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Out-of-hospital cardiac arrest rectilinear biphasic to monophasic damped sine defibrillation waveforms with advanced life support intervention trial (ORBIT)☆

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Abstract

Background: Although biphasic defibrillation waveforms appear to be superior to monophasic waveforms in terminating VF, their relative benefits in out-of-hospital resuscitation are incompletely understood. Prior comparisons of defibrillation waveform efficacy in out-of-hospital cardiac arrest (OHCA) are confined to patients presenting in a shockable rhythm and resuscitated by first responder (basic life support). This effectiveness study compared monophasic and biphasic defibrillation waveform for conversion of ventricular arrhythmias in all OHCA treated with advance life support (ALS).

Methods and results: This prospective randomized controlled trial compared the rectilinear biphasic (RLB) waveform with the monophasic damped sine (MDS) waveform, using step-up energy levels. The study enrolled OHCA patients requiring at least one shock delivered by

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ALS providers, regardless of initial presenting rhythm. Shock success was defined as conversion at 5 s to organized rhythm after one to three escalating shocks. We report efficacy results for the cohort of patients treated by ALS paramedics who presented with an initially shockable rhythm who had not received a shock from a first responder (MDS: $n = 83$; RLB: $n = 86$). Shock success within the first three ascending energy shocks for RLB (120, 150, 200 J) was superior to MDS (200, 300, 360 J) for patients initially presenting in a shockable rhythm (52% versus 34%, $p = 0.01$). First shock conversion was 23% and12%, for RLB and MDS, respectively ($p = 0.07$). There were no significant differences in return of spontaneous circulation (47% versus 47%), survival to 24 h (31% versus 27%), and survival to discharge (9% versus 7%). Mean 24 h survival rates of bystander witnessed events showed differences between waveforms in the early circulatory phase at 4–10 min post event (mean (S.D.) RLB 0.45 (0.07) versus MDS 0.31 (0.06), $p = 0.0002$) and demonstrated decline as time to first shock increased to 20 min.
Conclusion: Shock success to an organized rhythm comparing step-up protocol for energy settings demonstrated the RLB waveform was superior to MDS in ALS treatment of OHCA. Survival rates for both waveforms are consistent with current theories on the circulatory and metabolic phases of out-of-hospital cardiac arrest.

Keywords: Cardiac arrest; Defibrillation; Cardioversion; Cardiopulmonary resuscitation (CPR); Advanced life support (ALS)

1. Introduction

Currently available external defibrillators for routine use by emergency medical services (EMS) personnel deliver monophasic (damped sinusoidal) or biphasic (current flow reversal during the shock) waveform shocks. The issue about which waveform is more effective in out-of-hospital cardiac arrest remains undecided. Biphasic waveforms defibrillate with lower energy, and initial shocks are more often successful in the electrophysiology laboratory, with implanted defibrillators [1–16] and when used by first responders in the setting of out-of-hospital cardiac arrest (OHCA) [7–10]. However, none of the prior randomized trials in out-of-hospital ventricular fibrillation (VF) were able to show improved survival to hospital admission or discharge despite greater efficacy in terminating VF [8,9]. This may in part be attributed to the fact that both out-of-hospital trials were randomized at the level of the first responder using automated external defibrillators. Neither out-of-hospital trial studied the relative efficacy of using ascending biphasic energy levels nor did they conduct lower energy level comparisons between biphasic and monophasic waveforms. In addition, not all biphasic waveforms are identical. Current ALS guidelines recommend either waveform, specifically ascending monophasic energy levels and either fixed or ascending biphasic energy levels [11].

The purpose of this study was to compare patient outcomes after VF treated with ascending energy shocks using a rectilinear biphasic waveform or a monophasic damped sine waveform in an advanced life support setting for the resuscitation of OHCA patients treated by Emergency Medical Technician-Paramedics (EMT-P).

2. Materials and methods

2.1. Study design

The out-of-hospital rectilinear biphasic trial (ORBIT), was a prospective, randomized, controlled trial of OHCA patients, comparing a control group receiving monophasic damped sine (MDS) defibrillation with a treatment group receiving rectilinear biphasic (RLB) defibrillation. The study used block randomization where a single ambulance station represented one block ("proc plan" SAS v 8.02). A central randomization unit used computer-generated random number tables to prepare a separate block randomization schedule for each station with a goal to provide an overall 1:1 device distribution ratio. A field logistics coordinator ensured compliance at the station through monthly scheduled checks and spot checks throughout the duration of the trial cross checking the serial number of the device and the station with the randomization schedule. Compliance at the patient was verified through the serial number of the device and station number abstracted from the ECG summary for each patient recruited in the trial. By design paramedics were not blinded to the treatment assigned. A central validation committee, blinded to treatment assignment, verified protocol adherence, ECG interpretation and patient outcomes.

2.2. Study population

Adult OHCA patients who experienced spontaneous, sustained, hemodynamically unstable ventricular arrhythmias (VF, pulseless VT) during the course of ALS treatment by EMT-P personnel were eligible for enrollment. Patients who received at least one shock at any time during resuscitation were enrolled, regardless of the initial presenting rhythm. Patients were excluded if they were under the age of 18 or presented with an unstable ventricular arrhythmia due to trauma.

2.3. EMS system

The city of Toronto (population 2.5 million) is served by a single EMS system. There are 22 stations housing 54 EMT-P staffed ambulances and 400 EMT-Ps under one medical director. EMT-P paramedics provide advanced life support by medical directive with medical oversight by telephone. In addition, there are 3000 firefighters, 400 EMT-Defibrillator only providers, and 20 Public Access Defibrillation Programs.

2.4. Intervention protocol

Patients who met the inclusion criteria received advanced airway management, ALS medications and defibrillation in ascending energy levels in accordance with the ILCOR 2000 ALS guidelines [11]. MDS defibrillation was delivered using M-Series monophasic defibrillators (ZOLL Medical, Corporation, Boston, USA) in a step-up protocol: 200, 300, and 360 J. Similarly, RLB defibrillation was delivered using M-Series biphasic defibrillators (ZOLL Medical, Corporation, Boston, USA); (120,150, and 200 J). If the patient received a shock from a first responder device prior to the arrival of the EMT-P provider, the subsequent shock energy level was adjusted depending on prior shock success in accordance with AHA guidelines [11]. An electrocardiogram (ECG) strip was recorded continuously from 6 s prior to a shock until 9 s after a shock. Return of spontaneous circulation (ROSC) was defined using the ILCOR definition as any return of a spontaneous pulse, detectable by palpitation of the carotid or femoral artery with no minimum duration [11].

2.5. Study outcomes

The primary outcome was shock success defined as a conversion to an organized rhythm at 5 s after one to three shocks administered by a randomized device. The initial cardiac arrest rhythm was obtained on review of the chart by trained data abstractors with strict rules of determination. Secondary outcomes were conversion with the first, second, and third shocks, ROSC, survival to arrival to the Emergency Department (ED), 24 h survival, hospital discharge, 30-day survival, and cerebral performance category (CPC) at discharge. A central validation committee, blinded to intervention group, validated the ECG interpretations, all outcomes and determined adverse events.

The primary and secondary outcomes were evaluated on all patients who received defibrillation using a randomized device regardless of presenting rhythm as well as the 'shockable' patient subgroup, defined as patients presenting with VF or pulseless VT on their initial rhythm recorded by the EMT-P unit. The "non-shockable" subgroup of patients, those patients whose initial rhythms recorded by the EMT-P unit were asystole or pulseless electrical activity, were not analyzed separately from the all patients group. Patients with EMS witnessed cardiac arrest or AED prior defibrillation are generally considered to have a survival advantage and have routinely been removed in previous comparable studies. Therefore, in this study, the subgroup of patients who arrested in the presence of the EMT-P unit and the subgroup of patients who were treated prior to the arrival of the EMT-P unit by first responders using automated external defibrillators (AEDs) were removed from the study analysis.

2.6. Safety and efficacy monitoring

A safety and efficacy committee (SEC) performed interim safety and efficacy analyses at 20% and 60% recruitment intervals. The efficacy stopping rule was set at a 15% absolute difference (from 55% to 70%) in the primary outcome measure without any safety concerns, with a p-value adjusted for multiple looks at the data [12,13]. The SEC committee would rule to stop the study if the adverse event rate in the treatment group exceeded the rate of the control group. All committee members were free of conflict of interest with the study results and the sponsor.

2.7. Statistical analysis

All statistical analyses were performed blinded to treatment group assignment. Continuous variables were expressed as mean $\pm$ S.D. Time intervals were also reported as medians and interquartile ranges. The appropriate two sample t-tests for samples with equal and unequal variance were used to compare mean values [14]. Two sample χ^2-tests and associated confidence intervals for differences between two proportions were used to compare proportions [15]. Since the baseline incidence of conversion success with the MDS waveform was previously reported as 69% [8] the conversion outcomes were reported as relative risk of shock failure and number needed to treat to convert an additional patient to an organized rhythm [16]. Randomization compliance was reported at both station and patient levels. The α-values adjusted for the: two interim and one final analyses were <0.0001, 0.0076, and 0.0424, respectively [13]. For all other comparisons, a χ^2 p-value of ≤ 0.05 was considered to be statistically significant. The continuity adjusted chi square p-value was used when cell size was small.

A sample size of 180 patients per group for a total of 360 OHCA patients was determined, based on an estimated 60% success rate for conversion to an organized rhythm after one to three shocks for the control arm (MDS waveform) [8], with a clinically significant difference of a 15% higher success rate for the study arm (RLB waveform); $p = 0.05$, 80% power (PASS 2000). The study was not powered to show a difference in survival.

2.8. Research ethics board

The Institutional Research Ethics Board approved the study to recruit without patient consent.

3. Results

3.1. Study enrollment

There were 538 patients enrolled (Fig. 1). Ninety-six cases were removed prior to validation because of incomplete documentation (53), non-randomized device (41), and family

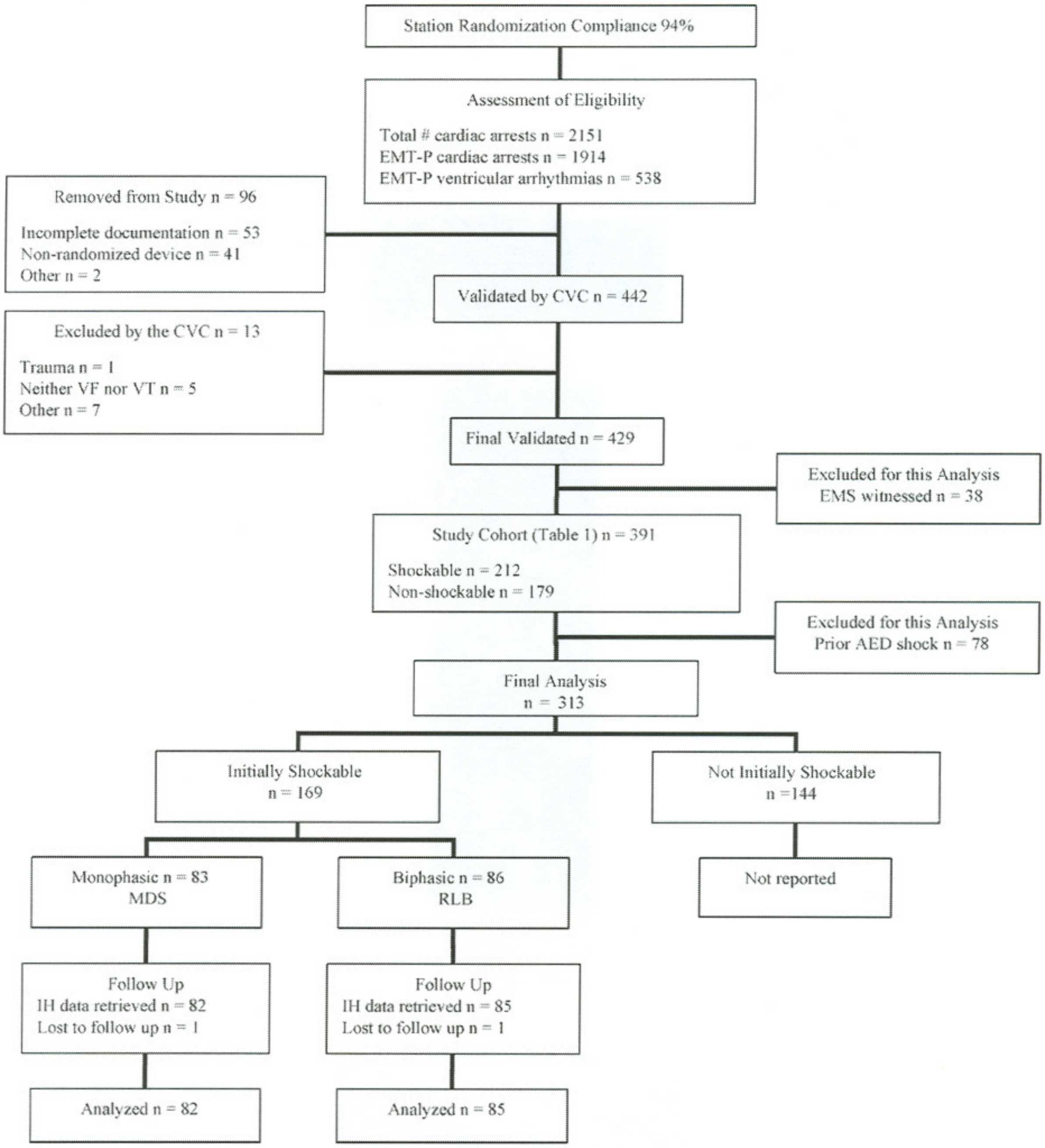

Fig. 1. EMT-P: emergency medical technician-paramedic, CVC: central validation committee, VF: ventricular fibrillation, VT: ventricular tachycardia, EMS: emergency medical services, AED: automated external defibrillator, OHCA: out-of-hospital cardiac arrest, MDS: monophasic damped sine, RLB: rectilinear biphasic, IH: in-hospital.

request (2). The central validation committee removed 13 cases of which 5 were not in VT or VF, one was traumatic in origin and 7 cases which were grouped as other (Fig. 1) leaving 429 validated cases. Thirty-eight EMS witnessed cases were removed prior to describing the study population demographics (see Section 2). There were 391 patients defibrillated regardless of presenting rhythm and of these 212 presented to EMT-Ps in a shockable rhythm (VF or pulseless VT on initial rhythm). The demographics and relevant covariables of these two groups are presented in Table 1. There were no significant differences in important covariables between treatment assignments. Seventy-eight cases received an AED shock prior to EMT-P arrival and were removed for the outcome analysis (see Section 2.5). The outcomes were evaluated on the 313 validated cases remaining of which 169 presented in a shockable rhythm and 144 patients presented

Table 1
Covariables

	All patients shocked during OHCA ($n=391$)		Patients shockable on arrival ($n=212$)	
	MDS ($n=193$)	RLB ($n=198$)	MDS ($n=107$)	RLB ($n=105$)
Age in years mean (S.D.)[a]	67.0 (16.0) ($n=185$)	67.3 (14.5) ($n=186$)	67.1 (16.4) ($n=103$)	67.1 (12.4) ($n=98$)
Male (%)	139/193 (72.0)	140/198 (70.7)	76/107 (71.0)	79/105 (75.2)
Call received to ALS "vehicle stops" interval, min. mean (S.D.) and median IQR[a]	7.3 (2.9), 6.9, 3.3 ($n=187$)	7.5 (3.3), 7.0, 3.3 ($n=189$)	6.8 (2.8), 6.0,2.9 ($n=102$)	6.8 (2.3), 6.7, 2.8 ($n=101$)
Call received to "first ALS shock" interval, min. mean (S.D.) and median IQR[a]	16.3 (9.2), 13.5, 12.0 ($n=186$)	16.6 (9.7), 13.9, 12.5 ($n=190$)	11.0 (5.8), 9.9, 4.6 ($n=103$)	10.4 (3.9), 9.7, 3.9 ($n=102$)
Rhythm analysis to "ALS shock" interval, min. mean (S.D.) and median IQR[a]	6.2 (8.5), 2.0, 11.0 ($n=189$)	6.1 (8.0), 2.0, 11.0 ($n=194$)	1.6 (6.0), 1.0, 1.0 ($n=106$)	0.7 (1.0), 0.0, 1.0 ($n=103$)
Bystander witnessed (%)[a]	142/191 (74.4)	146/197 (74.1)	82/105 (78.1)	81/104 (77.9)
BW collapse to "at patient's side" interval, min. mean (S.D.) and median IQR[a]	10.5 (4.1), 10.0, 5.5 ($n=122$)	10.9 (4.9), 10.0, 5.0 ($n=129$)	10.0 (4.0), 9.0, 5.0 ($n=71$)	9.8 (3.8), 9.0, 5.0 ($n=71$)
Bystander CPR (%)[a]	68/189 (36.0)	81/192 (42.2)	42/105 (40.0)	48/101 (47.5)
AED shock(s) prior to ALS arrival (%)[a]	44/191 (23.0)	34/198 (17.2)	24/107 (22.4)	19/105 (18.1)
Amiodarone (%)	85/193 (44.0)	82/198 (41.4)	55/107 (51.4)	41/105 (39.1)

OHCA: out-of-hospital cardiac arrest, MDS: monophasic damped sine, RLB: rectilinear biphasic, ALS: advanced life support, AED: automated external defibrillator, BW: bystander-witnessed, CPR: cardiopulmonary resuscitation, IQR: interquartile range.
[a] Some data missing.

in a non-shockable rhythm (Table 2). Device randomization compliance at the station was 94% and at the patient was 80%.

3.2. Response and transport times

The time interval from 'call received' to 'arrival at scene' (EMS systems response interval) did not differ between waveform treatments for all patients and the shockable cohort. The time interval from bystander witnessed collapse to 'at patient's side' was similar for both treatment groups; RLB: 9.8 min $\pm$ 3.8 versus MDS: 10.10 min $\pm$ 4.0 (Table 1).

3.3. Patient conversion outcomes

Successful conversion to an organized rhythm after one to three shocks for RLB was significantly greater than with the MDS waveform (52% versus 34%, $p=0.01$). Successful conversion to an organized rhythm after first shock for RLB versus MDS was 23% versus 12%, $p=0.07$ (Table 2). The RLB waveform increased the relative probability of shock

Table 2
Patient outcomes

	All patients shocked during OHCA ($N=313$)			Patients shockable on arrival ($N=169$)		
	MDS ($n=149$)	RLB ($n=164$)[a]	p	MDS ($n=63$)	RLB ($n=86$)	p
Up to three shocks conversion* (%)	66/149 (44.3)	90/163 (552)	0.05	28/83 (33.7)	45/86 (52.3)	0.01
First shock conversion to organized rhythm[a] (%)	35/146 (24.0)	48/161 (29.8)	0.25	10/82 (12.2)	19/83 (22.9)	0.07
Second shock conversion to organized rhythm[a] (%)	23/114 (20.2)	24/116 (20.7)	ns	16/73 (21.9)	18/67 (26.9)	ns
Third shock conversion to organized rhythm[a] (%)	8/91 (8.8)	18/92 (19.6)	0.06[b]	2/57 (3.5)	8/49 (16.3)	0.06[b]
ROSC (%)	55/149 (36.9)	61/164 (37.2)	ns	39/83 (47.0)	40/86 (46.5)	ns
Survival to 24 h (%)	26/147(17.7)	31/163 (19.0)	ns	22/82 (26.8)	26/85 (30.6)	ns
Survival to hospital discharge (%)	6/147 (4.1)	8/163 (4.9)	ns	6/82 (7.3)	8/85 (9.4)	ns
Survival to 30 days (%)	6/147 (4.1)	7/162 (4.3)	ns	6/82 (7.3)	7/84 (8.3)	ns
Cerebral perfusion category at discharge (%)	$n=6$	$n=7$	ns	$n=6$	$n=7$	ns
1	3/6 (50.0)	4/7 (57.1)		3/6 (50.0)	4/7 (57.1)	
2	2/6 (33.3)	0 (0.0)		2/6 (33.3)	0 (0.0)	
3	0 (0.0)	3/7 (42.9)		0 (0.0)	3/7 (42.9)	
4	1/6 (16.7)	0 (0.0)		1/6 (16.7)	0 (0.0)	

OHCA: out-of-hospital cardiac arrest, AED: automated external defibrillator, MDS: monophasic damped sine, RLB: rectilinear biphasic, IQR: interquartile range. ns: not significant at $p \leq 0.05$. ROSC: return of spontaneous circulation.
[a] Some data missing.
[b] p-Value adjusted for continuity correction.
* p-Value must be <0.048 for significance.

success by 57% (95% confidence intervals; 9%, 125%) with a number needed to treat (NNT) of 5, i.e. five patients need to be treated with a RLB waveform by an ALS paramedic to convert one extra patient to an organized rhythm successfully.

3.4. Patient survival outcomes

There were no significant differences between waveforms (RLB versus MDS) for ROSC success (47%, 47%), survival to 24 h (31%, 27%), survival to hospital discharge (9%, 7%) and to 30 days (8%, 7%). (Table 2) A good CPC score (CPC score = 1) at discharge was not significantly different between waveforms (RLB; 57% versus MDS; 50%).

4. Discussion

The main result of this study indicates that for out-of-hospital VF initially treated by ALS paramedics, RLB shocks are more effective at converting VF and pulseless VT to an organized rhythm than MDS shocks within the first three shocks when administered in sequence with escalating energy levels beginning at 120 J for RLB and 200 J for MDS However, despite an increased rate of return to an organized rhythm, neither the rate of return of spontaneous circulation nor the survival rates were improved in the RLB group. These observations are consistent with the observations of van Alem et al. [9] and Schneider et al. [8], but extend their findings to patients receiving ALS from advanced pare paramedics and ascending energy levels in accordance with current ALS guidelines. These data and our results suggest that biphasic waveform de-fibrillation is more effective than monophasic when administered by advanced life support paramedics and hence suggests the current ALS guidelines need to be reexamined. Importantly, unlike Schneider et al. [8] who employed "termination of VF" (which could include asystole) as an endpoint, we used an endpoint of "organized rhythm". Thus the ORBIT data refute the hypothesis that the increased efficacy of the RLB waveform is attributed to a higher likelihood of converting VF to asystole.

The return of spontaneous circulation and survival rates in the ORBIT study were lower than the other two OHCA studies [8,9] (Table 3). The EMS response interval was similar in all three studies; however, the rate of bystander CPR and witnessed cardiac arrest was lower in the ORBIT population. Becker et al published a comparison of survivor rates in cities with populations of more than 1 million and reported significantly lower rates than those reported in the previous studies. The Chicago data suggests that logistical (obstruction to patient access), demographic and other special characteristics of large cites may affect the survival rate [17]. The lower rate of witnessed cardiac arrest may be related to the fact that elders are well represented in our study population, more cardiac arrests occur at home and there is a cultural emphasis

Table 3
Comparison of ORBIT shockable group to published results

Design	Schneider [8] (BLS)[a]		van Alem et al. [9] (BLS)[a]		ORBIT (ALS)[a]	
Waveform	MTE, MDS ($n = 61$)	BTE ($n = 54$)	MDS ($n = 69$)	BTE ($n = 51$)	MDS ($n = 107$)	RLB ($n = 105$)
Energy levels	200, 300, 360 J	150 J	200 J	200 J	200, 300, 360 J	120, 150, 200 J
Covariables						
Witnessed cardiac arrest (%)[b]	89	87	96	96	78	78
Bystander CPR (%)[b]	46	43	57	51	40	48
Time Interval from Call Received to First Shock (randomized device)[b]	8.9 (3.2)[c]	9.2 (2.9)	8 (2–15)[d]	8 (3–15)	11.0 (5.8)[c], 9.9 (4.6)[e]	10.4 (3.9)[c], 9.7 (3.9)[e]
Primary outcomes						
First shock to 2-complex rhythm within first minute after shock (%)			45	69 (53% increase)		
Up to first three shocks to non-VF rhythm for ≥first 5 s (includes asystole) (%)	69	98 (42% increase)				
Up to three shocks to organized rhythm ≤5 s (%)					34	52 (53% increase)

BLS: basic life support, ALS: advanced cardiac life support, MTE: monophasic truncated exponential waveform, MDS: monophasic damped sine waveform, BTE: biphasic truncated exponential form, RLB: rectilinear biphasic waveform, J: joules, CPR: cardiopulmonary resuscitation, IQR: interquartile range, AED: automated external defibrillator, VF = ventricular fibrillation.

[a] Level of care provided with randomized device.
[b] Some data missing.
[c] Mean (S.D.).
[d] Mean (range).
[e] Mean (IQR).

in Canada on independent living for the elderly. Hence few bystanders are present to witness the cardiac arrest or perform CPR in the population most likely to suffer an OHCA.

The time to first shock from call received varied in all three OHCA trials (Table 3). Van Alem et al. and Schneider et al. reported 8–9 min [8,9] where as the time to first shock was longer in the ORBIT trial by 2–3 min. Campbell et al. studied patient access time interval (the time interval from 'vehicle stopped to arrive patient') and reported that 25% of calls had patient access time intervals of more than 2.5 min and 10% were more than 5 min [18]. We have reported previously that the 90th percentile for the patient access time interval is prolonged by a little more than 4 min when the patient is located three or more floors above ground [19]. The access and speed of vertical transportation in high-rise buildings are especially relevant in a large urban or metropolis setting, where a significant proportion of the population works or resides in high-rise buildings. Among Toronto's population of over 2.5 million, for example, 31% of the urban population lives in apartments and 70% of apartment dwellers live five or more floors above ground [20]. The elderly, defined as age ≥65 years, account for 11% of this group of all apartment dwellers [20]. Large urban centers that are densely populated present access challenges that contribute to 'urban delay' and will ultimately determine the presenting rhythm, the response to defibrillation and survival.

The incidence of VF and of VT at some time during a cardiac arrest in the ORBIT trial (years 2001–2003) was 28% (538 eligible of 1914 EMT-P cardiac arrests or 280 per 1000, Fig. 1). This rate was below that reported for Seattle in the year 2000 (380 per 1000). The decline in ventricular arrhythmia incidence reported by Cobb et al. from 1980 to 2000 was attributed to the national decline in coronary heart disease mortality [22]. It is unlikely that Canadian mortality rates due to heart disease have declined sufficiently to account for this difference. It is more likely that the longer patient access time interval, time to first shock, the low rates of bystander CPR and witnessed events seen in the ORBIT trial may account for the observed differences in incidence of VP and VT.

The decreased rates of bystander CPR and witnessed events in the ORBIT study, added to the urban delay to first shock, may increase the probability that the patient will be in the circulatory or metabolic phase of cardiac arrest when the ALS paramedics arrives at the patient side, as proposed in the

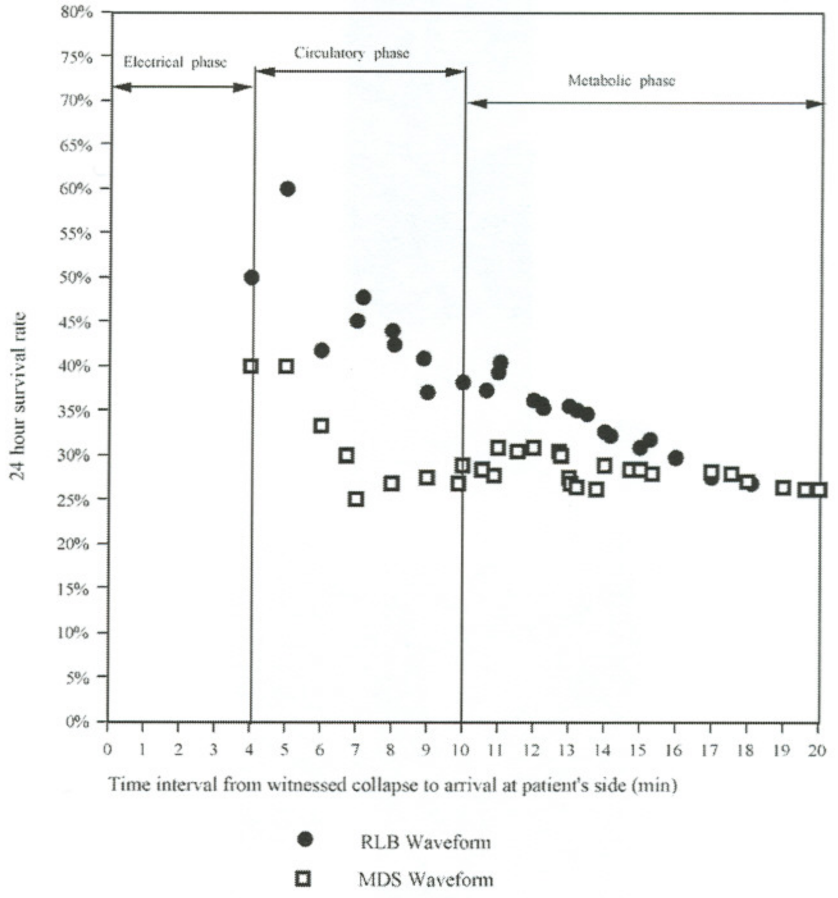

Fig. 2. Twenty-four hours survival rates for the RLB and UDS treated patients grouped by 1 min intervals, with respect to the three phases of OHCA [21]. The points indicate the observed survival rates for patients in the RLB and MDS groups, respectively, as a function of the interval between estimated witnessed cardiac arrest and the first shock, binned in 1 min intervals from 4 to 20 min. There were no patients with an interval less than 3 min.

3-phase temporal model of OHCA [21]. The 3-phase model suggests that defibrillation would be most effective during the electrical phase of VF (within 4 min of its onset), and defibrillation during the subsequent circulatory phase with little or no preceding CPR would be relatively ineffective at restoring circulation. The effectiveness of defibrillation may thus be time sensitive; for more effective defibrillation, it may have to be administered much earlier after the onset of VF. Operationally, this also means that the optimal intervention strategy for OHCA may need to be adjusted based on the 'downtime interval' (collapse to defibrillation) which should include the collapse to 911 call interval and the patient access time interval from 'vehicle arrive at scene to arrive patient'.

To conduct a post hoc analysis of the efficacy of either waveform as a function of time in VF we plotted the 24 h survival rate against the estimated time interval from witnessed collapse until delivery of first shock (Fig. 2). The time intervals were binned in 1 min intervals except where seconds were discriminating and permitted the plotting of individual data points within the binned time intervals. Fig. 2 demonstrates that, in the first 4–10 min of estimated VF duration, 24 h survival rates with RLB defibrillation were greater than MDS survival rates (mean (S.D.) RLB 0.45 (0.07) versus MDS 0.31 (0.06), $p = 0.0002$). This observation suggests that the RLB waveform has "clinical superiority" early after VF onset, during the circulatory phase of OHCA. The efficacy of defibrillation with this waveform in this phase of OHCA would likely improve further with CPR first [23,24] whereas in the metabolic phase [21] from 10 to 20 min neither waveform was as effective. In this analysis the RLB waveform continued to generate a higher 24 h survival rate from 11 to 15 min (mean (S.D.) RLB 0.35 (0.03) versus MDS 0.23 (0.02), $p < 0.001$). Whereas there was no significant difference in 24 h survival between waveforms when time to first shock was 16–20 min post event (mean (S.D.) RLB 0.28 (0.02) versus MDS 0.27 (0.01), $p = \text{ns}$). Our results imply that a higher rate of success with the biphasic waveform did not result in improved survival rates when downtimes exceeded 16 min, presumably because of ineffective cardiac contractile function after successful defibrillation. A survival rate of 60–50% with RLB for the time interval of 4–6 min after cardiac arrest would be predicted from the data shown in Fig. 2, and is very similar to survival rates estimated for the 3–6 min period in the study by Valenzuela et al., where biphasic defibrillation was delivered early after cardiac arrest onset [25]. Importantly, we estimated "total arrest duration" as the entire interval from collapse to defibrillation, not from 911 call to paramedic arrival at the scene. Where this time interval can be estimated it is clearly a more accurate reflection of the total time spent with no or low (during CPR) cardiac output, and likely to be more closely related to outcomes after treatment than the more commonly employed "911 call to arrival" interval. These results suggest both the potential value of early successful defibrillation using biphasic waveforms and the limitations of defibrillation late after VF onset, particularly when CPR is riot systematically provided prior to defibrillation. For these reasons, we believe that our findings in this large randomized OHCA trial support the concepts advanced in the 3-phase temporal model of OHCA [21].

5. Limitations

Randomization compliance was 94% at the level of the station and was 80% at the level of the patient. The unpredictable nature of the EMS environment, the size and complexity of the EMS system and the critical nature of the call necessitating creative immediate solutions to device failures or shortages contributed to a reduction in randomization compliance at the level of the patient This theory of random error was supported by an intention-to-treat analysis which was similar in magnitude and direction of the point estimate for the primary outcome measure (not shown). Regression analysis did not demonstrate any effect of compliance on waveform and primary outcome. And, finally this study compares two waveforms with ascending levels of energy. The results of this study may not be generalizeable to all types of biphasic or monophasic waveforms. The OHCA literature until now has used fixed biphasic energy levels of the truncated waveform to compare success against ascending monophasic levels. The ORBIT study evaluates the use of the rectilinear waveform with ascending levels of energy. Thus differentiating whether success was attributed to this different waveform or to ascending levels of energy will not be possible from this study.

6. Conclusions

Shock success to an organized rhythm comparing step-up protocol for energy settings demonstrated that the rectilinear biphasic waveform was superior to the monophasic damped sine waveform in advanced life support treatment of out-of-hospital cardiac arrest. Survival rates showed differences between waveforms in the early circulatory phase and demonstrated decline as the time to first shock increased.

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