The Refractory VF Arrest Patient: A Review of the Current Treatment Options

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- Board Member, MN Resuscitation Consortium
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Objectives

- Delineate Refractory Ventricular Fibrillation (RVF)
- Recurrent VF versus Refractory VF
- What is “Electrical Storm”
- Current Pre-hospital treatments
- Additional hospital treatments
- Dual/Double Sequential Defibrillation
- ECMO/ECLS-A New Hope?

A Standard Scenario

- 55 YOF collapses at stop light, and her car rolls into the car in front of her. Airbags do not deploy, and bystanders find her slumped over the steering wheel and pulseless.
- First responder/bystanders start CPR, and deliver three AED shocks prior to EMS arrival.
- On EMS arrival, a fourth shock is delivered, an IO and alternative airway placed. Automated CPR started.
- Epinephrine 2 mg (total) and Amiodarone 300 mg given, and the patient remains in VF.
- Patient downtime is now ~25 minutes, and repeat evaluation reveals persistent VF.

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What are your options

- Continue CPR for a total of 30 minutes with recurrent defibrillations, additional epinephrine, bicarbonate and Amiodarone?
- "Load and Go" to the local hospital with CPR enroute and continuing the resuscitation?
- "Load and Go" to the local CCL (Cardiac Cath Lab) hospital with CPR enroute and continuing the resuscitation, with possible PCI with ongoing CPR?
- Call HEMS unit for transfer to CCL hospital, but can they continue effective CPR in the helicopter?
- "Load and Go" to a ECMO/ECLS center with CPR enroute and continuing the resuscitation, on the basis they can accept the patient and continue resuscitation?

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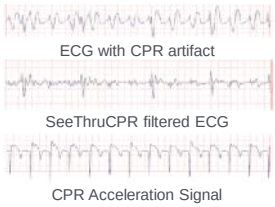
Defining the problem: What is recurrent versus refractory VF (RVF)?

- Recurrent VF is a rhythm that terminates with cardioversion, but then recurs rapidly.
- As CPR is immediately restarted after defibrillation, this may be missed due to CPR artifact.
- This rhythm is amenable to treatment with chemical antidysrhythmics if recognized and treated appropriately.
- (Courtesy of ZOLL Corp.)



ECG with CPR artifact

SeeThruCPR filtered ECG

CPR Acceleration Signal

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Defining the problem: What is recurrent versus refractory VF?

- **Refractory VF** is ventricular fibrillation that is thought to be "shock resistant" to standard cardioversion, due to ongoing myocardial ischemia fostering ongoing electrical instability.
- This is the concept of cardiac "Electrical Storm", where the myocardium is extremely resistant to stabilization.

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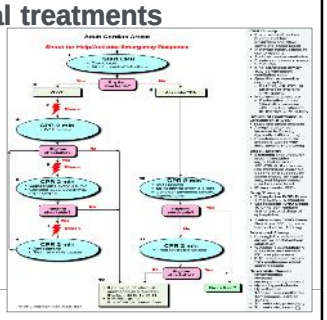
Current Pre-hospital treatments

- Current AHA guidelines for VF/VT call for three defibrillations with IV/IO epinephrine every 3-5 minutes.
- Amiodarone is then given if unable to convert.
- ***RVF exceeds the current AHA algorithm for VF/VT!!!***



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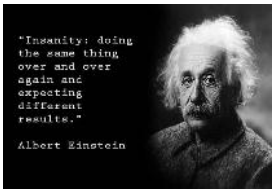
Current Pre-hospital treatments

- **With RVF, we are now past this algorithm, so what do we do next?**
  - Consider other antidysrhythmics such as magnesium, lidocaine or procainamide?
  - Administration of NaHCO3 to increase pH to more acceptable levels?



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Current Pre-hospital treatments

- **How about limiting or eliminating epinephrine?**
  - It has never been shown to improve survival to hospital discharge, and may actually decrease it.
  - Increases oxygen consumption.
  - Increases cerebral and myocardial vasoconstriction, so it impairs critical tissue oxygenation.
  - It is a dysrhythmic catecholamine, so it may actually make RVF harder to break.

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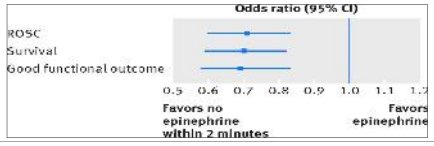
Current Pre-hospital treatments

Lars W Andersen et al: Early administration of epinephrine (adrenaline) in patients with cardiac arrest with initial shockable rhythm in hospital: propensity score matched analysis: BMJ 2016; 353



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Current Pre-hospital treatments

- Design: Prospective observational cohort study.
- Intervention: Epinephrine given within two minutes after the first defibrillation.
- Main outcome measures: Survival to hospital discharge. Secondary outcomes included return of spontaneous circulation and survival to hospital discharge with a good functional outcome.
- Results: 2978 patients were matched on the propensity score, and the groups were well balanced. 1510 (51%) patients received epinephrine within two minutes after the first defibrillation, which is contrary to current American Heart Association guidelines. Epinephrine given within the first two minutes after the first defibrillation was associated with decreased odds of survival in the propensity score matched analysis (odds ratio 0.70, 95% confidence interval 0.59 to 0.82; P<0.001). Early epinephrine administration was also associated with a decreased odds of return of spontaneous circulation (0.71, 0.60 to 0.83; P<0.001) and good functional outcome (0.69, 0.58 to 0.83; P<0.001).
- Conclusion: Half of patients with a persistent shockable rhythm received epinephrine within two minutes after the first defibrillation, contrary to current American Heart Association guidelines. The receipt of epinephrine within two minutes after the first defibrillation was associated with decreased odds of survival to hospital discharge as well as decreased odds of return of spontaneous circulation and survival to hospital discharge with a good functional outcome.

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Current Pre-hospital treatments

- How about limiting or eliminating epinephrine?
  - Preliminary research shows that lower doses of epinephrine does not impact outcomes.
  - There is a reasonable argument that to decrease the catecholamine surge associated with RVF, epinephrine should be reduced or eliminated in these patients.

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Hospital treatment

- **The "Pit Crew" approach to managing the RVF patient on arrival to the ED**
  - Management of these patients should not be left up to an individual physician's discretion and approach.
  - Have defined roles of all ED staff in the resuscitation.
  - Have an organized approach to this patient with set intervention protocols.
  - Take into account what has already been performed by the transporting EMS crew, such as:
    - Airway management
    - IV/IO access
    - Medications given (limiting epinephrine!!)
    - Continuing CPR (Manual versus Automated)

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Hospital treatment

- **What is you plan of action for this patient?**
  - Will this patient stay and be resuscitated in the ED?
  - What other medications should be considered?
  - Will the CCL/IC be notified and prepared to take this patient for emergent CC with ongoing CPR?
  - Does the CCL have the option/equipment for placing an LVAD or Impella device to extend the resuscitation window?
  - Is there the option for an ECMO/ECLS team to either receive the patient or mobilize to come to the patient?

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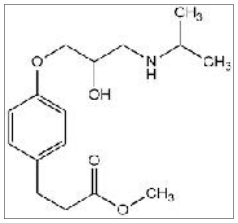
Hospital treatment: Other medications for RVF

- **Esmolol**
  - Esmolol decreases sympathetic tone and counteracts the catecholamine surge thought to occur during RVF arrest.
  - This is the only drug in cardiac arrest management that has been shown to increase the rate of survival to hospital discharge ***with*** favorable neurologic outcomes.



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Hospital treatment: Other medications for RVF

- **Esmolol**
  - Blocks beta-adrenergic receptors in the myocardium, thereby blocking the beta effects of the high concentrations of catecholamines.
  - This allows RVF to be more responsive to cardioversion.

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Hospital treatment: Other medications for RVF

- **INTRA-LIPID EMULSION THERAPY**
  - Recent research has shown that intra-lipids appear to open a different calcium channel into the myocardial conduction cells.
  - This allows the generation of ATP (energy) that can stimulate cardiac conduction and contractility.

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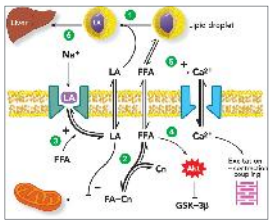
Hospital treatment- Other medications for RVF

- **INTRA-LIPID EMULSION THERAPY**
  - Postulated to augment the carnitine pathways in the myocardial cells during cardiac arrest.
  - Carnitine pathways help transport fatty acids into mitochondria to provide cardiac energy needs.



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Hospital treatment: PCI with automated CPR

- Cardiac catheterization with ongoing automated CPR has been described multiple times in the medical literature.
- It requires well trained staff, rapid transport directly to the CCL, and interventionalists adept at the intricacies of the procedure.

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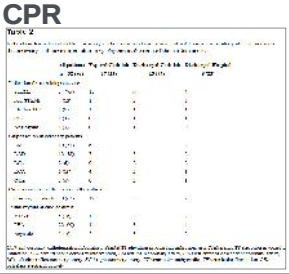
Hospital treatment: PCI with automated CPR

- The most recent series of 25 patients showed that 15 patients were discharged from the CCL, and that 8 were discharged with CPC 1-2 (32%).
- The practitioners felt that the automated CPR did not affect their ability to adequately perform their procedures.



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Pre-hospital and hospital treatment: Dual/Double Sequence Defibrillation (DSD)

- This mode of treatment has been around for over thirty years, and has been used mainly by EP cardiologists.
- It is based on the concept that very high doses of energy are needed when RVF is unresponsive to maximum standard defibrillations.
- DSD relies on the current delivered to the patient, and the vector that it goes through in order to maximally capture the fibrillating myocardium.
- In order to successfully defibrillate, ~90% of the myocardium must be depolarized with greater than 14A of current.

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Pre-hospital and hospital treatment: Dual/Double Sequence Defibrillation (DSD)

- Current (A)=Energy(J)/Impedance(ohms); with impedance being a function directly related to the patient. The higher the impedance, the less current delivered. (Ohm's Law)
- All current defibrillators measure patient impedance, and increase the delivered energy to increase the current delivered.
- Impedance can be lowered by improving the contact between patient and defibrillator pads by:
  - Cleaning skin prior to pad placement.
  - Removing excess body hair or sweat.
  - Increasing pressure on the pads (gloved hands with dry towels).

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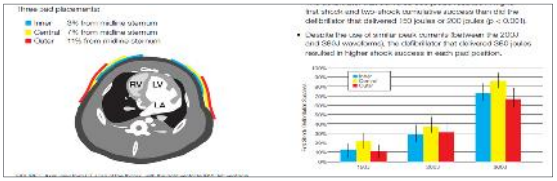
Pre-hospital and hospital treatment: Dual/Double Sequence Defibrillation (DSD)

- In addition, pad placement is a key factor in successful defibrillation:



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Pre-hospital and hospital treatment: Dual/Double Sequence Defibrillation (DSD)

- Shock success depends on a number of factors:
  - Vector of the shock (pad placement) and resulting current shunting (current going to areas other than the heart)
  - Location of the heart (axis deviation or degree of ventricular enlargement placing the myocardium in a suboptimal shock location)
  - Shock strength or size (e.g., more current)
  - Shock waveform (e.g., longer duration)

  (Two major determinants of energy (joules))
- The results from this experimental study show that even minor changes in pad placement (< 3 cm) can impact shock success.

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Pre-hospital and hospital treatment: Dual/Double Sequence Defibrillation (DSD)

Case Series	Patients	Conversion	DSD Shocks	Survivors
Cabanas	10	7	2	0
Cortez	12	9	2	3
Ross	50	14	unknown	3
Merlin	7	5	2	3
Emmerson	45	17	2.5±2	2
Totals:	129	52	2	11 (8.5%)

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Pre-hospital and hospital treatment: Dual/Double Sequence Defibrillation (DSD)

- All the listed studies attempted DSD after 3-5 standard defibrillation attempts.
- All were given amiodarone prior to DSD.
- Highest CPC 1-2 discharge rate was 28.7% (Merlin).
- Several ongoing studies currently.

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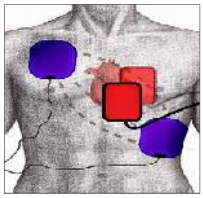
Pre-hospital and hospital treatment: Dual/Double Sequence Defibrillation (DSD)

- For successful defibrillation, we need to capture ~90% of the myocardium **and** exceed 14A in current.
- DSD runs the risk of excessive current delivery to the patient, potential damage of equipment, and prolonging field times for the patient.



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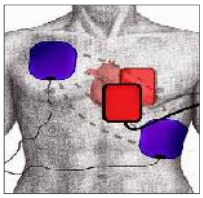
Pre-hospital and hospital treatment: Dual/Double Sequence Defibrillation (DSD)

- **Keys to maximizing early defibrillation success**
  - Initial proper angle of Anterior-Lateral pad placement.
  - Maximize pad contact to decrease electrical impedance.
  - If unsuccessful after three attempts, change to Anterior-Posterior position.
  - If still unsuccessful, **and** equipment is available, consider DSD.



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Hospital and Pre-hospital: ECMO/ECLS

- Currently our therapy relies on the premise that RVF must be stopped.
- What if we take conversion of RVF out of the picture, and instead concentrate on the rapid establishment of oxygenation and perfusion until PCI could be performed?
- LETS STOP THE CLOCK!!

- ECMO/ECLS

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Hospital and Pre-hospital: ECMO/ECLS

- **ECMO/ECLS**
  - Extracorporeal Membrane Oxygenation (or Life Support)
  - Provides oxygenation of the blood and pressure support for tissue perfusion.
  - Can also perform Therapeutic Hypothermia after ROSC.

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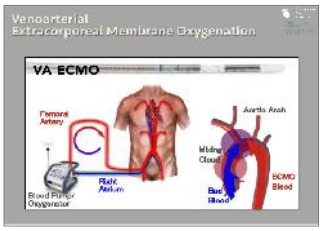
Hospital and Pre-hospital: ECMO/ECLS

- A cannula is inserted into the venous system and it takes returning venous blood into the ECMO circuit.
- Venous blood is then pushed through an oxygenator chamber and CO2 is removed.
- Oxygenated blood is then pumped into the aorta to perfuse the patient.
- Provides cardiac support to assist systemic circulation.



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ECMO/ECLS in Paris

- Mobile ICU = First responders
  - -physicians on ambulance
  - -"Exactly like trauma room"
- Prehospital ECMO Team
  - – 2 senior non-surgeon physicians with expertise in ECMO, 1 nurse, 1 paramedic
  - – Maquet™ Cardiohelp
  - – 2 units of packed RBCs and 2 units of FFP
  - – Sedation/Therapeutic Hypothermia

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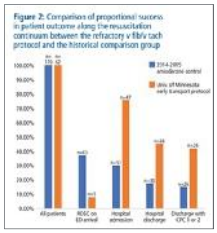
Hospital and Pre-hospital: ECMO/ECLS

- Patients with RVF have a high rate of acute and chronic CAD (~65%), such that emergent PCI may be their only option for successful resuscitation.
- When compared with standard ACLS protocol using amiodarone for RVF, survival rates with ECMO/ECLS are much higher.



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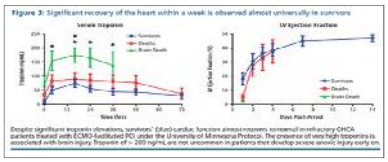
Hospital and Pre-hospital: ECMO/ECLS

- In addition, ECMO/ECLS now supports cardiac function after PCI, allowing survivors to regain excellent LV function as well as neurologic function.



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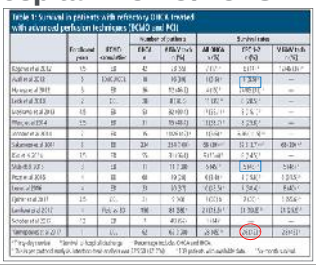
Hospital and Pre-hospital: ECMO/ECLS

- Sixteen studies have been completed over the last five years showing between a 5.5% to 45% CPC 1-2 survival rate.



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The MRC Refractory VF/VT Initiative

- Inclusion: Age 18-75, with presumed cardiac etiology.
- Exclusion: Known DNR/DNI, terminal medical condition, or active bleeding.
- All patients receive the standard ACLS treatment for VF/VT in cardiac arrest, airway management and ITD placement.
- Patients are placed onto automated CPR as soon as feasible.
- After three unsuccessful cardioversions by any combination of first responders (AED) or ALS crew, the patient is loaded into the ambulance and antidysrhythmic (amiodarone, lidocaine or magnesium) is administered.

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The MRC Refractory VF/VT Initiative

- Any patient that has VF/VT as the presenting rhythm, and then remains in VF/VT after treatment is considered to have RVF/VT.
- Patient can degenerate into PEA ***or*** asystole at any point after the initial diagnosis of RVF/VT, and/or get back to RVF/VT after requiring an antidysrhythmic, and they are still included.
- EMS transports the patient with automated CPR in progress if within a 60 minute window from 911 dispatch to arrival at the single designated ***"Resuscitation Center"*** (the University of Minnesota Hospital).

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The MRC Persistent VF/VT Initiative

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Our Starting Scenario

- Patient transported for emergent ECMO and PCI; found to have an acute coronary artery dissection (55 minutes of CPR).
- Undergoes repair, continued ECMO and Therapeutic Hypothermia. She is discharged 12 days later and returns back to her regular life.

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The Refractory VF Patient: Take Home Points:

- The current AHA guidelines do not adequately delineate the treatment of this condition.
- Automated CPR has markedly extended the "window of opportunity" for these patients.
- Epinephrine is arrhythmogenic and can worsen RVF, as well as cause cerebral/myocardial ischemia.
  - Limit epinephrine to a total of 3 mg, **OR** eliminate its use altogether in these patients.

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The Refractory VF Patient: Take Home Points:

- Have a plan for the RVF patient, including early transport, appropriate destination, and an organized approach when they arrive.
  - Consider Esmolol for decreasing sympathetic tone and counteracting the catecholamine surge.
  - Consider 20% Lipid infusion therapy for restoring energy flow to the myocardial mitochondria and possible associated drug intoxications.
  - PCI with ongoing automated CPR is feasible and extends our "window of opportunity", but requires skilled practitioners and a prepared CCL.

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The Refractory VF Patient: Take Home Points:

- DSD is another option for the termination of RVF, but first look to decrease patient impedance in cardioversion and changing pad placement/vectors.
- ECMO/ECLS is rapidly becoming more available, affordable, and easier to accomplish, but it is intensive and requires significant infrastructure.
  - Use of orchestrated GEMS/HEMS with automated CPR for rapid transport of these patients.
  - Consider the development of regional ECMO/ECLS programs.
  - While time is still of the essence, ECMO/ECLS can now provide a new "window of opportunity".

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- **Special Thanks to:**
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  Paramedic, Quality Supervisor; NMHAS
- **The Minnesota Resuscitation Consortium**
- **@ConteratoMarc**

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Questions?

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- **Esmolol therapy:**
  - Load: 0.5 mg/kg IV over 1 min, THEN
  - Maintenance: Start 0.05 mg/kg/min IV for 4 min, may increase by 0.05 mg/kg up to 0.2 mg/kg/min
  - If HR/BP not controlled after 5 min, repeat bolus (ie, 500 mcg/kg/min for 1 min), then initiate infusion of 0.1 mg/kg/min IV

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References

- **INTRA-LIPID EMULSION THERAPY**
  - Infuse 20% Lipid Emulsion (values in parenthesis are for a 70 kg patient)
  - Bolus 1.5 mL/kg (lean body mass) intravenously over 1 min (~100 mL).
  - Continuous infusion at 0.25 mL/kg/min (~18 mL/min; adjust by roller clamp).
  - Repeat bolus once or twice for persistent cardiovascular collapse
  - Double the infusion rate to 0.5 mL/kg per minute if blood pressure remains low.
  - Continue infusion for at least 10 minutes after attaining circulatory stability.
  - Recommended upper limit: approximately 10-12 mL/kg lipid emulsion over the first 30 minutes.

(Courtesy of http://lipidrescue.squarespace.com/)

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