Review
The controversial role of dual sequential defibrillation in shockable cardiac arrest

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ABSTRACT

Background: In the United States, over 350,000 cardiac arrests occur outside of the hospital and 209,000 occur in the hospital. Shockable rhythms such as ventricular fibrillation (VF) have a survival rate of 20–30% outside of the hospital setting. Dual Sequential Defibrillation (DSD) has demonstrated success in terminating VF that is refractory to multiple attempts using a single defibrillator.

Methods: The PubMed, and MEDLINE databases were reviewed in February of 2018 and literature reviewed on dual sequential defibrillation. The terms “dual”, “sequential”, “double sequential”, and “defibrillation” were added in the search builder. This search was limited to English-language articles. The results and their references were assessed for relevance to the topic and implications for dual sequential defibrillation in shockable cardiac arrest.

Result: Included search terms yielded 23 articles. Studies occurred in the emergency department and prehospital setting. There are two retrospective cohort studies and the majority of published studies are case reports/series. Sample size per study varied from 1 to 279 encounters.

Conclusion: Studies have shown success in using DSD to treat refractory VF. However, further studies are necessary to assess the efficacy and safety of DSD compared to the standard of care treating refractory VF.

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1. Introduction

Annually, over 350,000 cardiac arrests occur outside of the hospital and 209,000 occur in the hospital with a survival rate of 10% and 20%, respectively [1]. Survival rates vary by the type of abnormal rhythm causing the cardiac arrest. Shockable rhythms such as ventricular fibrillation (VF) and pulseless ventricular tachycardia (VT) have a survival rate of 21.4–29.3% outside of the hospital setting [2]. Current treatments guidelines are provided by the American Heart Association include basic life support (BLS) and advanced cardiovascular life support (ACLS) [1]. Increase in survival is associated with witnessed cardiac arrest, bystander cardiopulmonary resuscitation (CPR), early defibrillation and return of spontaneous circulation (ROSC) [3]. The role of external defibrillation is delivery of an electrical current to depolarize cardiac muscle cells, disrupt chaotic rhythms and re-establish sinus rhythm.

Refractory VF/VT occurs when there is persistent VF/VT despite defibrillation attempts. Patients with refractory VF/VT have higher mortality and poor neurologic outcomes [4]. Often these rhythms may be resistant to standard American Heart Association ACLS guidelines and therefore newer techniques are being developed to treat this issue. In addition to defibrillations, current standard treatment for VF/VT includes antiarrhythmic drugs such as lidocaine and amiodarone [5]. A recent study of esmolol showed some success in terminating refractory VF/VT and increasing ROSC compared to standard therapy [6].

The practice of dual sequential defibrillation (DSD) has demonstrated promise in terminating VF refractory to multiple single device defibrillations and antiarrhythmic medications. This practice has a growing body of literature suggesting DSD has a role in acute emergency situation. This literature review provides an overview and discussion to elucidate the current understanding and outlook of DSD in resuscitative medicine.

2. Methods

The PubMed and MEDLINE databases were reviewed to assess the literature on double sequential defibrillation. The terms “dual”, “sequential”, “double sequential”, and “defibrillation” searched in the PubMed and MEDLINE search builder. Search results were further limited to English language studies. Boolean operators and medical subject headings (MeSH) terms were used to combine search terms. Further literature was discovered using the Google Scholar database with the same search terms and using the reference section of articles found through the PubMed search. The result revealed 23 matches. The results and their references were assessed for relevance to the topic and implications for dual sequential defibrillation in shockable cardiac arrest.
2.1. Refractory ventricular fibrillation

Ventricular Fibrillation (VF) is an abnormal cardiac rhythm that can cause cardiac arrest. VF is often associated with a relatively higher chance of survival than other cardiac arrest rhythm such as pulseless electrical activity or asystole [7]. VF is caused by numerous underlying pathology, some examples are coronary heart disease, valvular heart disease, cardiomyopathy, electrolyte abnormalities, and congenital heart rhythm disorder (Brugada syndrome, prolong QT) [8]. These conditions disrupt the normal flow of electricity in the heart leading to an erratic pattern, which results in a heart that is not able to properly perfuse vital organs with blood.

The survival outcomes in refractory VF are 5.6–8.2% compared to non-refractory VF, which are 21.4–29.3% survival [2, 4, 9]. Refractory VF or shock resistant VF is defined as a rhythm that fails to achieve sustained ROSC after treatment with single defibrillation shocks and administration of anti-arrhythmic medication [10]. Refractory VF should be distinguished from recurrent VF (also known as electrical storm), which is defined as greater than 3 episodes of VF in 24 h [11]. Practically, it is challenging to distinguish given that CPR guidelines state chest compressions should be resumed after defibrillation and this distorts rhythm for at least 2 additional minutes [12].

2.2. Definition of dual sequential defibrillation

Dual or double sequential defibrillation is the application of two defibrillators that provide two shocks to a patient in refractory arrhythmias. The timing of delivering the sequential defibrillation is not clearly defined as techniques differ. The DSD techniques include defibrillation with a 1 to 2 second delay, overlapping shocks or completely synchronized. In the out of hospital setting, fully synchronized defibrillation is a challenge given the devices are not electrically connected, therefore true timing cannot be determined [13].

Two defibrillator types are used in the prehospital setting. The original device was the monophasic defibrillator, which delivers 200–360 joules of energy in a single direction. Introduced in the 1990’s, the biphasic defibrillator delivers bidirectional energy of 100–200 J. Wang et al. in a meta-analysis reported the biphasic and monophasic did not differ in out of hospital cardiac arrests in terms of survival rate to hospital discharge [14]. However, patients resuscitated with biphasic shocks were more likely to be neurologically intact upon leaving the hospital based on cerebral performance category (CPC) [15]. Clinicians use the CPC system to stratify the neurological level for cardiac arrest patients. [16] The effectiveness of biphasic defibrillation is postulated to be the use of multiple vectors. The myocyte vectors are not depolarized in a single direction during VF and the bidirectional waveform in biphasic devices maximizing the amount of depolarizing myocytes in cardiac muscle [15]. An additional benefit of the biphasic is the lower energy results in less post-shock myocardial damage [17].

Currently DSD is predominantly performed after multiple attempts of unsuccessful single device defibrillation. Growing clinical and theoretic evidence suggests the use of sequential shocks may alter the termination threshold and provide increased success in terminating refractory VF [18]. There are two ways the second set of pads can be applied to a patient. (Fig. 1A, B). With the first set in the anterior right chest and lateral left chest, with the second set either adjacent to the first set or in the anterior/posterior position. Charge both devices, ensure everyone is clear of the patient, press the shock button on both devices (either simultaneously or sequentially) and immediately resume CPR.

3. Levels of evidence

3.1. Animal models

The subject of DSD has been researched since the 1940’s in animal models and is an ongoing debate among researchers [19]. In 1986, the use of double and triple sequential defibrillation was trialed in dogs with induced VF that were with or without myocardial infarcts. The study concluded the use of sequential shocks would lower defibrillation threshold. The total energy and voltage required to terminate VF, and restore normal sinus was lower using DSD [20]. In 1994, VF was induced in closed-chested dogs and termination was attempted with either single or sequential overlapping electrical pulses of various energy levels (50 J, 100 J, 150 J). The study found the highest success in terminating VF to sinus with use of 150 J in sequential pulses [18].

3.2. Cohort study

Ross et al. conducted a retrospective cohort study on out of hospital cardiac arrests in a large urban emergency medical service (EMS) system between January 2013 and December 2015. Of the 3470 patients, 302 met inclusion criteria, which selected for patients in both recurrent and refractory VF treated with at least 4 single defibrillations as the
control or administration of DSD as the experimental group. The primary outcome was favorable neurologic outcome as defined by CPC 1 and 2 (1 = Good cerebral performance: conscious, alert, able to work, might have mild neurologic or psychological deficit; 2 = Moderate cerebral disability: conscious, sufficient cerebral function for independent activities of daily life) [8, 20]. The secondary outcomes include ROSC survival to hospital admission or survival to hospital discharge. Of the 302, 23 had incomplete data and were excluded, 229 received single 200 J defibrillation and 50 received a total of 400 J DSD. In the DSD group, a single person pushed both button simultaneously to deliver the 400 J. The orientation of the pads was one in the anterolateral and one in the anterior posterior orientation. Overall, the study showed no statistical difference in primary or secondary outcomes [21].

There was a statistically significant difference in the percentage of witnessed arrests between the groups of this study with 38% in DSD group versus 54.6% in the control group. A variable known to influence outcomes of resuscitation in VF/VT include age, sex, rate of bystander CPR and witness of arrest [3]. This resulted in a selection bias because a 2010 meta-analysis found the difference in survival for witness’s arrest to be 13.5% versus 6.4% in non-witnessed arrest. The author of this study discussed the limitations of the study including the selection bias as a confounder, the low population number and the inability to differentiate recurrent versus refractory VF. Refractory and recurrent is often used interchangeably in literature but distinguishing them may be beneficial to properly study the effectiveness of DSD. The result is the data skewed toward no difference if recurrent VF is being mischaracterized as refractory VF [21].

A similar retrospective cohort study by Emmerson et al. between July 2015 and December 2016 in London with 220 out of hospital cardiac arrest patients (45 treated with DSD and 175 treated with single defibrillations) found no significance in pre-hospital ROSC, ROSC at hospital admission and survival to discharge between the control and experimental groups. The study protocol aimed at no more than 6 single defibrillation shocks prior to DSD. Ultimately, an average of 10 single defibrillation shocks delivered before employing DSD and the time to DSD and ROSC was not recorded. The DSD group had 60% of arrests witnessed and the control group had 79.4% witnessed creating a selection bias similar to Ross et al. The study reported omission of recurrent VF but stated it cannot guarantee all recurrent VF was excluding. The study reinforces the need for isolating refractory VF/VT through analysis of strips and clarifying definitions to enable studying DSD in truly refractory VF cases [22].

3.3. Case reports

The first reported application of DSD in human dates back to 1994 with a retrospective case series of 5 patients out of 2990 patients over a 3-year period experiencing refractory ventricular fibrillation. Prior to attempt DSD, patients received 7 to 20 single defibrillation shocks. DSD was delivered externally 0.5 to 4.5 s apart by means of two defibrillators and all 5 (100%) patients reverted back to normal sinus rhythm [23]. DSD is regaining attention in recent years with several case reports attempting DSD. Sheikh et al. received 3 single 200 J defibrillations using a 200 J biphasic defibrillator. After these unsuccessful attempts, DSD using two defibrillators at 300 J each or 600 J in total was attempted. A second set of defibrillator pads were placed in an anteroposterior position directly adjacent to the first set of pads. The defibrillators were activated simultaneously and the patient reverted to normal sinus rhythm with return of spontaneous circulation (ROSC). The patient regained consciousness and was discharged from the hospital in neurologically intact after 7 days [27].

A similar in-hospital case reported by Gerstein et al. involved a 66-year-old man with an acute inferior ST-elevation myocardial infarction who went into VF. CPR was initiated with a biphasic 200 J device for 72 min. A total of 15 single defibrillation attempts occurred before DSD was tried. After the second DSD attempt, normal sinus rhythm was established with ROSC. Ultimately, the patient had anoxic brain injury and did not survive due to the prolonged CPR [28].

Several studies presented single case reports of cardiac arrest that occurred outside of the hospital [29-34]. The result was resuscitations using DSD reverted from VF to normal sinus rhythm with ROSC and complete neurological recovery in each case. A notable difference between these cases is the amount of single defibrillation attempts before attempting DSD. Sheikh et al. received 3 single 200 J defibrillations, two in anterolateral position and one in anteroposterior position, before receiving DSD [29]. Bell et al. had 4 attempts with single defibrillations before the use of two 200 J biphasic successfully terminated VF after 27 min. The patient has a recurrence of VF 60 s later and DSD was successful again [30]. Leacock et al. had 5 single defibrillations before the use of two 200 J defibrillators was attempted [31]. Lybeck et al. had 7 attempts with a single defibrillator before DSD was employed with 200 J biphasic and 360 J monophasic devices delivered within 1 s [32]. In Tawil et al., the patient received 7 single biphasic 200 J defibrillation attempts before DSD with two biphasic devices at a total of 400 J was attempted. ROSC occurred after 3 DSD shocks and this patient was later discharged neurologically intact after 61 min of resuscitative efforts. The number of shocks needed to terminate VF/VT is an independent risk factor for survival to hospital discharge [33]. A patient
requiring greater than or equal to 3 shocks is associated with less favorable outcomes [35]. In Johnston et al. a 28-year-old female with long QT syndrome had a cardiac arrest witnessed by her husband who initiated CPR immediately. She had 6 biphasic single defibrillations using 200 J before attempting DSD with two 200 J defibrillators. She recovered fully and was discharged neurologically intact [34] (Table 1).

### 3.4. Device and patient safety

A case report by Gerstein et al. reports the first known case of damage to a defibrillator linked to DSD. The case involves a 41-year-old man presenting to his primary care clinic with electrocardiogram (EGG) abnormalities. The physician sent him to the emergency department and an ECG displayed VT or supraventricular tachycardia secondary to left cardiac vessel occlusion. The patient received antiarrhythmic and defibrillation with a Zoll M Series CCT biphasic 200 J. This first shock was ineffective and a Physio-Control LIFEPAK LP15 360 J biphasic defibrillator was attempted. After both brands failed, DSD was attempted twice with two Zoll brand devices used simultaneously. Finally, DSD was attempted with two of the Physio-Control LIFEPAK LP15 and was again unsuccessful [36].

Next day, one of the LIFEPAK devices failed self-test and was nonfunctioning. The event code indicated the third shock delivered from the prior day, which occurred in parallel with the use of the Zoll device. DSD is an off-label use and manufacturers for the devices involved in this case have no safety standards or guidance surrounding this practice. The leading theory behind how the damage occurred was there was cross talk between devices that resulted in the device sending electricity to the other device instead of to the patient. DSD is increasingly being used and a few large EMS agencies have integrated it into their

### Table 1

<table>
<thead>
<tr>
<th>Studies/reports on dual sequential defibrillation</th>
<th>Author</th>
<th>Design</th>
<th>No.</th>
<th>Details</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gerstein et al. Case report</td>
<td>Ross et al.</td>
<td>Retrospective</td>
<td>229</td>
<td>received single 200 J defibrillation and 50 received DSD with a total of 400 J</td>
<td>Overall, the study showed no statistical difference in primary or secondary outcomes between DSD and single defibrillation. The study was subject to selection bias favoring outcomes for the control.</td>
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<tr>
<td>Hoch et al.</td>
<td>Emmerson et al.</td>
<td>Retrospective</td>
<td>175</td>
<td>received single 200 J defibrillation and 45 received two 200 J defibrillations in sequence for a total of 400 J</td>
<td>Average of 10 single shocks delivered prior to DSD</td>
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<tr>
<td>Cordero et al.</td>
<td>Cabanas et al.</td>
<td>Case series</td>
<td>10</td>
<td>patients (9 males and 1 female) with a median age of 76.5. In the</td>
<td>VF terminated after DSD in 7 cases and only 3 (42.3%) patients had ROSC in the field. The 10 patients, 0 (0%) survived to hospital discharge.</td>
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<tr>
<td>Cortez et al.</td>
<td>DSD was employed by paramedics after three unresponsive episodes of VF to single defibrillation. The mean resuscitation time was 34.3 min before first DSD. The mean number of single shocks was 5.4 prior to DSD ranging from 3 to 9, with a mean of 2 DSD shocks delivered.</td>
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<td>Sena et al.</td>
<td>Merlin et al.</td>
<td>Case report</td>
<td>1</td>
<td>56-year-old female in hospital became unresponsive and went into VF. CPR was initiated with delivery of four rounds of defibrillation using a 200 J biphasic defibrillator. After these unsuccessful attempts, DSD using two defibrillators at 300 J each and a 360 J monophasic devices delivered within 1 s.</td>
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<td>Gerstein et al.</td>
<td>Leacock et al.</td>
<td>Case report</td>
<td>1</td>
<td>66-year-old man had an acute inferior ST-elevation myocardial infarction out of the hospital went into VF. CPR was initiated with a biphasic 200 J devices for 72 min. A total of 15 single defibrillation attempts occurred before DSD was tried.</td>
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<td>Lybeck et al.</td>
<td>Tawil et al.</td>
<td>Case report</td>
<td>1</td>
<td>40-year-old male struck his chest against a pole during a basketball game and had sudden out-of-hospital cardiac arrest. 7 attempts with a single defibrillator before DSD was employed with 200 J biphasic and a 360 J monophasic devices delivered within 1 s.</td>
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<td>Johnston et al.</td>
<td>Gerstein et al.</td>
<td>Case report</td>
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<td>A 28-year-old female with long QT syndrome had a cardiac arrest witnessed by her husband who initiated CPR immediately. 6 biphasic 200 J single defibrillations were used before attempting DSD with two 200 J defibrillators.</td>
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<td>Bell et al.</td>
<td>Sheikh et al.</td>
<td>Case report</td>
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<td>A 41-year-old male with EKG showing VT secondary to coronary syndrome. DSD was attempted and one device was damaged and nonfunctioning the following day.</td>
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<td>The result was resuscitations using DSD reverted from VF to normal sinus rhythm with ROSC and placement of an automatic implantable defibrillator.</td>
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protocols. It is possible the defibrillator malfunction was unrelated to DSD but given that is a rare event DSD must be considered [36].

4. Discussion

The efforts are ongoing to optimize ACLS protocol and increase the survival rate of patients unresponsive to current standards of care. Large urban EMS agencies have begun to integrate dual sequential defibrillation into resuscitation protocols [21, 24] DSD has been an effective technique in treatment of refractory VF in many cases around the country.

Evidence supports that early intervention with defibrillation correlate with better outcomes [3]. Cortez et al. employed DSD after a mean 27 min and had better outcomes using DSD in comparison to Cabananas et al., which employed DSD after a mean of 51 min [24, 25]. The reported cases and series range from 3 to 15 single defibrillators before DSD was attempted [26–34]. Hasegawa et al. reports the success of defibrillation tapers off after multiple attempts and after three attempts survival outcomes decrease [35]. This poses a dilemma because classification of refractory VF requires three attempts at single defibrillation. Case reports have published showing success after 1 to 3 attempts with DSD. VF was reverted to sinus after a median of 2 attempts. Ross et al. found no significant difference in outcomes between the use of DSD and single defibrillation in a cohort analysis. However, the study had a selection bias that favored outcomes for control group and despite this had no significant difference in outcomes. Emphasis on timely incorporation of DSD into protocols would be beneficial given the outcomes measured are not based only on ROSC, but neurological preservation [21].

The underlying mechanism of DSD is not fully understood. Leading theories divide the mechanism into three components that likely have interplay. The components are duration, vector direction and energy. One theory proposes the defibrillation threshold is lowered with simultaneous or near simultaneous shocks because cardiac cells are in various stage of depolarization, repolarization and rest. The increase duration of shock allows for depolarization of missed cells that continue to propagate disorganized rhythms [18, 23]. Another theory postulates DSD maximizes on the vectors and allows for more cardiac mass to depolarize [18, 20, 23, 37]. This allows for increased likelihood of a shock aligning with the excitable cardiac cells. In refractory VF high-energy defibrillation may be required to successfully terminate VF as it may overcome factors such as suboptimal pad placement, anatomy differences and transthoracic impedance [38, 39]. Previously, weight was thought to be an independent risk factor for unsuccessful defibrillation due to the barrier created between the heart and external defibrillation, however this was found not to be a variable in a prehospital study using biphasic defibrillation [40]. It is likely the mechanism is a combination of these factors and understanding the mechanism of DSD may be useful in optimizing the timing of shock delivery.

The practice of DSD is corroborated by human and animal studies using sequential or overlapping shocks. The exact importance of magnitude versus direction of energy applied for termination of arrhythmias remains unclear [20, 23]. The survival rate in refractory DSD is only 5.6–8.2% compared to 21.4–29.3% in shockable VF [2, 4, 9]. Refractory VF is associated with underlying pathology that is acute or chronic ischemic. This causes scarring of the myocardium and predisposed individuals to a persisting arrhythmia [8]. The practice of transporting these patients was the standard of care for a time. However, evidence concludes resuscitation in the field is associated with better outcomes than patients transported to hospital [3]. Currently, standard interventions used in the VT/VF vary based on the clinical scenario, setting, (in or out of hospital) and available resources. The treatment involves combinations of the following: CPR, defibrillation, medications, relocation of defibrillator pads, cardiac catheterization, surgical interventions and protocols to minimize oxygen requirement such as inducing hypothermia in patients [41].

Patient safety was highlighted in Gerstein et al. after a device failed the day after being used in DSD. This was the first and only reported case of device malfunction, but the rise in this practice should incentivize manufactures to include DSD in future quality testing. The report concludes approaches to averting potential damage to defibrillators and danger to patients. Recommendations to providers include adding protocol to evaluate function of device after off label use such as DSD [36].

5. Conclusions

Survival rates remain low in refractory VF and current standards should continue to explore other treatment options. The emergence of the practice of DSD in treating refractory VF requires establishing guidelines surrounding the practice. Most of the data to date is based on case establish reports and series showing some successful resuscitation with intact neurological outcome. Overall, well-designed and high quality case control or double-blinded randomized trial will be necessary to completely elucidate the efficacy and role of DSD.

Author disclosure statement

No competing financial interests exist.

References


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