

## SUPPLEMENTAL DIGITAL CONTENT

### **Effect of Inhaled Xenon on Cardiac Function in Comatose Survivors of Out-of-hospital Cardiac Arrest – a substudy of the Xe-Hypotheca trial**

Antti Saraste\*, MD, PhD<sup>1</sup>, Haitham Ballo\*, MD<sup>1</sup>, Olli Arola, MD<sup>2</sup>, Ruut Laitio, MD; PhD<sup>2</sup>, Juhani Airaksinen, MD, PhD<sup>1</sup>, Marja Hynninen, MD, PhD<sup>3</sup>, Minna Bäcklund, MD, PhD<sup>3</sup>, Emmi Ylikoski, MD, PhD<sup>3</sup>, Johanna Wennervirta, MD, PhD<sup>3</sup>, Mikko Pietilä, MD, PhD<sup>1</sup>, Risto O. Roine, MD, PhD<sup>4</sup>, Veli-Pekka Harjola, MD, PhD<sup>5</sup>, Jussi Niiranen, MD<sup>6</sup>, Kirsi Korpi, MD<sup>6</sup>; Marjut Varpula, MD, PhD<sup>6</sup>, Harry Scheinin, MD, PhD<sup>2</sup>, Mervyn Maze, MB, ChB<sup>7</sup>, Tero Vahlberg, MSc<sup>8</sup>, Timo Laitio, MD, PhD<sup>2</sup>,  
for the Xe-HYPOTHECA Study Group

Supplemental Digital Content Table 1. Inclusion and Exclusion criteria

Supplemental Digital Content Figure 1. Study flowchart

Supplemental Digital Content Table 2. Clinical characteristics of patients enrolled in the Xe-HYPOTHECA main study only vs. echo substudy

Supplemental Digital Content Table 3. Hemodynamics on admission, during hypothermia and 24 ± 4 hours after rewarming.

Supplemental Digital Content Figure 2. Echocardiographic assessments of left ventricle ejection fraction and systolic longitudinal strain on admission and 24 hours after rewarming.

Supplemental Digital Content Table 1. Inclusion and exclusion criteria

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**Inclusion criteria**

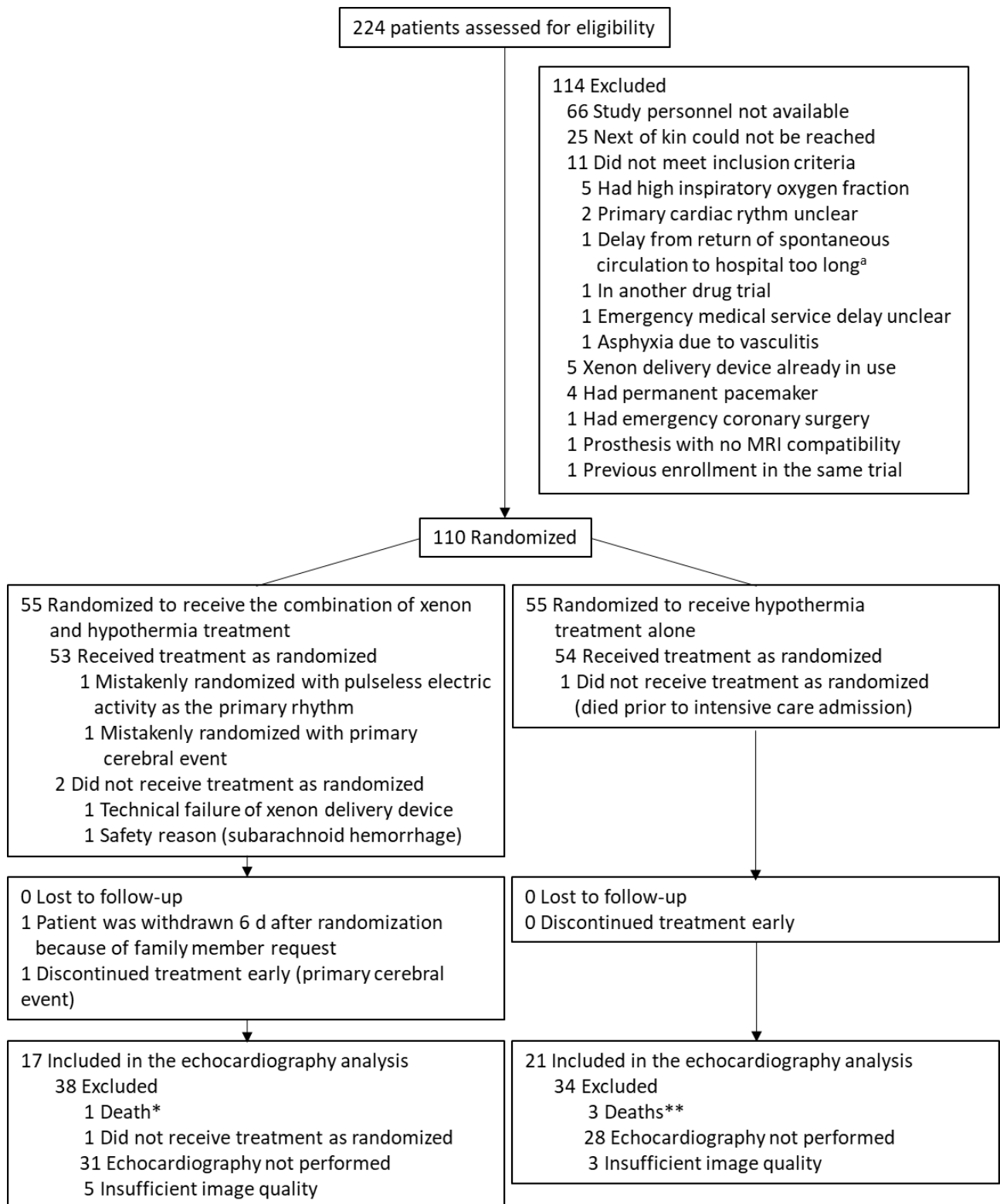
Witnessed cardiac arrest  
Ventricular fibrillation or  
Non-perfusing ventricular tachycardia  
Presumed cardiac origin  
Age 18-80 years  
Start of resuscitation by emergency medical personnel within 15 minutes  
Return of spontaneous circulation in 45 minutes  
Decision of therapeutic hypothermia treatment by attending physician

**Exclusion criteria**

Hypothermia (<30 oC core temperature)  
Unconsciousness before collapse (cerebral trauma, intoxication etc.)  
Computed tomography scan indicating cerebral pathological reason for the cardiac arrest  
Responding verbal commands after return of spontaneous circulation  
Pregnancy  
Coagulopathy  
Terminal phase of chronic disease  
Systolic arterial pressure less than 80 mmHg lasting >30 minutes after return of spontaneous circulation  
Mean arterial pressure less than 60 mmHg lastin > 30 minutes after return of spontaneous circulation  
Hypoxemia (arterial oxygen saturation <85%) lasting >15 minutes after return of spontaneous circulation  
Factors making participation in follow-up implausible  
Enrolment in another interventional trial

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Supplemental Digital Content Figure 1. Study flowchart



\*early termination of hypothermia treatment due to severe hypotension and multiple organ failure, \*\*1 withdrawal from life-sustaining treatment at 58 hours, 1 death at 3 hours, and 1 death at 51 hours after out-of-hospital cardiac arrest

Supplemental Digital Content Table 2. Clinical characteristics of patients enrolled in the Xe-HYPOTHECA main study only vs. echo substudy

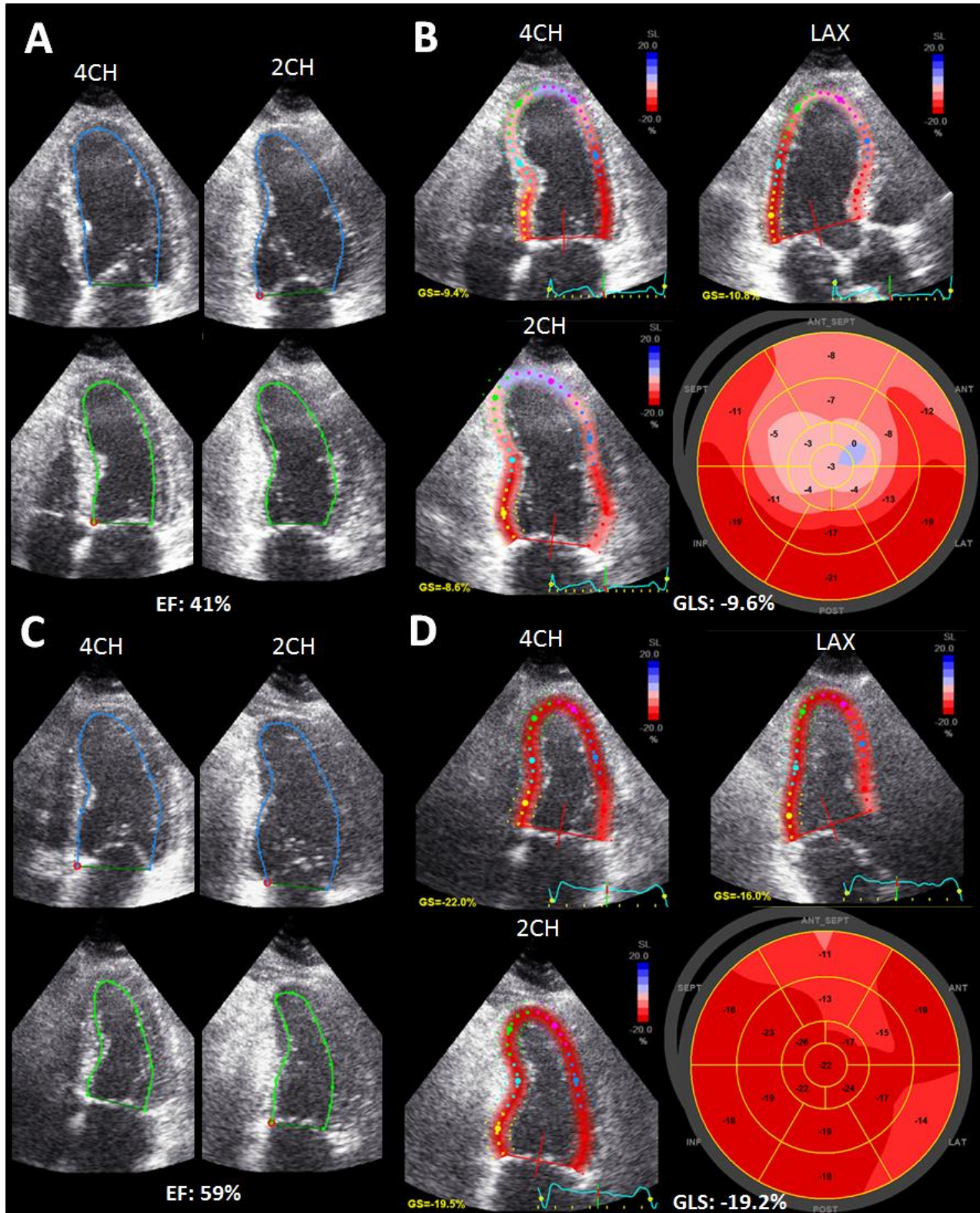
	Main study (n=72)	Echo substudy (n=38)	p-value
Age (years)	60 (11)	59 (12)	0.56
Male	52 (72%)	28 (74%)	0.87
Hypertension	32 (44%)	16 (42%)	0.81
Congestive heart failure	8 (11%)	2 (5%)	0.49
Diabetes	16 (22%)	1 (3%)	0.007
Dyslipidemia	28 (39%)	10 (26%)	0.19
Kidney dysfunction	22 (31%)	15 (39%)	0.35
Smoker	69 (96%)	37 (97%)	0.06
<b>Medication</b>			
Beta-blocker	23 (32%)	6 (16%)	0.06
ACE inhibitor/ARB	26 (36%)	10 (26%)	0.28
Calcium-channel blocker	13 (18%)	6 (16%)	0.74
Diuretics	10 (14%)	1 (3%)	0.09
Antiplatelet/anticoagulation	24 (33%)	10 (26%)	0.42
Statin	21 (29%)	7 (18%)	0.19
<b>Resuscitation</b>			
Bystander resuscitation	50 (69%)	27 (38%)	0.86
Emergency medical service delay (min)	8 (3)	9 (3)	0.04
Return of spontaneous circulation (min)	23 (8)	21 (6)	0.40
No-flow (min), median (IQR)	0 (5)	0 (6)	0.72
<b>Cooling</b>			
Core temperature prior start of cooling (°C)	35.1 (1.2)	35.0 (1.3)	0.67
Time from OHCA to target temperature (min), median (IQR)	295 (116)	316 (99)	0.24
Time from OHCA to initiation of xenon (min), median (IQR)	251 (72)	244 (71)	0.91
Previous CABG	6 (8%)	3 (8%)	1.00
Coronary artery disease	46 (64%)	32 (84%)	0.01
Number of diseased vessels			0.07
1-vessel disease	14 (30%)	15 (47%)	
2-vessel disease	12 (26%)	7 (22%)	
3-vessel disease	14 (30%)	6 (19%)	
STEMI	22 (31%)	15 (39%)	0.35
PCI on admission	16 (22%)	17 (45%)	0.01
<b>Troponin-T (ug/L), median (IQR)</b>			
Admission	0.09 (0.23)	0.08 (0.20)	0.77
72 h after OHCA	0.39 (1.54)	0.23 (1.31)	0.47

ACE=angiotensin converting enzyme, ARB=angiotensin receptor blocker, IQR=interquartile range, n=number, OHCA=out-of-hospital cardiac arrest, no-flow=time without any cardiopulmonary resuscitation, data are shown as mean (standard deviation) or number of patients (percentage) unless otherwise stated

Supplemental Digital Content Table 3. Hemodynamics on admission, during hypothermia and 24 ± 4 hours after rewarming.

	All	Xenon (n=17)	Control (n=21)	p-value
<b>Admission*</b>				
Heart rate (bpm)	69 (19)	65 (18)	72 (20)	0.28
Systolic arterial pressure (mmHg)	118 (24)	113 (18)	123 (28)	0.24
Central venous pressure (mmHg)	11 (4)	11 (5)	12 (4)	0.59
<b>During hypothermia**</b>				
Heart rate (bpm)	49 (10)	45 (6)	52 (11)	0.02
Systolic arterial pressure (mmHg)	110 (11)	110 (9)	110 (14)	0.96
<b>24 ± 4 hours after hypothermia*</b>				
Heart rate (bpm)	81 (14)	82 (15)	81 (13)	0.91
Systolic arterial pressure (mmHg)	134 (21)	135 (23)	133 (20)	0.84
Central venous pressure (mmHg)	12 (5)	10 (6)	13 (4)	0.08

bpm=beats per minute, n=number, \*at the time of echocardiography, \*\*mean of 2 or 5 min epochs during hypothermia, data are shown as mean (standard deviation)



Supplemental Digital Content Figure 2. Echocardiographic assessments of left ventricle (LV) ejection fraction (EF) and systolic longitudinal strain on admission (A and B) and 24 hours after rewarming (C and D). Stenosis of the left anterior descending coronary artery was treated percutaneously on

admission and inhaled xenon in combination with hypothermia was administered according to the study protocol. Apical 4-chamber (4CH) and 2-chamber (2CH) views demonstrate endocardial border delineation in systolic (green line) and diastolic (blue line) frames that were used for calculation of LV EF by Simpson's biplane method of discs (A and C). Systolic longitudinal strain was measured in apical 4CH, 2CH and long axis (LAX) views. Color coded views and polar maps demonstrate improvement of peak systolic global longitudinal strain (GLS) from -9.6% on admission to -19.2% at 24 hours after rewarming.