

# The impact of ventricular fibrillation amplitude on successful cardioversion, resuscitation duration, and survival after out-of-hospital cardiac arrest

Ziad Nehme, Steffi Burns, Jocasta Ball, Stephen Bernard and Karen Smith

Ventricular fibrillation is the most favourable electrocardiogram (ECG) finding in patients with out-of-hospital cardiac arrest (OHCA) and is associated with high rates of survival.<sup>1</sup> Over the past two decades, improvements in survival after initial ventricular fibrillation arrests have been driven by substantial investment in system-based initiatives that have improved rates of bystander cardiopulmonary resuscitation (CPR) and defibrillation.<sup>2-5</sup> Despite the widespread adoption of these initiatives, survival rates following initial ventricular fibrillation arrests can vary by as much fivefold across similar regions.<sup>6</sup>

Ventricular fibrillation is not a uniform finding in OHCA and population-specific variations in ventricular fibrillation amplitude could lead to variations in survival outcomes.<sup>7</sup> International guidelines recommend against the initial defibrillation of rhythms that are analysed by automated external defibrillators (AEDs) as being low in amplitude ( $\leq 0.2$  mV).<sup>8</sup> However, these criteria are difficult to administer using manual defibrillation, and this may result in a large number of low amplitude rhythms being treated as initially shockable by emergency medical services (EMS).

International data on the incidence of low amplitude ventricular fibrillation rhythms are lacking, and the majority of existing studies have examined the impact of ventricular fibrillation signal using methods that have limited application in the clinical setting.<sup>7,9</sup> A more useful approach, incorporating the analysis of ventricular fibrillation amplitude signal before the first defibrillation attempt, has been described,<sup>10,11</sup> but relatively little is known about the impact of these findings on outcomes such as successful cardioversion, duration of resuscitation, and survival to hospital discharge. Studies demonstrating an association between pre-shock ventricular fibrillation amplitude and clinical outcomes have also not adjusted for important confounding variables, including delays before the initial defibrillation.<sup>10</sup>

We sought to examine the incidence of low amplitude ventricular fibrillation rhythms, determine the factors associated with low amplitude ventricular fibrillation, and determine the impact of ventricular fibrillation amplitude

## ABSTRACT

**Objective:** We sought to examine the incidence of low amplitude ventricular fibrillation and its impact on successful cardioversion, duration of resuscitation, and survival to hospital discharge in patients with out-of-hospital cardiac arrest (OHCA).

**Design:** Retrospective analysis from a statewide registry.

**Setting:** Victoria, Australia.

**Participants:** Consecutive initial ventricular fibrillation arrests with an emergency medical service (EMS)-attempted resuscitation between 1 February 2019 and 30 January 2020.

**Main outcome measures:** Survival to hospital discharge, successful cardioversion, and duration of resuscitation.

**Results:** Of the 471 initial ventricular fibrillation arrests, 429 (91.1%) had sufficient electrocardiogram data for review. The median initial and final ventricular fibrillation amplitude did not differ (0.3 mV; interquartile range [IQR], 0.2–0.5 mV). The final pre-shock amplitude was  $\leq 0.1$  mV (very fine) and  $\leq 0.2$  mV (fine) in 22.8% and 37.5% of cases respectively. In a multivariable analysis, only the time between emergency call and first defibrillation was associated with a low initial ventricular fibrillation amplitude  $\leq 0.2$  mV (adjusted odds ratio [aOR], 1.07; 95% CI, 1.02–1.13;  $P = 0.004$ ). After adjustment for arrest factors, every 0.1 mV increase in final amplitude was independently associated with survival to hospital discharge (aOR, 1.26; 95% CI, 1.14–1.39;  $P < 0.001$ ) and initial cardioversion success (aOR, 1.19; 95% CI, 1.07–1.32;  $P = 0.001$ ). The duration of resuscitation also increased by 1.7 minutes (95% CI, 1.03–2.36;  $P < 0.001$ ) for every 0.1 mV increase in final amplitude.

**Conclusion:** More than one-third of initial ventricular fibrillation OHCA cases were low in amplitude. Comparative international data are needed to better understand how low amplitude ventricular fibrillation rhythms confound the measurement of OHCA interventions and international benchmarks for survival outcomes.

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on successful cardioversion, duration of resuscitation, and survival to hospital discharge in patients with OHCA.

## Methods

### Study design

Between 1 February 2019 and 30 January 2020, we performed a retrospective audit of all OHCA cases with an initial arrest rhythm of ventricular fibrillation. Patients shocked before EMS arrival and those with an arrest witnessed by EMS personnel were excluded. The study, including the collection and use of registry data, was approved by the Monash University Human Research Ethics Committee (Project No. 21046).

### Setting

The state of Victoria, Australia, operates a single statewide EMS system servicing 6.4 million people across 227 000 km<sup>2</sup>. Suspected cardiac arrest events receive a dual response consisting of advanced life support and intensive care paramedics. Basic life support-trained firefighters and community emergency volunteers are also dispatched in metropolitan Melbourne and some areas of regional Victoria.<sup>12</sup> Cardiac arrest treatment guidelines follow the recommendations of the Australian Resuscitation Council (<https://resus.org.au/guidelines>). Paramedics used manual defibrillation protocols and charged the monitor pre-emptively before rhythm analysis.

### Data sources

The Victorian Ambulance Cardiac Arrest Registry (VACAR) is a population-based register of more than 105 000 OHCA events attended by EMS in the state of Victoria. The VACAR has been described in detail elsewhere.<sup>2</sup> Briefly, cardiac arrest cases are identified from electronic patient care records using a highly sensitive search algorithm. Cases are entered into the registry by trained data processors according to consensus definitions.<sup>13</sup> The registry collects over 150 data elements, including the Utstein-style descriptors<sup>13</sup> and patient discharge outcomes from over 100 participating hospitals. Hospital discharge status is also cross-referenced against official statewide death records from the Victorian Registry of Births, Deaths and Marriages.

### Assessment of ventricular fibrillation amplitude

Two clinical reviewers assessed all electronic and paper-based ECG recordings for initial arrest rhythms. Disagreements in the initial arrest rhythm were adjudicated by a third clinical reviewer. Ventricular fibrillation amplitude was measured in millivolts (mV) — where 0.1 mV is equal to 1 mm — and

was defined as the median peak-to-peak amplitude over a 2-second interval. As ventricular fibrillation amplitude deteriorates without CPR, we measured amplitude at two points during the pre-shock interval: i) immediately after the cessation of chest compressions (initial pre-shock amplitude); and, ii) immediately before defibrillation (final pre-shock amplitude). If the pre-shock interval was short (< 2 seconds), we assessed amplitude based on the available recordings. As the measurement of amplitude was conducted across both paper and electronic mediums, we used reference ECGs with varying ventricular fibrillation amplitudes to standardise the assessment across reviewers.

### Data analysis

Statistical analyses were undertaken using Stata Statistical Software 15 (StataCorp, 2018, College Station, TX, USA). A two-sided significance level of less than 0.05 was considered statistically significant. The primary outcome was survival to hospital discharge. Secondary outcomes included ventricular fibrillation amplitude, duration of resuscitation and initial cardioversion success. We defined resuscitation duration as the total time between the commencement of EMS CPR and return of spontaneous circulation (ROSC) or termination of resuscitation. Initial cardioversion success was defined as ROSC after one defibrillation attempt.

Baseline characteristics were reported using descriptive statistics and stratified by final ventricular fibrillation amplitude groups ( $\leq 0.2$  mV,  $> 0.2$  to  $< 0.5$  mV, and  $\geq 0.5$  mV). Comparison of baseline characteristics across amplitude groups were made using the  $\chi^2$  and Kruskal–Wallis tests, as appropriate.

To examine the association between arrest characteristics and a final ventricular fibrillation amplitude  $\leq 0.2$  mV, we performed multivariable logistic regression with the following independent variables: age (per year increase), sex, witness status, bystander CPR, arrest aetiology, location of arrest, urban region, and time between call and initial defibrillation, which includes the EMS response time interval. Similarly, to examine the association between ventricular fibrillation amplitude (per 0.1 mV increase) and initial defibrillation success and survival to hospital discharge, we performed multivariable logistic regression adjusting for the variables described above. The models were performed as a complete case analysis, excluding a small number of cases with one or more missing variables ( $n = 3$ , 0.5%). Results from the logistic regression models were reported as adjusted odds ratios (aORs) with 95% confidence intervals (CIs).

Finally, to examine the association between ventricular fibrillation amplitude (per 0.1 mV increase) and duration of resuscitation efforts, we performed multivariable linear

regression, also adjusting for the arrest factors described above. The results of this model were reported as mean differences with 95% CIs.

**Results**

**Population sample**

Between 1 February 2019 and 30 January 2020, EMS attempted resuscitation on 2771 OHCA cases not witnessed by EMS, of which 647 (23.3%) were initially shockable. After excluding those shocked before EMS arrival ( $n = 162$ ) and cases involving initial pulseless ventricular tachycardia ( $n = 14$ ), 471 cases (72.8%) were eligible to undergo measurement of ventricular fibrillation amplitude. Of those eligible, 429 cases (91.1%) had an electronic or paper ECG available.

**Ventricular fibrillation amplitude**

The initial and final pre-shock amplitudes for the 429 ventricular fibrillation cases are shown in Figure 1. The median initial and final amplitudes did not differ (median, 0.3 mV; interquartile range [IQR], 0.2–0.5 mV), although 51 cases (11.9%) increased in amplitude and 150 cases (35.0%) decreased in amplitude over the first pre-shock

interval. Ninety-eight (22.8%) and 161 cases (37.5%) had a final pre-shock amplitude  $\leq 0.1$  mV and  $\leq 0.2$  mV respectively.

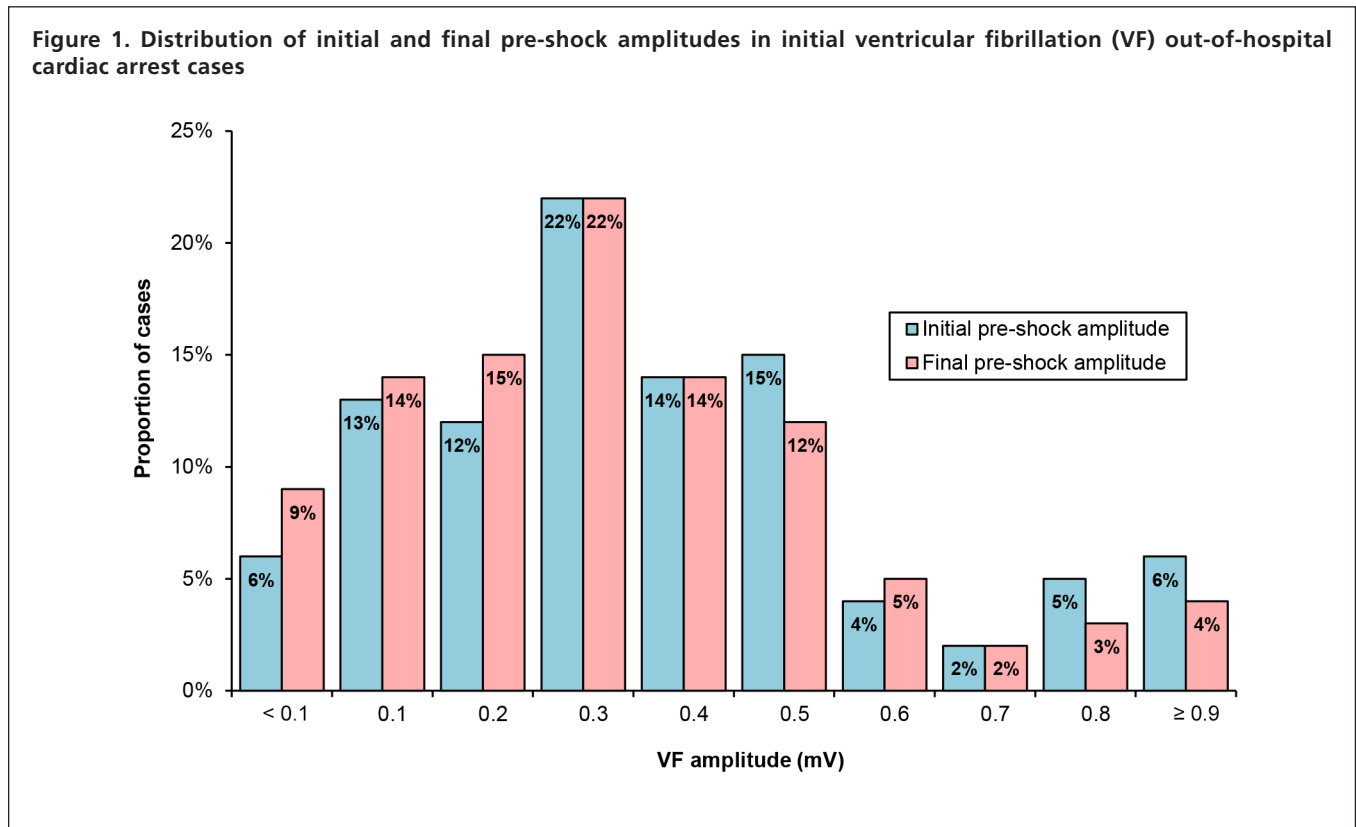
**Baseline characteristics and ventricular fibrillation amplitude**

The arrest characteristics of initial ventricular fibrillation cases are shown in Table 1. Although patients with lower ventricular fibrillation amplitudes were similar in age and sex and received similar levels of bystander CPR compared with higher ventricular fibrillation amplitudes, they experienced longer delays to EMS arrival and first defibrillation.

**Unadjusted outcomes and ventricular fibrillation amplitude**

Table 1 shows the differences in unadjusted outcomes across the final ventricular fibrillation amplitude groups. The median duration of resuscitation was significantly longer in low amplitude ventricular fibrillation compared with higher amplitude groups (37 min  $\nu$  19 min  $\nu$  20 min;  $P < 0.001$ ). Unadjusted rates of cardioversion success and survival to hospital discharge were lower in cases with low amplitude ventricular fibrillation ( $P < 0.001$  for both comparisons).

The distribution of survival to hospital discharge rates across initial and final pre-shock amplitudes is presented



**Table 1. Arrest characteristics of initial ventricular fibrillation cases stratified by final amplitude**

	Overall	Final pre-shock amplitude			P	Missing n (%)
		≤ 0.2 mV	> 0.2 to < 0.5 mV	≥ 0.5 mV		
Total number of patients	429	161	153	115		
Median age, years (IQR)	66 (53–76)	66 (53–76)	66 (54–76)	68 (54–75)	0.97	0
Sex, male	358 (83.5%)	140 (87.0%)	128 (83.7%)	90 (78.3%)	0.16	0
Public location	103 (24.0%)	37 (23.0%)	38 (24.8%)	28 (24.4%)	0.92	0
Presumed cardiac aetiology	414 (96.5%)	154 (95.7%)	150 (98.0%)	110 (95.7%)	0.44	0
Urban region	288 (67.1%)	102 (63.4%)	105 (68.6%)	81 (70.4%)	0.41	0
Bystander-witnessed	328 (76.5%)	118 (73.3%)	117 (76.5%)	93 (80.9%)	0.34	0
Bystander CPR	349 (83.4%)	124 (77.0%)	129 (84.3%)	96 (83.5%)	0.20	0
Median time intervals, min (IQR)						
Call to EMS arrival	7 (6–10)	8 (6–11)	7 (6–10)	7 (6–9)	0.004	0
Call to first defibrillation	10 (8–13)	10 (9–14)	10 (8–12)	10 (8–12)	0.03	0
Duration of resuscitation	27 (12–41)	37 (21–46)	19 (10–36)	20 (10–35)	< 0.001	0
Cardioversion success						7 (1.6%)
ROSC within one shock	69 (16.4%)	10 (6.3%)	34 (22.5%)	25 (22.1%)	< 0.001	
ROSC within three shocks	154 (36.5%)	35 (22.2%)	70 (46.4%)	49 (43.3%)	< 0.001	
Scene outcome						0
Efforts ceased at scene	167 (38.9%)	94 (58.4%)	38 (24.8%)	35 (30.4%)	< 0.001	
Transported with ROSC	242 (56.4%)	57 (35.4%)	109 (71.2%)	76 (66.1%)	< 0.001	
Transport with ongoing CPR	20 (4.7%)	10 (6.2%)	6 (3.9%)	4 (3.5%)	0.49	
Any pre-hospital ROSC	264 (61.5%)	66 (41.0%)	117 (76.5%)	81 (70.4%)	< 0.001	0
Event survival	242 (56.4%)	56 (34.8%)	109 (71.2%)	77 (67.0%)	< 0.001	0
Discharged alive	142 (33.3%)	22 (13.7%)	68 (45.3%)	52 (45.2%)	< 0.001	3 (0.5%)

CPR = cardiopulmonary resuscitation; EMS = emergency medical service; IQR = interquartile range; ROSC = return of spontaneous circulation. Proportions exclude missing data.

in Figure 2. Survival rates for final amplitudes of < 0.1 mV, 0.1 mV and 0.2 mV were 2.6%, 6.7% and 27.0% respectively. In comparison, survival to hospital discharge remained consistently above 40%, with final amplitudes > 0.2 mV. Similar findings were observed for the unadjusted rate of cardioversion success across final ventricular fibrillation amplitude groups (Figure 3).

#### Association between ventricular fibrillation amplitude, survival and cardioversion success

Table 2 shows the results of the multivariable logistic regression model for the association between final ventricular fibrillation amplitude, survival to hospital discharge, and initial cardioversion success. The risk-adjusted odds of survival to hospital discharge and initial

cardioversion success increased by 25.6% (aOR, 1.26; 95% CI, 1.14–1.39;  $P < 0.001$ ) and 18.6% (aOR, 1.19; 95% CI, 1.07–1.32;  $P = 0.001$ ) for every 0.1 mV increase in the final ventricular fibrillation amplitude. Results were similar for initial ventricular fibrillation amplitude (data not shown).

#### Association between arrest characteristics and ventricular fibrillation amplitude

The results of the multivariable logistic regression model for the association between arrest characteristics and a final ventricular fibrillation amplitude ≤ 0.2 mV are described in Table 2. After adjustment for arrest characteristics, only the time between call and initial defibrillation was independently associated with a final ventricular fibrillation amplitude ≤ 0.2 mV (aOR, 1.07; 95% CI, 1.02–1.13;  $P = 0.004$ ).

Figure 2. Unadjusted survival to hospital discharge in initial ventricular fibrillation (VF) out-of-hospital cardiac arrest cases across initial and final pre-shock amplitudes

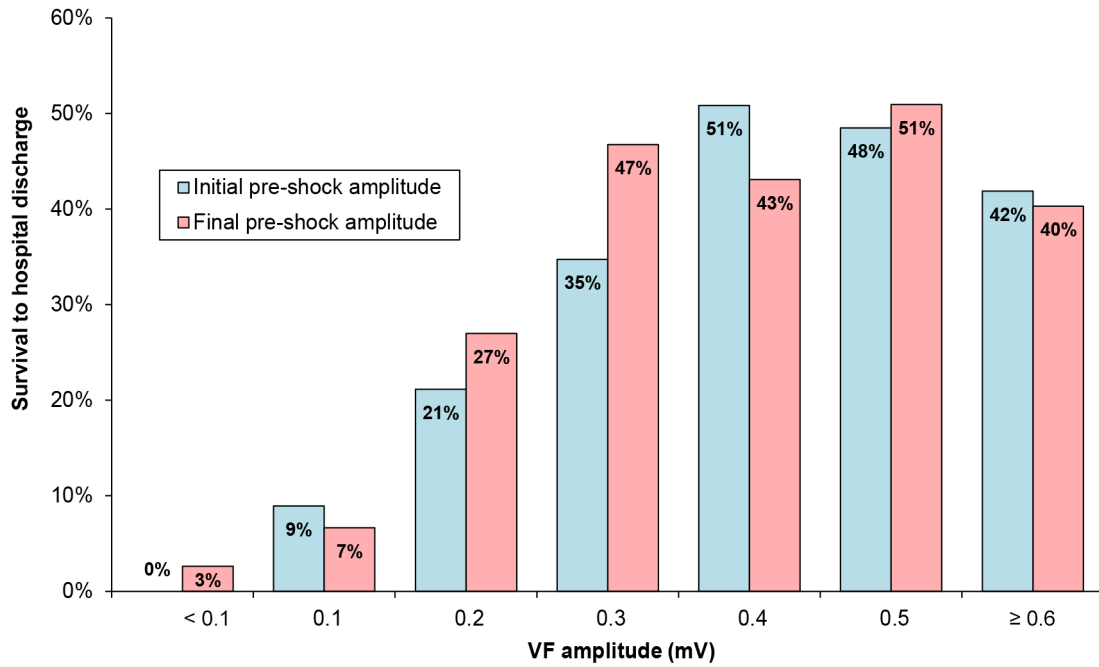
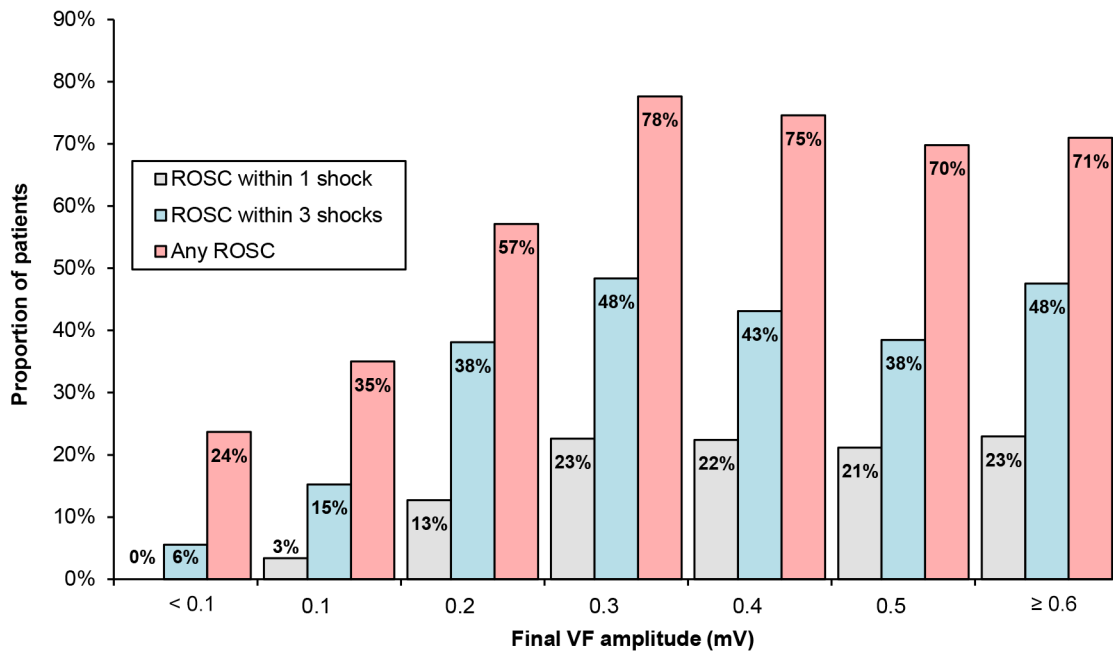


Figure 3. Unadjusted rates of return of spontaneous circulation (ROSC) within one shock, ROSC within three shocks, and any pre-hospital ROSC across final ventricular fibrillation (VF) amplitudes



**Table 2. Multivariable logistic regression of the association between final ventricular fibrillation amplitude, survival to hospital discharge and initial cardioversion success, and the association between arrest characteristics and a final ventricular fibrillation amplitude  $\leq 0.2$  mV**

	Survival to hospital discharge		Initial cardioversion success		Final ventricular fibrillation amplitude $\leq 0.2$ mV	
	aOR (95% CI)	P	aOR (95% CI)	P	aOR (95% CI)	P
Age, per year increase	0.97 (0.95–0.98)	< 0.001	1.00 (0.98–1.01)	0.72	1.00 (0.99–1.01)	0.76
Sex, male	0.76 (0.42–1.38)	0.36	0.62 (0.31–1.22)	0.16	1.66 (0.94–2.94)	0.08
Public location	1.76 (1.05–2.92)	0.03	2.43 (1.35–4.36)	0.003	1.06 (0.65–1.72)	0.81
Presumed cardiac aetiology	2.61 (0.74–9.15)	0.14	0.68 (0.17–2.69)	0.58	0.55 (0.19–1.59)	0.27
Urban region	0.71 (0.43–1.17)	0.18	0.72 (0.40–1.29)	0.27	0.87 (0.56–1.34)	0.52
Bystander-witnessed	1.35 (0.77–2.37)	0.29	1.93 (0.90–4.16)	0.09	0.81 (0.50–1.30)	0.38
Bystander CPR	1.67 (0.86–3.23)	0.13	1.21 (0.55–2.69)	0.63	0.72 (0.43–1.21)	0.21
Call to defibrillation time, per min increase	0.86 (0.79–0.92)	< 0.001	0.95 (0.88–1.02)	0.18	1.07 (1.02–1.13)	0.004
Final pre-shock amplitude, per 0.1 mV increase	1.26 (1.14–1.39)	< 0.001	1.19 (1.07–1.32)	0.001	na	na

aOR = adjusted odds ratio; CPR = cardiopulmonary resuscitation; na = not applicable; ROSC = return of spontaneous circulation.

Figure 4 shows the predicted probability of a final pre-shock amplitude  $\leq 0.2$  mV stratified across the time between call and initial defibrillation, after holding other covariates at their mean.

### Association between ventricular fibrillation amplitude and duration of resuscitation

The results of the multivariable linear regression model for the association between final ventricular fibrillation amplitude and the duration of resuscitation are presented in Table 3. After adjustment for arrest characteristics, every 0.1 mV increase in the final ventricular fibrillation amplitude reduced the duration of resuscitation by 1.7 minutes (95% CI, 1.03–2.36;  $P < 0.001$ ). Results were similar for initial ventricular fibrillation amplitude (data not shown).

### Discussion

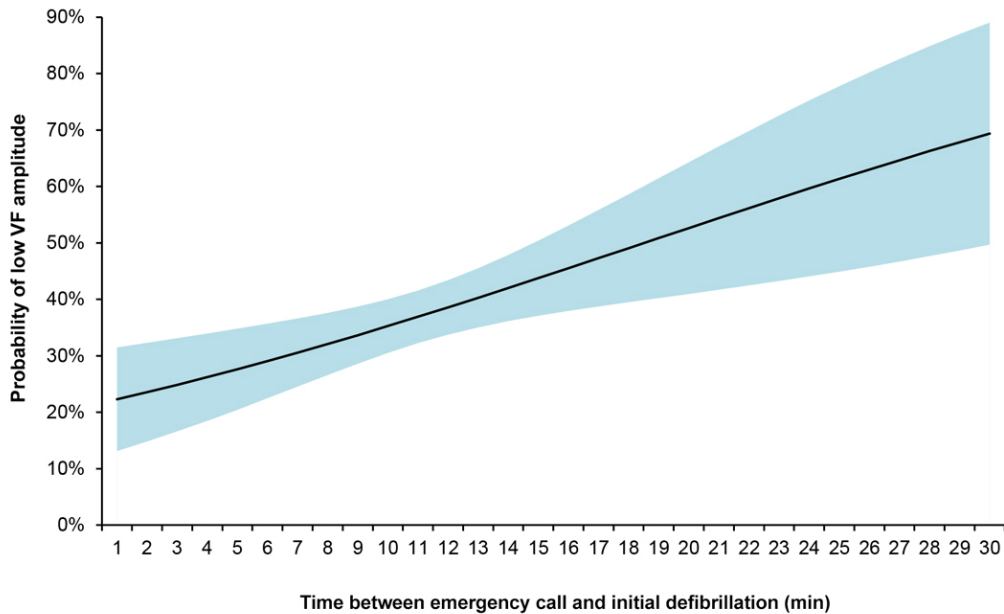
In this study of initial ventricular fibrillation cases undergoing manual defibrillation, the incidence of fine and very fine ventricular fibrillation was high, affecting more than one-third of cases. Ventricular fibrillation amplitude correlated closely with unadjusted rates of survival and cardioversion success, and our multivariable analysis indicates that only the time to initial defibrillation was associated with pre-shock ventricular fibrillation amplitude. After adjustment for arrest characteristics including the time to defibrillation, ventricular fibrillation amplitude was significantly associated with cardioversion success, the duration of resuscitation,

and survival to hospital discharge, with the effect size being larger than most other arrest characteristics.

There are relatively little international data on the incidence of low amplitude ventricular fibrillation rhythms in patients with OHCA. This is in part due to the variety of approaches used to assess ventricular fibrillation signal, many of which consider both amplitude and frequency.<sup>9</sup> While these approaches are certainly more useful for the validation of automated defibrillator technology,<sup>8</sup> they have limited clinical application in settings where manual defibrillation is used.

To date, only a small number of studies have examined the impact of initial ventricular fibrillation amplitude on clinical outcomes. Weaver and colleagues<sup>11</sup> examined the initial amplitude of 394 patients with ventricular fibrillation and reported a mean peak-to-peak amplitude of 0.55 mV, with only 17% of patients presenting with an amplitude of 0.2 mV or less. Although the authors showed that initial ventricular fibrillation amplitude was associated with survival to hospital discharge, the analysis did not completely account for differences in arrest characteristics. Balderston and colleagues<sup>10</sup> examined 80 patients with initial ventricular fibrillation arrest shocked by an AED, and compared the prognostic value of both ventricular fibrillation amplitude immediately before defibrillation and the maximal ventricular fibrillation amplitude in the 3 seconds before defibrillation. The authors showed that ventricular fibrillation amplitude immediately before defibrillation correlated strongly with unadjusted clinical outcomes such

**Figure 4. Predicted probability of a final pre-shock amplitude  $\leq 0.2\text{mV}$  stratified across the time between call and initial defibrillation, holding other covariates at their mean**



VF = ventricular fibrillation.

as survival, ROSC and successful defibrillation. However, the analysis did not report or account for differences in arrest characteristics, including delays to the initiation of resuscitation.

Although international variation in the initial amplitude of ventricular fibrillation is likely to be related to system effectiveness (eg, response and/or treatment delays), our analysis indicates that initial ventricular fibrillation amplitude may also be independent of arrest characteristics. Although our analysis did not account for comorbidity and medication use, a recent study evaluating the effect of comorbidity and medication use on ventricular fibrillation amplitude spectrum area did not find clinically meaningful associations between the two factors.<sup>14</sup> This could suggest that ventricular fibrillation amplitude is an important independent predictor of patient outcomes after OHCA, which could also confound the measurement of interventions<sup>15</sup> or regional benchmarking of OHCA outcomes.<sup>6</sup>

If the frequency of low amplitude ventricular fibrillation is increasing over time, this would also have a temporal impact on OHCA outcomes that is seldom considered in OHCA outcome reports.

Guidelines for specifying and reporting the performance of AEDs define low amplitude ventricular fibrillation

**Table 3. Multivariable linear regression of the association between final ventricular fibrillation amplitude and the duration of resuscitation efforts**

	Mean difference (95% CI)	P
Age, per year increase	-0.01 (-0.11 to 0.09)	0.90
Sex, male	2.35 (-1.96 to 6.67)	0.28
Public location	-4.32 (-8.15 to -0.50)	0.03
Presumed cardiac aetiology	0.64 (-8.13 to 9.41)	0.89
Urban region	1.06 (-2.42 to 4.54)	0.55
Bystander-witnessed	-1.70 (-5.51 to 2.10)	0.38
Bystander CPR	1.71 (-2.50 to 5.91)	0.43
Call to first defibrillation time, per min increase	0.84 (0.48-1.20)	< 0.001
Final pre-shock amplitude, per 0.1 mV increase	-1.70 (-2.36 to -1.03)	< 0.001

CPR = cardiopulmonary resuscitation.

( $\leq 0.2$  mV) as “intermediate rhythms”, where the benefits of defibrillation are limited.<sup>8</sup> Comparable criteria for cases undergoing manual defibrillation do not exist, and it is unclear how EMS systems differ with respect to their definitions of ventricular fibrillation in clinical practice. It is possible that EMS agencies that use AEDs would identify fewer cases of fine ventricular fibrillation in the field, and this may contribute to international variation in the incidence and outcomes of OHCA.<sup>16</sup> Importantly, our findings indicate that survival for low amplitude ventricular fibrillation rhythms are not as poor as previously reported,<sup>11</sup> and it is therefore possible that some populations of fine ventricular fibrillation patients have benefitted from temporal improvements to OHCA systems of care over time.<sup>2-5</sup>

### Limitations

Our study should be interpreted in the context of its limitations. Our sample size was modest, and some subgroups had a small number of patients. Our approach to measuring ventricular fibrillation amplitude was pragmatic and intended to categorise ventricular fibrillation amplitude without minimising the efficiency of the registry. More sophisticated approaches have been described elsewhere<sup>7,9</sup> but are also less practical. We were unable to examine the amplitude of cases shocked before EMS arrival, as the registry does not maintain complete ECG recordings from first responder AEDs. Finally, our analysis did not adjust for the effect of comorbidity and post-resuscitation interventions on survival outcome.

### Conclusion

More than one-third of initial ventricular fibrillation cases were considered fine in amplitude and were associated with significantly poorer risk-adjusted odds of survival and initial cardioversion success. A lack of existing data on the incidence of low amplitude ventricular fibrillation rhythms could contribute to both regional and international variation in the reported incidence and outcomes following OHCA.

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### Competing interests

No relevant disclosures.

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