JOURNAL WATCHER

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THIS WEEK IN BRIEF

Cardiogenic shock and ECMO lead again. The 2026 SCAI SHOCK update stages shock by perfusion physiology and trajectory. In DAPT-SHOCK-AMI, crushed ticagrelor gave effective platelet inhibition at the end of PCI in 22% of patients against 100% with cangrelor, but a 1-point margin left the clinical endpoint inconclusive. OnScene reported 40% vs 20% survival with helicopter ECPR in a nonrandomized design, and in HERACLES the IABP improved a myocardial supply-demand estimate on VA-ECMO where Impella CP did not.

Bicarbonate lowered RRT starts without a clear survival effect; albumin did not prevent AKI, and 20% albumin was linked to more RRT. HFNO may reduce intubation in one immunocompromised subgroup, APRV improved oxygenation only, thrombectomy for PE showed observational associations, and funobactam met a wide non-inferiority margin.

Strategic priorities. Cardiogenic shock, MCS and ECMO: Baran (rank 1), SCAI SHOCK 2026; Motovska (rank 2), cangrelor in infarct-related shock; Reis Miranda (rank 3), OnScene prehospital ECPR; Ezad (rank 4), IABP vs Impella unloading on VA-ECMO. Ventilation: Maillard (rank 6) on HFNO and Sajawal (rank 7) on APRV. The Thiele editorial on the SCAI update was summarized and not briefed. No supplementary strategic article was added this week.

22%
of patients loaded with crushed ticagrelor had effective platelet inhibition at the end of PCI, against 100% with cangrelor (Motovska, DAPT-SHOCK-AMI)

40%
survived to discharge with helicopter-delivered on-scene ECPR vs 20% with conventional care, nonrandomized (Reis Miranda, OnScene)

0.74
risk ratio for RRT initiation with sodium bicarbonate, 97.2% probability of benefit (Kitisin)

AT A GLANCE

#	Study	Design	Result in one line	Signal
1	**Baran: SCAI SHOCK 2026** Baran et al, JSCAI 2026	Expert consensus, ungraded	Normotensive hypoperfusion is stage C; restage by 2 to 6 h	Consider locally
2	**Motovska: cangrelor in MI shock** Motovska et al, Lancet 2026	Double-blind RCT, 605 adults	Platelet inhibition 100% vs 22%; 30-day composite 38% vs 41%	Consider locally
3	**Reis Miranda: OnScene** Reis Miranda et al, N Engl J Med 2026	Nonrandomized stepped-wedge, 231 adults	Survival 40% vs 20%; adjusted OR 2.66	Consider locally
4	**Ezad: IABP vs Impella on ECMO** Ezad et al, Circ Cardiovasc Interv 2026	Mechanistic RCT, 24 adults	Supply-demand ratio 1.48 vs 0.97; P=0.036	Consider locally
5	**Kitisin: bicarbonate meta-analysis** Kitisin et al, Intensive Care Med 2026	Bayesian meta-analysis, 4 RCTs	RRT RR 0.74 (95% CrI 0.59 to 0.98)	Confirms practice
6	**Maillard: HFNO subgroups** Maillard et al, Intensive Care Med 2026	Post hoc analysis of HIGH, 704 adults	Best tercile IMV 32.2% vs 53.0%	Watch
7	**Sajawal: APRV meta-analysis** Sajawal et al, Lung 2026	Meta-analysis, 9 RCTs, 585 adults	Mortality RR 0.95 (95% CI 0.72 to 1.26)	Confirms practice
8	**Ismayl: thrombectomy in PE** Ismayl et al, JSCAI 2026	Meta-analysis, 1 RCT, 11 cohorts	In-hospital death RR 0.72 (95% CI 0.31 to 1.69)	Watch
9	**Jeanmougin: albumin and AKI** Jeanmougin et al, Crit Care 2026	Meta-analysis, 9 RCTs, 11,778 adults	AKI RR 1.00; RRT RR 1.26 with 20% albumin	Confirms practice
10	**Chang: funobactam for HABP** Chang et al, Lancet Infect Dis 2026	Non-inferiority RCT, 450 adults	14-day death 3.0% vs 2.7%	Watch

Signals: CHANGE PRACTICE CONSIDER LOCALLY CONFIRMS PRACTICE WATCH Click a title to jump to its card · This week on SharePoint

The studies

1. SCAI SHOCK 2026: every stage now rests on perfusion physiology and trajectory, with drugs and devices as supporting evidence

CONSIDER LOCALLY Baran et al, JSCAI 2026 · Expert consensus, ungraded · Certainty: **Very low** · PDF · Briefing

Bottom line. The third SCAI SHOCK classification, endorsed by eight societies including SCCM, assigns stage from physiology and trajectory alone. Vasoactive dose, the vasoactive-inotropic score and new mechanical circulatory support (MCS) are complementary evidence and cannot define a stage. Hypoperfusion with or without hypotension marks stage C, stage D is failure of initial support after time for treatment to act, and ECLS alone no longer defines stage E. The arrest modifier is reserved for comatose post-arrest patients. No new data are analyzed.

Population: Patients with an acute or acute-on-chronic cardiac event or a defined high-risk cardiac procedure, from prehospital care to the ICU, including children • **Scope:** Stages A to E, the arrest modifier, restaging, and phenotypes: infarct-related, heart failure, RV-predominant, mixed, postcardiotomy and pediatric shock • **Evidence:** Narrative literature review; votes by members without relevant industry ties at a 75% threshold; no systematic search or grading

RESULTS

- Stage C descriptors include lactate 2 mmol/L or more, creatinine 1.5 times baseline, urine output below 30 mL/h and, where invasive hemodynamics are measured (strongly recommended), cardiac index below 2.2 L/min/m2 and PCWP above 15 mm Hg. Stage E descriptors include lactate 8 mmol/L or more, pH 7.2 or lower and ongoing CPR.
- Restaging at about 2 to 3 hours identifies clear worsening, and up to 4 to 6 hours judges failure to respond; renal and hepatic markers can lag by more than 12 to 24 hours.
- Mixed cardiogenic and vasodilatory shock, about 20% of cardiac ICU shock admissions, is supported by an SVR below 1000 to 1200 dyn·s/cm5. As a consensus document, no NNT or fragility index applies.

CAVEATS

- Narrative review plus opinion, with no evidence grading or reported vote tallies; reassessment windows and SVR cut-offs lack prospective validation.
- Moving normotensive hypoperfusion into stage C departs from the Cardiogenic Shock Working Group construct without a systematic comparison, and interrater agreement across disciplines is unquantified.
- The pre-proof descriptor table still links stages C and D to therapy, at odds with the text, and several members report MCS industry relationships.

How it fits. *The update keeps the 2019 and 2022 criteria largely intact while changing what a stage means. In the accompanying editorial, Thiele, Hassager and Freund support staging by physiology, since escalation reflects institutional preference and device access as much as severity, and propose reporting stage and support intensity as parallel variables. They flag residual therapy-based wording, untested restaging windows and the unexplained divergence on normotensive hypoperfusion. Nothing here shows that stage-based escalation improves survival.*

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2. DAPT-SHOCK-AMI: cangrelor achieved platelet inhibition that crushed ticagrelor rarely did, but a 1-point margin left the clinical endpoint inconclusive

CONSIDER LOCALLY Motovska et al, Lancet 2026 · Double-blind RCT, 605 adults · Certainty: **Moderate** · PDF · Briefing

Bottom line. In 605 patients with infarct-related cardiogenic shock (AMI-CS) undergoing primary PCI, 61% ventilated and 55% after out-of-hospital arrest, cangrelor achieved effective P2Y12 inhibition at the end of PCI in 56 of 56 tested patients against 15 of 68 (22%) with crushed ticagrelor. The 30-day composite of death, myocardial infarction or ischemic stroke was 38% vs 41%, risk difference -4 points (90% CI -10 to 3), and non-inferiority within a 1-point margin was not shown. Major bleeding did not differ.

Population: Adults with AMI-CS scheduled for primary PCI; 89% STEMI; no pre-admission P2Y12 load • **Intervention:** Cangrelor bolus and infusion for at least 2 hours, bridged to crushed ticagrelor • **Comparison:** Crushed ticagrelor 180 mg orally or by nasogastric

tube, with placebo infusion • **Outcome:** Platelet reactivity index below 50% at end of PCI (superiority); 30-day death, MI or ischemic stroke (non-inferiority)

RESULTS

- Primary clinical endpoint 112 of 298 vs 126 of 307; HR 0.86 (95% CI 0.68 to 1.08). All-cause death at 30 days 37% vs 40%. Definite stent thrombosis 0 vs 9 (3%) and reinfarction 0 vs 5; ischemic stroke 4 vs 1.
- Exploratory 1-year all-cause death 44% vs 49%, and cardiovascular death, MI, urgent revascularization or heart failure 33% vs 42% (HR 0.76, 95% CI 0.59 to 0.99), unadjusted for multiplicity. BARC 3b or higher bleeding at 30 days 6% vs 5%.
- No NNT for the clinical endpoint, which was not significant; fragility index not applicable to it. For the platelet co-primary endpoint the fragility index is 35 (Fisher's exact test), so that result is robust.

CAVEATS

- A 1-point non-inferiority margin paired with an assumed 10-point benefit made the test close to a superiority test, and observed event rates were below the assumed 50%.
- Platelet testing covered only 124 of 605 patients at selected centres; the encouraging ischemic and late mortality signals rest on small, exploratory counts.
- Baseline differences (median LVEF 35% vs 30%, less MCS with cangrelor) could favour cangrelor; adverse events were not systematically collected.

How it fits. *The landmark P2Y12 trials barely enrolled patients in shock, so this is the first randomized evidence in AMI-CS. Pre-publication commentary by Grand, Vranckx and van Diepen judged the projected effect optimistic and the 12-month findings hypothesis-generating, and a PCRonline review called the margin unusually conservative. The pharmacodynamic gap is the most secure finding; whether it costs lives remains untested.*

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3. OnScene: helicopter teams carrying ECMO reached flow 30 minutes sooner, and survival to discharge doubled in a nonrandomized national design

CONSIDER LOCALLY Reis Miranda et al, N Engl J Med 2026 · Nonrandomized stepped-wedge, 231 adults · Certainty: **Low** · PDF · Briefing

Bottom line. As all four Dutch helicopter emergency medical service (HEMS) stations switched from conventional care to carrying ECMO, adults aged 18 to 50 with refractory out-of-hospital cardiac arrest survived to discharge in 57 of 144 (40%) in ECMO-capable periods vs 17 of 87 (20%) before: adjusted OR 2.66 (95% CI 1.56 to 4.55). Favourable neurological outcome at 6 months was 36% vs 13%, and median time to ECMO flow was 45 vs 77 minutes. Allocation followed calendar period and was never randomized.

Population: Age 18 to 50, witnessed or with signs of life, shockable rhythm or PEA with suspected PE, refractory more than 20 minutes after dispatch, end-tidal CO2 at least 1.2 kPa • **Intervention:** HEMS team with ECMO onboard: ultrasound-guided femoral cannulation and VA-ECMO on scene • **Comparison:** HEMS team without ECMO; transport for in-hospital ECPR allowed (24 of 87) • **Outcome:** Survival to hospital discharge; CPC 1 or 2 at 6 months

RESULTS

- Cannulation was attempted in 98 of 144 intervention patients; 32 reached ROSC first. Unadjusted OR for survival 2.72 (95% CI 1.59 to 4.66).
- CPC 1 or 2: 51 of 141 vs 11 of 85, OR 4.22 (95% CI 2.82 to 6.32). Observational NNT about 5 for survival and about 4 for favourable neurological outcome. Fragility index not applicable, as the study was not randomized.
- Cannulation failure 15 of 98 on scene vs 4 of 24 in hospital; lethal cannulation bleeding 1 of 98 vs 2 of 24. Survival 35% with on-scene ECPR vs 25% (6 of 24) with in-hospital ECPR in the conventional arm.

CAVEATS

- Every station moved to the intervention later in calendar time, so secular change is confounded with treatment, and four clusters are too few for robust standard errors.
- Ventricular fibrillation or tachycardia 89% vs 75% and PE as cause 11% vs 23% favoured the intervention arm; eligibility was judged by unblinded teams.
- One unblinded assessor graded CPC, enrolment stopped at 231 of 390, and the intervention is a bundle of training, ultrasound, telemedicine and downstream care.

How it fits. *ARREST, Prague-OHCA and INCEPTION used transport-based ECPR with collapse-to-flow times near an hour and gave mixed results; OnScene points to time to flow as the modifiable driver. An accompanying NEJM editorial could not be opened. Lorne Porayko (BC ICU Doc) called the result "impressive, plausible, and unrandomized" and argued for a trial that randomizes crossover order and blinds outcome assessment.*

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4. HERACLES: on VA-ECMO, the IABP improved an invasive myocardial supply-demand estimate where Impella CP did not

CONSIDER LOCALLY Ezad et al, Circ Cardiovasc Interv 2026 · Mechanistic RCT, 24 adults · Certainty: **Low** · PDF · Briefing

Bottom line. In 24 patients on VA-ECMO for cardiogenic shock (median age 51, LVEF 10%, 96% SCAI D or E), randomized to intra-aortic balloon pump (IABP) or Impella CP and measured with each device off and then on, the IABP raised the estimated myocardial oxygen supply-demand ratio to a median 1.48 (IQR 1.23 to 2.10) while Impella left it at 0.97 (IQR 0.92 to 1.39); P=0.036. Both lowered LV end-diastolic pressure similarly; the difference came mainly from a larger fall in myocardial work with the IABP.

Population: Adults on peripheral VA-ECMO for cardiogenic shock needing catheterization and LV unloading; postcardiotomy shock excluded • **Intervention:** IABP at 1:1 • **Comparison:** Impella CP at P5, with a P3 step • **Outcome:** Within-patient change in coronary flow (thermodilution) over tension-time index times heart rate

RESULTS

- Estimated demand fell 25% with the IABP vs 6% with Impella (P=0.05); coronary flow changed little with either device, and Impella raised distal coronary pressure by 3 mm Hg without more flow.
- LVEDP fell 4 vs 5 mm Hg (P=0.92). The pressure-based Buckberg index rose with the IABP (1.31) with no between-group difference (P=0.35).
- Exploratory 30-day mortality 38% vs 45% (P=0.84). The primary endpoint is continuous, so no fragility index applies, and no NNT is derivable.

CAVEATS

- Twenty-four patients, the minimum of a target of 36, with one significant primary comparison and many unadjusted secondary ones.
- The ratio is a composite of surrogates without LV volumes or measured oxygen consumption, and Impella was never tested above P5.
- IABP patients had higher LVEDP and lower pulse pressure at baseline, and the authors caution that IABP benefit depends on residual native ejection.

How it fits. *Prior pressure-volume work suggested that venting and true unloading differ; HERACLES is the first randomized head-to-head physiological comparison in patients. It offers no outcome evidence, which UNLOAD-ECMO, EULODIA, EASE-ECMO, REMAP-ECMO and ANCHOR should supply. No editorial or other commentary was found.*

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5. Bicarbonate for metabolic acidemia: little evidence of a survival effect and a 97% probability of fewer RRT starts

CONFIRMS PRACTICE Kitisin et al, Intensive Care Med 2026 · Bayesian meta-analysis, 4 RCTs · Certainty: **Moderate** · PDF · Briefing

Bottom line. Pooling BICAR-ICU, BICARICU-2 and both SODa-BIC trials (1,544 adults with metabolic acidosis), intravenous sodium bicarbonate gave a short-term mortality RR of 0.94 (95% CrI 0.73 to 1.22), a 72.1% posterior probability of benefit. Renal replacement therapy (RRT) initiation was lower, RR 0.74 (95% CrI 0.59 to 0.98), with a 97.2% probability of benefit, consistent across sceptical and optimistic priors and a frequentist model.

Population: Adult ICU patients with metabolic acidosis; French trials pH 7.20 or below (BICARICU-2 also KDIGO AKI 2 to 3), SODa-BIC trials pH below 7.30 on vasopressors • **Intervention:** IV sodium bicarbonate titrated to pH 7.30 or higher (4.2% boluses or continuous infusion) • **Comparison:** No bicarbonate (open-label) or 5% dextrose placebo (double-blind) • **Outcome:** Day 28 or 30 all-cause mortality; RRT initiation

RESULTS

- RRT starts 221 of 768 vs 313 of 776 summed across trials; applying RR 0.74 to the pooled control rate of 40.3% gives an NNT of about 10. Mortality NNT not derivable, as the effect was uncertain.
- 90-day mortality RR 0.99 (95% CrI 0.72 to 1.34); RRT dependence RR 0.82 (95% CrI 0.53 to 1.27, post hoc). Vasopressor-free days and length of stay did not differ.
- Predictive interval for RRT 0.46 to 1.30. A post hoc analysis gave an 85.4% probability that timing of RRT differed by less than 12 hours, arguing against simple postponement.

CAVEATS

- The two open-label French trials supplied 434 of 534 RRT events, and RRT initiation is clinician-dependent.
- Populations differ sharply (median pH 7.15 with lactate 5 to 6 mmol/L vs pH 7.26 with lactate about 2.5), and kidney recovery beyond day 30 was not consistently reported.
- Three authors led included trials and the journal's editor-in-chief is an author (declared, with recusal); hypernatremia, alkalosis and hypocalcemia were numerically more frequent.

How it fits. *The Surviving Sepsis Campaign advises against bicarbonate for lactic acidemia to improve hemodynamics and suggests it for severe acidemia with AKI; this synthesis supports that split. The Bottom Line's review of SODa-BIC endorsed selective use for physiological goals. MOSAICC is ongoing. No commentary on this paper was found.*

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6. A causal forest reanalysis of HIGH suggests HFNO may reduce intubation in a subgroup of immunocompromised patients

WATCH Maillard et al, Intensive Care Med 2026 · Post hoc analysis of HIGH, 704 adults · Certainty: **Low** · PDF · Briefing

Bottom line. In 704 immunocompromised adults from the HIGH trial without a do-not-intubate order, high flow nasal oxygen (HFNO) did not significantly change day-28 invasive ventilation overall (42.2% vs 47.8%). A causal forest ranked patients by predicted benefit, with modest discrimination (c-for-benefit 0.59, 95% CI 0.51 to 0.67). In the tercile with the highest predicted benefit, invasive ventilation was 32.2% with HFNO vs 53.0% with conventional oxygen (sHR 0.55, 95% CI 0.37 to 0.80); the other terciles showed no difference, and there was no mortality interaction.

Population: Immunocompromised adults with acute hypoxemic respiratory failure in 32 French ICUs, mostly hematologic or solid malignancy · **Intervention:** HFNO as randomized in HIGH · **Comparison:** Conventional oxygen · **Outcome:** Day-28 invasive ventilation, a secondary non-adjudicated trial outcome

RESULTS

- The highest-benefit group was older (median 69 years), on higher oxygen flow (13 L/min), with lower PaO2/FiO2 and non-respiratory SOFA, and fewer myeloid malignancies or aplasia. Interaction P=0.010 for intubation and P=0.109 for death.
- Day-28 mortality 33.9% vs 34.3% overall. In the best stratum an NNT of about 5 follows from the counts, but it describes a model-derived group and does not transfer to individual patients; fragility index not applicable to a post hoc analysis.
- In an external French cohort of 565 patients (107 on HFNO), c-for-benefit was 0.82 (95% CI 0.77 to 0.86), though absolute HFNO benefit was overestimated.

CAVEATS

- Post hoc, with intubation decided without protocol criteria, so part of any effect may run through clinician behaviour.
- The lower confidence bound of the c-for-benefit sits near chance, and the subgroup comparisons use the same patients that trained the model.
- The external cohort is observational and miscalibrated; both datasets are French and the trial data are a decade old.

How it fits. *HIGH found no benefit of HFNO on mortality or intubation, and that result still sets expectations for hard outcomes. This analysis is best read as a hypothesis about whom to enrich in a future trial. Several authors report support from an HFNO manufacturer. No external commentary was found.*

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7. APRV in ARDS: better PaO2/FiO2 and higher mean airway pressure, with no demonstrated survival benefit

CONFIRMS PRACTICE Sajawal et al, Lung 2026 · Meta-analysis, 9 RCTs, 585 adults · Certainty: **Very low** · PDF · Briefing

Bottom line. Across nine small randomized trials (585 adults with or at risk of ARDS), airway pressure release ventilation (APRV) did not change mortality: RR 0.95 (95% CI 0.72 to 1.26), an interval compatible with a 28% relative reduction or a 26% increase. PaO2/FiO2 was 56.21 mm Hg higher (95% CI 24.63 to 87.79) and mean airway pressure 3.97 cm H2O higher. Ventilator-free days and ventilation duration did not clearly differ, and certainty was very low for every outcome except peak airway pressure.

Population: Adults with ARDS or acute lung injury (six trials), at high risk of ARDS (two) or ventilated after cardiac surgery (one) • **Intervention:** APRV with varied P-low, release time and spontaneous breathing settings • **Comparison:** Low tidal volume ventilation (three trials), SIMV with PEEP or pressure support, or pressure control with paralysis • **Outcome:** Mortality at trial-defined follow-up

RESULTS

- Mortality diverged by time point: RR 1.22 (95% CI 0.94 to 1.59) in the three 28-day trials and 0.74 (95% CI 0.52 to 1.05) in the three with later follow-up.
- ICU stay 2.53 days shorter (95% CI 0.64 to 4.43), losing significance with Hartung-Knapp intervals. Excluding high-risk-of-bias trials, the oxygenation gain was 45.86 mm Hg (95% CI -2.46 to 94.18).
- No NNT is derivable, as no outcome effect was demonstrated. Barotrauma and hemodynamic effects were not pooled.

CAVEATS

- No trial exceeded 138 patients, and postoperative, at-risk and established ARDS populations with outdated comparators were pooled.
- Continuous outcomes rely on median-to-mean conversions and digitized figures, and Table 3 gives a ventilation-duration interval that contradicts the text.
- Most sensitivity analyses were not prespecified, and reporting bias could not be tested.

How it fits. *Earlier meta-analyses reported lower hospital mortality with APRV; assembled cleanly, with the duplicate Varpula cohort linked to its parent, that signal does not reproduce. The oxygenation response is a surrogate with the usual trade-offs of higher mean airway pressure. No external commentary was found.*

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8. Thrombectomy for intermediate-risk PE: no in-hospital mortality difference, with later survival associations confined to observational cohorts

WATCH Ismayl et al, JSCAI 2026 · Meta-analysis, 1 RCT, 11 cohorts · Certainty: **Low** · PDF · Briefing

Bottom line. Across one 100-patient randomized trial and 11 observational cohorts (4,268 adults with intermediate-risk pulmonary embolism), mechanical thrombectomy added to anticoagulation was not associated with lower in-hospital mortality: RR 0.72 (95% CI 0.31 to 1.69). It was associated with lower 30-day (RR 0.24, 95% CI 0.09 to 0.67), 1-year (RR 0.34) and 2-year (RR 0.45) mortality and less chronic thromboembolic pulmonary hypertension (CTEPH; RR 0.40, 95% CI 0.17 to 0.94), all from observational data. Major bleeding did not clearly differ.

Population: Adults with acute intermediate-risk PE (RV dysfunction or troponin rise without instability); some cohorts included higher-risk patients • **Intervention:** Mechanical thrombectomy plus anticoagulation, mostly FlowTriever • **Comparison:** Anticoagulation alone • **Outcome:** In-hospital mortality

RESULTS

- Major bleeding RR 1.46 (95% CI 0.43 to 4.91). In STORM-PE, the only RCT, 7-day PE-related mortality was 4.3% with thrombectomy vs 0%.
- Restricted to cohorts enrolling only intermediate-risk PE, 30-day mortality was no longer significant: RR 0.29 (95% CI 0.04 to 2.20).
- One-year, 2-year and CTEPH estimates each rest on two studies pooled with fixed-effect models. NNT not derivable: pooled absolute event rates are not reported and the estimates are adjusted observational ratios.

CAVEATS

- The RCT contributes to none of the outcomes that showed benefit, and confounding by indication is the dominant threat.
- A 55% fall in 2-year all-cause death is larger than clot removal plausibly explains, and active cancer was less frequent in thrombectomy arms in several cohorts.
- Three cohorts used historical comparators, populations and devices varied, and publication bias was not assessed.

How it fits. *The 2026 AHA/ACC PE guideline gives thrombectomy a Class IIb recommendation, and PulmCCM's review of STORM-PE noted physiological gains without patient-centred benefit. PEERLESS II and PE-TRACT should test early routine thrombectomy on clinical outcomes. No independent commentary was found.*

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9. Albumin did not prevent AKI across nine trials, and 20% albumin carried a low-certainty signal of more RRT

CONFIRMS PRACTICE Jeanmougin et al, Crit Care 2026 · Meta-analysis, 9 RCTs, 11,778 adults · Certainty: **Low** · PDF · Briefing

> **Bottom line.** In nine randomized trials of 11,778 non-cirrhotic critically ill adults, albumin for fluid resuscitation did not reduce acute kidney injury (AKI): RR 1.00 (95% CI 0.91 to 1.11), and trial sequential analysis crossed the futility boundary for a 15% relative reduction. In four trials of 3,226 patients, all using 20% albumin after cardiac surgery or in sepsis, new renal replacement therapy (RRT) was more frequent: RR 1.26 (95% CI 1.07 to 1.48), low certainty. Mortality did not differ.

Population: Adult ICU patients needing resuscitation fluid: sepsis, cardiac surgery, burns, major surgery and an unselected ICU cohort · **Intervention:** Albumin 4%, 5% or 20%; median total dose 70 g · **Comparison:** Crystalloid (five trials) or standard care (four) · **Outcome:** AKI as defined by each trial

RESULTS

- Mortality RR 0.98 (95% CI 0.92 to 1.05); ICU stay 0.33 days longer (95% CI 0.12 to 0.55). No subgroup modified the AKI effect.
- Required information size 14,039 patients; the Z-curve crossed the futility boundary at 11,778, assuming a 21% control AKI rate.
- NNH for RRT not derivable: per-trial RRT counts were in figures unavailable in the text, and pooled absolute rates are not reported.

CAVEATS

- AKI definitions varied, and SAFE and ALBIOS contribute renal SOFA changes, which capture worsening of existing dysfunction.
- SAFE (6,997 patients, 4% albumin, 2004) dominates the AKI estimate.
- The RRT signal is a secondary outcome from four of nine trials, with unstandardized RRT initiation and only two trials blinding participants and staff.

How it fits. *The RRT finding contrasts with a 2015 sepsis network meta-analysis and aligns with the higher AKI rate in ALBICS AKI and the hyperoncotic starch experience. Read with Kitisin (rank 5): both turn on RRT initiation, a clinician-dependent outcome. No external commentary was found.*

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10. Imipenem-funobactam met a 10-point non-inferiority margin for HABP and VABP at a 2.7% control mortality

WATCH Chang et al, Lancet Infect Dis 2026 · Non-inferiority RCT, 450 adults · Certainty: **Low** · PDF · Briefing

Bottom line. In 449 treated adults with hospital-acquired or ventilator-associated bacterial pneumonia (HABP or VABP), almost all in China and over 60% with primary neurological disease, 14-day mortality was 3.0% (9 of 299) with imipenem-cilastatin-funobactam vs 2.7% (4 of 150) with imipenem-cilastatin-relebactam, difference 0.2% (95% CI -3.5 to 4.0), within the 10% margin. Clinical success was 63% in both arms; 28-day mortality was 7.7% vs 3.3%, difference 4.1% (95% CI -0.4 to 8.7).

Population: Adults with Gram-negative HABP, ventilated HABP or VABP; APACHE II 30 or below; immunocompromise excluded • **Intervention:** Imipenem-cilastatin-funobactam every 6 h for 7 to 14 days • **Comparison:** Imipenem-cilastatin-relebactam, randomized 2:1 • **Outcome:** 14-day all-cause mortality, 10% non-inferiority margin

RESULTS

- Carbapenem-resistant subset (76 patients, 16.9%): 14-day mortality 1.9% vs 8.7%, clinical success 64% vs 44%; intervals wide and comparator inactive against most A baumannii isolates.
- Treatment-related hepatic events 22.1% vs 33.3% (post hoc). No drug-related deaths.
- No NNT or NNH, as no difference was significant; fragility index not applicable to a non-inferiority result without a significant difference.

CAVEATS

- At 2.7% control mortality, a 10-point margin would accept a several-fold relative increase in death; the authors concede the margin no longer fits current care.
- The 28-day imbalance is attributed post hoc to neurological deaths and case mix and cannot be dismissed.
- Sponsor-funded with sponsor employees as authors; follow-up non-completion was asymmetric (38 vs 11) and breakpoints are provisional.

How it fits. *Funobactam is a diazabicyclooctane inhibitor with class D activity, so its potential lies in OXA-producing carbapenem-resistant A baumannii, where options are scarce and this trial was not powered. An accompanying Lancet Infectious Diseases Comment could not be accessed, and no other commentary was found.*

Pattern of the week. Statistical framing shaped three randomized results as much as the data did: DAPT-SHOCK-AMI failed a 1-point non-inferiority margin with point estimates favouring cangrelor, the funobactam trial passed a 10-point margin at a control mortality under 3%, and HERACLES rested on one physiological composite in 24 patients. Two kidney meta-analyses turned on RRT initiation, a clinician-dependent outcome, without survival effects. APRV and thrombectomy showed surrogate or observational gains only, and OnScene and the SCAI update both put time and trajectory at the centre of shock and arrest care.

Issue 778: 97 items catalogued (94 new, 3 cited again); 10 ranked articles briefed, all from the full-text articles, plus 16 editorial and commentary summaries. AI generated; go to the original paper when in doubt.

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