Literature Update

Critical Care BC

Nov 2023

Review

STRATUS Trial

Original Investigation | Caring for the Critically Ill Patient ONLINE FIRST FREE

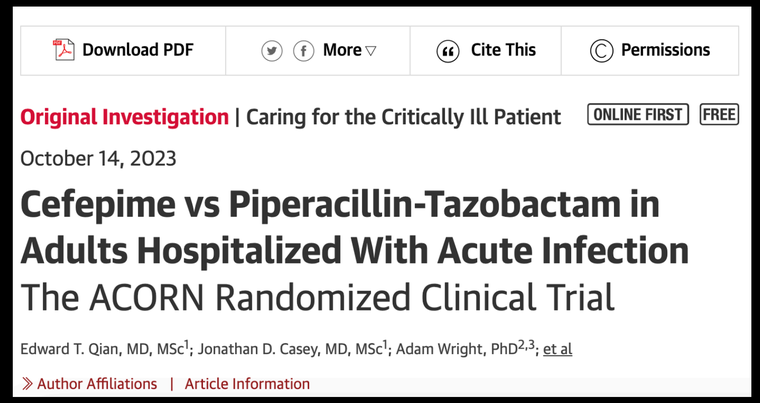
October 12, 2023

Small-Volume Blood Collection Tubes to Reduce Transfusions in Intensive Care

The STRATUS Randomized Clinical Trial

Deborah M. Siegal, MD[1,2,3,4]; Emilie P. Belley-Côté, MD, PhD[1,2,8]; Shun Fu Lee, PhD[1,8]; et al

ACORN



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Original Investigation | Caring for the Critically Ill Patient ONLINE FIRST FREE

October 14, 2023

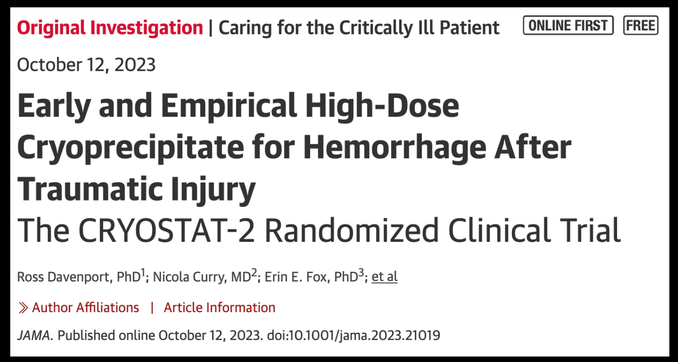
Cefepime vs Piperacillin-Tazobactam in Adults Hospitalized With Acute Infection

The ACORN Randomized Clinical Trial

Edward T. Qian, MD, MSc[1]; Jonathan D. Casey, MD, MSc[1]; Adam Wright, PhD[2,3]; et al

Author Affiliations | Article Information

CRYOSTAT-2



Original Investigation | Caring for the Critically Ill Patient ONLINE FIRST FREE

October 12, 2023

Early and Empirical High-Dose Cryoprecipitate for Hemorrhage After Traumatic Injury

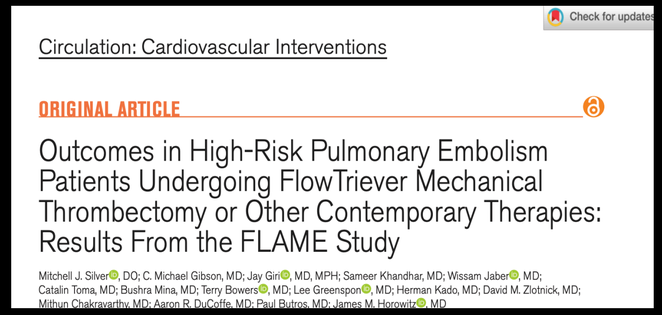
The CRYOSTAT-2 Randomized Clinical Trial

Ross Davenport, PhD[1]; Nicola Curry, MD[2]; Erin E. Fox, PhD[3]; et al

Author Affiliations | Article Information

JAMA. Published online October 12, 2023. doi:10.1001/jama.2023.21019

FLAME Trial



Check for updates

Circulation: Cardiovascular Interventions

ORIGINAL ARTICLE

Outcomes in High-Risk Pulmonary Embolism Patients Undergoing FlowTriever Mechanical Thrombectomy or Other Contemporary Therapies: Results From the FLAME Study

Mitchell J. Silver, DO; C. Michael Gibson, MD; Jay Giri, MD, MPH; Sameer Khandhar, MD; Wissam Jaber, MD; Catalin Toma, MD; Bushra Mina, MD; Terry Bowers, MD; Lee Greenspon, MD; Herman Kado, MD; David M. Zlotnick, MD; Mithun Chakravarthy, MD; Aaron R. DuCoffe, MD; Paul Butros, MD; James M. Horowitz, MD

This Month


ILCOR
IRC

Circulation

ILCOR SUMMARY STATEMENT

2023 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations: Summary From the Basic Life Support; Advanced Life Support; Pediatric Life Support; Neonatal Life Support; Education, Implementation, and Teams; and First Aid Task Forces

RESUSCITATION

EUROPEAN RESUSCITATION COUNCIL

ILCOR SUMMARY STATEMENT | ARTICLES IN PRESS, 109992

2023 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations: Summary From the Basic Life Support; Advanced Life Support; Pediatric Life Support; Neonatal Life Support; Education, Implementation, and Teams; and First Aid Task Forces

ACLS

ECPR
OHCA

ECPR
IHCA

DSED &
Vector
Change

Calcium
OHCA

Calcium
IHCA

ACLS

Neuro Prog in patients comatose post ROSC

GCS Motor >3 in 4 days PROSC, good prob

MRI 72hrs - 7 days post ROSC, good prob

NSE <17 microgram/L within 72 hrs after ROSC

EEG? Continual (Near Continuous) with no PEDs or Seizure

Neuro Prog in patients comatose post ROSC

ECPR OHCA

ECPR IHCA

DSED of VC

Calcium OHCA

Calcium IHCA

GCS Motor >3 in 4 days PROSC, good prob

MRI 72hrs - 7 days post ROSC, good prob

NSE <17 microgram/L within 72 hrs after ROSC

EEG? Continual (Near Continuous) with no PEDs or Seizure

PALS

ECPR
OHCA

Unknown

ECPR
IHCA

PALS

Neuro Prog in patients comatose post ROC

GCS Motor >3 in 4 days PROSC, good prob — Unknown

Pupil Reflex > 12 hrs ROC — 

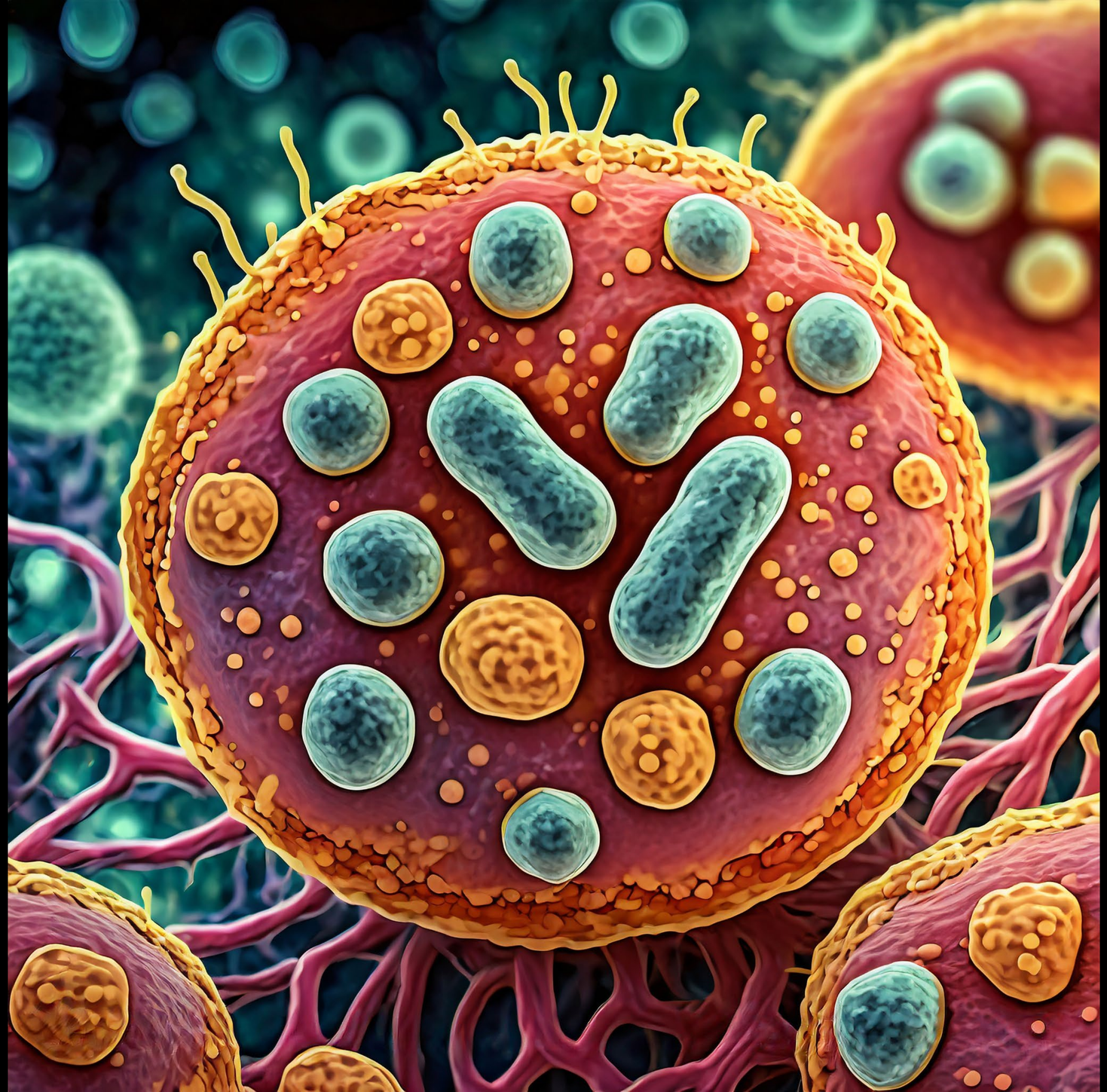
Brainstem reflexes? — Unknown

Normal Lactate <12 hrs post ROC — 

pH post ROC — 

MRI 72hrs - 14 days post ROSC, good prob — 

Prophylaxis



AMIKINHAL Trial

RESEARCH SUMMARY

Inhaled Amikacin to Prevent Ventilator-Associated Pneumonia

Ehrmann S et al. DOI: 10.1056/NEJMoa2310307

CLINICAL PROBLEM

Ventilator-associated pneumonia is the most frequent presentation of hospital-acquired infection of the lower respiratory tract. Microaspirations around the tracheal-tube cuff and the formation of biofilm can lead to progressive bacterial spread in the tracheobronchial tree, ultimately leading to pneumonia. Inhaled antibiotic therapy enables delivery of very high antibiotic concentrations to the tracheobronchial tree, lung parenchyma, and tracheal-tube biofilm. Whether preventive inhaled antibiotics may reduce the incidence of ventilator-associated pneumonia is unclear.

CLINICAL TRIAL

Design: A multicenter, double-blind, randomized, placebo-controlled trial in France examined the efficacy and safety of inhaled amikacin in critically ill adults who had undergone invasive mechanical ventilation for ≥72 hours.

Intervention: 847 patients were randomly assigned to receive inhaled amikacin at a dose of 20 mg per kilogram of ideal body weight or placebo once daily for 3 days. The primary outcome was a first episode of ventilator-associated pneumonia through day 28.

RESULTS

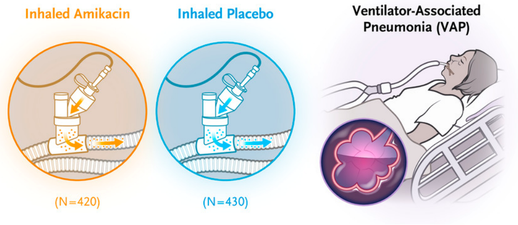
Efficacy: At 28 days, ventilator-associated pneumonia had developed in fewer patients in the amikacin group than in the placebo group.

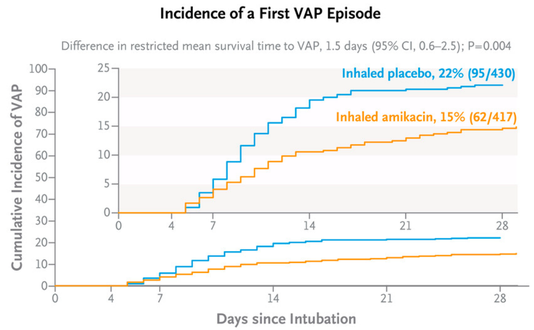
Safety: Trial-related serious adverse effects were seen in 7 patients in the amikacin group and 4 patients in the placebo group.

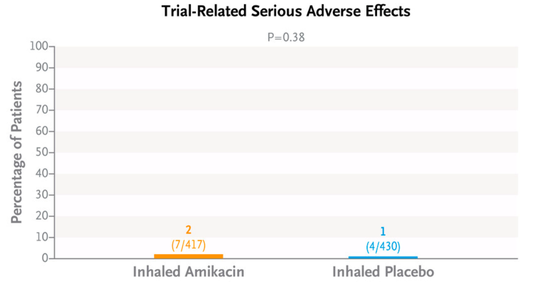
LIMITATIONS AND REMAINING QUESTIONS

- The trial was not powered to investigate other patient-centered outcomes, such as death or length of stay in the ICU and hospital.
- The trial was also not powered to detect whether preventive inhaled antibiotics could reduce the use of systemic antibiotics to limit antibiotic-resistance selection pressure.

Links: Full Article | NEJM Quick Take



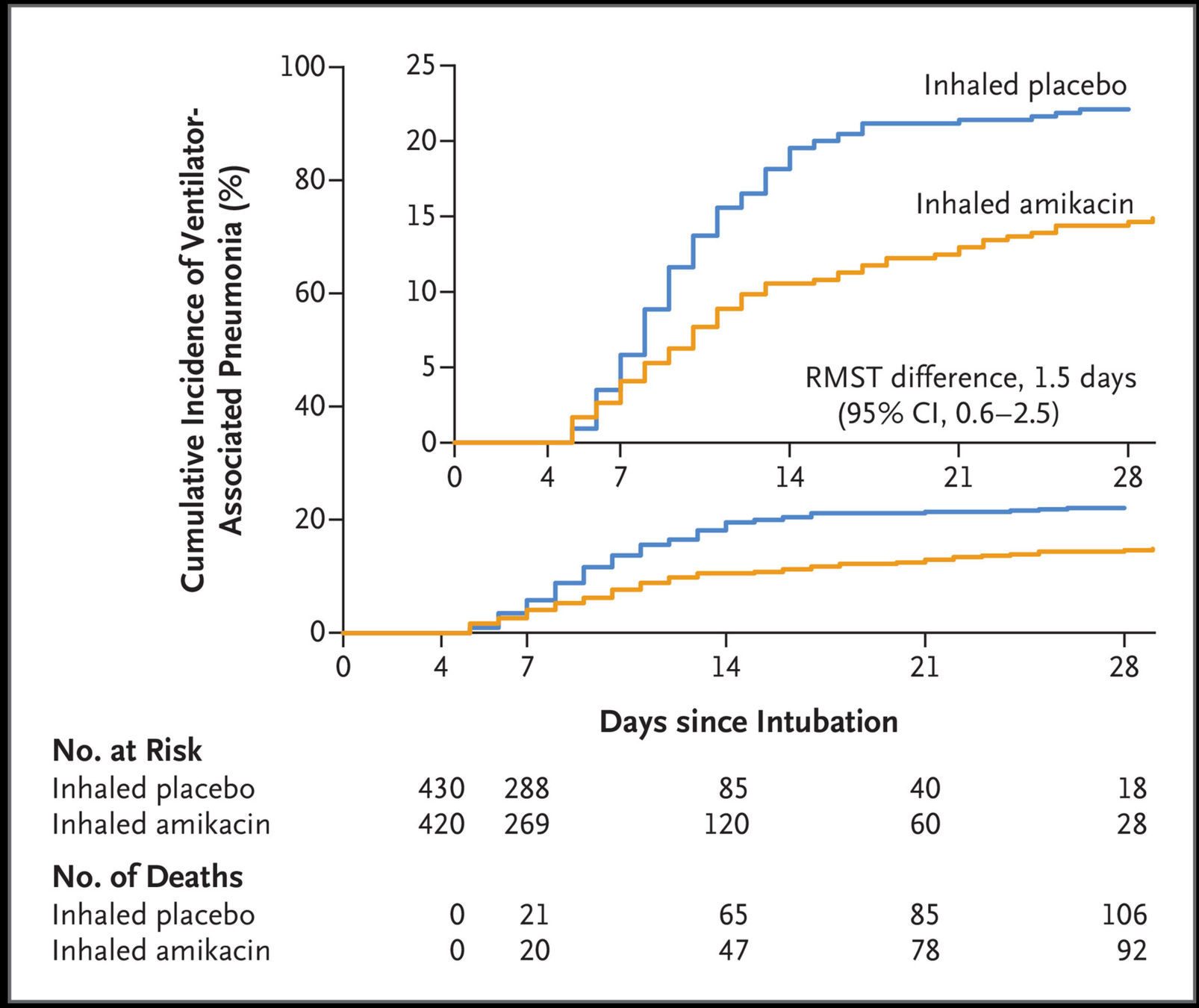




CONCLUSIONS

Among critically ill patients who had undergone mechanical ventilation for more than 3 days, a subsequent 3-day course of inhaled amikacin reduced the burden of ventilator-associated pneumonia during 28 days of follow-up.

AMIKINHAL Trial



No. at Risk					
Inhaled placebo	430	288	85	40	18
Inhaled amikacin	420	269	120	60	28
No. of Deaths					
Inhaled placebo	0	21	65	85	106
Inhaled amikacin	0	20	47	78	92

This Issue Views 24,100 | Citations 0 | Altmetric 155

Original Investigation | Caring for the Critically Ill Patient

October 10, 2023

Nasal Iodophor Antiseptic vs Nasal Mupirocin Antibiotic in the Setting of Chlorhexidine Bathing to Prevent Infections in Adult ICUs

A Randomized Clinical Trial

JAMA®

QUESTION Does nasal iodophor antiseptic work as well as nasal mupirocin antibiotic for preventing *Staphylococcus aureus* clinical cultures in intensive care unit (ICU) patients receiving daily chlorhexidine gluconate (CHG) bathing?

CONCLUSION This clinical trial found that nasal iodophor was inferior to nasal mupirocin in preventing *S aureus* clinical cultures in ICU patients.

POPULATION

430 764 Men
370 587 Women

Adult ICU patients

Mean age: **63.4** years

LOCATIONS

137
Community hospitals in the US

INTERVENTION

137 Hospitals randomized

69

Iodophor-CHG

Mupirocin-CHG then switched to twice-daily intranasal 10% povidone-iodine swabs for 5 days + daily CHG bath

68

Mupirocin-CHG

Twice-daily intranasal 2% mupirocin ointment for 5 days + daily CHG bath

PRIMARY OUTCOME

S aureus clinical cultures attributed to the ICU (occurring from ICU day 3 through 2 days after ICU discharge) from baseline to intervention period

FINDINGS

ICU-attributable days

Iodophor-CHG

Baseline: 4.3/1000
Intervention period: 5.0/1000

Mupirocin-CHG

Baseline: 4.0/1000
Intervention period: 4.1/1000

Clustered HR, iodophor-CHG: 1.17
Clustered HR, mupirocin-CHG: 0.99

HR difference in differences, 18.4%
(95% CI, 10.7% to 26.6%)

Huang SS, Septimus EJ, Kleinman K, et al. Nasal mupirocin vs iodophor in the setting of chlorhexidine bathing to prevent infections in adult ICUs: a randomized clinical trial. *JAMA*. Published October 10, 2023. doi:10.1001/jama.2023.17219

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Restrictive or Liberal Transfusion Strategy in Myocardial Infarction and Anemia

J.L. Carson, M.M. Brooks, P.C. Hébert, S.G. Goodman, M. Bertolet, S.A. Glynn, B.R. Chaitman, T. Simon, R.D. Lopes, A.M. Goldsweig, A.P. DeFilippis, J.D. Abbott, B.J. Potter, F.M. Carrier, S.V. Rao, H.A. Cooper, S. Ghafghazi, D.A. Fergusson, W.J. Kostis, H. Noveck, S. Kim, M. Tessalee, G. Ducrocq, P. Gabriel Melo de Barros e Silva, D.J. Triulzi, C. Alsweiler, M.A. Menegus, J.D. Neary, L. Uhl, J.B. Strom, C.B. Fordyce, E. Ferrari, J. Silvain, F.O. Wood, B. Daneault, T.S. Polonsky, M. Senaratne, E. Puymirat, C. Bouleti, B. Lattuca, H.D. White, S.F. Kelsey, P.G. Steg, and J.H. Alexander, for the MINT Investigators*

ABSTRACT

70-80 Vs >100

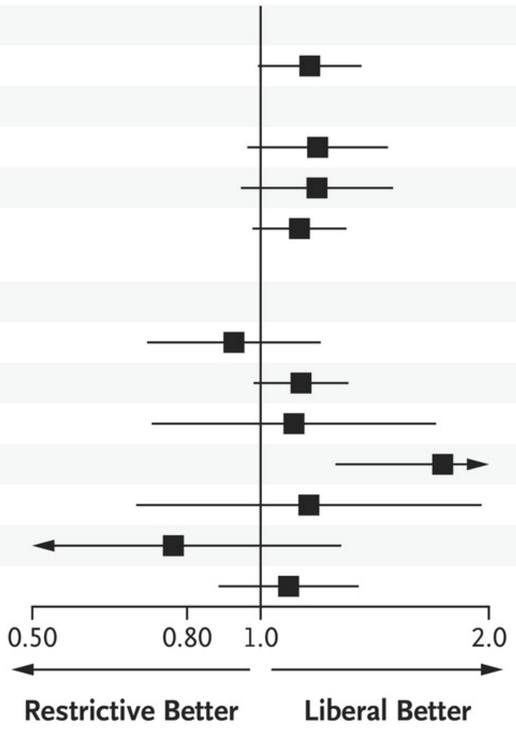
Table 1. Characteristics of the Patients at Baseline.*

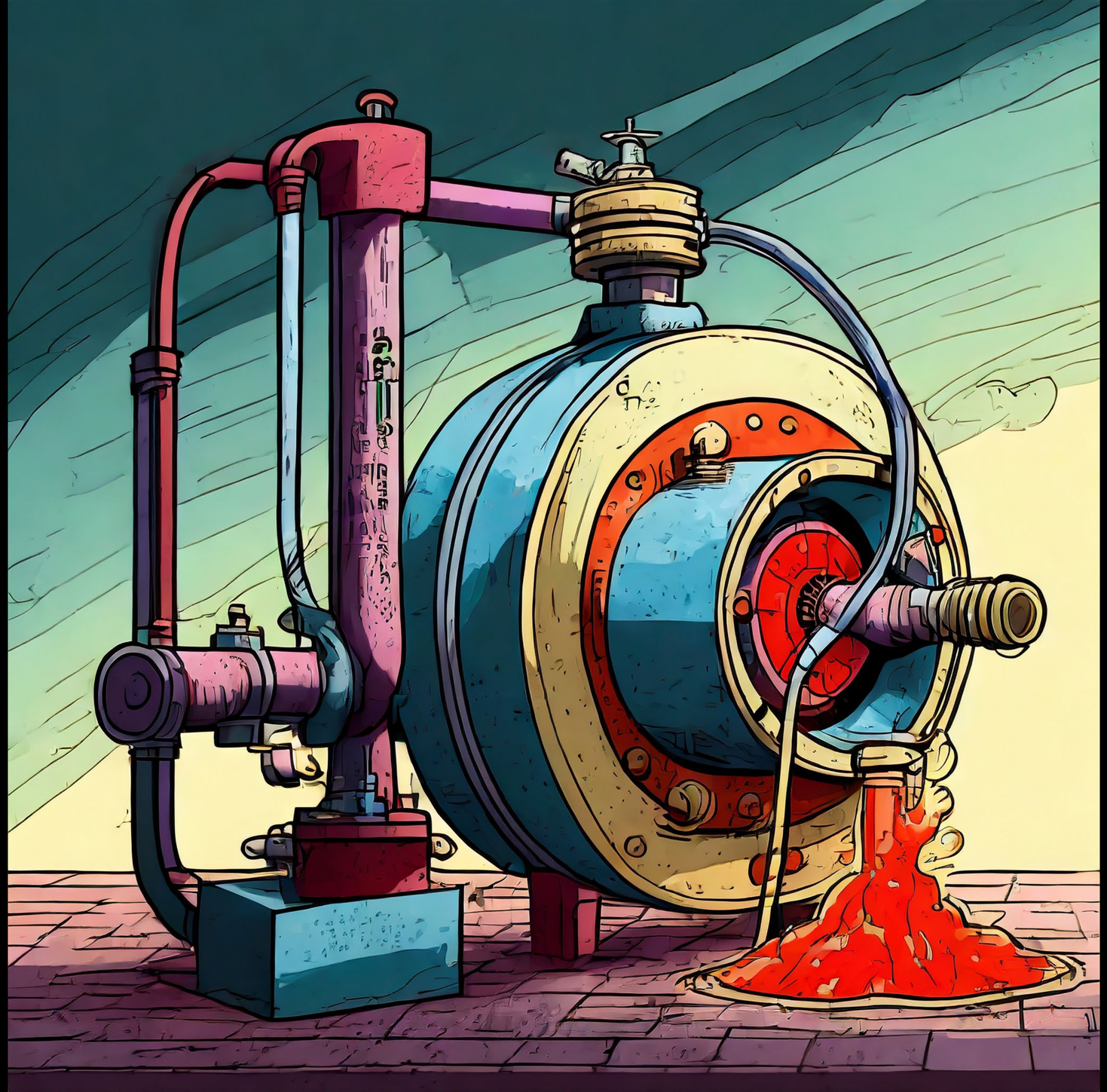
Characteristic	All Patients (N=3504)	Restrictive Strategy (N=1749)	Liberal Strategy (N=1755)
Age — yr	72.1±11.6	72.2±11.5	72.1±11.6
Female sex — no. (%)	1593 (45.5)	774 (44.3)	819 (46.7)
Race or ethnic group — no. (%)†			
White	2474 (70.6)	1229 (70.3)	1245 (70.9)
Black	440 (12.6)	217 (12.4)	223 (12.7)
Other	244 (7.0)	129 (7.4)	115 (6.6)
Missing	346 (9.9)	174 (9.9)	172 (9.8)
Medical history — no./total no. (%)			
Myocardial infarction	1138/3504 (32.5)	589/1749 (33.7)	549/1755 (31.3)
Percutaneous coronary intervention	1200/3503 (34.3)	623/1749 (35.6)	577/1754 (32.9)
Coronary-artery bypass grafting	762/3504 (21.7)	372/1749 (21.3)	390/1755 (22.2)
Heart failure	1066/3504 (30.4)	527/1749 (30.1)	539/1755 (30.7)
Angiography — no./total no. (%)			
Results available before randomization	1738/3504 (49.6)	885/1749 (50.6)	853/1755 (48.6)
Multivessel coronary artery disease: >50% obstruction	1103/1679 (65.7)	565/856 (66.0)	538/823 (65.4)
Left ventricular ejection fraction			
Quantitative assessment available — no. (%)	2558 (73.0)	1282 (73.3)	1276 (72.7)
Most recent result in past year — %	47.4±13.5	47.3±13.4	47.5±13.7
Categorical assessment available — no./total no. (%)			
30 to <45%: moderate	807/2929 (27.6)	397/1460 (27.2)	410/1469 (27.9)
<30%: severe	292/2929 (10.0)	145/1460 (9.9)	147/1469 (10.0)
Index myocardial infarction — no. (%)			
NSTEMI	2848 (81.3)	1430 (81.8)	1418 (80.8)
Type 1	1460 (41.7)	730 (41.7)	730 (41.6)
Type 2	1955 (55.8)	967 (55.3)	988 (56.3)
Medical finding or therapy before randomization			
Revascularization for treatment of index myocardial infarction — no. (%)	1002 (28.6)	509 (29.1)	493 (28.1)
In-hospital heart failure — no. (%)	780 (22.3)	377 (21.6)	403 (23.0)
Mechanical ventilation — no. (%)	481 (13.7)	250 (14.3)	231 (13.2)
Active bleeding — no. (%)	459 (13.1)	246 (14.1)	213 (12.1)
Red-cell transfusion — no. (%)	1237 (35.3)	599 (34.2)	638 (36.4)
Hemoglobin — g/dl	8.6±0.8	8.6±0.8	8.6±0.8
Median creatinine (IQR) — mg/dl	1.4 (0.9–2.5)	1.4 (0.9–2.6)	1.4 (0.9–2.5)
Renal dialysis — no./total no. (%)	415/3503 (11.8)	203/1748 (11.6)	212/1755 (12.1)

* Plus–minus values are means ±SD. To convert the values for creatinine to micromoles per liter, multiply by 88.4. IQR denotes interquartile range, and NSTEMI non–ST-segment elevation myocardial infarction.

† Race or ethnic group was reported by the patients. The "other" category included patients who identified as Asian, American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, First Nations Inuit or Metis, or multiracial. Data were missing for 323 patients in France (where racial data are not reported) and for 23 patients in other countries.

Outcome	Restrictive Strategy	Liberal Strategy	Risk Ratio (95% CI)
	no. of patients/total no. (%)		
Primary outcome			
Myocardial infarction or death	295/1749 (16.9)	255/1755 (14.5)	1.16 (1.00–1.35)
Secondary outcomes			
Death	173/1749 (9.9)	146/1755 (8.3)	1.19 (0.96–1.47)
Myocardial infarction	149/1749 (8.5)	126/1755 (7.2)	1.19 (0.94–1.49)
Death, myocardial infarction, revascularization, or rehospitalization	342/1749 (19.6)	305/1755 (17.4)	1.13 (0.98–1.29)
Other outcomes			
Heart failure	102/1749 (5.8)	111/1755 (6.3)	0.92 (0.71–1.20)
Death, myocardial infarction, or unstable angina	338/1749 (19.3)	300/1755 (17.1)	1.13 (0.98–1.30)
Unscheduled revascularization	43/1749 (2.5)	39/1755 (2.2)	1.11 (0.72–1.70)
Cardiac death	97/1749 (5.5)	56/1755 (3.2)	1.74 (1.26–2.40)
Stroke	30/1749 (1.7)	26/1755 (1.5)	1.16 (0.69–1.95)
Pulmonary embolism or deep venous thrombosis	26/1749 (1.5)	34/1755 (1.9)	0.77 (0.46–1.27)
Pneumonia or bacteremia	166/1749 (9.5)	153/1755 (8.7)	1.09 (0.88–1.34)





JAMA®

QUESTION Does continuously delivered β-blockade with landiolol for up to 14 days reduce risk of organ failure as measured by the Sequential Organ Failure Assessment (SOFA) score among patients with tachycardia while being treated with norepinephrine for septic shock?

CONCLUSION These results do not support the use of landiolol for managing patients with tachycardia treated with norepinephrine for established septic shock.

POPULATION

74 Men **52** Women

Adults ≥18 years in intensive care unit (ICU) with septic shock receiving ≥0.1 μg/kg/min norepinephrine and heart rate ≥95/min

Mean age: **55.6** years

LOCATION

40
National Health Service ICUs in the UK

INTERVENTION

126 Patients randomized

63
Landiolol infusion
Continuous infusion during ICU stay of landiolol starting at 1.0 μg/kg/min and titrated to reach target heart rate

63
Standard care
Did not receive landiolol during stay in the ICU

PRIMARY OUTCOME

Mean SOFA score over the first 14 days after trial entry while in the ICU (SOFA score range, 0-20; higher score, worse organ dysfunction)

FINDINGS

Mean (SD) SOFA score

Landiolol infusion	Standard care
8.8 (3.9)	8.1 (3.2)

These results do not support the use of landiolol for managing patients with tachycardia and established septic shock:

Mean difference, 0.75
(95% CI, −0.49 to 2.0)

Whitehouse T, Hossain A, Perkins GD, et al; the STRESS-L Collaborators. Landiolol and organ failure in patients with septic shock: the STRESS-L randomized clinical trial. *JAMA*. Published online October 25, 2023. doi:10.1001/jama.2023.20134

JAMA®

QUESTION Is the exclusion of aspirin as part of the antithrombotic regimen with a fully magnetically levitated left ventricular assist device (LVAD) safe?

CONCLUSION Aspirin is not required to maintain outcomes with a magnetically levitated LVAD in advanced heart failure.

POPULATION

456 Men
133 Women

Adults with advanced heart failure receiving LVAD support

Mean age: **58** years

LOCATION

51
Medical centers in North America, Europe, Kazakhstan, and Australia

INTERVENTION

628 Patients randomized
589 Patients analyzed

314
Placebo
Placebo added to antithrombotic regimen with a fully magnetically levitated LVAD and vitamin K antagonist therapy

314
Aspirin
Aspirin (100 mg/d) added to antithrombotic regimen with a fully magnetically levitated LVAD and vitamin K antagonist therapy

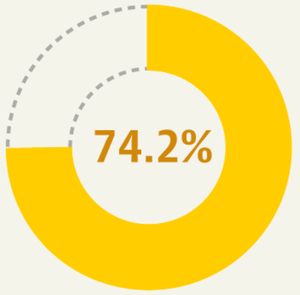
PRIMARY OUTCOME

Survival free of a major nonsurgical hemocompatibility-related adverse event (stroke, pump thrombosis, major bleeding, or arterial peripheral thromboembolism) at 12 months

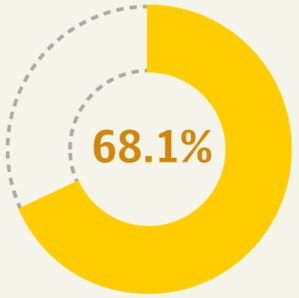
FINDINGS

Patients with composite primary outcome

Placebo
201 of 271 patients



Aspirin
186 of 273 patients



Noninferiority (−10% margin) of placebo was demonstrated:

Between-group difference, 6.0% improvement in event-free survival with placebo
(lower 1-sided 97.5% confidence limit, -1.6%); *P* < .001

Mehra MR, Netuka I, Uriel N, et al; for the ARIES-HM3 Investigators. Aspirin and hemocompatibility events with a left ventricular assist device in advanced heart failure: the ARIES-HM3 randomized clinical trial. *JAMA*. Published online November 11, 2023. doi:10.1001/jama.2023.23204

Kotani *et al. Critical Care* (2023) 27:465
https://doi.org/10.1186/s13054-023-04755-5

Critical Care

RESEARCH Open Access

Positive single-center randomized trials and subsequent multicenter randomized trials in critically ill patients: a systematic review

Yuki Kotani[1,2,3], Stefano Turi[1], Alessandro Ortalda[1], Martina Baiardo Redaelli[1], Cristiano Marchetti[1], Giovanni Landoni[1,2*] and Rinaldo Bellomo[4,5]