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Medium Voltage Therapy for Preventing and Treating Asystole and PEA in ICDs

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Abstract — ***Introduction:*** **Sudden cardiac death (SCD) takes up to 500,000 lives each year before a victim can even be treated. To address this the implantable cardioverter defibrillator (ICD) was developed to treat those identified at high risk of SCD. Unfortunately, there are a significant number of cases in which the ICD does not successfully return a victim to normal rhythm and effective perfusion of the blood.**
Methods: **The vast majority of cases that are not responsive to the ICD therapy require cardio-pulmonary resuscitation (CPR) according to current resuscitation guidelines. A novel electrical stimulus called medium voltage therapy (MVT) has shown efficacy in producing coronary and carotid blood flow during ventricular fibrillation. This report presents the case that the same stimulus may be effective and feasible for use in ICD patients that do not respond to their ICD therapy, or do not have a rhythm in which, an ICD shock is indicated.**
Conclusion: **The inclusion of MVT technology in implantable devices may be effective in preparing the heart for successful defibrillation or in improving the metabolic condition of the heart to the extent that a pulsatile rhythm may spontaneously develop.**

Keywords — **Arrhythmia, Cardiac, Cardiac Arrest, CPR, Electric CPR, Fibrillation.**

I. INTRODUCTION

Sudden cardiac death (SCD) is among the largest killers in the developed world. In fact nearly 500,000 SCDs occur in the United States every year[1]. SCD is usually caused by ventricular fibrillation (VF), which can be converted to a normal rhythm if treated within minutes using a high-energy defibrillation shock. The development of the implantable cardioverter defibrillator (ICD) has provided an effective therapy for the victims of SCD[2]. Unfortunately, a significant number of ICD recipients still succumb to SCD because their initial post-shock rhythm may be or may deteriorate into rhythms that until now have not be treatable with electrical therapy. Among these arrhythmias are ventricular tachycardia (VT)/VF storm (repeated episodes of VT or VF i.e. 3 or more in a 24 hour period), asystole, pulseless electrical activity (PEA), and persistent VF. Anderson observed that failed rescue shocks accounted for 32% of the cardiac deaths in ICD patients[3]. Benditt, et. al. identified the mechanisms by which rescues shocks in ICD patients fail. These are shown in figure 1 (used with permission)[4]. An analysis

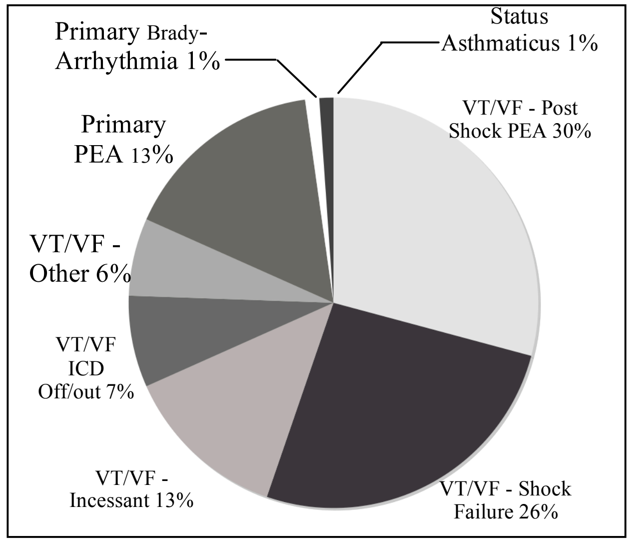

Fig. 1. The rhythms observed for patients not responding to ICD therapy. Note that in nearly all cases CPR is indicated for the observed rhythm

of these causes reveals that cardiopulmonary resuscitation (CPR) is indicated in 90% of the cases.

We have previously reported on the efficacy of a medium voltage electrical therapy (MVT) that produces coronary and cerebral perfusion and ventilation during VF when applied transthoracically or via an intracardiac route. [5,6] MVT refers to an electrical stimulus greater than that used for pacing but less than that used for defibrillation. In this report we discuss the prospect of using MVT to treat PEA, asystole and persistent VT/VF whether it occurs as the initial rhythm of SCD or following unsuccessful defibrillation attempts.

II. METHODS

The efficacy of MVT waveforms is very sensitive to the nature of the waveform. A series of factorial design experiments evaluating the influence of the waveform parameters was conducted in a preclinical setting. The waveforms evaluated consist of a series of pulse trains defined by five variables (Fig. 2): pulse amplitude (current of 0.2, 0.25, 0.5, 0.75, and 1 ampere), pulse width (PW: 0.15 ms and 7.5 ms), and pulse period (PP; 15 ms and 30 ms). Train width (TW) and Train Rate (TR) were fixed at 200 ms and 100 pulse trains/min respectively.[5,6]

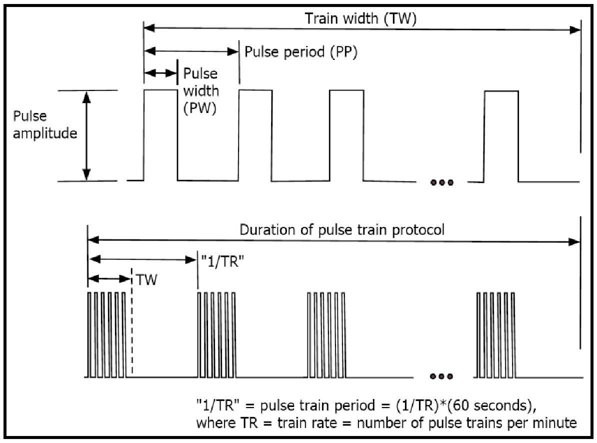

Fig. 2. Shows the nature of the pulse trains that were tested and found to be effective for producing coronary and carotid blood flow.

Figure 3 shows the results of the application of an optimal MVT waveform. The three channels shown are the ECG, arterial and atrial pressures. Coronary perfusion pressure (CPP) is the figure of merit most commonly used in resuscitation experiments because it a good measure of the perfusion of the heart. CPP is calculated as the difference between arterial and atrial pressure at the end of the diastolic phase. CPP of 15 mm Hg is considered to be the accepted minimum value (AMV) of CPP consistent with successful resuscitation.[7,8] Optimal MVT pulse trains produce CPP up to 30 mm Hg. Panel A shows a brief period of VF followed by the administration of MVT and the resultant arterial and venous blood pressure waveforms. Typical arterial peak pressures are 80 - 90 mm Hg. In this experiment MVT was continued only long enough (20 seconds) to reveal its efficacy then ceased and a defibrillation shock administered. At the end of the panel one can see the rescue shock and the normal ECG rhythm and blood pressure.

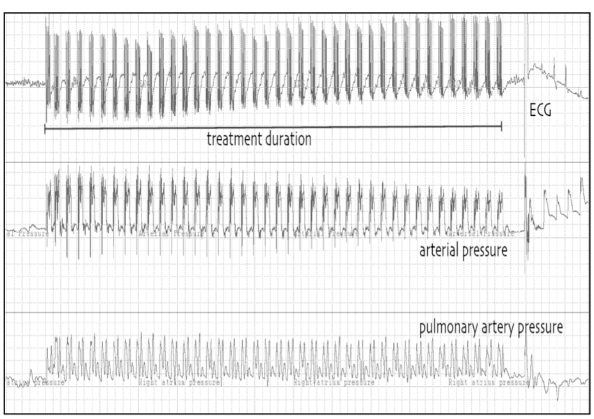

Fig. 3a. Shows a tracing of a preclinical test of MVT. Starting with VF on the far left MVT can be seen on the ECG (top tracing). The arterial and venous pressures resulting from the MVT can be seen on the next two tracings respectively. (Pressure tracings are 20 mm Hg/faint line).

Figure 3b is an expanded view of Figure 3a. The ECG tracing clearly shows the VF preceding the MVT and the NSR after the MVT. In the expanded panel 3B the individual pulses of a pulse train are individually visible. Each pulse train corresponds to a constriction (equivalent to a heartbeat.)

The time constants associated with cellular polarization and depolarization of skeletal muscle vs. cardiac muscle have been reported to be vastly different with the cardiac time constant being approximately 50 times longer than that for cardiac muscle.[9] By selecting pulse widths of 150 μs and 7.5 ms we were able to selectively stimulate skeletal muscle versus cardiac muscle.[10] This can be demonstrated by comparing waveform effectiveness after the administration of pancuronium[11].

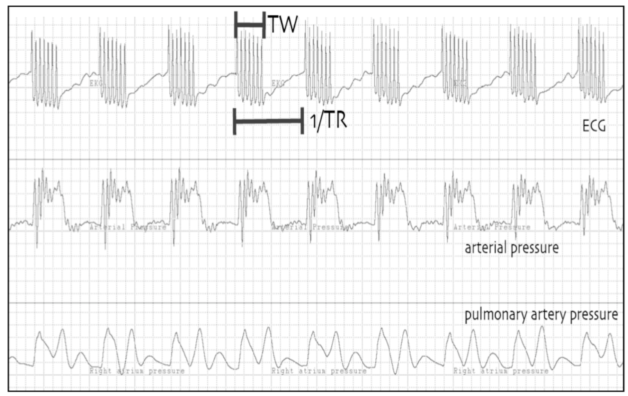

Fig. 3b. Shows an expanded section of the tracing of figure 3a in which the individual pulses of the MVT can be clearly seen in the ECG

While the testing reported to date has been performed during VF, we hypothesize that the same stimulation waveforms would be effective during PEA and other non-pulsatile rhythms and would be of great benefit to ICD patients who fail to convert to a pulsatile rhythm.

III. HISTORICAL BACKGROUND

Work by others has shown that when pulse trains similar to those described above are administered during VF the hemodynamic recovery is dramatically improved[12]. This in turn could prevent or reduce the incidence of post-shock asystole or PEA by improving the metabolic condition of the heart and making more receptive to a defibrillation shock.

The upper tracing in Figure 4 shows a “No Therapy” episode in which hemodynamic recovery from VF proceeds with severely reduced systolic and diastolic pressures. In contrast, the lower tracing shows that when only a few MVT pulse trains are administered the systolic pressures are immediately returned to normal. This improvement in hemodynamic recovery following defibrillation when MVT is administered during VF suggests that corresponding improvement in blood flow may also be realized when MVT is administered during PEA and asystole; and may also improve the likelihood of success with subsequent defibrillation shocks.

Further support that MVT may be useful in treating PEA, asystole or persistent VT/VF is based on observation shown in Figure 5. In Figure 5 we see that after 30 seconds of MVT applied during VF the subject spontaneously converted to a normal rhythm with good hemodynamic recovery. This observation can be coupled with the knowledge that the recommended therapy for PEA, asystole or persistent VT/VF is CPR.

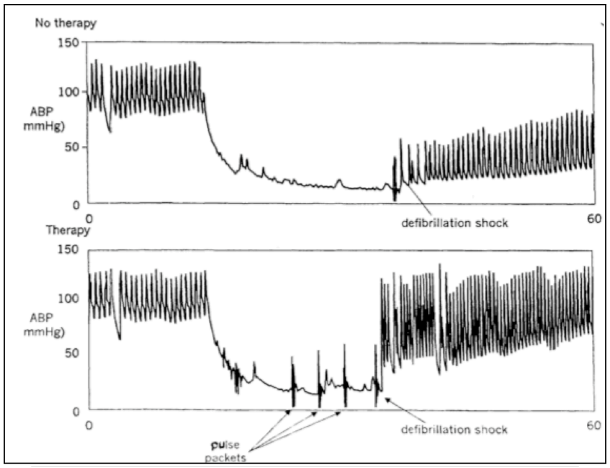

Fig. 4. A "no therapy" example (top tracing) shows very low blood pressure after defibrillation, while the MVT in the bottom tracing shows very strong pulse pressures

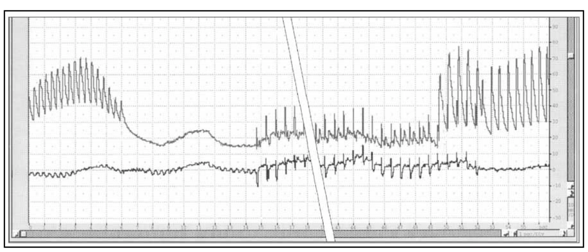

Fig. 5. In this example of MVT during VF we see that a pulsatile rhythm began spontaneously after 30 seconds of VF.

Independently, Rosborough and Deno showed that in a study of 38 episodes of induced PEA, animals that received MVT were 3 times more likely to return to a spontaneous circulation (ROSC) with no additional intervention than subjects without MVT[13].

Another advantage of short-pulse MVT is the stimulation of pre-synaptic sympathetic nerve axons. This is especially true for the "skeletal" waveform as the shorter pulses are more efficient for stimulating the sympathetic axon. Sympathetic stimulants are the standard of care for asystole.[14,15] While this is typically provided pharmacologically —with epinephrine — it can also be provided electrically as with MVT.[16]

IV. CONCLUSIONS

Research has shown that the vast majority of ICD patients that experience a SCD episode and do not respond to an ICD shock or have a rhythm for which a shock is not indicated should have CPR. MVT has been shown to be an effective method of electric CPR and could be incorporated into and ICD to provide the proper therapy in cases where CPR is indicated. An ICD enabled with MVT and an algorithm to determine whether to deliver MVT or a defibrillation shock could result in a substantial improvement in the survival of ICD patients that do not respond to ICD therapy.

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