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Modern Management of Cardiac Arrest

Guest: Dr. Joshua Reynolds

Background

- > 500,000 adults and children experience cardiac arrest (CA) annually in the US.
- CA claims more lives than colorectal cancer, breast cancer, prostate cancer, influenza, pneumonia, auto accidents, HIV, and firearms *combined*.
- Only 5% to 15% survive to hospital DC.

Hemodynamic-Directed Resuscitation

- ROSC and survival after CPR are dependent upon restoring myocardial blood flow.
- Coronary perfusion pressure (CPP) during relaxation phase of CPR is the primary determinant of myocardial blood flow.
- CPP = Aortic diastolic pressure – right atrial pressure
- *Meaney PA, et al. Circulation 2013*
    1) Arterial line + central venous line
        a. Target CPP > 20 mm Hg
        b. Optimal CPP not established
    2) Arterial line only
        a. Target diastolic blood pressure > 25 mm Hg
        b. Improve quality of CPR or give vasopressors
    3) Capnography only
        a. Target ETCO2 > 20 mm Hg
- There are no human trials studying the optimal titration of these parameters
- **Take Home Point: focus CA resuscitation on CPP**

High-Quality CPR

- Background
    - The cornerstone of cardiac arrest resuscitation
    - Patient survival linked to quality of CPR
    - Goal is to deliver oxygen/substrate to vital tissues
    - Provides only 10-30% of normal coronary flow; 30-40% of normal cerebral flow
    - Providers frequently deliver compressions that are too slow, too shallow, and don't allow for complete recoil
- Critical components
    - Chest compression fraction (CCF)
        - CCF = proportion of time compressions are performed during arrest
        - Target > 80%; lower CCFs assoc with decreased ROSC and survival to DC
        - Minimize interruptions!

                - Team Leader
                    - Communicate clearly about impending pauses - direct team to perform simultaneous actions during pause
                - Pulse checks
                    - Manual palpation unreliable and results in long pause
                    - Not recommended as a means of monitoring the effectiveness of CPR
                - Airway
                    - Optimal time for insertion of advanced airway unknown
                    - Consider supraglottic airway or passive oxygenation
                    - First attempt laryngoscopy during compressions; if unsuccessful, attempt to intubate in < 10 seconds
                - Perishock pauses
                    - Minimize preshock pauses
                    - *Cheskes S, et al. Circulation 2011*
                        - Survival significantly lower for patients with preshock pause > 20 secs compared to preshock pause < 10 secs
                        - 18% reduction in survival for every 5 sec increase in preshock pause
                    - Charge the defibrillator during compressions
                    - Hands-on defibrillation?
                    - Restart compressions immediately after shock and deliver for 1-2 min before postshock rhythm analysis
    - Rate
        - AHA/ECC Guidelines recommend compression rate ≥ 100 /min
        - Optimum target likely 100-120 /min
    - Depth
        - Guidelines recommend compression depth ≥ 2 inches (50 mm) in adults; improved defibrillation success and ROSC
        - Numerous studies demonstrating providers do not compress chest deep enough; depth < 38 mm associated with decreased ROSC/survival.
    - Chest Recoil
        - Allow the chest to fully recoil
            - Animal data: improves MAP, CPP, myocardial blood flow
            - No studies in humans
        - Avoid leaning: increases RA pressure, decreases cerebral and coronary perfusion, and decreases LV myocardial flow
- Mechanical CPR Devices
    - Theory: offers improved quality compressions while allowing defibrillation
    - *Westfall M, et al. Crit Care Med 2013*
        - Meta-analysis
        - Examines rates of ROSC from load-distributing band and piston-driven devices compared with manual CPR.
        - 12 studies (6,538 patients; 1,824 with ROSC)
            - 8 load-distributing devices

            - 4 piston-driven devices
        - Results
            - No benefit observed for piston-driven devices
            - 1 observational study demonstrated improved outcome for load-distributing device
    - *Perkins GD, et al. Lancet 2014 [published online]*
        - Pragmatic, cluster-randomized, open-label trial of adults with non-traumatic OHCA in the UK.
        - Objective: determine if the introduction of the LUCAS-2 mechanical CPR into EMS response vehicles would improve survival over manual CPR.
        - Study
            - Patients
                - Adults > 18 years of age
                - Non-traumatic OHCA
            - Primary outcome: 30-day survival
        - Results
            - 4471 patients
                - 1652 assigned to LUCAS-2 device (638 did not receive)
                - 2819 assigned to the control group
            - 30-day survival
                - LUCAS-2 group: 6%
                - Control group: 7%
    - **Take Home Point: no statistical difference in survival with mechanical devices.**

Defibrillation

- Biphasic vs. monophasic devices: no difference in survival
- Deliver single shock then resume compressions before rhythm analysis

Airway & Ventilation

- Airway
    - Optimal timing of advanced airway placement is unknown
    - Prolonged attempts at airway management lead to interrupted compressions.
    - Consider delayed intubation, passive oxygen delivery via NRB mask during first few minutes of arrest.
    - Supraglottic airways: data is mixed regarding outcomes.
    - <u>Use ETCO2 waveform capnography to confirm placement.</u>
- Oxygenation
    - Administer 100% FiO2, though animal data indicates 100% FiO2 may result in worse outcomes compared with room air.
- Ventilations
    - Goal – provide sufficient oxygen without impeding perfusion during CPR
    - Positive-pressure ventilation lowers cardiac output and reduces CPP during CPR
    - Metabolic demands for oxygen are decreased in the arresting patient
    - <u>Current recommendations: 8 – 10 bpm</u>
    - Ventilate to produce no more than visible chest rise

End-tidal CO2

- CO2 levels can reflect tissue production, cardiac output, and ventilation
- *Heradstveit B, et al. PQRST-A unique aide-memoire for capnography interpretation during cardiac arrest. Resuscitation 2014; 85:1619-20.*
  - P – Position of the tube
    - Capnography superior to auscultation and capnometry
  - Q – Quality of CPR
    - Monitor for signs of fatigue in rescuer – drop in levels
  - R – ROSC
    - Sudden increase to normal (35-40 mm Hg) reliable indicator of ROSC
  - S – Strategy
    - Reduced levels described in patients with PE, tension PTX, and hemorrhage
  - T – Termination
    - ETCO2 < 10 mm Hg after 20 min predicts unsuccessful resuscitation.
    - Current data insufficient for specific cut-off values at certain time intervals.

Vasopressors

- Rationale: vasopressors increase aortic pressure w/o concomitant increase in RAP, thereby improving both coronary and cerebral perfusion pressure.
- Epinephrine reported to cause:
  - Decreased microcirculatory cerebral blood flow
  - Increased myocardial oxygen consumption
  - Increased post-defibrillation ventricular arrhythmias
  - Increased post-ROSC myocardial dysfunction
- *Olasveengen TM, et al. JAMA 2009*
  - Prospective, RCT of consecutive adults with OHCA in Oslo, Norway
  - Objective: determine whether removing IV drug administration from ACLS would improve survival to hospital DC after OHCA
  - Results
    - 851 patients (418 in ACLS group; 433 in no IV drugs group)
    - No statistical difference in survival to hospital DC or long-term survival
- *Jacobs IG, et al. Resuscitation 2011*
  - Double-blind, randomized, placebo-controlled trial of epinephrine in OHCA
  - Objective: determine the effect of epinephrine on patient survival to hospital DC
  - Results
    - 601 patients
    - ROSC 8.4% vs. 23.5% for those who got epinephrine
    - Survival to hospital DC 1.9% vs. 4% (not statistically significant)
- *Hagihara A, et al. JAMA 2012*
  - Prospective, nonrandomized, observational propensity analysis of OHCAs occurring in Japan
  - Objective: evaluate the association between epinephrine use before hospital arrival and short- and long-term survival
  - Results

        - 417,188 patients
        - ROSC: 18.5% in the epinephrine group vs. 5.7% in no epi group
        - Negative association between prehospital epi use and long-term mortality (adjusted OR 0.46)
- *Larabee TM, et al. Resuscitation 2012*
    - Systematic review
    - 53 articles evaluating:
        - Any vasopressor to placebo
        - Vasopressin (w/ or w/o epinephrine) to epinephrine
        - High-dose epinephrine to standard dose epinephrine
        - Alternative vasopressors to epinephrine
    - Results
        - <u>Epinephrine associated with improved rate of ROSC</u>
        - <u>No long-term benefit demonstrated</u>
        - <u>Alternative vasopressors (dopamine, phenylephrine, norepinephrine) provide no long-term survival benefit</u>
- *Dumas F, et al. J Am Coll Cardiol 2014*
    - Background
        - International guidelines recommend epinephrine every 3-5 minutes during cardiac arrest resuscitation.
        - However, epi may have adverse effects during post-resuscitation phase and contribute to myocardial dysfunction.
        - Olasveengen, et al (*JAMA* 2009) and Hagihara, et al (*JAMA* 2012) reported no overall benefit to long-term survival with epinephrine.
    - Objective: evaluate relationship between epinephrine and survival among cohort of patients with ROSC from out-of-hospital cardiac arrest.
    - Study
        - Observational cohort study
        - All patients with nontraumatic OHCA who achieved ROSC and were admitted to a large, single center in Paris.
        - Primary outcome: favorable neurologic outcome (CPC of 1 or 2) at discharge.
    - Results
        - 1556 patients
            - 1134 (73%) received epinephrine
                - Older
                - Less likely to have witnessed arrest
                - Less likely to present with shockable rhythm
                - Longer duration of resuscitation
            - 422 (27%) did not get epinephrine
            - PCI performed in 44%, hypothermia performed in 70%
        - Survival
            - Epinephrine group: 193/1134 (17%)
            - No epinephrine group: 255/422 (60%)
        - Epinephrine use was negatively associated with favorable neurologic survival (adjusted OR 0.32).
        - Adverse association of epinephrine persisted across subgroups defined by initial rhythm, length of resuscitation, and post-arrest care.

    - Patients who received epinephrine within first 9 min of arrest had a better outcome (aOR 0.54) than those who received between 10-15 min (aOR 0.33).
  - Limitations: observational design, single center
- Combinations
  - *Mentzelopoulos SD, et al. JAMA 2013*
    - Randomized, double-blind, placebo-controlled, parallel-group trial
    - Objective: to determine whether the combination of vasopressin-epinephrine-corticosteroids during and after CPR improved survival to hospital DC in IHCA patients.
    - Results
      - 268 patients (VSE group: 130; control group: 138)
      - VSE group had higher probability for ROSC and survival to hospital DC with good neurologic outcome (13.9% vs. 5.1%)
- **Take Home Points**
  - <u>No definitive evidence that any vasoactive drugs improve long-term survival.</u>
  - No definitive evidence that any antiarrhythmic (i.e., amiodarone) has improved survival to hospital DC.

Unproven Therapies

- Calcium
  - Theory: acidosis during cardiac arrest may cause hypocalcemia that, if corrected, it may restore cardiac function during arrest.
  - *Kette F, et al. Eur J Emerg Med* 2013
    - Systematic review
    - 10 articles (2 RCTs); most studies rated as 'fair' quality
    - <u>No evidence that calcium in cardiac arrest resuscitation improves survival regardless of presenting rhythm</u>
  - Consider in cases of hyperkalemia, hypocalcemia, calcium channel blocker overdose, hypermagnesemia
- Thrombolytics
  - Theory: large % of patients with OHCA are due to ACS or PE
  - *Bottiger BW, et al. NEJM 2008*
    - Double-blind, multicenter trial in adults with OHCA
    - Randomized to tenecteplase or placebo
    - Primary outcome: 30-day survival
    - Results
      - 1050 patients (525 to tenecteplase)
      - 30-day survival
        - Tenecteplase group: 14.7%
        - Placebo group: 17%
    - Trial terminated early for <u>no benefit</u>
- Active Compression-Decompression CPR
  - Active compression-decompression CPR uses a device with a suction cup to perform CPR; differs from traditional CPR where chest is allowed to passively recoil.
  - Initial small studies demonstrated possible improvement in mortality and neurologic injury.

- *Lafuente-Lafuente C, et al. Cochrane Database Syst Rev 2013; 9:CD002751.*
    - Systematic review
    - 10 trials (8 OHCA, 1 INHCA, 1 both)
    - OHCA – 4162 patients
    - <u>No difference in mortality or neurologic impairment between ACDR CPR and standard CPR.</u>
- Aminophylline
  - Bradyasystole is most common initial rhythm in OHCA.
  - Survival from 'nonshockable' rhythms is very poor (< 3%).
  - Theory: aminophylline believed to counteract the effects of endogenous adenosine and may lead to improved survival.
  - *Hurley KF, et al. Cochrane Database Syst Rev 2013; 8:CD006781.*
    - Systematic review of all RCTs comparing IV aminophylline with administered placebo in adults with non-traumatic, normothermic, bradyasystolic cardiac arrests.
    - 5 trials (1254 patients; risk of bias low in 4 studies)
    - <u>Aminophylline had no effect on survival to hospital admission, ROSC, or survival to DC.</u>

Refractory Cardiac Arrest - Novel Therapies

- **Definition**
  - *Reynolds JC, et al. Circulation 2013*
    - Retrospective cohort study of cardiac arrest database (ROC) at single center (Pittsburgh site)
    - Objective: to determine the duration of CPR after which repeated traditional interventions cease to result in meaningful survival.
    - Study
      - Patients
        - Adults > 18 years of age with non-traumatic OHCA
        - Received chest compressions from professional provider or rescue shocks
      - Primary endpoint: survival to hospital DC with favorable neurologic status (mRS 0-3)
    - Results
      - 1014 patients
      - 47% achieved ROSC, 11% survived to hospital DC, 6% had a favorable functional status
      - 90% of patients who had favorable neurologic status at hospital DC had ROSC within 16 minutes
    - Limitations: single center, retrospective cohort of database
    - Take Home Points
      - Conventional resus strategies most effective w/in 10-15 min.
      - After 15 min, prob. of good functional recovery falls to < 2%.
- **ECLS**
  - Background
    - Literature on ECLS for refractory cardiac arrest present since 1980s
    - Most of literature for OHCA limited to small case series/case reports often comparing to historical controls.

        - *Kagawa, et al. Circulation 2012*: 42 pts, 21% survival with good neurologic outcome
        - *Maekawa, et al. Crit Care Med 2013*: 53 pts; 32% survival
        - *Leick, et al. Clin Res Cardiol 2013*: 28 pts; 39% survival
    - <u>Large randomized controlled trials have not yet been completed</u>
    - Extracorporeal Life Support Organization Registry
        - Over 5600 patients received ECLS for cardiac arrest
        - 1657 received ECPR: <u>28% survival to hospital DC</u>
    - Growing body of literature on use of ECLS in ED
        - *Bellezzo JM, Shinar Z, et al. Resuscitation 2012*: 18 patients, 8 survived to hospital DC, 5 neurologically intact
- Recent Literature
    - *SAVE-J Study Group, et al. Resuscitation 2014*
        - Objective: How does ECPR effect neurologic outcomes for patients with OHCA
        - Study: prospective observational study of 46 facilities in Japan (26 assigned to ECPR, 20 assigned to CPR)
        - Inclusion
            - Adults 20 – 75 years of age
            - VF/VT on initial ECG
            - CA on hospital arrival w/ or w/o pre-hospital ROSC
            - Arrival to ED within 45 min from 911 call
            - No ROSC at least during the 15 min after hospital arrival
        - Outcome: Favorable neurologic status (CPC 1 or 2) at 1 month and 6 months after CA
        - Results - 454 patients (234 in ECPR; 159 in CPR)
            - 1 m favorable outcomes (12.3% ECPR vs. 1.5% in CPR)
            - 6 m favorable outcomes (11.2% in ECPR vs. 2.6% in CPR)
            - Limitations
                - Differences in care between facilities
                    - TH: 91.5% in ECPR vs. 54%
                    - IABP: 92.7% in ECPR vs. 62.2%
                    - Coronary angio: 89% in ECPR vs. 68%
                - Non-randomized study
    - *Stub D, et al. The CHEER trial. Resuscitation 2014*
        - Study: prospective, pilot study from single center in Melbourne, Australia (The Alfred Hospital)
        - Patients (OHCA + IHCA)
            - OCHA
                - Aged 18-65 years
                - Cardiac arrest due to suspected cardiac etiology
                - CPR w/in 10 min by bystanders or EMS
                - Initial rhythm of VF
                - Mechanical CPR machine
        - Protocol

        - Eligible after 30 min of persistent cardiac arrest
        - 2L iced saline infused with mechanical CPR device
        - Intubated with 100% FiO2
        - Epinephrine 1 mg every 4 min
        - ECMO
            - 2 CCM physicians
            - Cannulated femoral artery and vein
            - Heparin bolus, blood flow at 3L/min with oxygen gas flow 3L/min
            - MAP of 70 mm Hg targeted with epi infusion
        - Transported to the cardiac catheterization lab
    - Results
        - 26 patients (11 OHCA and 15 IHCA)
            - Initial rhythm VF in 11 OCHA
            - Underlying cause of arrest ACS in 73%
        - Median time from collapse to ECMO initiation: 56 min
        - ROSC: 92%
        - Survival to hospital DC: 56%
            - 5/11 (45%) for OHCA
            - All survivors DC with full neurologic recovery
    - Complications
        - Blood transfusion required in 69%
        - Vascular surgery required in 42% - fem artery repair; arterial backflow cannula placement, ischemic limb
- *Johnson NJ, et al. Resuscitation 2014*
    - Study: analysis of single center prospective registry (U Penn)
    - Objective: describe the institution's experience with ECLS as a rescue strategy in adults with OHCA.
    - Patients
        - Age 18-70
        - Witnessed arrest (out-of-hospital, in the ED, or shortly after arrival to inpatient unit or cardiac cath lab)
        - Bystander initiated CPR
        - VF or VT as initial rhythm or obvious cardiac cause
        - Collapse to EMS arrival < 15 min
    - Results
        - 26 patients (15 OHCA, 5 in the ED, 3 after arriving to inpatient unit, 3 en route for transfer)
        - 42% with VF or pulseless VT
        - Average time from arrest to initiation of ECLS: 77 min
        - All patients cannulated via the femoral artery, femoral vein, or internal jugular vein
        - 4 patients (15%) survived to DC; 3 neurologically intact
        - 69% suffered complications: ischemia to lower extremity, stroke, hemorrhage, and organ failure.
    - Limitations
        - Retrospective, observational case series
        - Protocol developed largely by consensus

        - Low rate of VF/pulseless VT as initial rhythm
        - Low rates of bystander CPR
  - ECLS Take Home Points
    - No RCT or universally accepted protocol
    - Resource intensive therapy
    - Best outcomes appear to be adults with witnessed arrest, bystander CPR w/in minutes, shockable rhythm, short EMS transport time, short time to initiation of ECMO, rapid cooling once ECMO initiated, and emergent cardiac catheterization.
    - High rate of complications: hemorrhage, ischemia to lower extremity, and arterial injuries.
- **Esmolol**
  - *Driver BE, et al. Resuscitation 2014*
    - Patients in cardiac arrest have high levels of endogenous and exogenous epinephrine.
    - The $\beta 1$ and $\beta 2$ effects of epinephrine can increase myocardial oxygen requirements, worsen ischemic injury, lower VF threshold, worsen post-ROSC myocardial function
    - Objective: compare outcomes of patients who received esmolol to those who did not during refractory VF arrest in the ED.
    - Study
      - Retrospective, observational, analysis
      - Single, urban, academic county hospital (Hennepin County Medical Center)
    - Patients
      - Initial rhythm of VF or pulseless VT
      - CA in the ED or prehospital setting and remained in CA in ED
      - Received at least 3 defibrillation attempts
      - Got 300 mg amiodarone and 3 mg epinephrine
      - Had manual CPR by EMS followed by automated CPR with LUCAS device
      - All intubated
    - Results
      - 25 patients (6 received esmolol)
      - Esmolol group
        - All achieved temporary ROSC
        - 4 of 6 achieved sustained ROSC; all taken to Cath Lab
        - 3 of 6 survived to DC with good neurologic outcomes
      - No esmolol group
        - 8 of 19 achieved temporary ROSC
        - 6 survived to ICU admission
        - 2 survived to DC with good neurologic outcomes
    - Limitations: retrospective, small sample size

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