ECC CS CQ

CS 患者の治療において，PDEⅢ阻害薬の使用は患者の転帰を改善するか？

Clinical Importance of Phosphodiesterase 3 Inhibitors on Outcomes in Patients with Cardiogenic Shock：A Systematic Review

PROSPERO CRD42024542488

P (patients): Adult (18 years and older) patients admitted to the hospital with CS.
I (interventions): Administration of PDE3i with or without inotropes.
C (comparisons, controls): No PDE3i with or without inotropes such as dopamine, dobutamine, and levosimendan.
O (Main outcomes): Survival at 1 or 3 months, all-cause death, and cardiovascular death.
O (Additional outcomes): Length of stay in the emergency department, fatal arrhythmia, multiple organ failure, and use of mechanical circulatory support.
S (Study type): RCT.
T (Time frame): All published literature until October 31, 2024.

Yamamoto M, Hosoya Y, Hanada H, Osawa T, Arai M, Sakamoto K, Okazaki Y, Katasako-Yabumoto A, Ishizu T, Kondo T, Kirigaya J, Nakayama N, Yamamoto T, Hashiba K, Nakashima T, Tsujita K, Noguchi T, Tsujimoto Y, Kikuchi M, Tahara Y, Nonogi H, Matoba T. Clinical Importance of Phosphodiesterase 3 Inhibitors on Outcomes in Patients With Cardiogenic Shock — A Systematic Review —. Circ Rep. 2025;7(11):CR-25-0152.
doi:10.1253/circrep.CR-25-0152

Search strategies of literature databases

Search strings

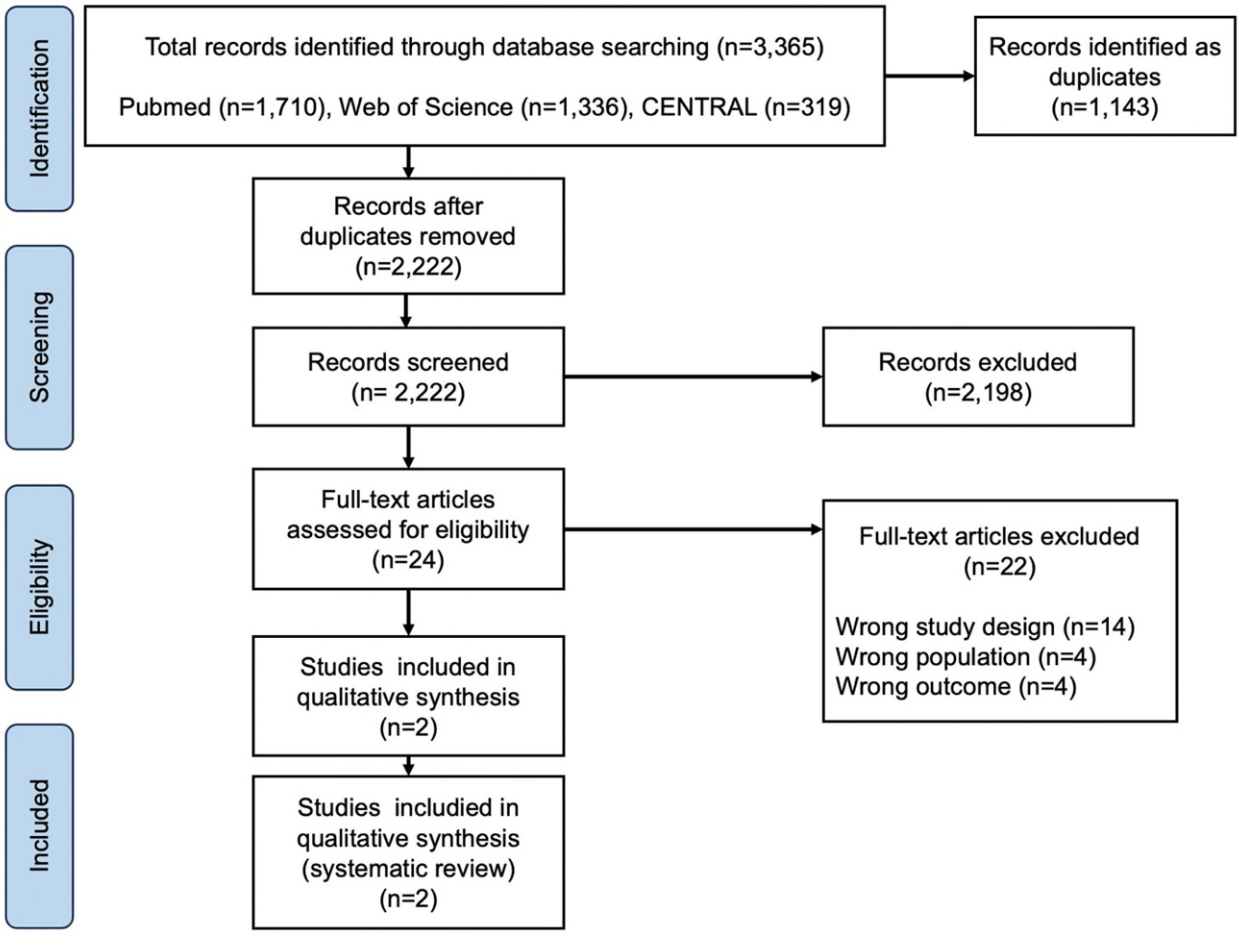
1. PubMed (MEDLINE & PMC)
#1: "cardiac shock"[Title/Abstract] OR "cardiogenic shock"[Title/Abstract] OR ("myocardial infarction"[MeSH Terms] AND "shock"[MeSH Terms:noexp]) OR "shock, cardiogenic"[MeSH Terms] OR "hypoperfusion"[Title/Abstract] OR ("hypotension"[Title/Abstract] AND ("heart failure"[Title/Abstract] OR "cardiac failure"[Title/Abstract] OR "myocardial failure"[Title/Abstract] OR "heart failure"[MeSH Terms] OR "HF"[Title/Abstract] OR "AHF"[Title/Abstract] OR "CHF"[Title/Abstract] OR "ADHF"[Title/Abstract]))
#2: "inotropic agent*"[Title/Abstract] OR "inotropic drug*"[Title/Abstract] OR "inotropic support*"[Title/Abstract] OR "inotropic therap*"[Title/Abstract] OR "cardiotonic agents"[MeSH Terms] OR "inotrope*"[Title/Abstract] OR "inodilator*"[Title/Abstract] OR "cardioprotective agent*"[Title/Abstract] OR "cardiac stimulant*"[Title/Abstract] OR "cardiotonic drug*"[Title/Abstract] OR "cardiotonic agent*"[Title/Abstract] OR "myocardial stimulant*"[Title/Abstract] OR "milrinone"[MeSH Terms] OR "milrinone"[Title/Abstract] OR "olprinone"[Title/Abstract] OR "olprinone"[Supplementary Concept] OR "phosphodiesterase 3 inhibitors"[MeSH Terms] OR "Phosphodiesterase-3"[Title/Abstract] OR "Phosphodiesterase-III"[Title/Abstract] OR "PDE-III"[Title/Abstract] OR "PDE-3"[Title/Abstract] OR "Phosphodiesterase3"[Title/Abstract] OR "PhosphodiesteraseIII"[Title/Abstract] OR "PDEIII"[Title/Abstract] OR "PDE3"[Title/Abstract] OR "PDI"[Title/Abstract] OR "levosimendan"[Title/Abstract] OR "simendan"[MeSH Terms] OR "enoximone"[MeSH Terms] OR "enoximone"[Title/Abstract]
#3: #1 AND #2

2. Web of Science (Science Citation Index Expanded(SCIE))
#1: (TS="cardiac shock" OR TS="cardiogenic shock" OR ((TS="myocardial infarction") AND (TS="shock")) OR TS=hypoperfusion OR ((TS=hypotension) AND ((TS="heart failure" OR TS="cardiac failure" OR TS="myocardial failure" OR TS=HF OR TS=AHF OR TS=CHF OR TS=ADHF))))
#2: TS="inotropic agent*" OR TS="inotropic drug*" OR TS="inotropic support*" OR TS="inotropic therap*" OR TS="cardiotonic agent*" OR TS=inotrope* OR TS=inodilator* OR

TS="cardioprotective agent*" OR TS="cardiac stimulant*" OR TS="cardiotonic drug*" OR TS="myocardial stimulant*" OR TS=milrinone OR TS=olprinone OR TS=Phosphodiesterase-3 OR TS=Phosphodiesterase-III OR TS=PDE-III OR TS=PDE-3 OR TS=Phosphodiesterase3 OR TS=PhosphodiesteraseIII OR TS=PDEIII OR TS=PDE3 OR TS=PDI OR TS=levosimendan OR TS=simendan OR TS=enoximone
#3: #1 AND #2

3. Cochrane Library (Cochrane Central Register of Controlled Trials(CENTRAL))
#1: "cardiac shock":ti,ab,kw OR "cardiogenic shock":ti,ab,kw OR ([mh "myocardial infarction"] AND [mh ^shock]) OR [mh "shock, cardiogenic"] OR hypoperfusion:ti,ab,kw OR (hypotension:ti,ab,kw AND ("heart failure":ti,ab,kw OR "cardiac failure":ti,ab,kw OR "myocardial failure":ti,ab,kw OR [mh "heart failure"] OR HF:ti,ab,kw OR AHF:ti,ab,kw OR CHF:ti,ab,kw OR ADHF:ti,ab,kw))
#2: ("inotropic" NEXT agent*):ti,ab,kw OR ("inotropic" NEXT drug*):ti,ab,kw OR ("inotropic" NEXT support*):ti,ab,kw OR ("inotropic" NEXT therap*):ti,ab,kw OR [mh "cardiotonic agents"] OR inotrope*:ti,ab,kw OR inodilator*:ti,ab,kw OR ("cardioprotective" NEXT agent*):ti,ab,kw OR ("cardiac" NEXT stimulant*):ti,ab,kw OR ("cardiotonic" NEXT drug*):ti,ab,kw OR ("cardiotonic" NEXT agent*):ti,ab,kw OR ("myocardial" NEXT stimulant*):ti,ab,kw OR [mh milrinone] OR milrinone:ti,ab,kw OR olprinone:ti,ab,kw OR [mh "phosphodiesterase 3 inhibitors"] OR Phosphodiesterase-3:ti,ab,kw OR Phosphodiesterase-III:ti,ab,kw OR PDE-III:ti,ab,kw OR PDE-3:ti,ab,kw OR Phosphodiesterase3:ti,ab,kw OR PhosphodiesteraseIII:ti,ab,kw OR PDEIII:ti,ab,kw OR PDE3:ti,ab,kw OR PDI:ti,ab,kw OR levosimendan:ti,ab,kw OR [mh simendan] OR [mh enoximone] OR enoximone:ti,ab,kw
#3: #1 AND #2

PRISMA Flow Chart



本資料の図表および記載内容は、Yamamoto M, et al. Circ Rep. 2025;7:1021-1028. より引用。

Summary of the included studies.

Author	Year	n (%)*	Age, sex	Study design	Country	Definition of CS	Cause of CS	Early death†
Fuhrman JT, et al.[13]	2008	Enoximon: 16 (50%) Levosimendan: 16 (50%)	Enoximon: mean 68 years, male 69% Levosimendan: mean 68 years, male 56%	Single-center, Open-label, RCT	Germany	(1) Deteriorating hypotension as manifested by sBP 90mmHg or requirement of inotropic amines and vasopressors to maintain sBP of at least 90 mmHg (2) CI below 2.5 L/min/m2 (3) Pulmonary capillary occulusion pressure above 18 mmHg (4) Clinical signs of peripheral hypoperfusion (cold skin, mental confusion, or oliguria)	Any cause (Ischemic and nonischemic)	Enoximon:10(63%) Levosimendan:5(31%)
Mathew R, et al.[14]	2021	Milrinone: 96 (50%) Dobutamine: 96 (50%)	Milrinone: mean 68.9 years, male 62% Dobutamine: mean 72.0 years, male 65%	Multi-center, Double-blinded, RCT	Canada	Meeting the SCAI definition of cardiogenic shock stage B, C, D, or E‡	AMI	Miilrinone:35(37%) Dobutamine:41(43%)

*Crude number of patients.

†30-day death in “Fuhrmann JT, 2008”, and in-hospital death from any case in “Mathew R, 2021” were summarized.

‡SCAI Stage B - ”Beginning” (Pre-shock), Stage C - ”Classic” Cardiogenic Shock, Stage D - ”Deteriorating”, Stage E - ”Extremis”

RCT, Randomized control trial. sBP, systolic blood pressure below. CI, Cardiac index. AMI, Acute myocardial infarction. SCAI, Society for Cardiovascular Angiography and Interventions

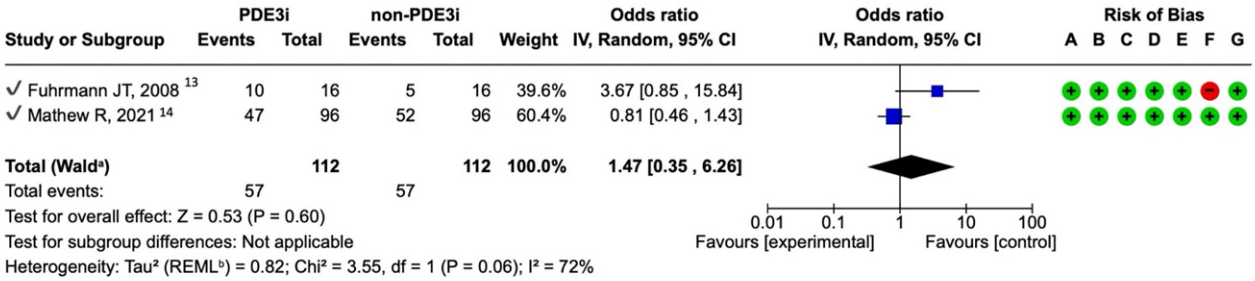
Evidence Profile

Certainty assessment							No of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CQ7	[placebo]	Relative (95% CI)	Absolute (95% CI)		
All-cause death: early death												
2	randomised trials	not serious	serious	serious	serious	none	57/112 (50.9%)	57/112 (50.9%)	**OR 1.47** (0.35 to 6.26)	**95 more per 1,000** (from 243 fewer to 358 more)	⨁◯◯◯ Very Low	CRITICAL
Cardiac Arrest (VT/VF)												
2	randomised trials	not serious	serious	serious	serious	none	59/112 (52.7%)	52/112 (46.4%)	**OR 1.14** (0.42 to 3.14)	**62 more per 1,000** (from 67 fewer to 190 more)	⨁◯◯◯ Very Low	CRITICAL
Initiation of renal replacement therapy												
2	randomised trials	not serious	not serious	not serious	serious	none	94/112 (83.9%)	52/112 (80.4%)	**OR 1.53** (0.80 to 2.92)	**43 more per 1,000** (from 83 fewer to 119 more)	⨁⨁⨁◯ Moderate	IMPORTANT

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

本資料の図表および記載内容は、Yamamoto M, et al. Circ Rep. 2025;7:1021-1028. より引用。

(A) Early death [13,14]



Footnotes

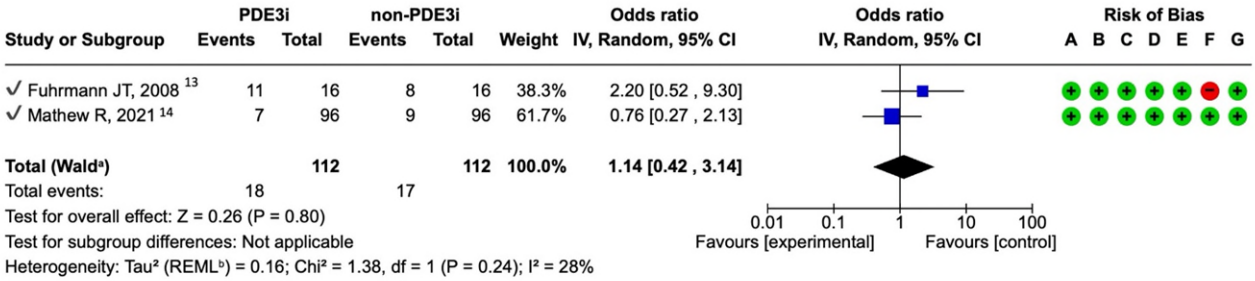
[a]CI calculated by Wald-type method.

[b]Tau² calculated by Restricted Maximum-Likelihood method.

Risk of bias legend

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

(B) Cardiac arrest (VT/VF)[13,14]



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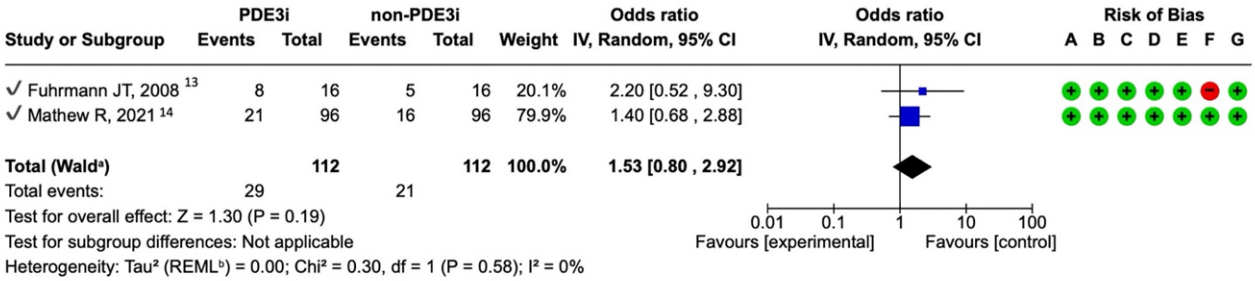
(F) Selective reporting (reporting bias)
(G) Other bias

(C) Initiation of renal replacement therapy[13,14]



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