10-2023

Pulmonary & Critical Care Insider: Issue 3

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PULMONARY & CRITICAL CARE INSIDER

Issue 3

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VIEWPOINTS

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ADOPTED FROM PULMCC AND CITED ARTICLES.

Lactated Ringer's or Normal Saline in Acute Pancreatitis?

Early administration of intravenous fluid is crucial to improve outcomes and help prevent pancreatic necrosis. Neither lactated Ringer's solution nor normal saline has been shown to be definitively superior for acute pancreatitis (AP); both fluids are recommended by the latest guidelines from *American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis*, 2018. Furthermore, a recent meta-analysis from 2021 in *Journal of Pancreatology* comparing lactated Ringer's and saline in AP showed no difference in mortality or the development of the systemic inflammatory response syndrome, but fewer intensive care unit admissions occurred with lactated Ringer's.

To examine outcomes with the two fluid types, researchers conducted a prospective, observational, 22-site international study of 1000 patients with acute pancreatitis who received lactated Ringer's or normal saline within the first 24 hours of hospitalization; 36% received saline, 33% received lactated Ringer's, and 31% received a combination of the two. Moderate-to-severe pancreatitis (i.e., organ failure or local complications) occurred in 236 patients. After adjusting for potentially confounding factors, patients who received lactated Ringer's were significantly less likely to develop moderate-to-severe pancreatitis than those who received saline (adjusted odds ratio, 0.52).

Conclusion:
This large observational study suggests that lactated Ringer's might prevent moderate-to-severe pancreatitis more effectively than normal saline. However, one limitation is that we do not know if physiologic treatment goals differed between the groups and affected outcomes. While we wait for further clarity from the upcoming WATERLAND randomized, controlled trial, clinicians might preferentially consider using lactated Ringer's in patients with AP.

Clinical Trial Link: https://clinicaltrials.gov/study/NCT05781243

VIEWPOINTS

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Don’t complain about too many CT scans being ordered by your ED doctor!

Pulmonary embolism (PE) and acute exacerbations of chronic obstructive pulmonary disease (COPD) can present with similar symptoms of dyspnea, hypoxemia, and cough. Prospective observational studies have suggested that pulmonary embolism is present in at least 5% of patients (1 in 20) diagnosed with COPD exacerbations requiring hospitalization, and possibly many more.
In most of these studies, diagnostic imaging was only performed on patients at higher pretest probability for PE according to Wells criteria or other risk stratification.

In a prospective study enrolling 1580 mostly elderly patients in China diagnosed with COPD exacerbation, all subjects underwent ultrasonography of the legs as well as CT pulmonary angiography.
Prevalence of pulmonary embolism was 17%, and overall prevalence of deep venous thrombosis or PE was 25%.

These findings certainly seem to justify the lower threshold for CTA chest and lower extremity ultrasound to rule out DVT among patients with COPD exacerbations and elevated D-Dimers.

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Stroke care for intensivists – Not as complicated after all!

Blood pressure targets in acute ischemic stroke after thrombectomy

In the new era of thrombectomy for ischemic strokes with large vessel occlusion, blood pressure targets remain a topic of interest.

Two randomized trials testing blood pressure targets after thrombectomy for acute ischemic stroke suggest permissive hypertension is appropriate for these patients, too.
In the OPTIMAL-BP randomized trial (JAMA 2023), 306 patients were randomized to intensive BP control (<140 mm Hg) or permissive (140-180 mm Hg) for 24 hours after successful endovascular therapy for acute ischemic stroke. Those randomized to the higher target had improved rates of functional independence at 3 months (54% vs 39%). The trial was planned for >660 patients but was stopped early due to a clear harm signal with intensive BP control.

The BEST-II trial (JAMA 2023) was a phase 2 trial intended to assess the likelihood (or futility) of finding a benefit in a future trial for aggressive BP control after thrombectomy. It only enrolled 120 patients, but suggested it was only 25% likely that intensive BP control (to a target <140 mm Hg) could feasibly be shown in a future trial to produce better outcomes than a target of <180 mm Hg.

Keeping it simple, post revascularization for a stroke (tPA or Thrombectomy) clinically relevant target is < 180 mmHg with goal for permission hypertension.

ORIGINAL ARTICLE SUMMARIES:

SAFETY OF SWITCHING FROM A VITAMIN K ANTAGONIST TO A NON-VITAMIN K ANTAGONIST ORAL ANTICOAGULANT IN FRAIL OLDER PATIENTS WITH ATRIAL FIBRILLATION: RESULTS OF THE FRAIL-AF RANDOMIZED CONTROLLED TRIAL. (CIRCULATION, 2023)

Aim of study: To determine whether Non-vitamin K antagonist oral anticoagulant (NOAC) is superior to Vitamin K antagonist (VKA) as stroke prevention for older frail patients with Atrial Fibrillation (AF).

Methods, Inclusion, Exclusion:
The FRAIL-AF study: a pragmatic randomized multicenter open-label clinical trial in older AF patients living with frailty. 1,330 patients in the Netherlands (mean age of 83 years; 38.8% women).

Inclusion:

- Patients 75 and older
- Managed on INR-guided VKA treatment for AF by a study participating service center
- Groningen Frailty Indicator (GFI) ≥3
- Willingness to switch from VKA management to a NOAC-based treatment strategy.

Exclusion:

- Valvular AF
- Mechanical Heart Valve
- Severe Mitral Valve Stenosis
- An estimated glomerular filtration rate (eGFR) below 30 ml/min/1.73 m2
- Involved in another research study
- Unwilling or unable to provide written informed consent.

Patients were first randomized to a NOAC-based treatment strategy started NOAC therapy when the INR was <2.0 after stopping VKA therapy. It was observed that there was a tendency of more bleeding during the switching period. Thus, randomization was adjusted for 102 patients in the intervention arm and an INR level <1.3 was used to prevent too high anticoagulation during the switching period.
7 more patients were excluded after randomization for missed exclusion criteria.
The “Intention to Treat” (ITT) population included 662 patients that switched from a VKA to a NOAC and 661 patients that continued with INR- guided VKA management. The ITT population was used for all further analyses and primary and secondary outcomes.

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The median duration for the intervention arm was 52 days. The mean follow-up time was 344 days.

NOAC switches

- Dabigatran: 57 patients
- Rivaroxaban: 332 patients
- Apixaban,: 115 patients
- Edoxaban: 109 patients
- Information on type of NOAC missing: 3 patients
- Patients meant to switch to a NOAC, but did not: 22 patients

NOAC dosing and dose adjustments in principle followed the summary of product characteristics guidelines, unless the treating physician deliberately opted for a different dose (typically off-label dose reduction in 6.6%), which was then accepted.

Results:
The occurrence of a major or clinically relevant non-major (CRNM) bleeding complication was the primary outcome.

- 90 patients died during follow up period. (Intervention arm: 44 patients, Control arm: 46 patients)
- 31 deaths were cardiovascular related: terminal heart failure and fatal myocardial infarction.
- 10 fatal bleeding related deaths (equal in both arms).

After having observed 163 bleeding complications (101 in the NOAC arm (15.3%) and 62 (9.4%) in the VKA-arm), this superiority trial was halted. It was decided to stop inclusion and complete follow-up for all participants in the study. While it was noted that there was a reduction in thromboembolic events with the NOAC switch, this did not off-set the higher bleeding risks- especially since risk of thrombo-embolic events was low in both treatment arms.

ORIGINAL ARTICLE SUMMARIES:

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Clinical Interpretation: In the FRAIL-AF study, switching INR-guided VKA-management to a NOAC based treatment strategy was associated with a 69% increase in bleeding complications and should not be a considered treatment in older AF patients living with frailty. Authors showed that the better efficacy of standard-dose NOAC treatment over VKA treatment was mainly driven by the results in patients who are VKA naïve. Moreover, an interaction of ageing on safety outcomes was observed: for standard-dose NOAC-treatment every 10-year increase in age led to a 10.2% increase in HR for major bleeding (P-value for interaction 0.02) and for reduced-dose NOAC-treatment every 10-year increase in age led to a 17.6% increase in the HR for major bleeding (P-value for interaction 0.01).

ORIGINAL ARTICLE SUMMARIES: EFFECTS OF CORRECTION RATE FOR SEVERE HYPONATREMIA IN THE INTENSIVE CARE UNIT ON PATIENT OUTCOMES. (J CRIT CARE, 2023)

Aim of study: To Investigate the association between “slow correction” vs. “rapid correction” and in-hospital mortality, hospital and ICU-free days, and development of neurological complications in ICU patients with sodium serum concentrate (serum [Na+] ≤120 mEq/L), specifically risk of osmotic demyelination syndrome (ODS).

Methods, Inclusion, Exclusion:
A retrospective cohort analysis using patient data using a large multi-center public database of 200,859 unique ICU patient encounters at 208 hospitals across the US from 2014 to 2015. A total of 1024 patients were included in the analysis
Cut-off for slow vs rapid correction was defined at 8 mmol/L/day. This cut-off was chosen because it falls within the recommended correction range for individuals at high risk for ODS.

Inclusion: Patients with severe hyponatremia, defined as subjects who had sodium serum during their ICU admission.
Exclusion: Patients less than 18 years old, on dialysis, discharged from the ICU within 24 hours of admission, glucose levels of greater than 360 mg/dL, or no recorded serum levels. Serum sodium values were documented and any sodium values from whole blood measurements were excluded. Only the first ICU admission was documented if a patient had multiple admissions.

Study set the exposure as “rapid correction,” defined as a serum [Na+] correction rate of >8 mEq/L/day, and the control as “slow correction,” defined as a serum [Na+] correction rate of ≤8 mEq/L/day. Our cohort included 1024 patients; 451 rapid and 573 slow correctors.

Results:
The primary outcome was in-hospital mortality. Secondary outcomes included hospital-free days, ICU-free days, and neurological complications at discharge.
Rapid correction was associated with lower in-hospital mortality, longer hospital-free days, and longer ICU-free days. There was no significant difference in neurological complications. In this study, rapid correction (>8 mEq/L/day) of severe hyponatremia within the first 24 h of ICU admission was associated with better patient outcomes.

ORIGINAL ARTICLE SUMMARIES: EFFECTS OF CORRECTION RATE FOR SEVERE HYPONATREMIA IN THE INTENSIVE CARE UNIT ON PATIENT OUTCOMES. (J CRIT CARE, 2023)

Clinical interpretation: These retrospective chart study results are promising and encourage prospective studies to establish evidence-based practice. Just like anything else in medicine extremes are to be avoided, although this study tells us that rapid correction defined as > 8 mEq/L/day may be safe, it does not tell us if > 10 or 12 mEq/L/day is safe. Clinical applicability of the results, however, reassures me that it might be ok to be less stressed about rapid correction or refrain from urgently starting someone on a hypotonic infusion for rapid correction of hyponatremia. Rather, decrease or stop the ongoing hypertonic infusion in the right clinical setting. Certainly, monitor the sodium levels frequently, allowing for self-correction of serum sodium levels.

SNAPSHOTS

Balloon pulmonary angioplasty or riociguat in patients with inoperable CTEPH?

Kawakami et al (Lancet Respir Med 2022) report results of a multicentre randomized trial comparing BPA and riociguat in the treatment of inoperable CTEPH at 12 months. Of 338 patients screened, 61 were randomised to BPA (n=32) or riociguat (n=29). Compared with medical therapy, BPA produced a greater reduction in pulmonary artery pressure (mean group difference −9.3 mm Hg, 95% CI −12.7 to −5.9 mm Hg; p<0.0001). At 12 months, BPA also demonstrated greater improvements in WHO functional class (p=0.0012) and reduction in home oxygen requirements (p=0.031). Interestingly, riociguat improved cardiac output (−0.8 L/min, 95% CI −1.28 to −0.33; p=0.0013), likely due to medical therapy treating microvascular lesions not amenable to BPA catheter. Although no clinical worsening or severe adverse procedure-related events were reported in the BPA group, higher rates of hemoptysis occurred (44% vs 4%). While the study provides reassurance of the clinical value of BPA, concerns regarding the generalizability of such intensive BPA procedures remain. The role of combination therapy also needs to be explored.

SNAPSHOTS

Cannot go wrong with a Mediterranean diet even in IPF!

Gastrointestinal pirfenidone adverse events in idiopathic pulmonary fibrosis depending on diet: the MADIET clinical trial. The Mediterranean diet is characterized by a high ratio of monounsaturated fatty acids (MUFA) to saturated fatty acids (SFA). Cohort had 49 in the Monounsaturated fatty acids and 37 in the Saturated fatty Acids arm. Baseline demographic characteristics were similar between both groups, including age, BMI, and hepatic metabolic markers.

MUFA-rich diet was associated with a lower incidence of pirfenidone related GI AEs (Adverse Event) (26.5%) compared to SFA-rich diet (64.9%) (p=0.001) (Link to Table 1), increasing the odds of not having a GI AE (Adverse Event) by more than nine-fold.

In conclusion, this study demonstrates that a SFA diet is associated with worse tolerability and higher risk of GI AEs in patients with IPF taking pirfenidone. This identifies diet as an important modifiable target to reduce pirfenidone-related GI AEs. Additional studies are required to analyze the effect on GI AEs of a dietary intervention, such as reducing saturated fat intake or cooking with olive oil.

SNAPSHOTS

Prognostication for out of hospital cardiac arrest could be useful when talking to family!

Table 2 Comparison (total sample size $N=658$)

	Utstein	CAHP	sCAHP	mCAHP	OHCA	CREST	C-GRApH	TTM	NULL-PLEASE	rCAST	MIRACLE2
Number of items for score determination	8	7	6	6	5	5	5	10	9	5	7
Number of patients with calculated score	658	649	649	649	640	544	607	557	640	625	620
Proportion of patients with score available as compared to full cohort	100.0%	98.6%	98.6%	98.6%	97.3%	82.6%	92.2%	84.6%	97.3%	94.9%	94.2%
Median score, IQR	NA	147 [111–175]	132 [101–156]	94 [73–110]	28 [13–41]	2 [1–3]	2 [1–3]	17 [12–20]	5 [3–6]	9 [6.5–12]	4 [2–5]
AUROC (95% CI)	0.79 [0.76–0.83]	0.87 [0.84–0.90]	0.85 [0.81–0.87]	0.86 [0.83–0.89]	0.84 [0.81–0.88]	0.79 [0.75–0.83]	0.76 [0.71–0.80]	0.88 [0.86–0.91]	0.81 [0.77–0.84]	0.82 [0.78–0.85]	0.85 [0.82–0.88]
Hosmer–Lemeshow											
Absolute value	5.48	11.03	4.83	7.63	11.92	8.84	4.43	12.14	3.84	9.28	16.64
P-value	0.70	0.19	0.77	0.47	0.15	0.26	0.48	0.14	0.87	0.32	0.03
Comparison versus Utstein Delta AUROC (95% CI)	NA	0.08 [0.07–0.08]	0.05 [0.04–0.06]	0.07 [0.06–0.07]	0.05 [0.05–0.05]	0 [0–0]	−0.03 [−0.03 to 0.05]	0.09 [0.08–0.10]	0.01 [0.01–0.02]	0.02 [0.02–0.03]	0.06 [0.05–0.06]
P-value		< 0.0001	< 0.001	< 0.001	< 0.001	0.28	0.03	< 0.001	0.20	0.16	< 0.001
Added AUROC per item	0.09	0.12	0.14	0.14	0.17	0.16	0.15	0.08	0.09	0.16	0.12

NA: Not applicable. AUROC: Area under the ROC curve. IQR: interquartile range

Table from Prospective comparison of prognostic scores for prediction of outcome after out-of-hospital cardiac arrest: results of the AfterROSC1 multicentric study. 2023

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