We've got ROSC!
...Now what?
Transitioning to Post-Resuscitative Care

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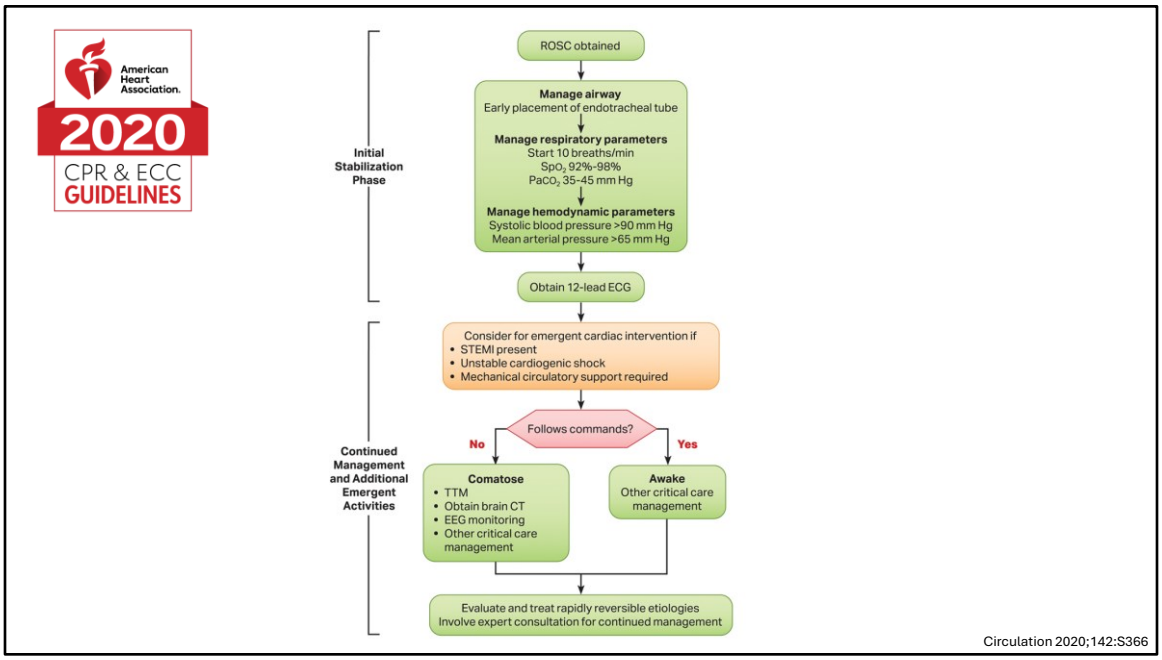

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The good news is, the AHA pretty much tells us what we need to do!

So, this is “ROSC 101” – just follow the ACLS post-ROSC algorithm.

But I want to dive a little deeper into some of these topics and present the latest evidence. The good news is, largely, the AHA guidelines remain reasonably accurate.

Just like the framework we’ve all been taught for patient assessment and management, we can use the ABCD framework to guide our post-resuscitation care

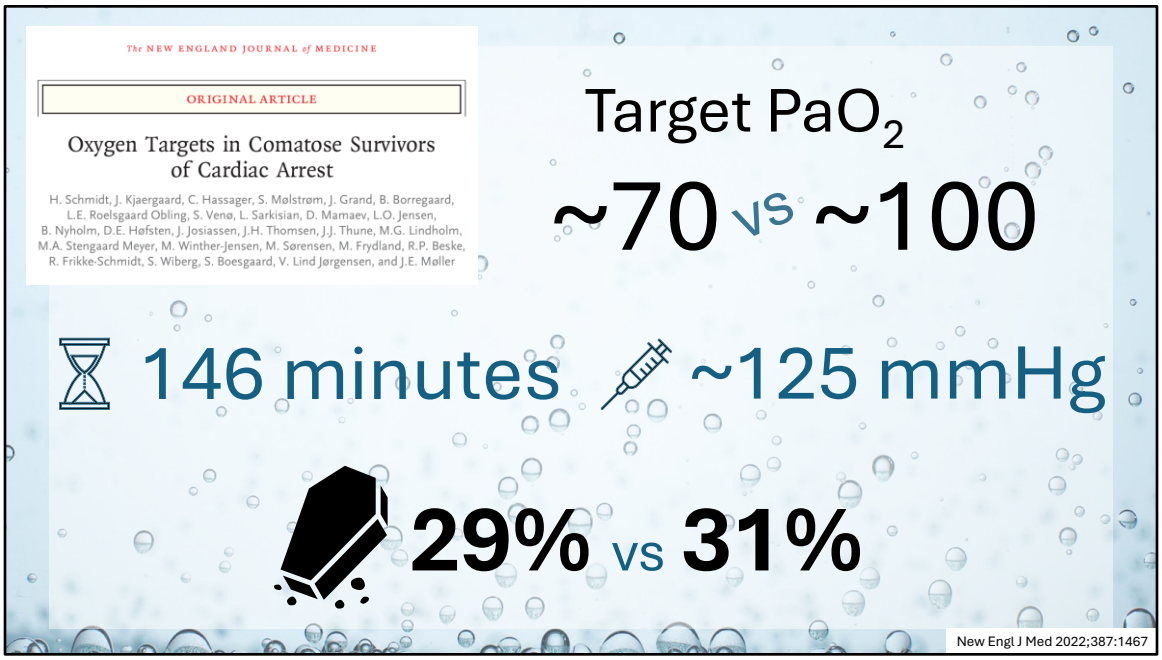
Now, obviously if your patient wakes up and is neurologically intact, some of these measures may not apply. But for those patients that remain comatose post-ROSC, we need to provide early, aggressive critical care to prevent secondary sequela, focusing especially on mitigating brain injury and preventing multiorgan failure.

When it comes to airway management, thought should be given to placing an endotracheal tube if the patient was not already intubated during resuscitation.

In general, once ROSC is attained, consider performing RSI to secure the airway, rather than attempting without any medications.

If the patient has tenuous hemodynamics, remember to consider adjusting your pharmaceutical selection and dose to account for the physiologically difficult airway.

From a respiratory standpoint, the AHA guidelines really only provide two recommendations:
Target an SpO_2 of 92-98%, and
Target a $PaCO_2$ of 35-45 mmHg



The BOX trial (Blood pressure and OXygenation targets after OHCA) sought to compare liberal versus restrictive oxygenation in the post-resuscitation period.

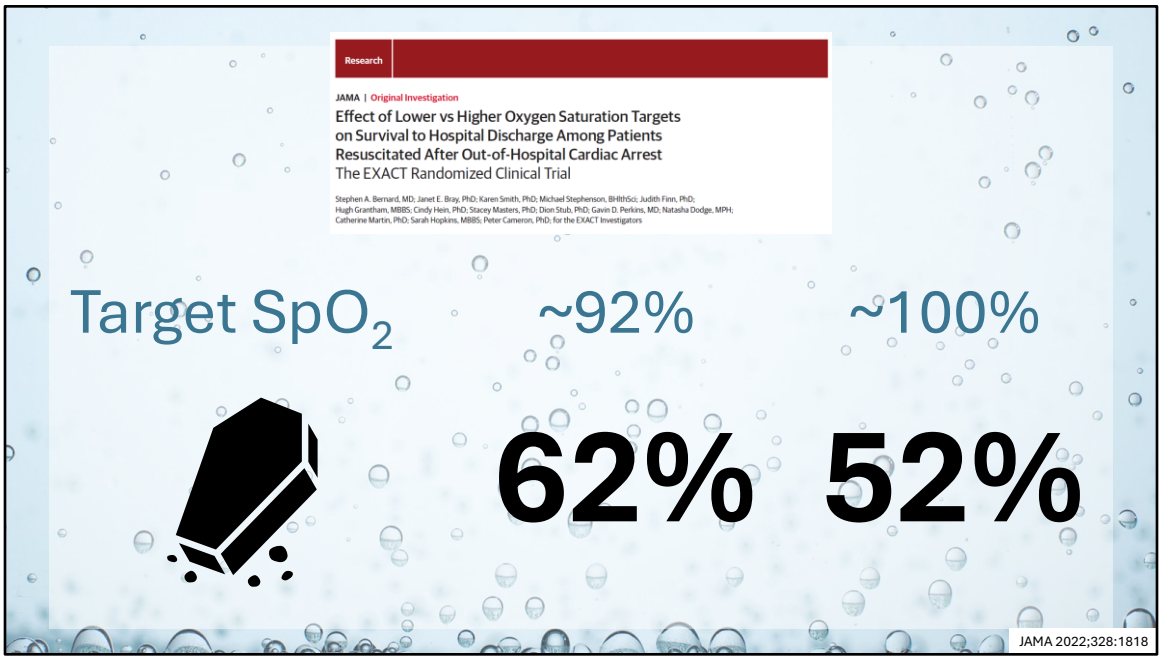
Patients were randomized to a target PaO_2 of either ~70 mmHg [9-10 kPa] in the restrictive group versus ~100 mmHg [13-14 kPa] in the liberal group.

(Recall that a normal PaO_2 is usually considered 75–100 mmHg [10.5–13.5 kPa], so this was comparing oxygen targets slightly below normal with those at the high end of normal.)

In general, there was no statistically significant difference in any of the endpoints of survival, severe disability, or cognitive outcome. Restrictive oxygenation patients tended to have a *slightly* worse modified Rankin score (median mRS 2 in the restrictive versus 1 in the liberal cohort), but this was not statistically significant.

Of note, however, the patients were randomized an average of 2½ hours after ROSC was achieved, most commonly after arriving to the ICU, and the first recorded PaO_2 values (at, or shortly after, randomization) were hyperoxic in both groups:
The first measured PaO_2 in the restrictive group was 16.1 kPa (121 mmHg), and the first measured PaO_2 in the liberal group was 17.1 kPa (128 mmHg)

So, in essence, both groups were hyperoxic for up to 2-3 hours after ROSC, and then were targeted to maintain high-normal versus low-normal PaO2, without much difference in outcomes.



The EXACT trial evaluated pulse ox targets in the immediate post-resuscitation, out-of-hospital period by paramedics.

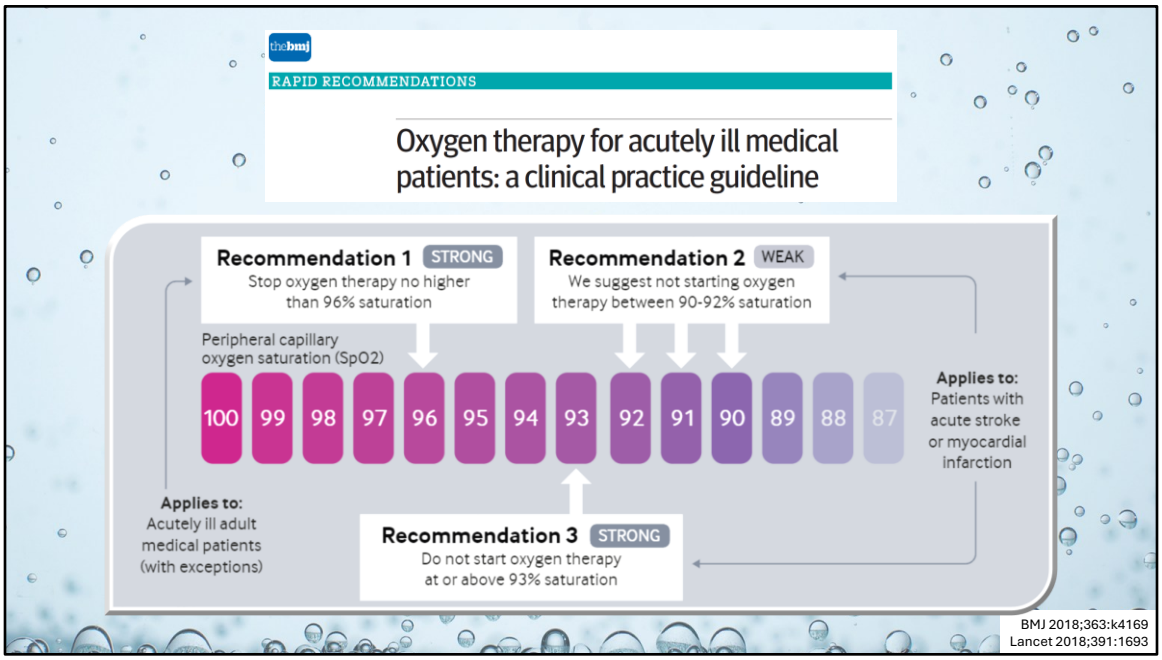
Patients were randomized to a target SpO_2 of either 90-94% in the restrictive group versus 98-100% in the liberal group, and that target was maintained until arrival in the ICU.

The trial was stopped early due to COVID, enrolling less than a third of the planned patient (428 enrolled of 1416 planned), so we should use some caution interpreting these results.

However, this trial found considerably higher mortality in the low saturation target: 62% mortality versus 52%

Secondary outcomes were similar between the two groups, except there were more cases of hypoxia (defined as SpO_2 <90%) in the lower oxygen target group.

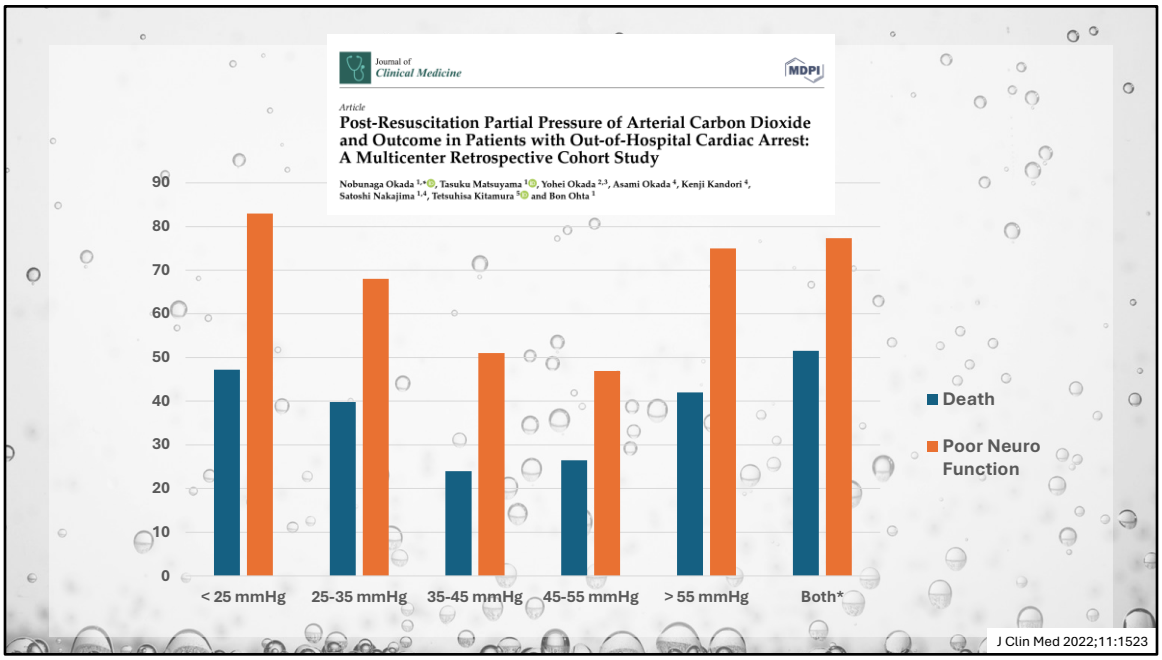
There was a trend toward more favorable neurologic function and more patients discharged to home in the higher target group, but this was not significant and with the limitation of the smaller-than-intended sample size, this should be hypothesis-generating at best.



So, what happens if your patient isn't intubated?

Are the oxygenation targets any different?

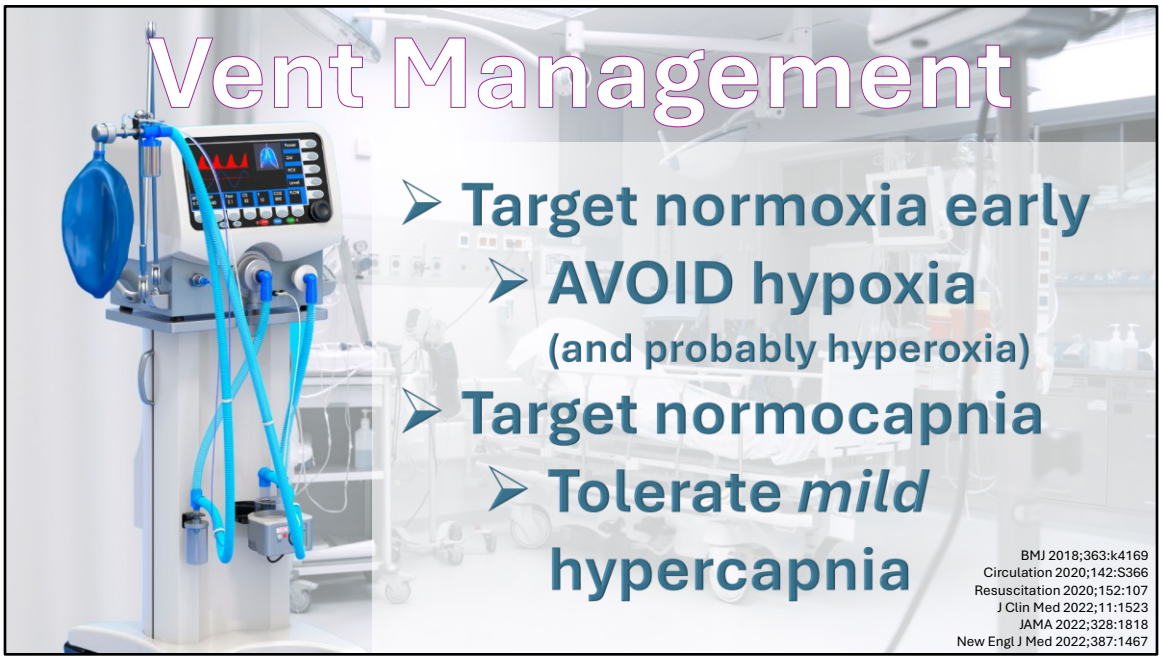
Not really. The best evidence we have to date comes from the 2018 guidelines published in BMJ, based heavily on the IOTA data published the same year in Lancet. IOTA found that exposure to hyperoxia increased the risk for mortality across all time periods, including in-hospital, 30-day, and longest follow-up, in the included studies. This included patients with acute stroke, acute myocardial infarction, and general critical medical illness.

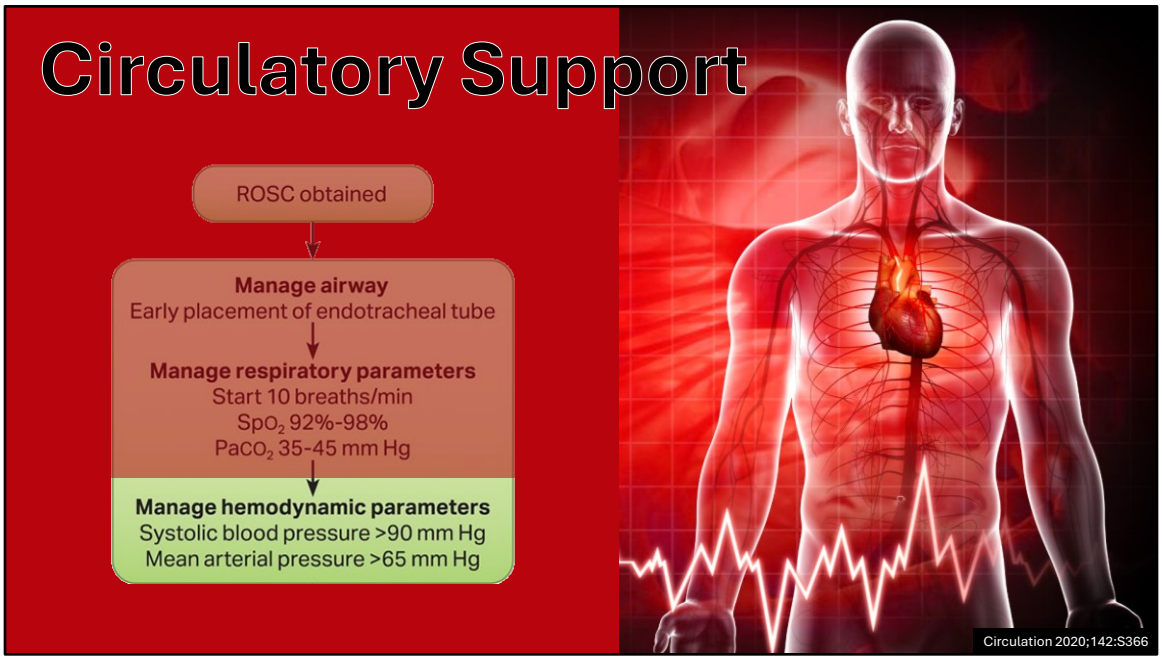


So now, let's take a look at ventilation guidelines in post-resuscitation care.

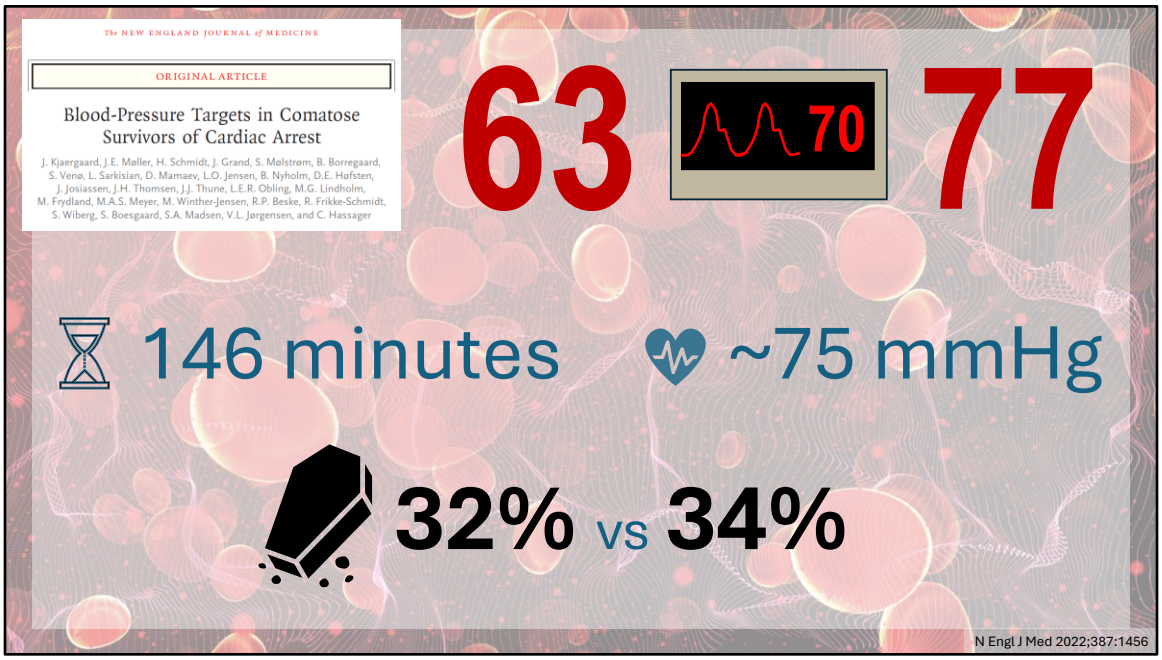
These authors analyzed over 600 patients with ROSC, finding that those with normocapnia or mild hypercapnia ($PaCO_2$ of 35-55 mmHg) had the best odds of survival with favorable neurologic function.

Those with any hypocapnia ($PaCO_2$ <35 mmHg), severe hypercapnia ($PaCO_2$ >55 mmHg), or exposure to both hyper- and hypo-capnea had significantly higher odds of mortality as well as poor neurologic function.


Vent Management
Target normoxia early
AVOID hypoxia
(and probably hyperoxia)
Target normocapnia
Tolerate *mild* hypercapnia
BMJ 2018;363:k4169
Circulation 2020;142:S366
Resuscitation 2020;152:107
J Clin Med 2022;11:1523
JAMA 2022;328:1818
New Engl J Med 2022;387:1467



Now, let's turn to circulatory support. The only guidance given by the AHA guidelines is to maintain a SBP >90 and MAP >65.



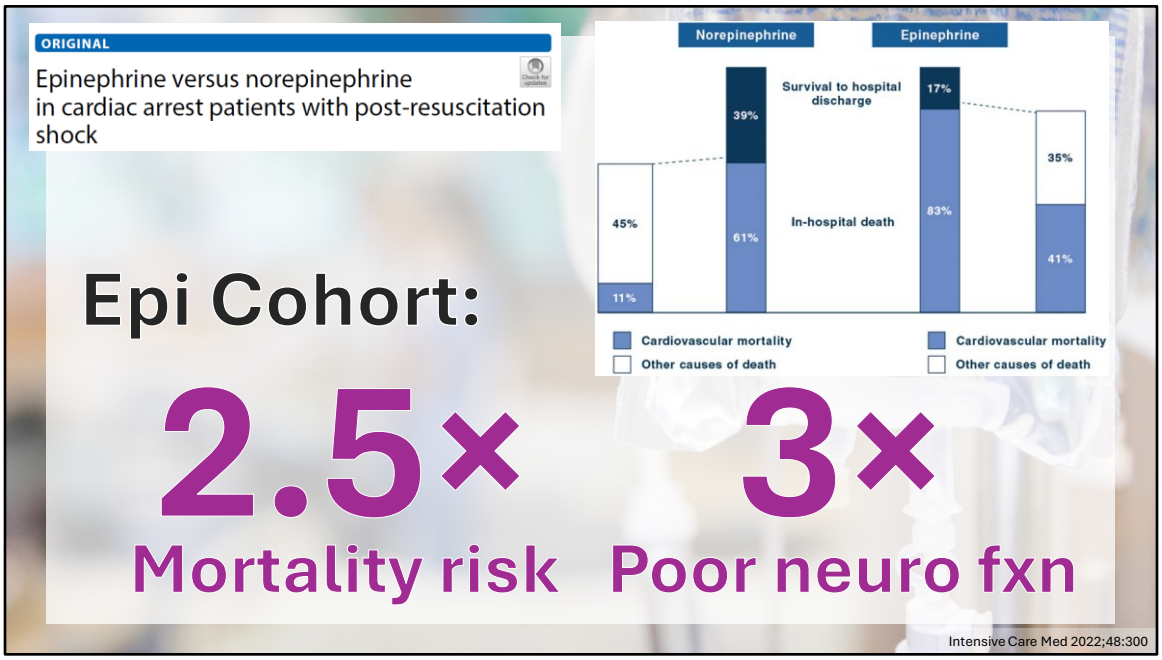
We've already discussed the oxygenation portion of the BOX trial (Blood pressure and OXygenation targets after OHCA) – now it's time to review the Blood Pressure portion of that study.

The authors also compared a target MAP of 63 mmHg versus 77 mmHg (their BP readout was randomized to deliver a 10% overestimation or 10% underestimation of the actual blood pressure, and had everyone target a MAP of 70 – rather clever way to randomize!)

Just like the oxygenation arm of this study, the patients were randomized an average of 2½ hours after ROSC was achieved, most commonly after arriving to the ICU.
Enrolled patients also had an average MAP of around 75 mmHg at the time of randomization – meaning, that MAP had been achieved and maintained for up to 2½ hours before the goal was adjusted (63 vs 77 mmHg).

Also similar to the oxygenation arm, there was no significant difference in mortality between the two groups: 32% in the low-MAP and 34% in the high-MAP cohort.

My take-home from this is that a MAP of 65 mmHg is probably sufficient, and there's no added benefit to augmenting that BP any higher in most patients.



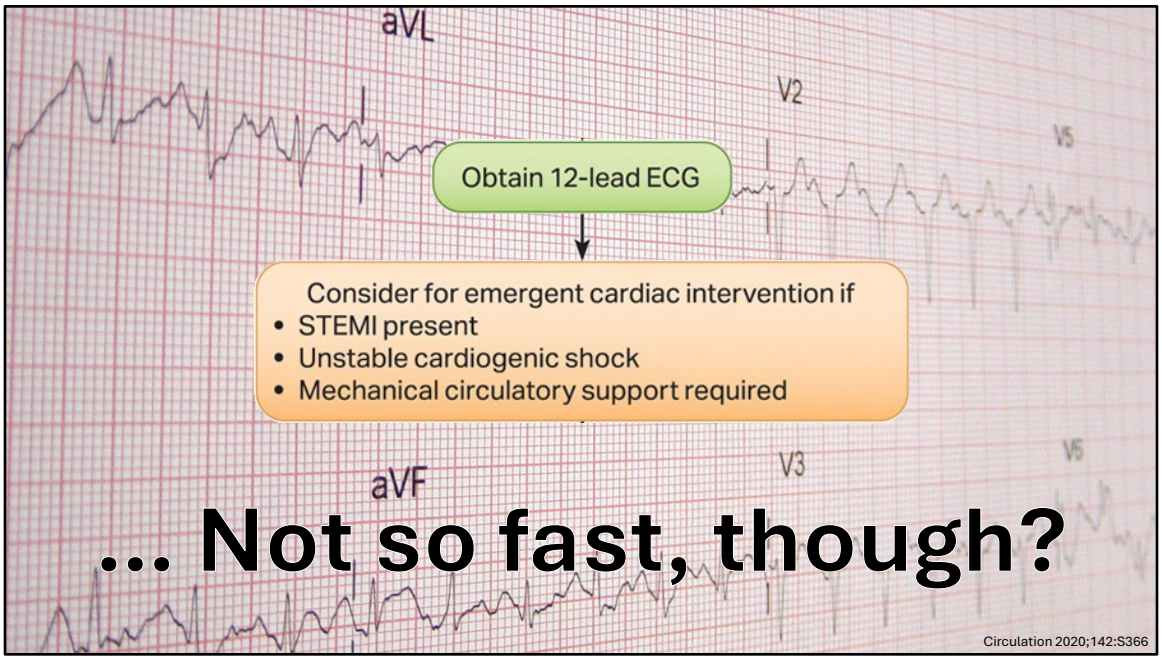
So which vasopressor (if any) is the better choice to maintain these MAP targets in the resuscitated patient patient?

This study evaluated, prospectively, the outcomes of patients that received either epinephrine (alone) or norepinephrine (alone) following resuscitation. They excluded any patient that received both agents (or, obviously, those that received neither)

They found that patients who received epinephrine were more likely to have significant morbidity or mortality

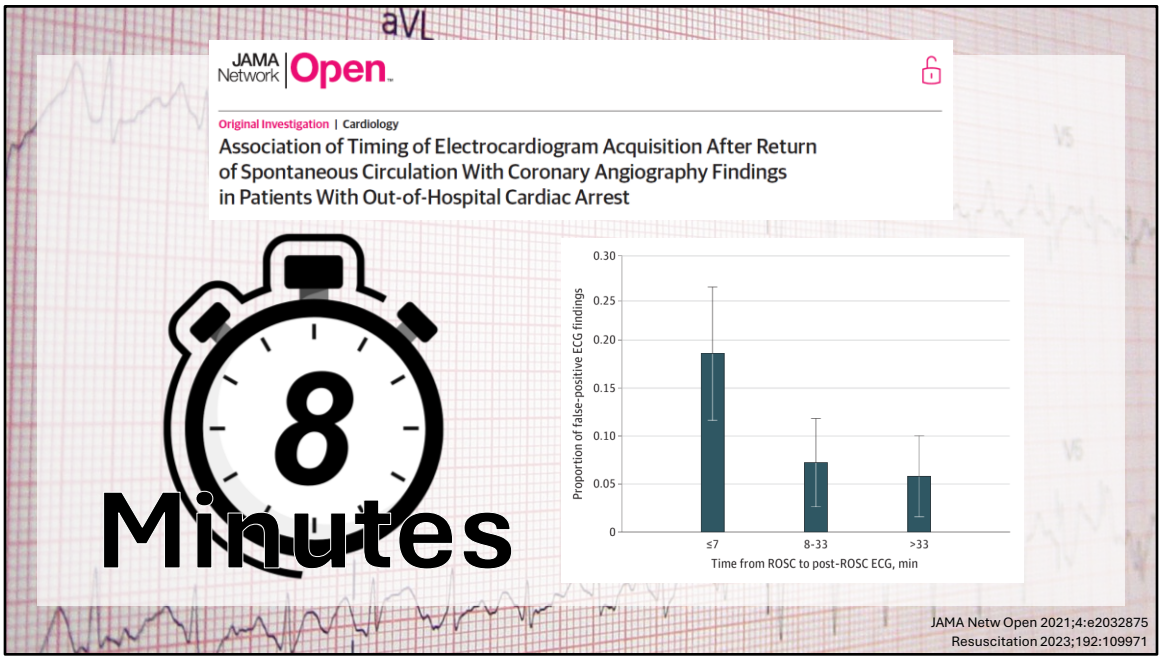
Specifically, epinephrine was associated with a 2.5-fold increase in risk of all-cause mortality and a 3-fold increased risk of unfavorable neurologic outcome (CPC score of 3-5) over norepinephrine.

To be fair, this was an observational study, not a blinded RCT, so there is certainly risk of bias in these results, but it adds to other data suggesting a potential harm with continued epinephrine administration post-resuscitation.



AHA recommends, once the patient is hemodynamically stabilized, the next priority should be obtaining a 12 lead ECG.

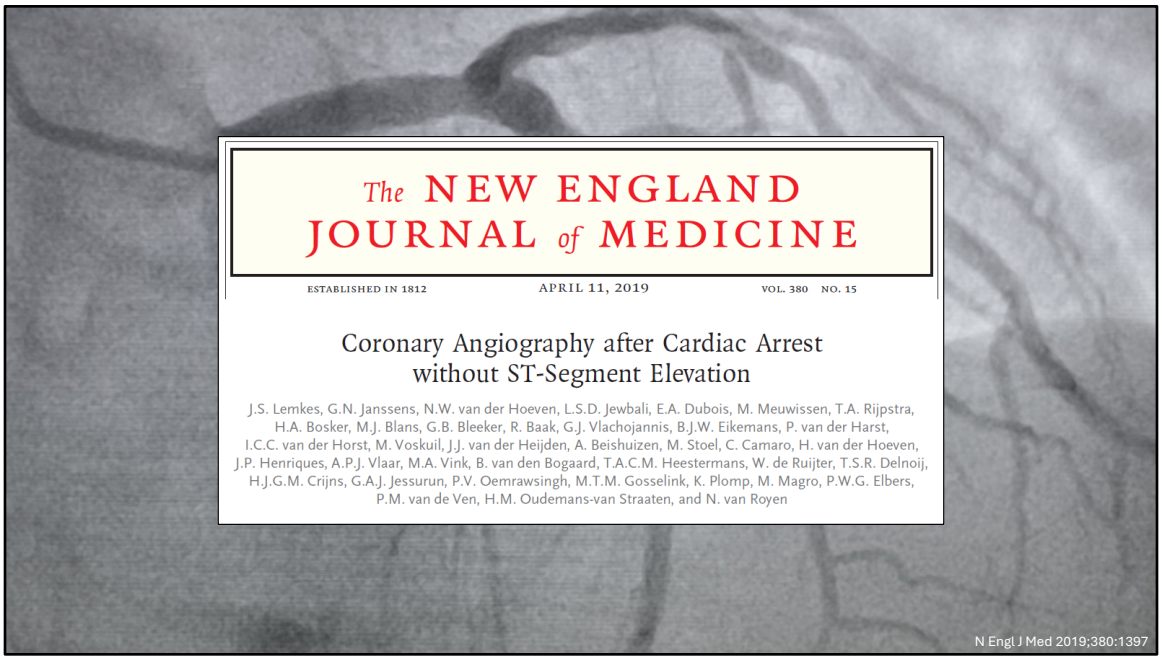
However, how quickly should we be getting that ECG? Does it matter?



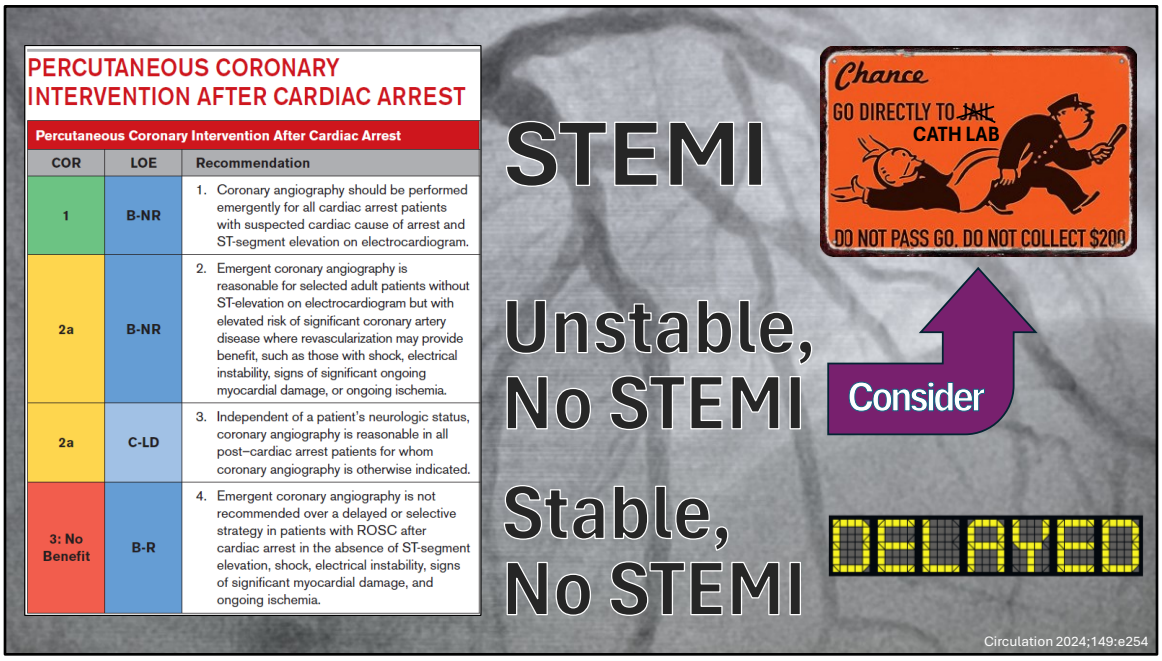
The authors found that the rate of false-positive ST elevation was highest in the first ~7 minutes post-ROSC (18.5% false-positive rate).

It may be reasonable to delay the ECG for a few minutes after ROSC, or at least repeat an ECG if there are any concerning findings.

Of note, there was still a ~5.8% false-positive rate in those ECGs acquired >30 minutes after ROSC, so it's likely not possible to eliminate all false-positives.

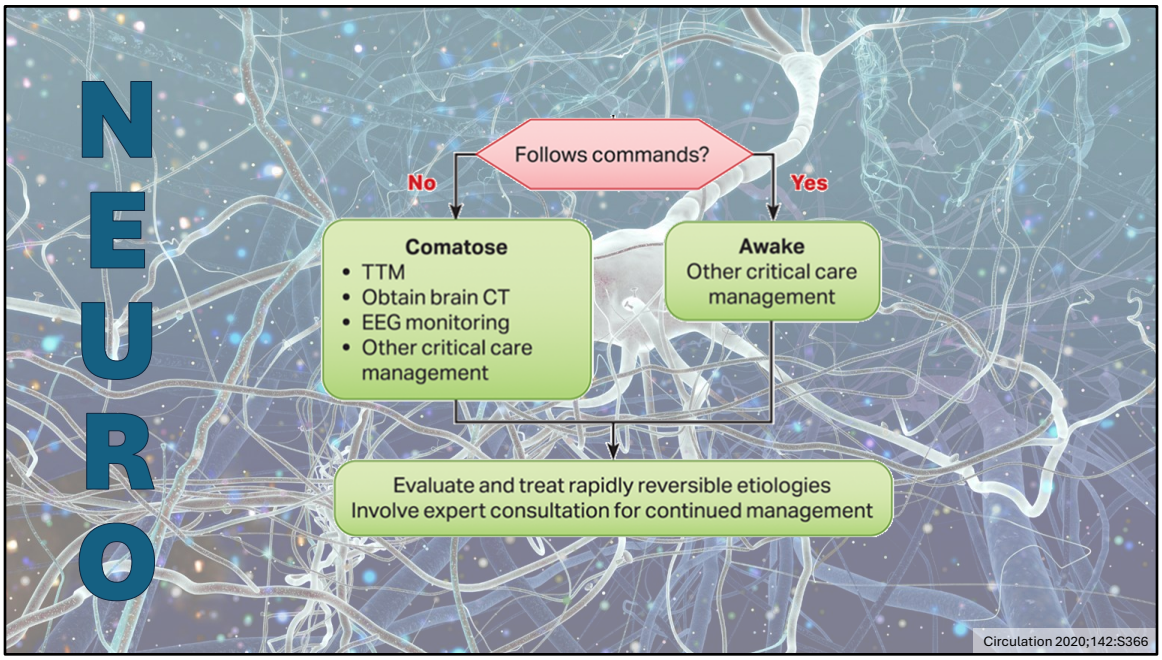


By now, I think most of us have heard about the COACT trial published in 2019. This trial showed that in post-resuscitation patients *without* ST-segment changes on ECG, immediate angiography was no better than delayed angio.

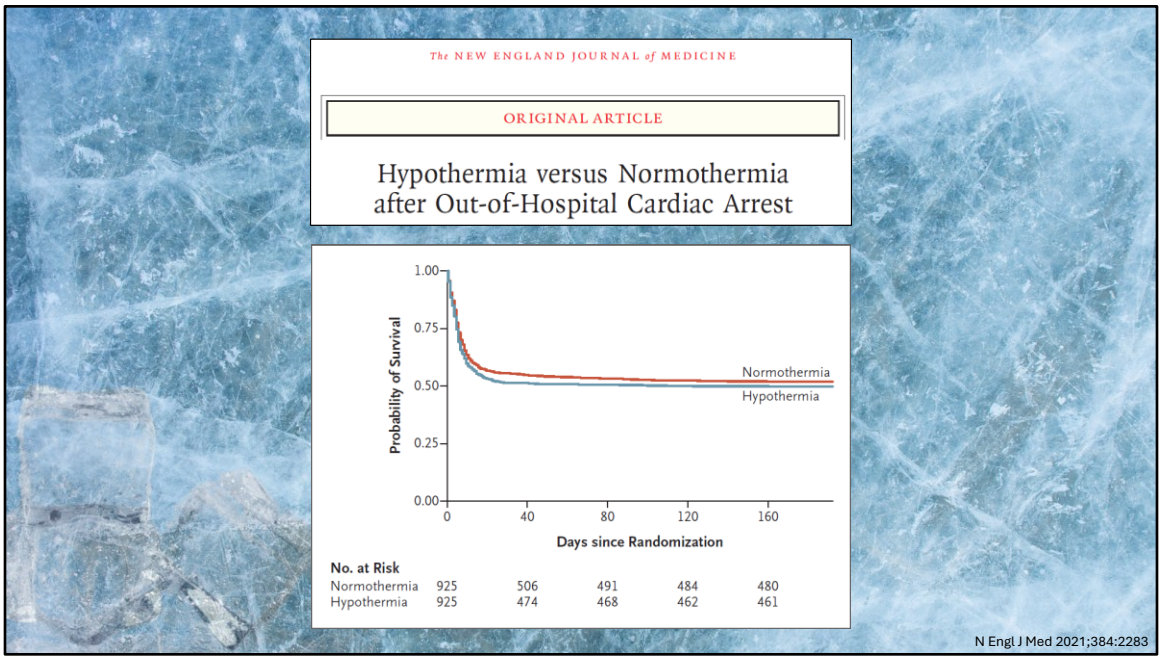


The latest focused update for CPR/ECC make the following recommendations on who should go for angio following resuscitation:

- STEMI = Emergent angio!
- Those with "shock, electrical instability, …or ongoing ischemia" = Consider emergent cath
- Stable without ST elevation = Delayed/selective (no benefit to emergent angio)

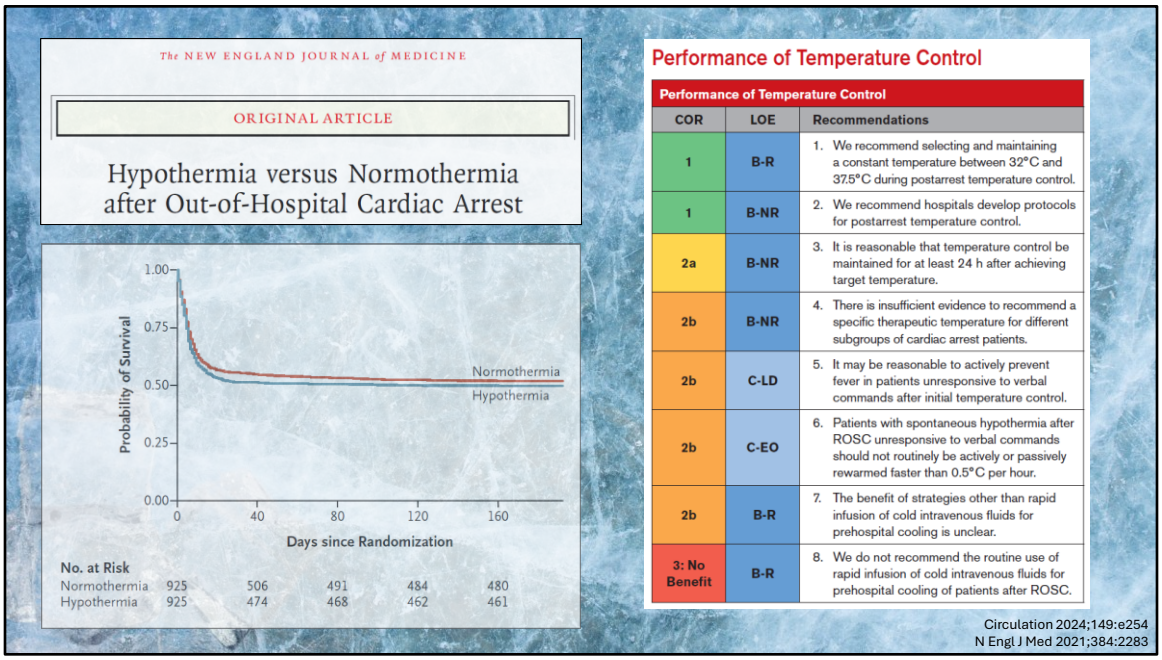


We've gone through the ABCs, now let's focus on our "Disability" – or neuro management.



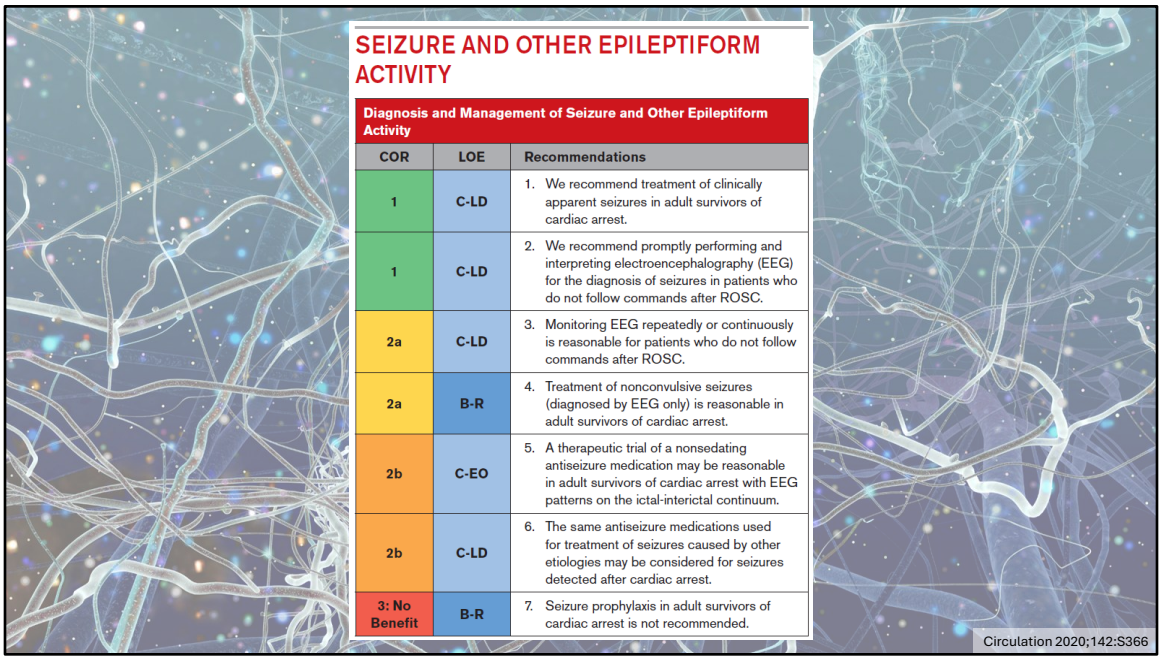
The TTM2 trial, published in 2021, compared hypothermia (32–34°C) to targeted normothermia (37°C, with early treatment of fever for any temperature >37.8°C).

They found no difference in mortality or favorable neurologic outcome between the two groups, although hypothermia had a higher risk of arrhythmia with hemodynamic compromise.



The updated CPR/ECC guidelines essentially suggest picking a target somewhere between hypothermia and normothermia (and probably reasonable to prevent fever), then develop protocols to make it consistent.

Otherwise, there is no specific guidance for any subgroup of patients. They also offer no guidance on *how* to achieve hypothermia or normothermia, other than explicitly advocating against use of cold IV fluids in the prehospital setting.



SEIZURE AND OTHER EPILEPTIFORM ACTIVITY

Diagnosis and Management of Seizure and Other Epileptiform Activity

COR	LOE	Recommendations
1	C-LD	1. We recommend treatment of clinically apparent seizures in adult survivors of cardiac arrest.
1	C-LD	2. We recommend promptly performing and interpreting electroencephalography (EEG) for the diagnosis of seizures in patients who do not follow commands after ROSC.
2a	C-LD	3. Monitoring EEG repeatedly or continuously is reasonable for patients who do not follow commands after ROSC.
2a	B-R	4. Treatment of nonconvulsive seizures (diagnosed by EEG only) is reasonable in adult survivors of cardiac arrest.
2b	C-EO	5. A therapeutic trial of a nonsedating antiseizure medication may be reasonable in adult survivors of cardiac arrest with EEG patterns on the ictal-interictal continuum.
2b	C-LD	6. The same antiseizure medications used for treatment of seizures caused by other etiologies may be considered for seizures detected after cardiac arrest.
3: No Benefit	B-R	7. Seizure prophylaxis in adult survivors of cardiac arrest is not recommended.

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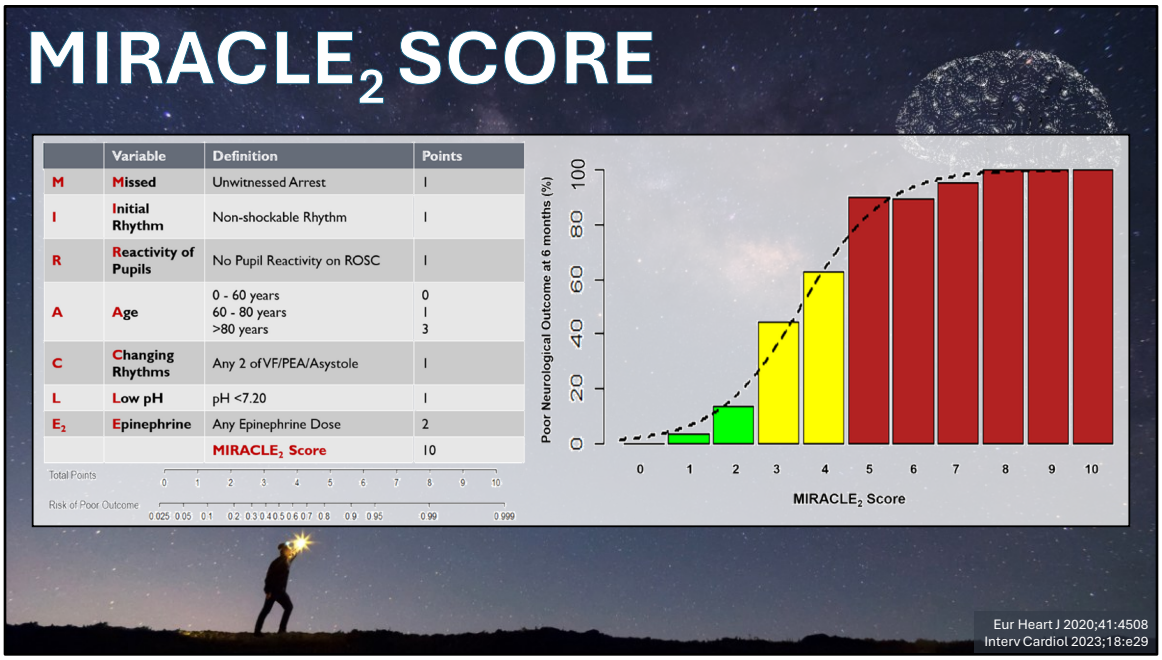
With regards to neurologic monitoring and management, the latest CPR/ECC updates continue to advocate for early EEG, treatment of clinically evident seizures, and avoidance of routine seizure prophylaxis.

Lastly, let's touch briefly on the topic of neuroprognistication

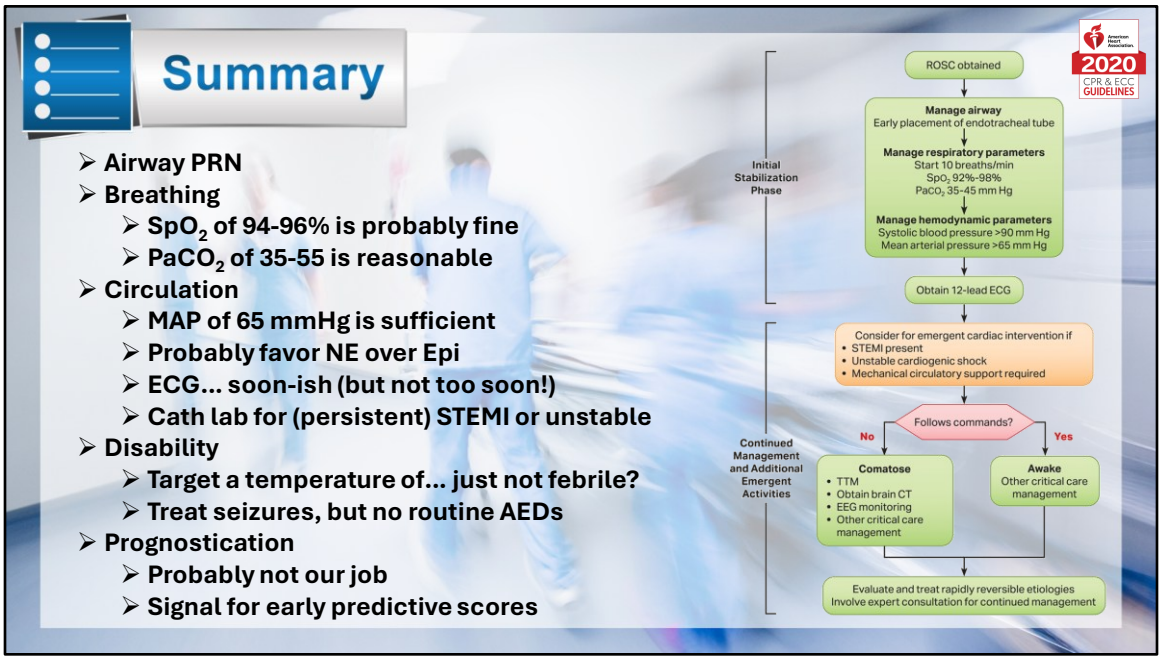
We know from AHA guidelines (and others, including Neurocritical Care Society) that neuroprognostication in comatose survivors of cardiac arrest should be delayed at least 72 hours.

Hopefully, these patients should be well out of the emergency department by the 72-hour mark, so I won't spend any more time discussing this topic in detail.



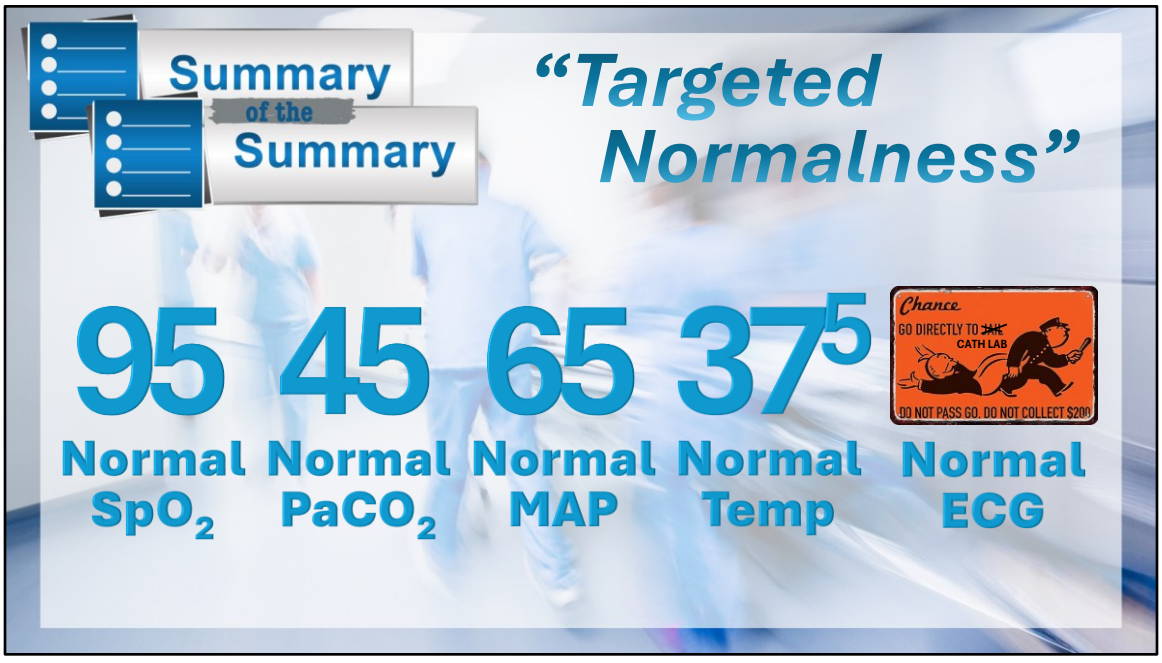
Despite the need to formally wait 72 hours for prognosis, researchers are actively looking for ways to identify patients early-on who may have favorable, or unfavorable, outcomes.

The MIRACLE$_2$ Score, developed in the UK, has shown promising results, with a score of ≤2 providing a 94% negative predictive value for poor outcome, while a score of ≥5 has a positive predictive value of 95% for poor outcome.



So, in summary:

- Airway PRN
- Breathing
  - SpO_2 of 94-96% is probably fine
  - $PaCO_2$ of 35-55 is reasonable
- Circulation
  - MAP of 65 mmHg is sufficient
  - Probably favor NE over Epi
  - ECG… soon-ish (but not too soon!)
  - Cath lab for (persistent) STEMI or unstable
- Disability
  - Target a temperature of… just not febrile?
  - Treat seizures, but no routine AEDs
- Prognostication
  - Probably not our job
  - Signal for early predictive scores



Or, the executive summary:
Maintain Target Normalness!

Normal SpO_2 (Probably around 95%)
Normal $PaCO_2$ (Probably around 45 mmHg)
Normal MAP (Probably 65 mmHg)
Normal temp (Probably 37.5°C – or around 98.5°F – just to keep with the "5" theme)
And, lastly, a normal ECG – otherwise, get them to the cath lab emergently for STEMI or other concerning high-risk findings

Jacob Miller, ACNP, ENP-C, CNS, NRP, FAEN, FAEMS

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