

Effect of diabetes and pre-hospital blood glucose level on survival and recovery after out-of-hospital cardiac arrest

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Out-of-hospital cardiac arrest (OHCA) is a leading cause of death in countries with populations of high-to-middle income.¹ Over the past three decades, reductions in the incidence of OHCA have been partly attributed to improvements in the treatment and prevention of common risk factors, such as dyslipidaemia,² smoking³ and congestive heart failure,⁴ but not all risk factors for OHCA are declining. In particular, diabetes mellitus, associated with a twofold increase in the relative risk of sudden cardiac death,⁵ is increasing, with as many as 415 million people estimated to be affected worldwide.⁶

Preliminary reports of in-hospital cardiac arrest show that patients with diabetes experience poorer survival and neurological recovery at hospital discharge.⁷ In addition, patients with and without diabetes experience derangements in blood glucose level (BGL) after cardiac arrest, and this is also believed to influence survival rates and neurological sequelae after successful resuscitation.^{8,9} Although diabetes is common among patients who have an OHCA, little is known about its influence on survival or long-term functional recovery outcomes.¹⁰⁻¹² Pre-hospital BGL is also seldom reported in OHCA populations, and its utility for predicting outcomes in patients with and without diabetes is yet to be determined.^{13,14}

We evaluated the impact of diabetes status on survival to hospital discharge and 12-month functional recovery outcomes after OHCA. In a subgroup of patients, we also determined the effect of pre-hospital capillary BGL on survival and 12-month functional recovery outcomes.

Methods

Study design

We conducted a retrospective analysis of registry-based data from the Victorian Ambulance Cardiac Arrest Registry (VACAR). We included patients aged over 15 years who experienced an OHCA of presumed cardiac aetiology and received an attempted resuscitation by emergency medical services (EMS) between 1 January 2007 and 30 June 2015. Patients who were witnessed to arrest by EMS personnel were excluded. The VACAR is classified as a quality assurance project by the Victorian Department of Health Human Research Ethics Committee, and our study had ethics approval from the Monash University Human Research Ethics Committee.

ABSTRACT

Objective: Diabetes mellitus and blood glucose level (BGL) are emerging as important prognosticators of outcome in critically ill patients. We evaluated the effect of diabetes and pre-hospital BGL on survival to hospital discharge and on 12-month functional recovery after out-of-hospital cardiac arrest (OHCA).

Design, setting and participants: We performed a retrospective analysis of data from a statewide cardiac arrest registry in Victoria, Australia. We included 11 873 adult patients who had had an OHCA of presumed cardiac aetiology between 1 January 2007 and 30 June 2015. Of these, 2438 (20.5%) had documented diabetes.

Main outcome measures: Survival to hospital discharge and 12-month functional recovery, measured using the Extended Glasgow Outcome Scale.

Results: Crude survival to hospital discharge differed among patients with and without diabetes (6.8% v 13.4%; $P < 0.001$). Diabetes significantly reduced the odds of survival to hospital discharge for patients presenting with a shockable rhythm (adjusted odds ratio [OR], 0.57; 95% CI, 0.38–0.86; $P = 0.007$) and reduced the odds of good 12-month functional recovery for patients discharged alive (OR, 0.57; 95% CI, 0.35–0.95; $P = 0.03$). In contrast, a mild-to-moderate elevation of pre-hospital BGL (8.0–15.9 mmol/L) was present in 695 of 1319 patients with available data (52.7%) and was associated with improved survival and functional recovery outcomes, which were independent of diabetes status.

Conclusions: Diabetes affects at least one in five patients who have had an OHCA and is associated with poorer survival and 12-month functional recovery after OHCA. In comparison, an elevated pre-hospital BGL is common in the peri-arrest period and may be associated with improved outcomes.

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Setting

Victoria, Australia, has a population of almost 5.8 million people, of whom 75% are concentrated in Melbourne. The state has a single EMS system which operates in a two-tiered fashion, sending advanced life support and intensive care paramedics to suspected cardiac arrest events. Basic life

support-trained firefighters and community volunteers are also dispatched to suspected cardiac arrest events in most parts of central and peripheral Melbourne.¹⁵ Local cardiac arrest treatment protocols follow the recommendations of the Australian Resuscitation Council (www.resus.org.au).

Data sources

Cases were identified from the VACAR, which has been described in detail.¹⁶ The VACAR is a population-based register of almost 80 000 OHCA events attended by EMS personnel in Victoria. The registry captures patient, operational and treatment data from eligible OHCA cases by conducting a highly sensitive search of electronic patient care records completed by paramedics in the field. The search strategy shortlists potential cardiac arrest cases, which are then checked and validated manually by registry personnel. The registry records more than 150 data elements, including but not limited to the Utstein-style descriptors.¹⁷ Hospital medical records are manually screened for transported cases to identify hospital discharge status and discharge direction. Hospital discharge status is also cross-referenced against official state death records from the Registry of Births, Deaths and Marriages, Victoria. For our study, we supplemented the core VACAR dataset with additional data elements sourced from pre-hospital patient care records, including a list of key pre-existing conditions and BGL measurements. All documented pre-existing conditions, including diabetes mellitus, were reported at the scene by a relative or friend of the patient. In 1477 included cases (12.4%), pre-existing conditions were either unknown or not documented. As the use of electronic patient care records was not universal at the beginning of the study period, a small number of eligible OHCA cases were excluded because of missing patient care records ($n = 981$ [7.6%]).

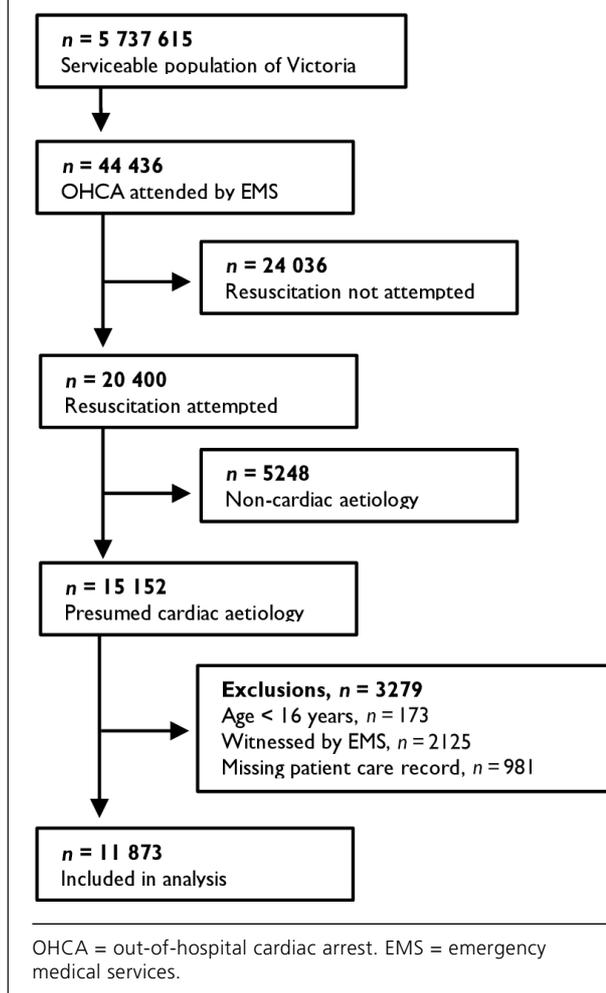
Blood glucose monitoring

BGL monitoring is performed in the field using point-of-care glucometers (Accu-Chek Performa, Roche Diagnostics), which provide a numeric display range of 0.6–33.3 mmol/L (10–600 mg/dL). Readings outside the measuring limits are indicated by either a low or high result. The recording of BGL during cardiac arrest is not routine practice in Victoria and, as a result, the assessment is performed relatively infrequently by paramedics. In our study, BGL data were available in a subgroup of cases included in the analysis ($n = 1319$ [11.1%]). BGL results outside the glucometer's measuring range were recoded as the highest or lowest limit, as appropriate (0.6 mmol/L or 33.3 mmol/L). For patients with two or more pre-hospital BGL readings ($n = 79$), we used only the first reading in our analysis.

Twelve-month follow-up

Since 1 January 2010, the VACAR has undertaken health-

Figure 1. Patient selection between 1 January 2007 and 30 June 2015 in Victoria, Australia



related quality-of-life telephone interviews with survivors to hospital discharge at 12 months after cardiac arrest. The methodology has been described in detail.¹⁸ Patients who undergo telephone follow-up complete responses to a number of health-related quality-of-life assessment tools, including the Extended Glasgow Outcome Scale (GOSE), which measures functional outcomes on an eight-point scale ranging from 1 (death at follow-up) through to 8 (upper good recovery).¹⁹ In our study, 12-month GOSE outcomes are reported for the period 1 January 2010 to 30 June 2014.

Statistical analysis

We performed analyses using IBM SPSS Statistics, version 22 (SPSS Inc). A two-sided significance level of 0.05 was considered statistically significant for all hypothesis tests. The main outcome measures were survival to hospital discharge and 12-month survival with good functional recovery (GOSE ≥ 7). For analysis, BGLs were grouped

Table 1. Baseline characteristics of patients with and without diabetes

Characteristic	All (N = 11 873)	Diabetes (n = 2438)	No diabetes (n = 9435)	P
Median age, years (IQR)	70 (57–80)	72 (62–80)	69 (56–80)	< 0.001
Male, n (%)	8236 (69.4)	1639 (67.2)	6597 (70.0)	0.009
Pre-existing conditions, n (%)				
Hypertension	4570 (38.5)	1381 (56.6)	3189 (33.8)	< 0.001
Dyslipidaemia	2515 (21.2)	934 (38.3)	1581 (16.8)	< 0.001
Ischaemic heart disease	3353 (28.2)	1051 (43.1)	2302 (24.4)	< 0.001
Heart failure	1589 (13.4)	566 (23.2)	1023 (10.8)	< 0.001
Arrhythmia	1312 (11.1)	357 (14.6)	955 (10.1)	< 0.001
Stroke or transient ischaemic attack	804 (6.8)	251 (10.3)	553 (5.9)	< 0.001
Vascular disease	643 (5.4)	169 (6.9)	474 (5.0)	< 0.001
Renal insufficiency	575 (4.8)	259 (10.6)	316 (3.3)	< 0.001
Chronic obstructive pulmonary disease	1006 (8.5)	232 (9.5)	774 (8.2)	0.04
Neurodegenerative disorder	770 (6.5)	175 (7.2)	595 (6.3)	0.12
Cancer	871 (7.3)	174 (7.1)	697 (7.4)	0.67
Nil known	503 (4.2)	–	–	–
Unknown/not documented	1477 (12.4)	–	–	–
Median emergency medical services response time, minutes (IQR)	8.1 (6.4–11.0)	8.0 (6.4–10.8)	8.2 (6.4–11.1)	0.11
Emergency medical services response time unknown, n (%)	5 (< 0.1)	0	5 (0.1)	–
Public location, n (%)	2420 (20.4)	299 (12.3)	2121 (22.5)	< 0.001
Bystander witnessed, n (%)	6900 (58.4)	1386 (57.0)	5514 (58.8)	0.13
Unknown if bystander witnessed, n (%)	59 (0.5)	8 (0.3)	51 (0.5)	–
Bystander cardiopulmonary resuscitation, n (%)	7505 (63.2)	1451 (59.5)	6054 (64.2)	< 0.001
Initial arrest rhythm, n (%)				
Shockable	4428 (37.5)	745 (30.7)	3683 (39.3)	< 0.001
Pulseless electrical activity	2208 (18.7)	511 (21.1)	1697 (18.1)	0.001
Asystole	5072 (42.9)	1153 (47.5)	3919 (41.8)	< 0.001
Other	102 (0.9)	84 (0.9)	18 (0.7)	0.47
Unknown	63 (0.5)	11 (0.5)	52 (0.6)	–
Metropolitan region, n (%)	7130 (75.6)	1953 (80.1)	7130 (75.6)	< 0.001

IQR = interquartile range.

into five equally spaced categories: ≤ 3.9 mmol/L, 4.0–7.9 mmol/L, 8.0–11.9 mmol/L, 12.0–15.9 mmol/L and ≥ 16.0 mmol/L. We described cardiac arrest characteristics, crude survival outcomes and BGLs using descriptive statistics, and compared them by diabetes status using the χ^2 or Mann–Whitney *U* test, as appropriate. Crude survival rates to hospital discharge were also compared across BGL categories for patients with and without diabetes, using the χ^2 test.

To assess the impact of diabetes on survival to hospital discharge and 12-month survival with good functional recovery, we performed multivariable logistic regression with the following covariates: age, male sex, EMS response time, shockable arrest rhythm, public location, bystander

witnessed, bystander cardiopulmonary resuscitation and metropolitan region. We also included factors that were identified from univariate analyses as having differed between patients with and without diabetes, including a documented history of hypertension, dyslipidaemia, ischaemic heart disease, heart failure, arrhythmia, stroke or transient ischaemic attack, vascular disease, renal insufficiency and chronic obstructive pulmonary disease. To optimise the model, we backward-eliminated the covariates with the largest significance values until a parsimonious model was achieved, retaining all variables with $P \leq 0.1$. Models were tested for interactions between diabetes and other relevant covariates, but only one (an interaction term between diabetes and shockable arrest rhythm) was

found to be significant in the model predicting survival to hospital discharge. In patients with available data, we also tested the contribution of pre-hospital BGL in each of the optimised models. We provide two additional models evaluating the impact of pre-hospital BGL on survival to hospital discharge in patients with and without diabetes in the Appendix (online at cicm.org.au/Resources/Publications/Journal). In these analyses, we chose the BGL range between 4.0 mmol/L and 7.9 mmol/L as the reference category. Results from the regression analyses are shown as odds ratios (ORs) with 95% confidence intervals.

Results

Sample population

Between January 2007 and June 2015, 44 436 cases of OHCA attended by EMS in Victoria were identified. We

included 11 873 of these cases in our analysis (Figure 1). Diabetes was documented as a pre-existing condition in 2438 cases (20.5%). The baseline characteristics of OHCA patients with and without diabetes are shown in Table 1.

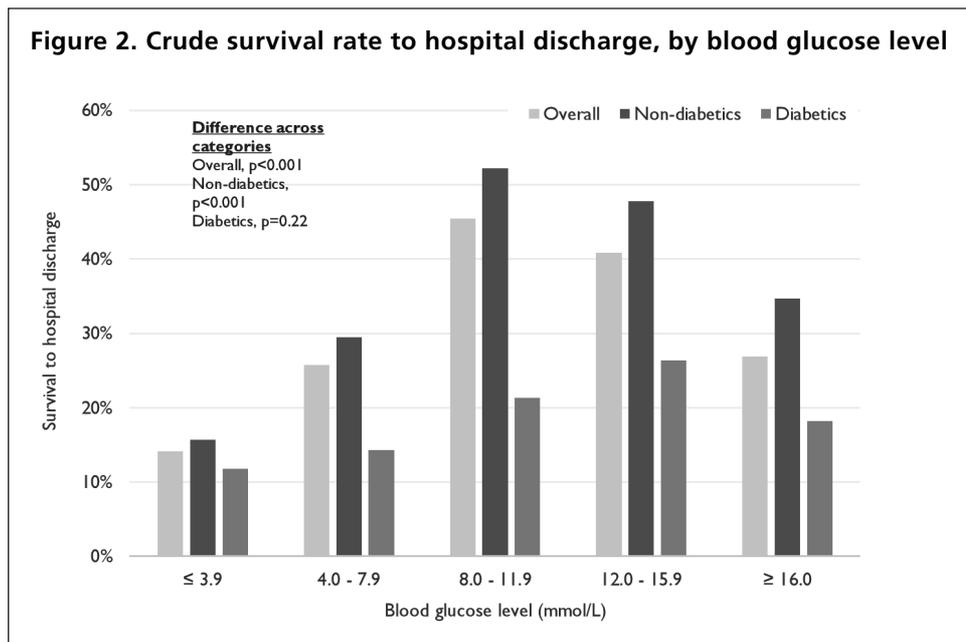
Crude survival and 12-month functional recovery

Crude survival outcomes for OHCA patients with and without diabetes are shown in Table 2. The crude survival rate to hospital discharge of patients with diabetes was about half that of patients without diabetes (6.8% v 13.4%; $P < 0.001$). In survivors to hospital discharge who were eligible for 12-month follow-up, the rate of good functional recovery (GOSE ≥ 7) was lower in patients with diabetes compared with those without diabetes (41.6% v 60.4%; $P = 0.002$). In contrast, the rate of death, vegetative state or severe disability at 12 months was higher in people with diabetes compared with people without diabetes (37.7% v 15.9%; $P < 0.001$).

Table 2. Pre-hospital blood glucose level, survival to hospital discharge and 12-month GOSE outcomes in patients with and without diabetes

Characteristic	All (N = 11 873)	Diabetes (n = 2438)	No diabetes (n = 9435)	P
Median pre-hospital blood glucose level (IQR)*	9.9 (6.8–13.4)	11.2 (7.0–15.3)	9.6 (6.8–12.8)	< 0.001
Pre-hospital blood glucose level, mmol/L, n (%)*				
≤ 3.9	85 (6.4)	34 (8.8)	51 (5.5)	0.02
4.0–7.9	350 (26.5)	85 (22.0)	265 (28.4)	0.02
8.0–11.9	419 (31.8)	90 (23.3)	329 (35.3)	< 0.001
12.0–15.9	276 (20.9)	87 (22.5)	189 (20.3)	0.35
≥ 16.0	189 (14.3)	90 (23.3)	99 (10.6)	< 0.001
Return of spontaneous circulation at any time, n (%)	4638 (39.1)	888 (36.4)	3750 (39.7)	0.003
Scene outcome, n (%)				
Efforts ceased on scene	7502 (63.2)	1648 (67.6)	5854 (62.1)	< 0.001
Transport with return of spontaneous circulation	3837 (32.3)	706 (29.0)	3131 (33.2)	< 0.001
Transport with CPR ongoing	532 (4.5)	84 (3.4)	448 (4.7)	0.006
Survived to hospital, n (%)	3881 (32.8)	707 (29.1)	3174 (33.8)	< 0.001
Unknown if survived to hospital, n (%)	43 (0.4)	8 (0.3)	35 (0.4)	–
Survival to hospital discharge, n (%)	1421 (12.1)	166 (6.8)	1255 (13.4)	< 0.001
Unknown if survived to hospital discharge, n (%)	102 (0.9)	13 (0.5)	89 (0.9)	–
12-month GOSE in survivors to hospital discharge, n (%) [†]				
1 (death)	47 (6.8)	12 (15.6)	35 (5.7)	0.001
2 (vegetative state)	3 (0.4)	1 (1.3)	2 (0.3)	0.22
3–4 (lower or upper severe disability)	76 (11.0)	16 (20.8)	60 (9.8)	0.004
5–6 (lower or upper moderate disability)	161 (23.4)	16 (20.8)	145 (23.7)	0.56
7–8 (lower or upper good recovery)	401 (58.3)	32 (41.6)	369 (60.4)	0.002
Lost to follow-up/unknown	143 (17.2)	22 (22.2)	121 (16.5)	–

GOSE = Extended Glasgow Outcome Scale. IQR = interquartile range. CPR = cardiopulmonary resuscitation. * Subgroup includes 1319 of 11 873 cases (11.1%). † Subgroup includes 831 of the total 1421 survivors to hospital discharge (subgroup with available data who had a cardiac arrest between 1 January 2010 and 30 June 2014).

Figure 2. Crude survival rate to hospital discharge, by blood glucose level

diabetes and an initial shockable arrest rhythm suggested that diabetes was associated with a significant reduction in the odds of survival to hospital discharge when the initial rhythm was shockable (OR, 0.57; 95% CI, 0.38–0.86; $P = 0.007$), but not when the rhythm was non-shockable (OR, 1.01; 95% CI, 0.72–1.43; $P = 0.95$). Diabetes also reduced the odds of survival with good functional recovery at 12 months among patients who underwent an attempted resuscitation (OR, 0.45; 95% CI, 0.30–0.67; $P < 0.001$) and among patients who survived to hospital discharge (OR, 0.57; 95% CI, 0.35–0.95; $P = 0.03$).

Pre-hospital blood glucose levels

Pre-hospital BGL results are shown in Table 2 for 1319 cases (11.1%) which had available data. When compared with patients without a pre-hospital BGL recorded, patients with a pre-hospital BGL were younger, more often male and more often had diabetes, arrests in public locations and shockable arrest rhythms (data not shown). The median pre-hospital BGL was 9.9 mmol/L (interquartile range, 6.8–13.4 mmol/L), but was significantly higher in patients with diabetes compared with those without diabetes ($P < 0.001$). The proportion of patients with a BGL ≤ 3.9 mmol/L or ≥ 16.0 mmol/L was also higher in patients with diabetes compared with those without diabetes.

The vast majority of patients with a recorded pre-hospital BGL had achieved return of spontaneous circulation (ROSC) (81.2%) and survived to hospital (75.4%), and about one-third survived to hospital discharge (34.6%). When compared with patients who did not achieve ROSC, patients who did achieve ROSC had a higher median pre-hospital BGL (7.2 mmol/L v 10.4 mmol/L; $P < 0.001$). In addition, patients who did not achieve ROSC more often experienced a BGL ≤ 3.9 mmol/L (16.5% v 4.1%; $P < 0.001$), and this was a consistent finding in patients with diabetes (15.2% v 6.2%; $P = 0.005$) and patients without diabetes (17.6% v 3.4%; $P < 0.001$). The highest crude survival rates to hospital discharge were seen in patients with a pre-hospital BGL between 8.0 mmol/L and 15.9 mmol/L (Figure 2).

Multivariable analysis

Factors associated with survival to hospital discharge and 12-month survival with good functional recovery are shown in Table 3. A significant interaction between

The impact of pre-hospital BGL on survival and 12-month functional recovery after adjustment for diabetes and other arrest confounders is shown in Figure 3. The impact of pre-hospital BGL on survival to hospital discharge for patients with and without diabetes is also shown in the Appendix.

Discussion

In our large retrospective analysis, the prevalence of known diabetes among resuscitated patients who had had an OHCA of presumed cardiac aetiology was 20.5%. Patients with diabetes experienced poorer ROSC and survival-to-hospital outcomes, with the crude survival-to-hospital discharge rate being about half that of patients without diabetes. Specifically, patients with diabetes presenting with an initial shockable rhythm experienced a reduction in the odds of survival to hospital discharge of 43%, compared with patients without diabetes. Similarly, the odds of survival to 12 months with good functional recovery were also reduced by 55% in patients with diabetes compared with those without diabetes, regardless of the initial arrest rhythm.

The deleterious effect of diabetes on outcomes of OHCA appears to be larger in our study when compared with earlier reports. Existing evidence suggests that patients with diabetes who survive to hospital admission after an OHCA experience reductions in the odds of survival to hospital discharge of between 14% and 44%.^{10,12,20} A study from Korea reported that patients with diabetes who were admitted to hospital after an OHCA experienced a 20% reduction in the odds of good neurological recovery at hospital discharge when compared with patients without diabetes.¹² In contrast, two other reports from Sweden,

Table 3. Factors associated with survival and with 12-month survival with good functional recovery (GOSE \geq 7)

Characteristic	Survival to hospital discharge (<i>n</i> = 11 643)		Good functional recovery at 12 months in all attempted resuscitations (<i>n</i> = 6442)*		Good functional recovery at 12 months in patients discharged alive (<i>n</i> = 688)*	
	Adjusted OR (95% CI)	<i>P</i>	Adjusted OR (95% CI)	<i>P</i>	Adjusted OR (95% CI)	<i>P</i>
Age increase per year	0.97 (0.97–0.97)	< 0.001	0.98 (0.97–0.98)	< 0.001	Omitted	
Male	Omitted		1.36 (1.01–1.85)	0.05	1.53 (1.03–2.28)	0.04
Pre-existing conditions						
Hypertension	Omitted		0.78 (0.58–1.05)	0.10	Omitted	
Dyslipidaemia	Omitted		1.33 (0.95–1.87)	0.10	Omitted	
Heart failure	0.63 (0.48–0.83)	0.001	0.52 (0.29–0.93)	0.03	0.47 (0.23–0.97)	0.04
Arrhythmia	1.28 (1.03–1.60)	0.03	Omitted		Omitted	
Chronic obstructive pulmonary disease	0.71 (0.50–1.01)	0.06	0.38 (0.15–0.94)	0.04	0.30 (0.10–0.86)	0.02
Stroke or transient ischaemic attack	0.68 (0.49–0.96)	0.03	0.36 (0.15–0.84)	0.02	Omitted	
Diabetes	1.01 (0.72–1.44)	0.94	0.45 (0.30–0.67)	< 0.001	0.57 (0.35–0.95)	0.03
Initial shockable rhythm	7.94 (6.64–9.49)	< 0.001	7.42 (5.32–10.36)	< 0.001	Omitted	
Diabetes x initial shockable rhythm [†]	0.57 (0.38–0.86)	0.007	Omitted		Omitted	
Response time increase of emergency medical services (per minute)	0.92 (0.91–0.94)	< 0.001	0.91 (0.88–0.94)	< 0.001	Omitted	
Public location	1.81 (1.58–2.07)	< 0.001	1.90 (1.50–2.42)	< 0.001	Omitted	
Bystander witnessed	2.59 (2.19–3.07)	< 0.001	2.44 (1.76–3.37)	< 0.001	Omitted	
Bystander cardiopulmonary resuscitation	1.45 (1.24–1.69)	< 0.001	2.41 (1.73–3.37)	< 0.001	2.20 (1.46–3.33)	< 0.001
Metropolitan region	1.56 (1.32–1.85)	< 0.001	1.37 (1.03–1.83)	0.03	Omitted	

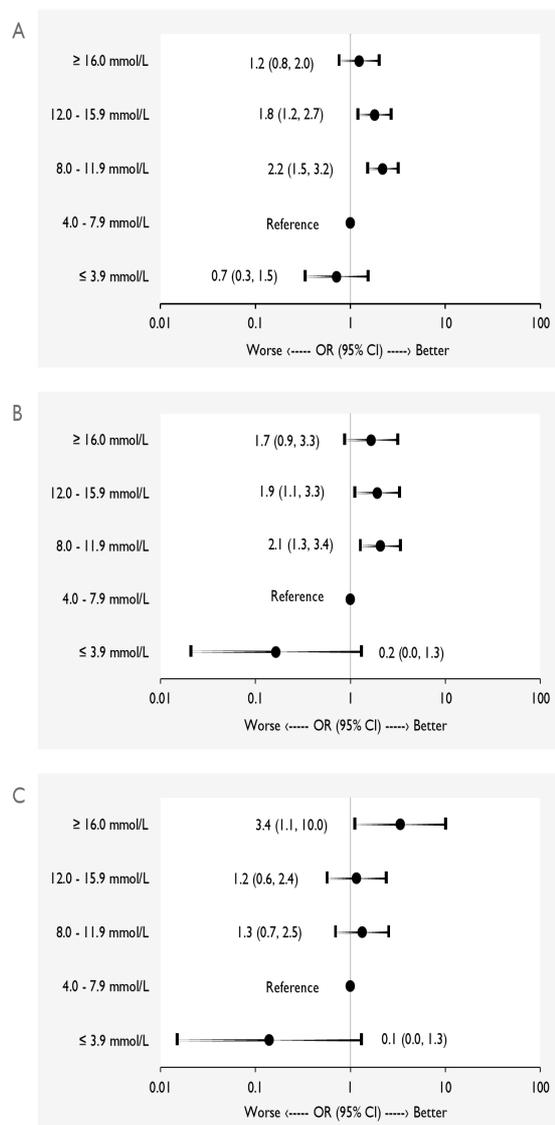
GOSE = Extended Glasgow Outcome Scale. OR = odds ratio. * Subgroup of patients who had a cardiac arrest between 1 January 2010 and 30 June 2014. † Interaction term between diabetes status and initial shockable rhythm.

conducted in both out-of-hospital and in-hospital cardiac arrest populations, suggested that the rate of good neurological recovery at hospital discharge did not differ between patients with and without diabetes.^{7,20}

Variation in these reported outcomes may be partly explained by differences in study designs and the included populations. For example, our data suggest that fewer people with diabetes achieve ROSC or survive to hospital, but this has not been examined in previous studies.^{10,12,20} Also, when compared with the Korean study,¹² our study included a much larger proportion of patients who had had an OHCA with an initial shockable rhythm (37.5% v 9.4%), and our findings show that this would be a key determinant of outcomes in patients with diabetes. In addition, functional outcomes at hospital discharge may not reflect those measured at 12-month follow-up, particularly as the recovery of patients with diabetes is typically complicated by a higher number of health complications, including recurrent cardiovascular events.²¹

In our study, patients with an elevated pre-hospital BGL of between 8.0 mmol/L and 15.9 mmol/L experienced better survival and 12-month functional recovery outcomes when compared with patients with a typical normal BGL range of 4.0–7.9 mmol/L. A mildly elevated BGL in patients who have had an OHCA is common on hospital arrival, and the BGL typically normalises in the hours after hospital admission.²² The severity of hyperglycaemia in populations who have had a cardiac arrest is believed to be affected by the duration of ischaemic insult, with longer resuscitation times leading to a pattern of increasing hyperglycaemia after ROSC.^{8,9} The release of counter-regulatory hormones such as catecholamines, cortisol and glucagon is proportional to the magnitude of ischaemia and reperfusion injury, and these hormones rapidly promote gluconeogenesis.²³ Thus, the lack of hyperglycaemia in critically ill patients could infer homeostatic dysfunction or an impaired counter-regulatory response.²³ This may explain why patients who had had an OHCA and had low or normal BGLs in our

Figure 3. Adjusted logistic regression analyses of the association between pre-hospital blood glucose level and survival to hospital discharge and good functional recovery at 12 months



(A) Survival to hospital discharge ($n = 1269$). (B) Good functional recovery at 12 months in all attempted resuscitations ($n = 998$). (C) Good functional recovery at 12 months in survivors to hospital discharge ($n = 315$). Model adjusted for covariates specified in Table 3.

study experienced worse survival and functional outcomes at 12 months when compared with those with a mild-to-moderate elevation of BGL.⁸

Although the frequency of BGLs ≤ 3.9 mmol/L in our overall population was low (6.4%), our data suggest that hypoglycaemia may occur more frequently among patients with diabetes and patients who do not achieve ROSC in

the field. It is notable that relatively low numbers of OHCA patients receive a BGL assessment in the pre-hospital setting. It is therefore possible that the frequency of glycaemic abnormalities is higher than that reported in our study, particularly as non-survivors were less likely to receive a pre-hospital BGL assessment. In our EMS system, routine screening of BGL is not currently recommended in cardiac arrest treatment guidelines, and the treatment of glycaemic abnormalities during and after arrest has not received significant attention. Similarly, international resuscitation guidelines do not specify glycaemic derangements as a potential cause or complication of OHCA and do not recommend routine assessment of BGL in the pre-hospital setting.^{24,25} Patients with hypoglycaemia may be at increased risk of autonomic dysfunction and arrhythmia,²³ and identification and treatment of hypoglycaemia may help improve outcomes after OHCA. Therefore, on the basis of these data, we recommend that all patients who have had an OHCA receive a pre-hospital BGL assessment to reduce the risk of unrecognised hypoglycaemia.

Study limitations

Our study has several limitations. It is a retrospective study and we are unable to show a causal relationship between diabetes or BGL and OHCA outcome. Our study is limited by the small number of patients with pre-hospital BGL data and, to a lesser extent, the incomplete capture of 12-month health-related quality-of-life outcomes across the study period. In addition, our 12-month GOSE outcomes were missing in 17.2% of patients (those lost to follow-up), and these patients may show poorer survival and functional outcomes at follow-up.¹⁸

Our analyses are also limited by the inclusion of pre-hospital-related variables collected by the VACAR. Other treatment factors present during in-hospital care were not collected, and these could also influence our findings. Our data could underestimate the true prevalence of diabetes, particularly as many patients and relatives are unaware of the diagnosis or are not present on scene to provide the information to paramedics. Although paramedics typically cross-check pre-existing conditions with patient medications and hospital medical records, this practice was not standardised in our study and it is possible that some patients may have been misclassified. In our study, 1477 patients (12.4%) had unknown or no pre-existing conditions documented on the pre-hospital patient care record. In addition, it is known that a significant proportion of the population have undiagnosed diabetes, and this may also confound our results. Despite this, the prevalence of diabetes we report in our study is higher than that observed in other populations of patients who have had an OHCA.^{10,11,20} Finally, our BGL measurements are taken from capillary samples, and the results may be less accurate

than, and may differ from, in-hospital studies reporting venous sampling.

In our study, at least one in five OHCA patients receiving attempted resuscitation had a documented history of diabetes. When compared with patients without diabetes, patients with diabetes had lower rates of survival and good long-term functional recovery outcomes, which persisted after adjustment for other potential confounders. The reasons for the differences in survival and functional recovery between patients with and without diabetes are unclear and are worthy of further research. Finally, a mild-to-moderate elevation of pre-hospital BGL was relatively common among patients who had had an OHCA, but the infrequent assessment of BGL in the pre-hospital setting could undermine their survival outcomes. Peri-arrest hypoglycaemia was associated with a lower likelihood of ROSC, and we therefore recommend its routine assessment during resuscitation.

Competing interests

None declared.

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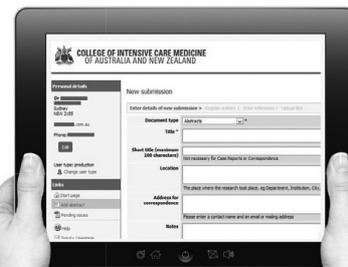
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Appendix

This appendix was part of the submitted manuscript and has been peer reviewed. It is posted as supplied by the authors.

The impact of diabetes and prehospital blood glucose on survival and 12-month functional recovery following out-of-hospital cardiac arrest

Supplementary appendix

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Supplementary Figure 1: Adjusted logistic regression analyses of the association between prehospital BGL and survival to hospital discharge in: [A] patients with diabetes (n=380), and; [B] patients without diabetes (n= 889). Model adjusted for the following covariates: age, heart failure, arrhythmia, COPD, stroke or TIA, initial shockable rhythm, EMS response time, public location, bystander witnessed, bystander CPR, and metropolitan region.

