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Outcomes of Mild therapeutic Hypothermia
in Out-of-hospital Cardiac arrest :
A Nationwide retrospective analysis

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Introduction

* Mild Therapeutic Hypothermia



* Previous Study

- * 2 RCTs in VF arrest
- * No RCTs in non-VF arrest
- * Few retrospective study but no nationwide analysis

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Korean EMS system

- Single-tiered system
- Government-based system (Fire Department)
- EMT-B to EMT-I service level
- CPR at scene and during transport
- No Termination of Resuscitation at scene
- Public access defibrillation program began in 2009

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Methods
Data Collection

- * **Cardiovascular Disease Surveillance (CAVAS) project**
 - * Since 2006 in collaboration with and supported by the
 - * National Emergency Management Agency (NEMA) and
 - * the Centers for Disease Control and Prevention (CDC) of the government of the Republic of Korea
- * **Nationwide cohort for EMS-assessed OHCA**
 - * EMS run sheet for demographic and Utstein information
 - * Hospital medical record review for hospital care and outcome
 - * Project Quality Management Committee (QMC)
 - * EM physicians, epidemiologists, statistical experts, cardiologist, and medical record review experts.

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Methods
Selection of Participants

- * **Inclusion**
 - * Patients in whom spontaneous circulation had been restored after OHCA
 - * Survived patient who admitted to the hospital
 - * Age >= 15years
 - * Presumed cardiac origin
- * **Exclusion**
 - * Non cardiac etiology
 - * Alert mental status at ED arrival

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Methods
Study Design


- * **Population-based retrospective study with historical control groups**
- * **Main exposure : Mild therapeutic hypothermia (MTH)**
 - * Case receiving mild therapeutic hypothermia using
 - * External cooling(water, fanning, or ice padding), Internal cooling(gastric lavage, bladder cooling, or IV cooling using a catheter) or Mixed cooling
 - * If the hospital attempted the procedure
 - * Regardless of either the duration or the withdrawal

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Methods

Outcome measure


- * **Primary Outcome**
 - * Survival to hospital discharge
- * **Secondary Outcome**
 - * Good neurologic status
 - * Cerebral Performance Categories (CPC) score of 1 (good recovery) or 2 (moderate disability)



Methods

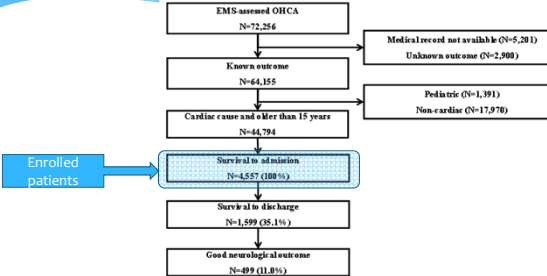
Statistical Analysis

- * **A Multivariable logistic regression analysis**
 - * to compare survival to discharge between the MTH and non-MTH groups adjusting for confounding and
 - * to calculate the adjusted ORs and 95% CI
- * **Propensity-score matched samples to control for selection bias**
 - * Propensity-score matched cohort was also analyzed by multivariable logistic regression
- * **Subgroup Analysis - initial rhythm**
 - * Shockable rhythm (VF or pulseless VT)
 - * Non-shockable rhythm (Asystole or PEA)




Results

Study population and outcomes



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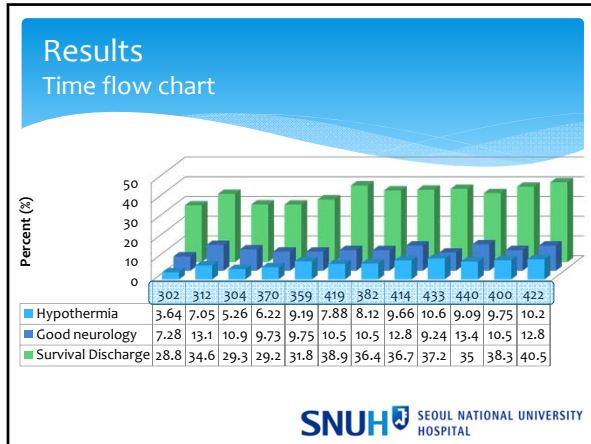
    graph TD
      A[EMS-assessed OHCA  
N=72,256] --> B[Known outcome  
N=64,355]
      A --> C[Medical record not available (N=2,200)  
Unknown outcome (N=2,200)]
      B --> D[Cardiac cause and <15 years  
N=44,794]
      B --> E[Pediatric (N=1,391)  
Non-cardiac (N=17,970)]
      D --> F[Survival to admission  
N=44,794 (100%)]
      F --> G[Survival to discharge  
N=1,599 (3.5%)]
      G --> H[Good neurological outcome  
N=499 (1.0%)]
  
```



Results Demographic findings							
Category	Total		Non Hypothermia Group		Hypothermia Group		p-value
	N	%	N	%	N	%	
Total, N (%)	4,557	100	4,180	100	377	100	
Sex, N (%)							<0.001
male	2,987	65.5	2,703	64.7	284	75.3	
female	1,570	34.5	1,477	35.3	93	24.7	
Age group, N (%)							<0.001
adult (15 to 64 years)	2,647	58.1	2,394	57.3	253	67.1	
elderly (older than 65 years)	1,910	41.9	1,786	42.7	124	32.9	
Metropolitan, N (%)							<0.001
no	2,016	44.2	1,885	45.1	131	34.8	
yes	2,541	55.8	2,295	54.9	246	65.2	
Witnessed status, N (%)							<0.001
no	1,219	26.8	1,134	27.1	85	22.5	
yes	3,129	68.7	2,840	68.0	289	76.7	
unknown	209	4.6	206	4.9	3	0.8	
Bystander CPR, N (%)							<0.001
no	4,204	92.3	3,899	93.3	305	80.9	
yes	353	7.7	281	6.7	72	19.1	

Results Demographic findings							
Category	Total		Non Hypothermia Group		Hypothermia Group		p-value
	N	%	N	%	N	%	
Total, N (%)	4,557	100	4,180	100	377	100	
Initial ECG, N (%)							<0.001
VF/VT	598	13.1	524	12.5	74	19.6	
PEA	357	7.8	306	7.3	51	13.5	
asystole	1,869	41.0	1,707	40.8	162	43.0	
unknown	1,813	39.8	1,643	39.3	90	23.9	
Interval, mean, STD (minutes)	mean	STD	mean	STD	mean	STD	
call to arrival at scene	6.6	3.6	6.7	3.6	6.2	2.5	0.02
call to arrival at ED	20.6	9.9	20.6	10.0	20	8.5	0.31
Pre-hospital defibrillation, N (%)							<0.001
no	3,902	85.6	3,614	86.5	288	76.4	
yes	655	14.4	566	13.5	89	23.6	
ED Level, N (%)							<0.001
level 1	712	15.6	557	13.3	155	41.1	
level 2	2,991	65.6	2,780	66.5	211	56.0	
level 3	792	17.4	782	18.7	10	2.6	
level 4	62	1.4	61	1.5	1	0.3	
Outcomes, N (%)							
survival to discharge	1,599	35.1	1,397	33.4	202	53.6	<0.001
good neurological status	499	11.0	430	10.3	69	18.3	<0.001

Results Type of Mild therapeutic hypothermia							
Covariates	Total	Mild therapeutic hypothermia					
		Any MTH procedure		EXT-EVA	EXT-SUR	IVD	INT-CAV
	N	N	%	%	%	%	%
Year, total	4,557	377	8.3	4.5	2.1	1	2.6
2008	1,288	72	5.6	5.1	0.2	0.1	0.6
2009	1,574	137	8.7	3.6	2.6	1.4	3
2010	1,695	168	9.9	5	3	1.4	3.7
ROSC at EMS							
no	4,061	331	8.2	4.5	2	0.9	2.5
yes	496	46	9.3	5.2	2.6	1.8	3
Outcomes							
Survival to discharge	1,599	202	12.6	6.9	3.8	1.8	4.3
Good neurological status	499	69	13.8	8.6	3.4	3.6	5.6



Results Effect of Mild Therapeutic Hypothermia

	Total	Survival		Unadjusted OR		Adjusted OR*	
	N	N	%	OR	95% CI	OR	95% CI
Survival to discharge							
non-MTH	4180	1397	33.4	1.00		1.00	
MTH	377	202	53.6	2.30	1.86 - 2.84	1.81	1.44 - 2.29
Good neurologic outcome							
non-MTH	4180	430	10.3	1.00		1.00	
MTH	377	69	18.3	1.95	1.48 - 2.58	1.37	1.00 - 1.89

OR, odds ratio, 95% CI, 95% confidence interval
 *Adjusted for age, sex, metropolitan vs. non-metropolitan, witness (yes, no, unknown), bystander cardiopulmonary resuscitation (yes, no), prehospital defibrillation (yes, no), return of spontaneous circulation at emergency medical service stage (yes, no), elapsed time interval from call to ambulance arrival at the scene (minutes), time interval from call to ambulance arrival at the emergency department (minutes), initial ECG, and emergency department level (level 1 to level 4).

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Result Demographic findings of Propensity matched cohort


Variables	Total	Post-resuscitation care		P-value
		Non-Hypothermia	Hypothermia	
Total, N (%)	752	376	376	
Sex, N (%)		100	100	0.866
male	564	281	283	74.7 - 75.3
female	188	95	93	24.7 - 24.7
Age, mean (SD), year		58.5	56.6	15.4 - 15.8
Metropolitan, N (%)				0.494
no	271	140	131	37.2 - 34.8
yes	481	236	245	62.8 - 62.2
Witnessed status, N (%)				0.149
no	554	266	288	70.7 - 76.6
yes	193	108	85	28.7 - 22.6
unknown	5	2	3	0.6 - 0.8
Bystander CPR, N (%)				0.853
no	144	73	71	19.4 - 18.9
yes	608	303	305	80.6 - 81.1
Initial ECG, N (%)				0.387
VF/ pulseless VT	144	70	74	18.6 - 19.7
PEA	94	44	50	11.7 - 13.3
asystole	347	185	162	49.2 - 43.1
unknown	167	77	90	20.5 - 23.9

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Result						
Demographic findings of Propensity matched cohort						
Variables	Total	Post-resuscitation care				P-value
		Non-Hypothermia		Hypothermia		
Total, N (%)	752	376	100	376	100	
Interval, mean (SD), minutes						
call to arrival to scene		6.4	2.8	6.2	2.5	0.354
call to arrival to ED		20.7	10.6	20.1	8.4	0.406
Prehospital defibrillation, N (%)						0.598
no	933	471	69.5	462	68.1	
yes	423	207	30.5	216	31.9	
ROSC at EMS, N (%)						0.836
no	1,097	547	80.7	550	81.1	
yes	259	131	19.3	128	18.9	
ED level, N (%)						0.783
level 1	307	153	40.7	154	40.9	
level 2	425	214	56.9	211	56.1	
level 3	19	9	2.4	10	2.7	
level 4	1	0	0	1	0.3	
Outcomes, N (%)						
Survival to discharge	346	144	41.6	202	58.4	<0.001
Good neurological status	123	54	43.9	69	56.1	<0.001

Results								
Effect of Mild Therapeutic Hypothermia in the Propensity matched cohort								
	Total	Survival		Unadjusted OR		Adjusted OR*		
	N	N	%	OR	95% CI	OR	95% CI	
Survival to discharge								
non-MTH	376	144	38.3	1.00		1.00		
MTH	376	202	53.7	1.87	1.40 2.50	1.83	1.33 2.50	
Good neurologic outcome								
non-MTH	376	54	14.4	1.00		1.00		
MTH	376	69	18.4	1.34	0.91 1.98	1.20	0.76 1.88	

OR: odds ratio, 95% CI: 95% confidence interval
*Adjusted for age, sex, metropolitan vs. non-metropolitan, witness (yes, no, unknown), bystander cardiopulmonary resuscitation (yes, no), prehospital defibrillation (yes, no), return of spontaneous circulation at emergency medical service stage (yes, no), elapsed time interval from call to ambulance arrival at the scene (minutes), time interval from call to ambulance arrival at the emergency department (minutes), initial ECG, and emergency department level (level 1 to level 4).




Subgroup analysis								
Outcome by Initial Rhythm								
Outcome by Initial Rhythm	Total	Survival		Unadjusted OR		Adjusted OR*		
	N	N	%	OR	95% CI	OR	95% CI	
VF or Pulseless VT								
Survival to discharge								
non-MTH	524	281	53.6	1		1.00		
MTH	74	54	73.0	2.34	1.36 4.01	2.04	1.15 3.62	
Good neurological outcome								
non-MTH	524	122	23.3	1		1.00		
MTH	74	29	39.2	2.12	1.28 3.53	1.86	1.07 3.21	
PEA or Asystole								
Survival to discharge								
non-MTH	2013	483	24.0	1		1.00		
MTH	213	95	44.6	2.55	1.91 3.40	2.05	1.51 2.79	
Good neurological outcome								
non-MTH	2013	69	3.4	1		1.00		
MTH	213	13	6.1	1.83	1.00 3.37	1.13	0.59 2.20	



Limitation


- * **Retrospective observational study**
 - * Information bias : Minimized by Quality Management Committee
 - * Selection bias : Propensity score analysis – Similar results
 - * Confounders : Hospital Level (High volume vs Low volume)




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Conclusion

- * The Mild therapeutic hypothermia treatment increased by year
- * **Survival to discharge rate was 1.8 times more in MTH than non MTH** in total cohort and propensity score matching cohort.
- * Especially in initial shockable rhythm in OHCA patients in nationwide data



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Thank you for your
Attention !!
