Analysis on Primary Outcome

Subgroup	31°C Group total no. of events	34°C Group total no. of patients	RR (95% CI)	Interaction p value
All Patients	89 / 184	83 / 183	1·07 (0·86 - 1·33)	0·56
Age				
<75 yr	64 / 151	63 / 151	1·02 (0·78 - 1·32)	0·41
≥75 yr	25 / 33	20 / 32	1·21 (0·87 - 1·68)	
Sex				
Male	75 / 152	62 / 146	1·16 (0·91 - 1·49)	0·13
Female	14 / 32	21 / 37	0·77 (0·48 - 1·25)	
Initial rhythm				
Shockable	68 /158	59 / 157	1·15 (0·87 - 1·50)	0·12
Nonshockable	21 / 26	24 / 26	0·88 (0·70 -1·09)	
STEMI				
No	58 / 120	54 / 110	0·98 (0·76 - 1·28)	0·37
Yes	31 / 64	29 / 73	1·22 (0·83 - 1·78)	
PCI within 12 hours				
No	38 / 80	40 / 76	0·90 (0·66 - 1·23)	0·17
Yes	51 / 104	43 / 107	1·22 (0·90 - 1·65)	



KM Curves for Survival at 180 days



No. at Risk							
31° Group	184	104	103	103	103	103	103
34° Group	183	110	109	108	108	108	108

Neuro Scores at 180 days

DRS Scores*

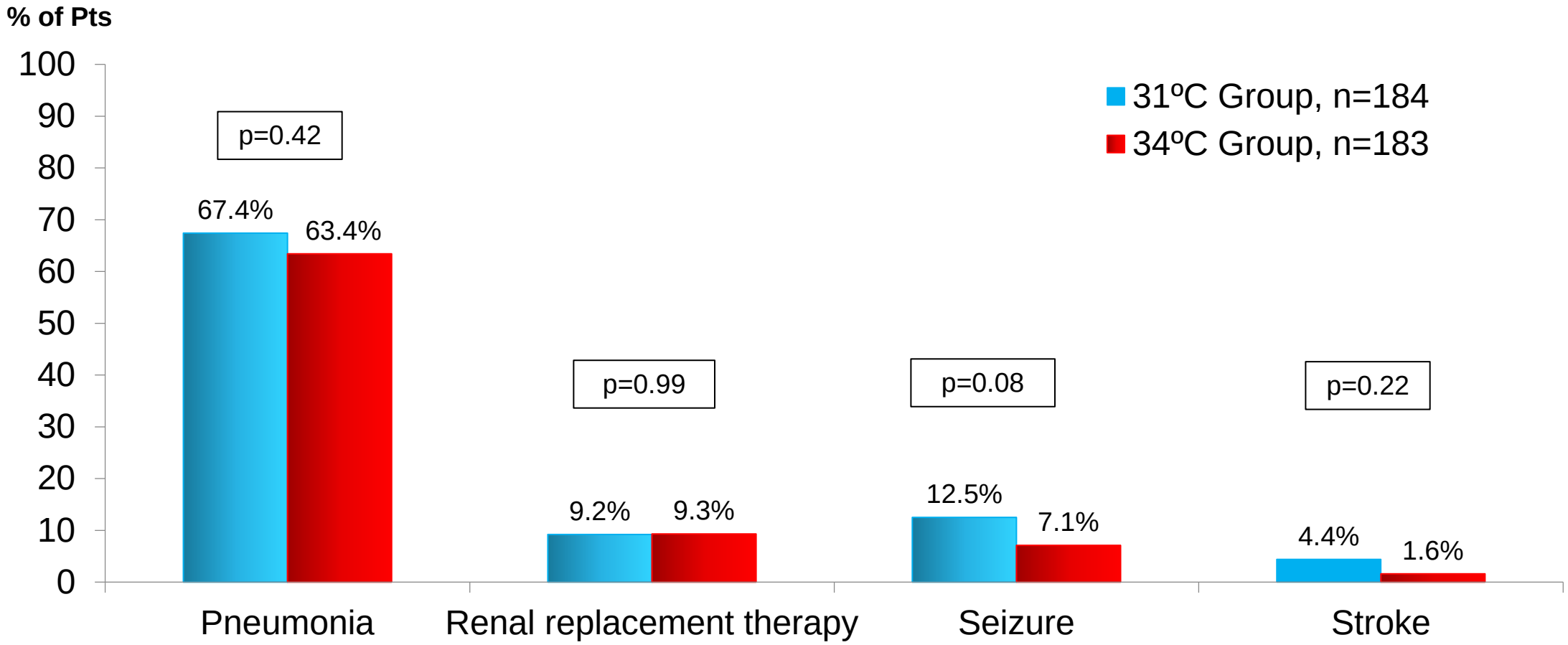
	31ºC Group (n=104)	34ºC Group (n=108)	P Value
>5	9%	8%	0.80
0-5	91%	93%	0·98
6-10	5%	5%	
11-15	1%	1%	
16-20	1%	0	
21-29	2%	2%	

*DRS assessed only in survivors;
†On MRS, 6 = death

Modified Rankin Scale Scores

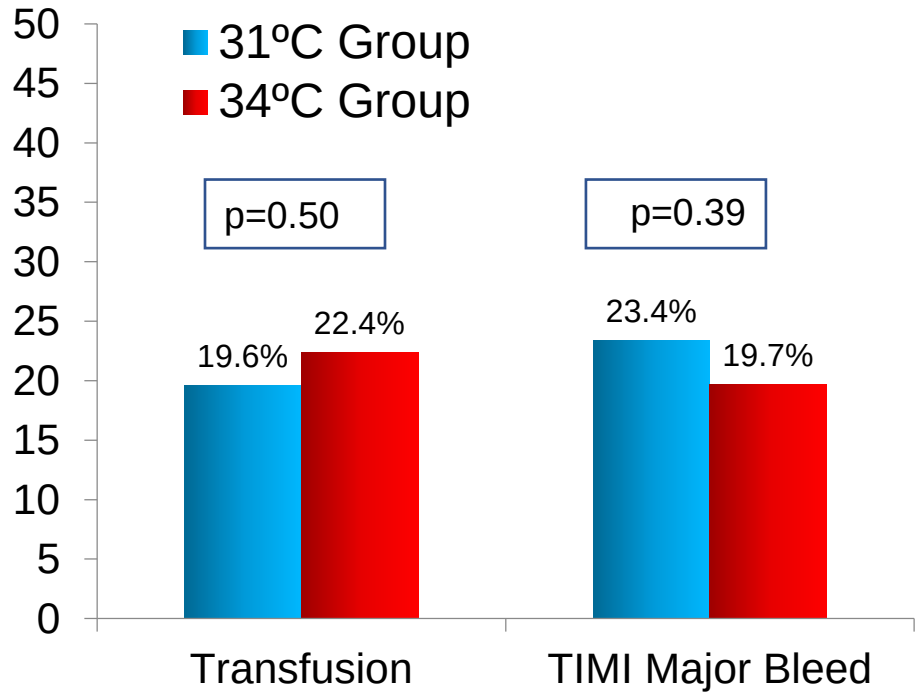
	31ºC Group (n=184)	34ºC Group (n=184)	P Value
4-6†	46%	44%	0.71
0	35%	37%	0.99
1	11%	12%	
2	4%	3%	
3	4%	4%	
4	1%	1%	
5	2%	2%	
6	44%	41%	

Key Secondary Outcomes

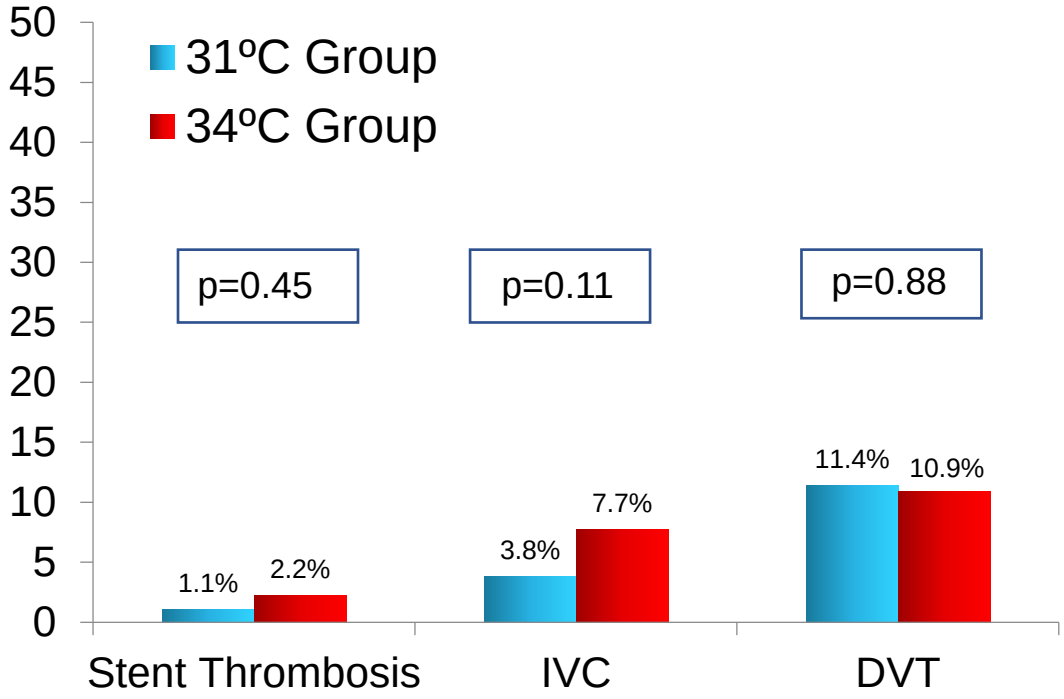


Bleeding vs Thrombosis

Bleeding



Thrombosis



Length of Stay

	31ºC Group (N=184)	34ºC Group (N=183)	p value
Length of stay in cardiac intensive care unit, days; median (IQR)	10 (7-15)	7 (6-12)	0.004
Length of stay in cardiac center, days; median (IQR)	22 (16-30)	20 (13-36)	0.27

Conclusion

- First randomized controlled trial to evaluate the benefits of therapeutic hypothermia with a target temperature below 32ºC
- In comatose survivors of out-of-hospital cardiac arrest, a target temperature of 31ºC did not reduce the rate of death or poor neurologic outcome at 180 days compared to a target temperature of 34ºC.

Acknowledgment

CICU nurses /staff
Cath lab nurses/staff
Coordinators
Cardiology residents
Adjudication committee
Members of DSMB