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Weekly Journal Scan

Out-of-Hospital Cardiac Arrest: Handle With Care–*Comment on the Resuscitation Outcomes Consortium Cardiac Epidemiologic Registry*

The results of 'Association of intra-arrest transport vs continued on-scene resuscitation with survival to hospital discharge among patients with out-of-hospital cardiac arrest' have been published on *JAMA* 2020;**324**(11):1058–1067 (doi:10.1001/jama.2020.14185).

Key points

- This cohort study prospectively analysed data from the population-based Resuscitation Outcomes Consortium (ROC) Cardiac Epidemiologic Registry, including consecutive Emergency Medical System (EMS)-treated patients with non-traumatic out-of-hospital cardiac arrest (people apnoeic and pulseless who received external defibrillation by bystanders or EMS or chest compression from EMS personnel) between April 2011 and June 2015 from 10 North American sites.
- Survival to hospital discharge (primary outcome) and survival with favourable neurological outcome (secondary endpoint) were compared between 11 625 subjects who underwent intra-arrest transport [transport initiated prior to return of spontaneous circulation (ROSC)] (exposed) and 32 344 individuals who received on-scene resuscitation until ROSC or termination of resuscitation (unexposed).
- The mean duration of attempted out-of-hospital resuscitation was 22 ± 12 min. Survival to hospital discharge was 3.8% for patients who underwent intra-arrest transport and 12.6% for those who received on-scene resuscitation. The majority (59%) of intra-arrest transport survivors achieved ROSC prior to hospital arrival.
- After a time-dependent propensity score matching (using potential confounders such as patient age, sex, episode location, witnessed status, bystander cardiopulmonary resuscitation, initial shockable rhythm, and presumed cardiac aetiology) a cohort of 27 705 patients was identified, consisting of 9406 exposed and 18 299 unexposed subjects. Survival to hospital discharge was significantly lower among exposed compared to unexposed patients [4% vs. 8.5%; risk difference of 4.6% (95% confidence interval, CI 4.0–5.1%)], so was survival with favourable neurological outcome [2.9% vs. 7.1%; risk difference of 4.2% (95% CI 3.5–4.9)].

Comment

Management of cardiac arrest in the out-of-hospital setting remains a largely unresolved challenge for EMS worldwide since the death toll is still unacceptably elevated (only about 10% survive) often with serious cognitive damage. In spite of that, development of more effective strategies has never been considered a priority in the public health agenda, and scientific literature is relatively poor.

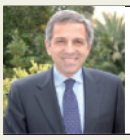
This observational cohort prospective study has the merit to provide a crisp snapshot of the current prevailing emergency strategies and of their comparison. With an approach based on a large and relatively homogeneous sample and a rigorous statistical approach, the authors report higher survival to hospital discharge in patients receiving on-scene resuscitation as compared to those managed with intra-arrest transport, the model currently prevailing in North America and other countries. This advantage persists after a propensity-matched analysis, as well as when cognitive outcomes are considered.

Of course, the on-site resuscitation manoeuvres require the intervention and assistance of well-trained personnel and the availability of proper equipment, and timing and duration of the manoeuvres are also of fundamental importance for the outcomes. In the ROC report, on-scene resuscitation time was 19 min, whereas intra-arrest transportation resuscitation time was 29 min and often patients reached the hospital still in arrest. Other factors that may advantage on-scene resuscitation are: clinical stabilization of vital parameters, impaired or delayed best cardiopulmonary resuscitation (CPR) practices during transportation, less effective quality of chest manual compression, and even less promptness of defibrillation or drug delivery in the ambulance. In fact, when exposure match time was analysed by strata, the worse outcomes of transported patients were those more rapidly moved from scene (within the first 15 min), whereas better survival was recorded when transportation was undertaken after 30 min.

An observational study can only detect an association, but not prove causation, and its findings are limited by unaccounted confounding. Moreover, the unavoidable heterogeneity of rescue and limited follow-up observation are additional limiting factors.

Randomized controlled studies should be encouraged and supported by public healthcare systems to assess the best practices to fight more effectively these fearful and dramatic events. By now, the dogma of rapidly transporting model needs to be challenged and the option 'handle with care' patients on the scene reconsidered.

Conflict of interest: Prof. Massimo Volpe reports personal fees for speaker bureau and/or consulting in Advisory Board from Amgen, Astra Zeneca, Daiichi-Sankyo, Menarini Int, MSD, Novartis Pharma, Novo Nordisk outside the submitted work. Prof. Carlo Patrono reports personal fees from Acticor Biotech, personal fees from Amgen, personal fees from Bayer, personal fees from GlaxoSmithKline, personal fees from Tremeau, personal fees from Zambon, grants from AIFA (Italian Drug Agency), grants from European Commission, other from Scientific Advisory Board of the International Aspirin Foundation, outside the submitted work.



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Weekly Journal Scan

Weak hypothesis? Wrong pharmacologic tool? Inadequate experimental design? Comment on the ATPCI trial

The results of the ATPCI trial have been presented at ESC 2020 and published in *The Lancet* (https://doi: 10.1016/S0140-6736(20)31790-6).

Key points

- The efficacy and safety of trimetazidine in patients with angina pectoris having been treated by percutaneous coronary intervention (ATPCI) study was designed to assess the potential long-term benefits of antianginal therapy after PCI.
- Approximately, 6000 patients who had had a successful PCI performed <30 days before inclusion, for stable angina or NSTE-ACS, regardless of the presence or absence of angina symptoms after the index PCI, were randomized to receive trimetazidine at the dose of 35 mg twice daily or placebo in addition to routine post-PCI treatment, and followed for up to 4 years.
- The incidence of the primary endpoint (a composite of cardiac death, hospital admission for a cardiac event, recurrence, or persistence of angina requiring the addition, switch, or increase of the dose of one of the antianginal drugs, or recurrent or persistent angina requiring coronary angiography) was not significantly different between the trimetazidine group [700 (23.3%) patients] and the placebo group [714 (23.7%); hazard ratio 0.98 (95% confidence interval 0.88–1.09); $P = 0.73$]. Similar results were obtained in the elective and urgent PCI subgroups. Serious adverse events occurred with similar frequencies in the two treatment groups.

Comment

The conceptual premise of ATPCI was that improvement in ischaemic myocardial metabolism by trimetazidine might be effective in improving outcomes after percutaneous coronary intervention (PCI), by preventing serious complications associated with angina. Numerous small studies had provided evidence for the efficacy of this compound in relieving angina and increasing exercise tolerance, but large randomized studies were lacking to define its place in the antianginal armamentarium. Unfortunately, major weaknesses in study design, patient selection, and drug effectiveness limit unequivocal interpretation of the ATPCI main findings. These include: (i) the presence of post-PCI angina before enrolment was not recorded and, at 1 month after randomization, angina was present in <20% of placebo-treated patients and not modified by trimetazidine; (ii) the observed annual event rate of the primary endpoint in the placebo arm of the trial was 40% lower than expected, perhaps reflecting the relatively young age of study participants (mean 61 years), their low atherosclerotic burden (>50% had single-vessel disease), and optimal evidence-based preventive therapy (including antianginal drugs in >90%); (iii) during the 4-year follow-up, angina leading to coronary angiography and angina leading to an increase or switch in antianginal therapies, were recorded in 17% and