CAT Block 9
Meagan Verbillion
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**Reference Article:** Jabre, P, et al. (2016). Early Identification of Patients With Out of Hospital Cardiac Arrest with No Chance of Survival and Consideration for Organ Donation. Annals of Internal Medicine, 65(11):770-778.

**PICO Question**: Can objective data be utilized to quickly identify patients with no chance of survival in out of hospital cardiac arrest in order to prioritize organ donation versus continuing with current standard of care measures?

**Study Design**: Retrospective assessment

**Introduction:** Mortality from out-of-hospital cardiac arrest (OHCA) is as high as 92-94%. Current standard of care for EMS personnel is to provide these patients with maximum resources in order to potentially achieve ROSC. Each EMS unit has clinical decision rules (CDR) currently in use that provide them with guidance as to when termination of resuscitation efforts is appropriate. The goal with termination in the field CDR is to spare cost of the ambulance transport and hospital staff utilization for a medically futile case. A 1% survival rate of patients with OHCA reflects medical futility and stopping CPR in these cases is reasonable. Despite the favorable utility of these CDR, none of them take into account organ donation. Organ transplantation saves lives and the major problem that the transplantation world faces is unavailability of organs. Unfortunately, many procedures must be in place to identify the appropriate candidates for donation and timelines of organ harvest from time of death are tight. In OHCA patients who could potentially be candidates for organ donation, rapid referral to the organ donation institution as well as mechanical ventilation and continuous external cardiac massage must be considered in order to harvest viable organs suitable for transplant. Many countries are now utilizing organs from Uncontrolled Donation after Cardiac Death (UDCD) which differs from current CDR in three respects. First and foremost, its use is intended exclusively for patients with no chance of survival. Second, the patient must be eligible to donate organs according to local policy, and third, the patient must be rapidly transported to an appropriate hospital under continuous resuscitative measures. This study aimed to find objective criteria that could be utilized within the first few minutes of OHCA to identify patients that have no chance of survival that are appropriate for organ donation.

**Methods**: This study utilized data from 3 different sources between the US and France. First, from the Paris Sudden Death Expertise Center (SDEC) a population based registry that covers Paris and its suburbs focusing solely on data from 2011-2014. All patients >18 years old with unexpected OHCA were included. Patients with DNR directives and those with obvious non cardiac causes to their death were excluded. Second, the PRESENCE Cohort study, a multi-center RCT was utilized. Ultimately after removing patients with extra-cardiac arrest, 486 patients were analyzed. Finally, the King Country Cohort, is an EMS database in Washington that has been collecting data about EMS-treated cardiac arrest since 1976. All patients 18-54 years who had OHCA without an obvious extra-cardiac cause that received ACLS care were included from the years 2006-2011. Three objective criteria that are known to be associated with lack of survival were selected based on a literature review that the authors felt were the most reliable, robust, objective, and easy to use in the pre-hospital setting to apply to OHCA patients. The criteria were: 1) OHCA not witnessed by EMS personnel or medical team members), 2) non-shockable initial cardiac rhythm, 3) no sustainable ROSC before receiving third 1 mg dose of epinephrine. These three criteria were applied to 1,771 patients from 2011-2012 of the SDEC registry. An internal prospective validation of the criteria was then conducted utilizing data from the SDEC registry for 2012-2015, the PRESENCE and King County cohorts, which comprised an additional 3,656 patients. The primary end point was the survival rate at hospital discharge among patients who met all 3 proposed criteria. The secondary end point was the number of patients eligible for organ donation according to the French protocol for kidney retrieval from UDCD criteria. UDCD Eligibility criteria included patients aged 18-54 years with no medical history of HTN, DM, cancer, sepsis, active viral infection (HBV/HCV/HIV) or renal disease and cardiac arrest not due to poly-trauma. In addition, time between

collapse and CPR initiation had to be less than 30 minutes and time from collapse to IABP insertion had to be less than 150 minutes. The survival rate and 95% CI were determined for patients with OHCA who fulfilled the objective criteria. They used standard $2 \times 2$ diagnostic test result tables to report prehospital or in-hospital mortality among patients meeting the objective criteria. They estimated the sensitivity (the probability that the criteria identify patients with no chance of survival [for patients who died]), specificity (the probability that the criteria recommend continuing ACLS [for patients discharged alive]), positive predictive value (PPV) (the probability of death when the criteria are met), and negative predictive value (NPV) (the probability of survival when ≥1 criterion is not met) and their respective 95% CIs for the objective criteria. The specificity and PPV were identified as the key test characteristics at the study design stage. Sensitivity analyses based on multiple imputation were used to account for missing data on outcomes and the objective criteria in the SDEC cohorts utilizing missing-at-random assumption. They assumed that for patients with OHCA who meet the objective criteria, the expected survival to discharge from the hospital is 0.001% (instead of 0% to allow sample size calculation). Therefore, 732 patients were required in order to detect a difference from a survival rate of 0.4%, with 90% power and a 1-sided type I error rate of 0.05 in a 1-sample test of proportions.

**Results**:  In the Paris SDEC 1-year cohort, the survival rate among the 772 patients with OHCA who met the objective criteria was 0% (95% CI, 0.0% to 0.5%), with a specificity of 100% (CI, 97% to 100%) and a positive predictive value of 100% (CI, 99% to 100%). These results were verified in the validation cohorts. 95 (12%) patients in the Paris SDEC 1-year cohort and 122 (8%) of the patients in the validation cohort may have been eligible for organ donation.

**Discussion**: In OHCA patients with no chance of survival, if appropriate candidates were identified within the first minutes of ACLS protocol and they met all of the aforementioned objective criteria we could increase the number of candidates eligible for organ donation thus saving the lives of patients desperately waiting for transplant. Obviously, initiating a plan such as the one outlined in this study would require significant resources. Many area EMS units would not be able to implement such a protocol as they are not close enough to a designated transplant facility. In addition, depending on the local protocols obtaining consent for donation could also lead to significant delays. This study highlighted the immense potential gains for the medical community if we were to switch our mindset from "always trying to achieve ROSC" to "maintenance of potentially viable organs" This will put a lot of onus on the prehospital community to have an upfront end of life discussion with family members and to coordinate efforts with local hospitals to ensure quick and timely initiation of appropriate procedures to ensure organ donation. The date presented in this study is however reassuring that we can utilize specific criteria, quickly and efficiently to identify futile efforts at resuscitation.

**Limitations**: This study had many limitations. First, there were several patients that had unknown outcomes. Second, UDCD protocol for kidney transplant only was applied as a secondary outcome. It is unknown whether or not other organs would be eligible for transplantation using this protocol. Third, exclusion criteria varied among the cohorts used with the Kings County cohort being the most restrictive.

**Bottom Line**: Utilizing the three objective criteria identified by this study could hasten identifying patients with OHCA eligible for organ donation.