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Cardiogenic Shock in Korea: Perspectives After the ECLS-Shock Trial

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DISCLOSURE

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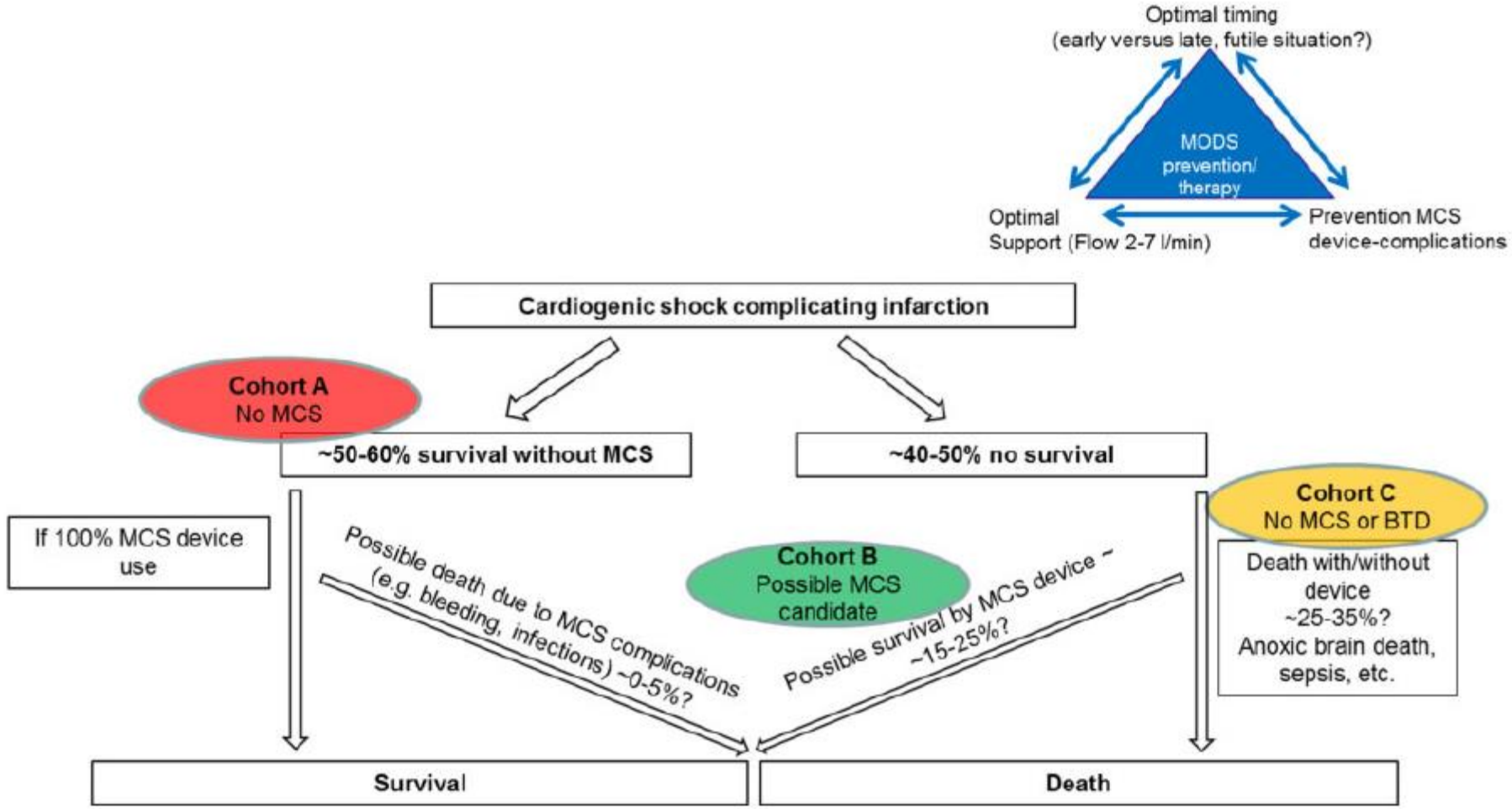
8. BiLab

Mechanical Circulatory Support Devices

Adequate patient selection and timing are very important !!



Thiele et al. European Heart Journal (2019) 40, 2671–2683

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Extracorporeal Life Support in Infarct-Related Cardiogenic Shock

H. Thiele, U. Zeymer, I. Akin, M. Behnes, T. Rassaf, A.A. Mahabadi, R. Lehmann, I. Eitel, T. Graf, T. Seidler, A. Schuster, C. Skurk, D. Duerschmied, P. Clemmensen, M. Hennersdorf, S. Fichtlscherer, I. Voigt, M. Seyfarth, S. John, S. Ewen, A. Linke, E. Tigges, P. Nordbeck, L. Bruch, C. Jung, J. Franz, P. Lauten, T. Goslar, H.-J. Feistritzer, J. Pöss, E. Kirchhof, T. Ouarrak, S. Schneider, S. Desch, and A. Freund, for the ECLS-SHOCK Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Microaxial Flow Pump or Standard Care in Infarct-Related Cardiogenic Shock

J.E. Møller, T. Engstrøm, L.O. Jensen, H. Eiskjær, N. Mangner, A. Polzin, P.C. Schulze, C. Skurk, P. Nordbeck, P. Clemmensen, V. Panoulas, S. Zimmer, A. Schäfer, N. Werner, M. Frydland, L. Holmvang, J. Kjærgaard, R. Sørensen, J. Lønborg, M.G. Lindholm, N.L.J. Udesen, A. Junker, H. Schmidt, C.J. Terkelsen, S. Christensen, E.H. Christiansen, A. Linke, F.J. Woitek, R. Westenfeld, S. Möbius-Winkler, K. Wachtell, H.B. Ravn, J.F. Lassen, S. Boesgaard, O. Gerke, and C. Hassager, for the DanGer Shock Investigators*

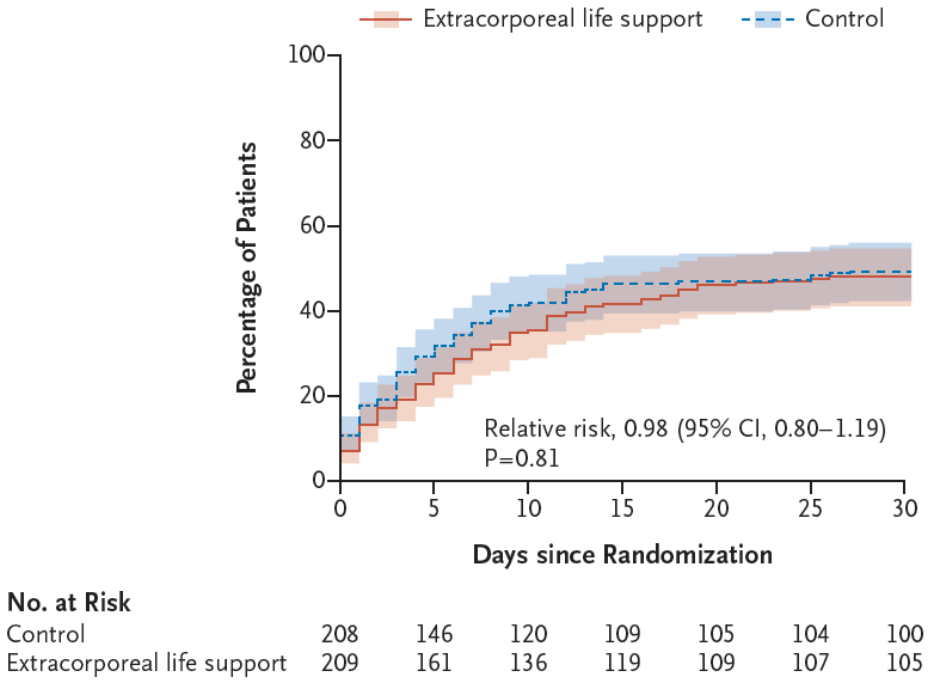
ECLS Shock vs DanGer Shock

	ECLS SHOCK trial	DanGer SHOCK trial
Study period	June 2019-November 2022	January 2013-July 2023
Study population	420	360
Center	44	14
Nation	Germany, Slovenia	Denmark, Germany, UK
Primary outcome	Death from any cause at 30 days	Death from any cause at 180 days
	47.8% in ECLS vs 49.0% in Control	45.8% in Impella vs 58.5% in Control
Bleeding	23.4% in ECLS vs 9.6% in Control	21.8% in Impella vs 11.9% in Control
Vascular complications	11.0% in ECLS vs 3.8% in Control	
Limb ischemia		5.6% in Impella vs 1.1% in Control

ECLS-SHOCK trial failed to show the benefit of VA-ECMO

- N=420, AMI with cardiogenic shock, planned early revascularization
- Early ECLS vs. usual medical treatment

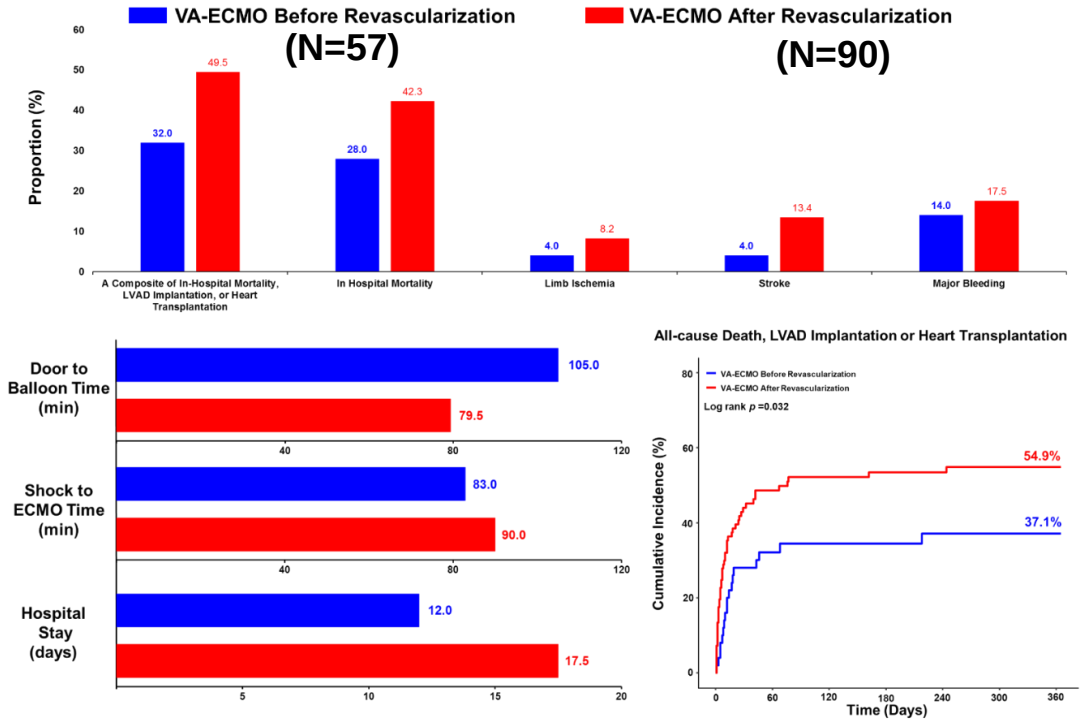
	Early ECLS	Medical therapy	HR [95% CI]
All-cause death	47.8%	49.0%	0.98 [0.80-1.19]
Moderate to severe bleeding	23.4%	9.6%	2.44 [1.50-3.95]
Peripheral vascular complications warranting intervention	11.0%	3.8%	2.86 [1.31-6.25]

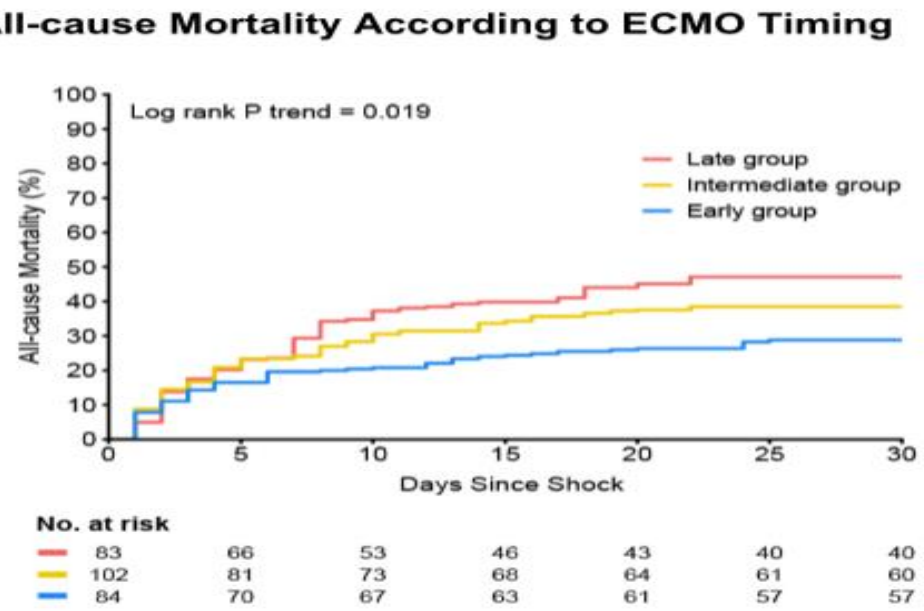


Thiele H, N Engl J Med 2023

Why is ECLS proved not beneficial in the ECLS-Shock trial?

1) Too late initiation of ECLS: ECLS before revascularization in 22%!





- Patients with AMI who underwent revascularization therapy with VA-ECMO were included.
- Patients with refractory CS but without E-CPR before revascularization

Choi KH and Yang JH et al. Cir J 2020

- From a multicenter registry, 362 patients with refractory CS who underwent ECMO between January 2014 and December 2018 were identified.

Ahn CM et al. JACC CVI 2021

Why is ECLS proved not beneficial in the ECLS-Shock trial?

2) Too severe futile patients?

- Altered mentality: 95%
- CPR before randomization: 78%
- Poor neurologic outcome in 24%
- SCAI stage E in 35%

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	ECLS (N=209)	Control (N=208)
Signs of impaired organ perfusion — no. (%)		
Altered mental status	200 (95.7)	198 (95.2)
Cold, clammy skin and limbs	202 (96.7)	204 (98.1)
Oliguria	150 (71.8)	150 (72.1)
Resuscitation before randomization — no. (%)	162 (77.5)	162 (77.9)
Median time until return of spontaneous circulation during longest continuous resuscitation (IQR) — min	20 (10–25)	20 (12–28)
Laboratory values on admission		
Median pH (IQR)	7.2 (7.1–7.3)	7.2 (7.1–7.3)
Median lactate (IQR) — mmol/liter	6.8 (4.5–9.6)	6.9 (4.6–10.0)
Median creatinine (IQR) — mg/dl	1.2 (1.0–1.5)	1.3 (1.1–1.6)
Median high-sensitivity cardiac troponin T (IQR) — ng/liter	1540 (232–6630)	987 (173–5700)
SCAI shock stage — no. (%)‡		
C	104 (49.8)	111 (53.4)
D	38 (18.2)	18 (8.7)
E	67 (32.1)	79 (38.0)

Why is ECLS proved not beneficial in the ECLS-Shock trial?

3) High complication rate	ECLS	Control
• Bleeding	23%	10%
• Ischemic vascular Cx	11%	4%

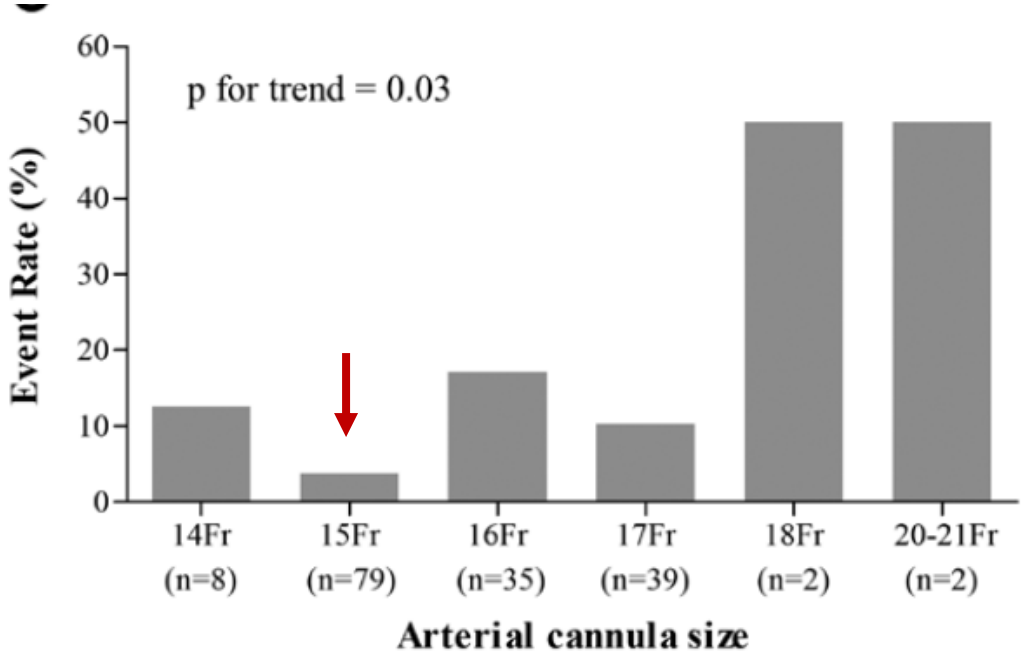
It is critical to reduce device-related complications for positive trial related to MCS.

Distal limb ischemia

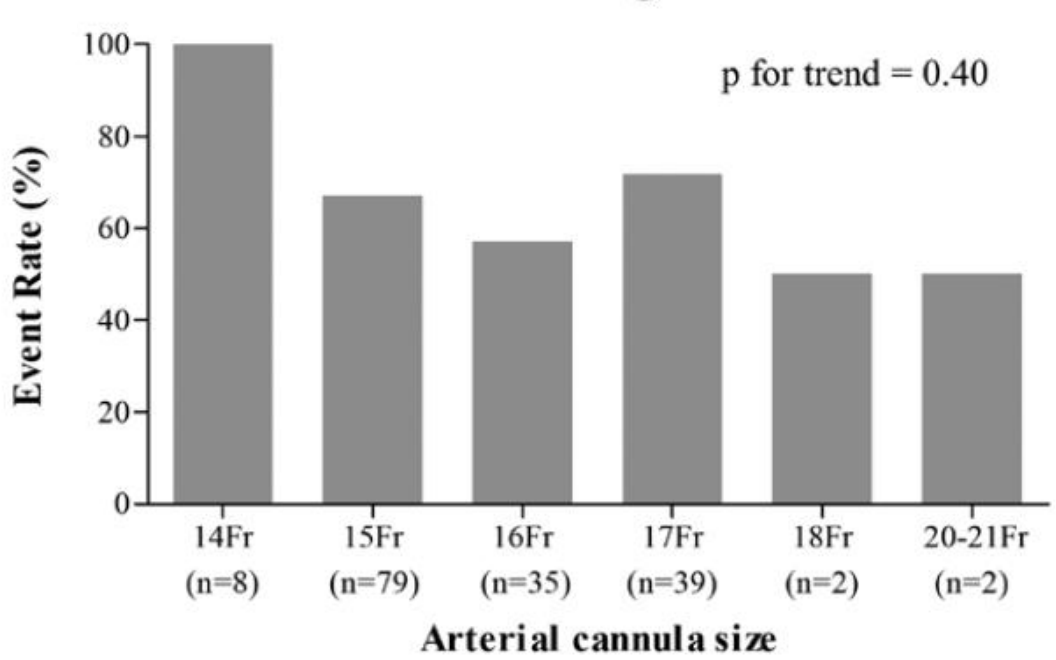
Small arterial cannula decreased lower limb ischemia

- N=165, VA-ECMO
- A smaller arterial cannula (14-15 Fr) was associated with a lower rate of limb ischemia

Limb ischemia



Successful weaning from ECMO

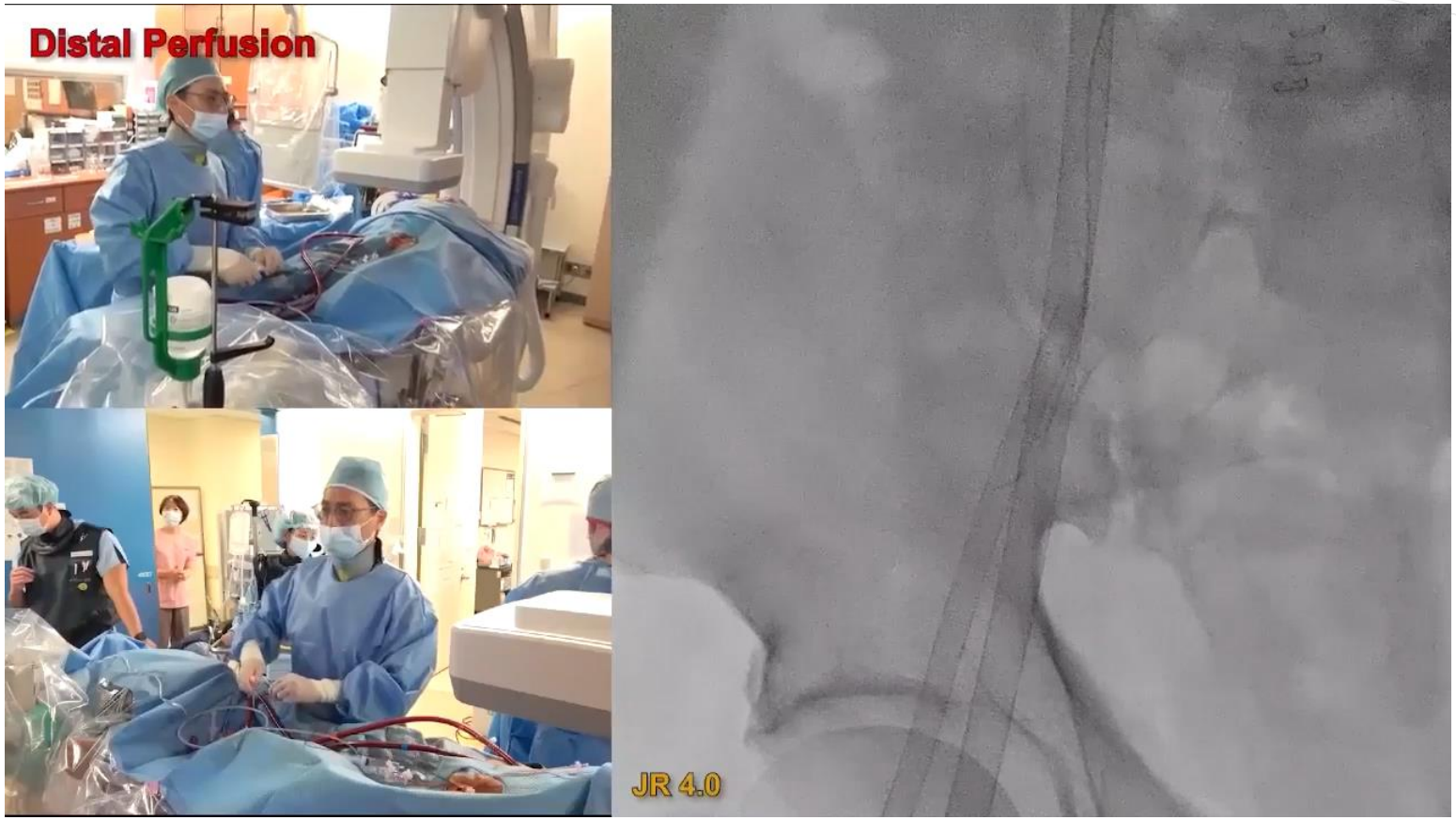


Kim J and Yang JH et al. ASAIO Journal 2018

Distal limb ischemia

Fluoroscopy-guided simultaneous distal perfusion

- Distal perfusion in 96 patients out of 230 patients treated with VA-ECMO
- Distal perfusion reduced the incidence of limb ischemia (8.2% vs. 2.1%, p=0.047) and in-hospital mortality (50.7% vs 38.5%, p=0.067).



Jang WJ and Yang JH et al, Ann Intensive Care 2018

Antiplatelet strategy

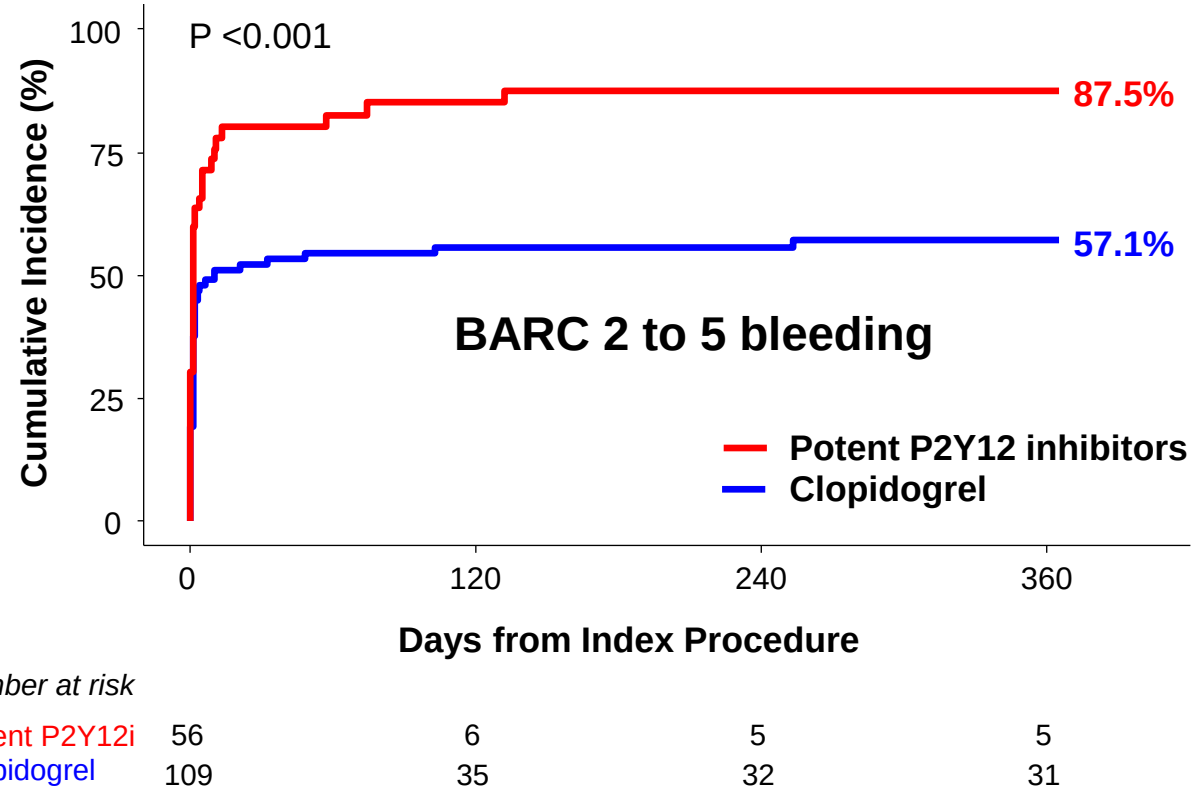
ECLS SHOCK

Table S2 – Antiplatelet drugs after the catheterization laboratory and until discharge

Medication	ECLS (n=209)	Control (n=208)
Aspirin; n/total (%)	174/202 (86.1)	170/198 (85.9)
Clopidogrel; n/total (%)	55/202 (27.2)	49/198 (24.7)
Prasugrel; n/total (%)	99/202 (49.0)	97/198 (49.0)
Ticagrelor; n/total (%)	45/202 (22.3)	48/198 (24.2)

72.3%

SMC ECMO registry



Number at risk

Potent P2Y12i	56	6	5	5
Clopidogrel	109	35	32	31

Park TK et al. Unpublished data

Access site bleeding

Percutaneous cannula removal

Percutaneous cannula removal

Puncture the arterial cannula

Hemostasis using two sets of Proglide®

- N=115 ECMO weaning (2012.09 ~ 2014.12)

	Percutaneous (N=56)	Surgical (N=59)	P-value
Procedural time	17.2 min	64.3 min	<0.001
Technical success[1]	85.7%	86.4%	1.0
Procedural complications[2]	17.9%	28.8%	0.19

1) Technical success = hemostatic control; no sign of immediate adverse events such as additive manual compression, dissection, occlusion, or stenosis; and unimpaired limb perfusion at the arterial cannulation site without need for access site-related adjunctive surgical or endovascular procedures from hemorrhagic, infectious, or ischemic complications.

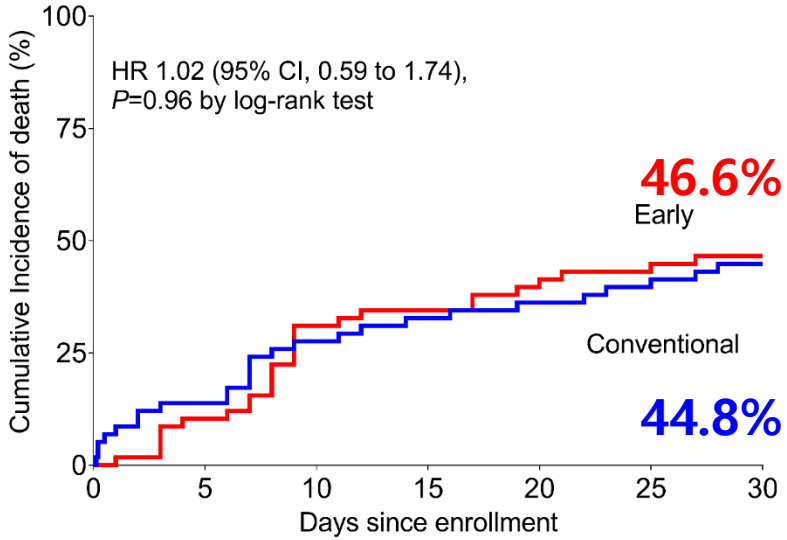
2) Procedural complication: open repair at the insertion site, limb ischemia after removal of the arterial cannula, removal site infection, pseudoaneurysm, distal part embolization, or 10 minutes or more manual compression at the weaning site.

Hwang JW and Yang JH et al, J Vasc Surg 2016

Why is ECLS proved not beneficial in the ECLS-Shock trial?

4) Limited LV unloading	ECLS	Control
• Active LV unloading	6%	32%
• Impella	0%	15%

At least routine early LV unloading is not beneficial.

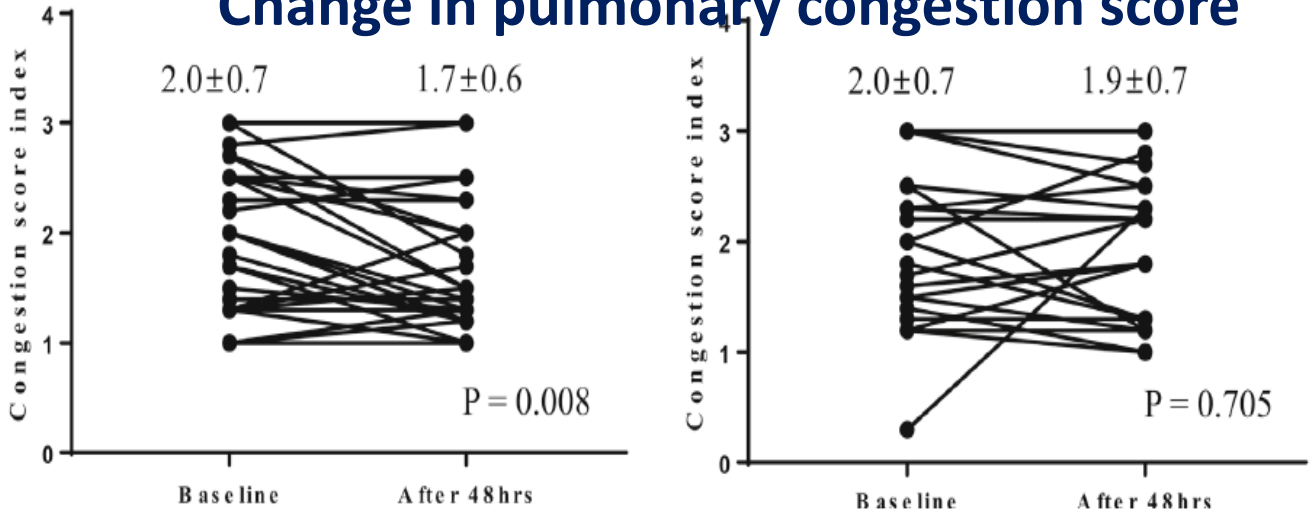


EARLY UNLOAD trial

Early LV unloading group

Conventional group

Change in pulmonary congestion score



EVOLVE ECMO trial

Lessons from ECLS SHOCK

- Although overall mortality was similar in both groups, the trial revealed meaningful increases in bleeding, limb ischemia, sepsis, and kidney injury in the ECLS group.
- These findings highlight the substantial importance of the critical care of patients after implantation of MCS.
- The opportunity to further improve outcomes with the development of strategies that might reduce these morbid complications both through clinical practices and continued device innovation.

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Association Between Presence of a Cardiac Intensivist and Mortality in an Adult Cardiac Care Unit

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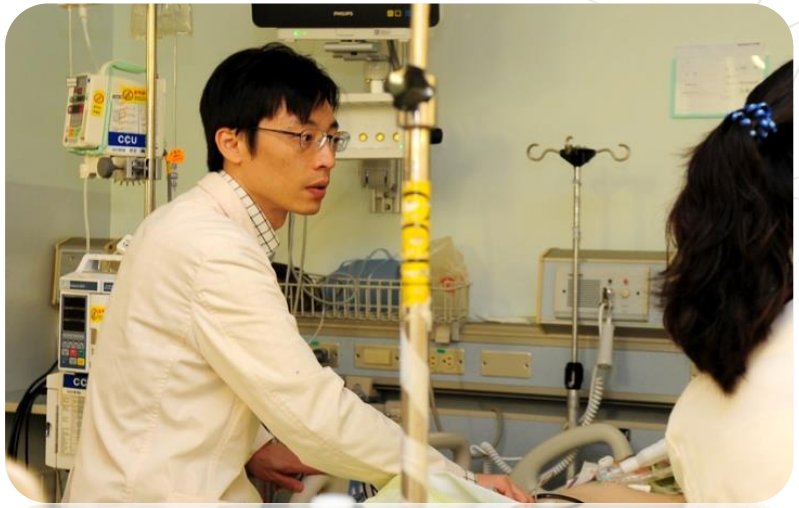
SMC CICU



2013

Low-intensity staffing

- Patients were managed by only their individual physicians

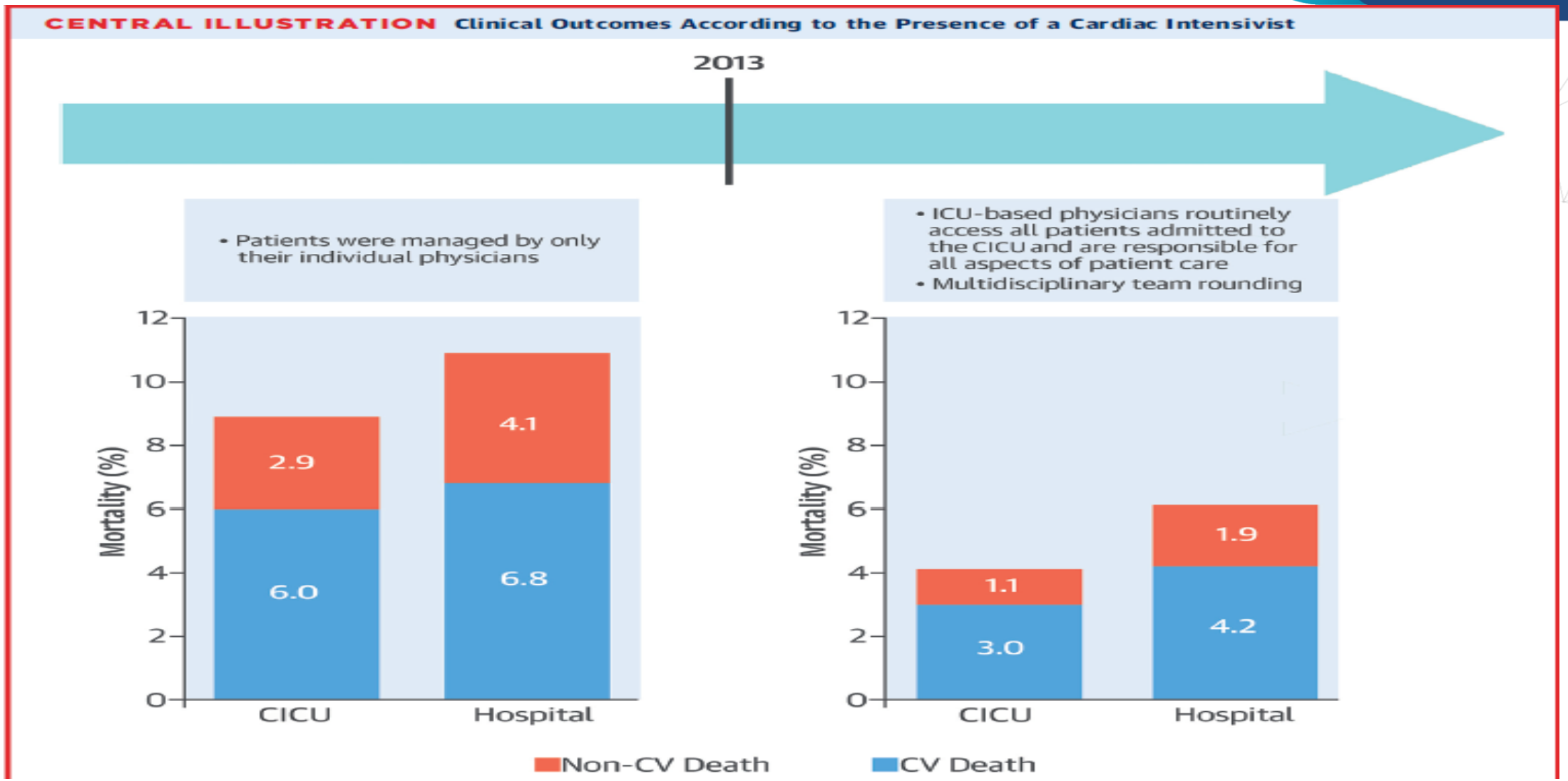
High-intensity staffing

- ICU-based physician evaluates all admissions and assumes primary responsibility for all aspects of patient care
- Multidisciplinary team rounding

Member

- A cardiologist who was board certified in interventional cardiology and critical care medicine
- 1 General cardiologist and 1 general intensivist
- Covered CICU with 3 senior residents of internal medicine
- Received phone calls and text messages from home overnight (CICU was made up of in-house general cardiologist and senior residents)
- Pharmacist and nutritionist
- Respiratory therapist
- Advanced nurse (CRRT)
- Registered nurse (Patient: bed=2:1)

SJ Na and JH Yang et al. JACC 2016

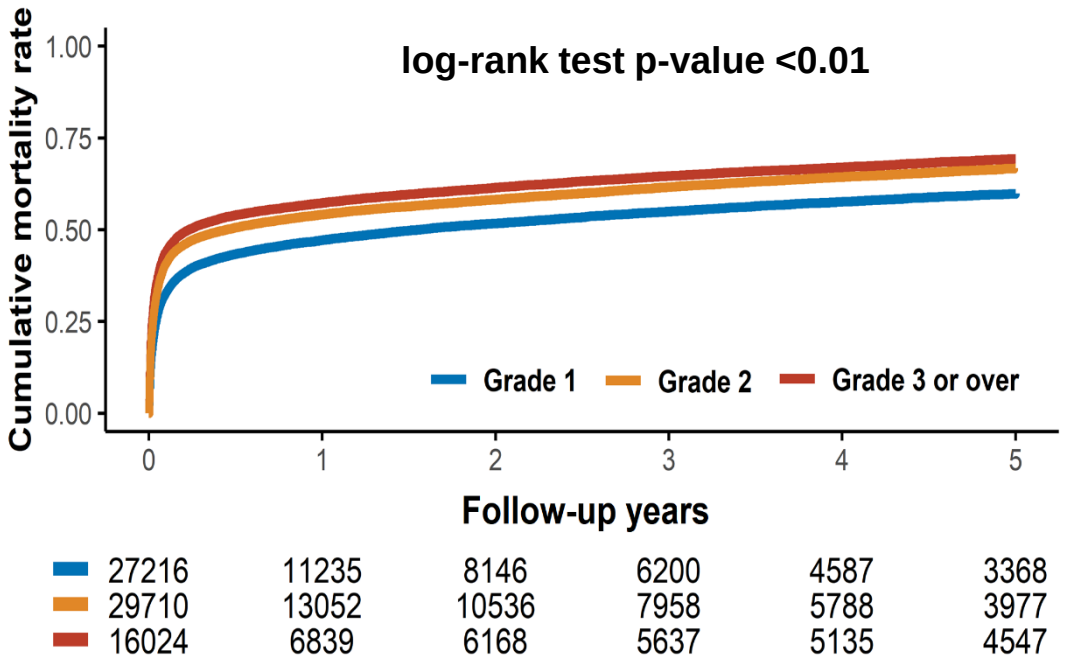


After the implementation of a multidisciplinary team including a dedicated cardiac intensivist, the in-hospital and CICU mortality was dramatically improved

SJ Na and JH Yang et al. JACC 2016

The Effect of Bed-to-Nurse Ratio on Clinical Outcomes of Cardiogenic Shock: A Nationwide-Population Based Study

	ICU Grade 1	ICU Grade 2	ICU Grade 3 or more	p-value
	(N=27,216)	(N=29,710)	(N=16,024)	
Age, mean (SD)	69.3 (14.5)	69.5 (14.5)	69.5 (14.0)	0.19
Sex, male	16,885 (62.0)	17,725 (59.7)	9,234 (57.6)	<.001
Charlson's index, mean (SD)	3.5 (2.8)	3.4 (2.8)	3.1 (2.7)	<.001
Medical aid, yes	1,393 (5.1)	2,238 (7.5)	1,461 (9.1)	<.001
History of myocardial infarction	3,741 (13.8)	4,054 (13.7)	2,393 (14.9)	<.001
History of congestive heart failure	8,997 (33.1)	9,505 (32.0)	4,701 (29.3)	<.001
Diabetes mellitus	11,878 (43.6)	12,749 (42.9)	6,540 (40.8)	0.21
Hypertension	15,716 (57.8)	17,439 (58.7)	9,058 (56.5)	0.002
Chronic kidney disease	4,382 (16.1)	4,197 (14.1)	1,779 (11.1)	0.002
Cause of admission				<.001
Acute myocardial infarction	8,834 (32.5)	9,624 (32.4)	5,756 (35.9)	
Heart failure-related shock	18,382 (67.5)	20,086 (67.6)	10,268 (64.1)	
Admission from emergency room	22,063 (81.1)	25,770 (86.7)	13,979 (87.2)	<.001
CPR at admission	2,942 (10.8)	6,235 (21.0)	4,570 (28.5)	<.001
Multiple vasopressors	14,881 (54.7)	18,425 (62.0)	10,094 (63.0)	<.001
Concomitant use of Inotropes	8,478 (31.2)	9,747 (32.8)	5,663 (35.3)	<.001
Mechanical ventilation	15,934 (58.6)	19,587 (65.9)	10,733 (67.0)	<.001
ECMO	2,620 (9.6)	2,158 (7.3)	1,089 (6.8)	<.001
CRRT	6,158 (22.6)	6,540 (22.0)	2,834 (17.7)	<.001
Length of stay (days)	22.4 (55.8)	20.3 (37.6)	18.8 (34.8)	<.001



- This cohort study obtained data from the Korean National Health Insurance Service (K-NHIS) database. The Korean NHIS covers approximately 97% of Koreans, while the Medical Aid Program covers the 3% of remaining Koreans who cannot afford national insurance
- We selected all patients ≥18 years old who were diagnosed with cardiogenic shock and admitted to the ICU at a tertiary or general hospital from January 1, 2010 to December 31, 2020
- ICU nursing grade was categorized as grade 1 (< 0.5 beds per nurse), grade 2 (<0.63 beds per nurse), and grade 3 or above.

Choi KH, Kang D and Yang JH et al. Critical Care 2024

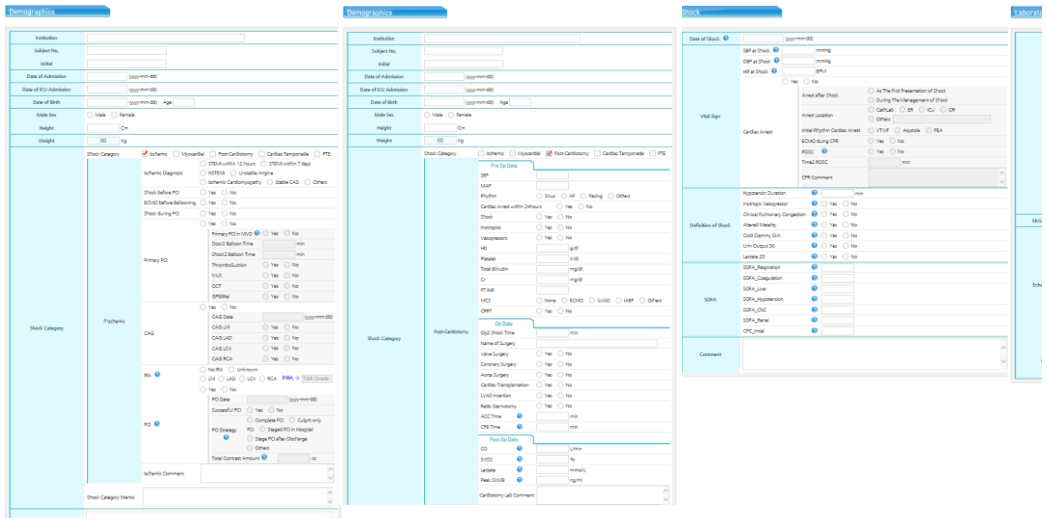
RESCUE registry

- Korean multicenter registry of cardiogenic shock with or without ECMO
  - Enrolment period: 2014.01 ~ 2018.12.
  - N= 1,247 (retrospective 954, prospective 293)

Center	N	Center	N
Samsung Medical Center	249	Ilsan Baik Hospital	78
Shinchon Severance Hospital	181	Jungang Univ. Hospital	67
Korea Univ. Ananm Hospital	134	Buchon Sejong Hospital	66
Samsung Changwon Hospital	122	Chungnam Univ. Hospital	57
Konkuk Univ. Hospital	112	Inha Univ. Hospital	52
Chungbuk Univ. Hospitial	91	Dankook Univ. Hospital	38

RESCUE II Registry

- Prospective multicenter registry of cardiogenic shock
- Improved design of case record form
- Collaborative work with Korean centers and Mayo Clinic
- Expected numbers: 1,370 patients



Study Design

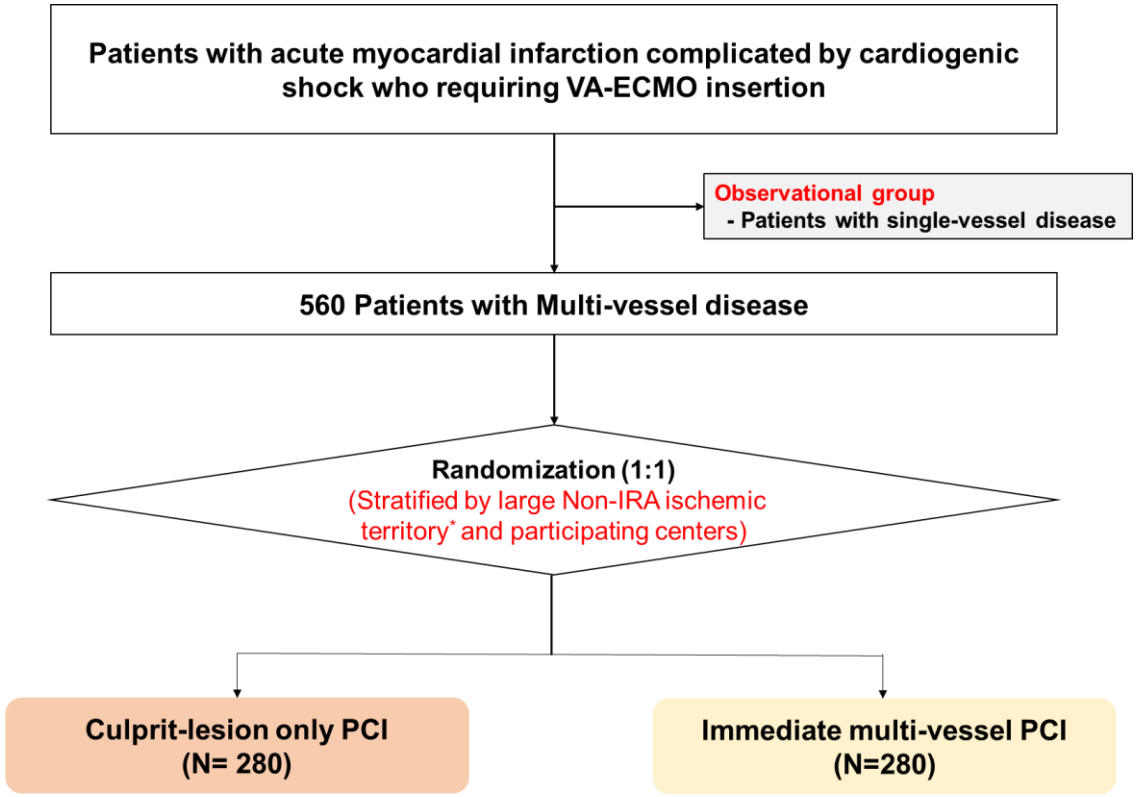
Study Type :	Observational [Patient Registry]
Estimated Enrollment :	1000 participants
Observational Model:	Cohort
Time Perspective:	Prospective
Target Follow-Up Duration:	1 Year
Official Title:	SMart Angioplasty Research Team: **Shock** II: SMART-RESCUE II
Actual Study Start Date :	May 30, 2019
Estimated Primary Completion Date :	December 31, 2023
Estimated Study Completion Date :	December 31, 2024

My Perspectives on revascularization in AMICS underwent VA ECMO

- It is unclear whether the role of immediate multi-vessel PCI differed for an extremely advanced form of CS, underreported in the CULPRIT-SHOCK trial.
- The clinical role of NCL revascularization may be different from that of other MCS devices capable of left ventricular unloading because VA-ECMO may induce pulmonary edema along with an increase of left ventricular filling pressure by increasing the afterload
- It may result in aggravation of the ischemia in the NCL territory and delay the recovery of cardiac function, leading to failure of ECMO weaning.
- Transporting the patient to the catheterization laboratory for staged PCI under ECMO support can be risky and burdensome.

RESCUE-SHOCK Trial

Principal Investigator: Jeong Hoon Yang
5-years enrollment from 31 tertiary centers in Korea



Primary endpoint

90-day all-cause mortality or advanced heart failure requiring cardiac replacement therapy (LVAD insertion or heart transplantation)

*Large Non-IRA (non-infarct related artery) ischemic territory was defined as left main or proximal left anterior descending artery involvement, proximal left circumflex artery involvement (left dominance), and proximal to distal right coronary artery involvement (right dominance).

1) Revascularization strategy for non-IRA in the culprit-only PCI group

Except the culprit lesion, all other lesions should be left untreated in the acute setting. If needed, staged PCI or coronary artery bypass surgery for non-IRA lesions could be allowed.

2) Revascularization strategy for non-IRA in the immediate multi-vessel PCI group

All additional lesions in other major coronary arteries defined by a diameter >2.5 mm with significant stenoses (>70% by visual assessment) should be revascularized during primary PCI using the standard techniques. **In case of chronic total occlusion as a non-IRA lesion, revascularization attempt is left in operator's discretion.**

ClinicalTrials.gov Identifier: NCT05527717

Thank you for your attention