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Haifa M. Algethamy
Assistant Professor
Faculty of Medicine
King Abdulaziz University

Anesthesia, Critical Care and Neurocritical Care Consultant
Department of Anesthesia and Critical Care
King Abdulaziz University Hospital
Jeddah, Saudi Arabia

halgethami@kau.edu.sa

Out-of-Hospital Cardiac Arrest

Long-term outcomes and their predictors

Out-of-hospital cardiac arrests (OHCA) are associated with very high rates of mortality and poor cognitive outcome. This paper reviews long-term outcomes post OHCA and the pre-hospitalisation factors that predict them.

Introduction

Cardiac arrest is among the most common health emergencies worldwide, suffered by over a half million patients annually in the United States alone. Among these, roughly six in ten (61%) occur outside a hospital (Kronick et al. 2015). Estimates of mortality from out-of-hospital cardiac arrest (OHCA) vary widely, largely depending on the time point from which mortality is measured e.g., among all patients who suffer an OHCA or only among those who have already survived to hospital discharge. Considering all OHCA patients, the survival rate is low, generally ranging from 2-12% (Brison et al. 1992; Debaty et al. 2017; Hamilton et al. 2016; Hollenberg et al. 2005; Holler et al. 2007; Horsted et al. 2007; Geri et al. 2017; Sasson et al. 2010; Shuvy et al. 2017; Andrew et al. 2017a; Bunch et al. 2004a; Hawkes et al. 2017; Kempton et al. 2019). Alternatively, among patients who already have survived to hospital admission or discharge, long-term survival rates are much higher, with one-year survival of almost 50% reported amongst patients who survive long enough to receive treatment in an intensive care unit (Abazi et al. 2019), up to 90% or better among those surviving to hospital discharge (Andrew et al. 2017b; Shuvy et al. 2017).

Survival is not the only outcome of importance however, as some OHCA patients suffer potentially catastrophic, long-term cognitive and other neurological deficits that markedly impair their quality of life and level of independence, as well as activity-limiting fatigue in roughly half, and psychological symptoms like depression, anxiety and post-traumatic stress in roughly one third of patients (Moulaert et al. 2017). Of these, by far the most studied has been cognitive status which, in itself, is a predictor of long-term survival (Martinell et al. 2017). The purpose of the current paper is to review current knowledge on pre-hospitalisation predictors of long-term survival and long-term cognitive outcomes among adults who have experienced a non-traumatic OHCA.

Predictors of Long-Term Survival and Function

Compiling data from three large patient registries in which all non-traumatic cases of OHCA were counted, and for which data are published on survival both at hospital discharge and one-year post OHCA — from Australia (Andrew et al. 2017b) (n=33,212), Canada (Shuvy et al. 2017) (n=28,611), and the USA (Chan et al. 2016) (n=16,208) - totalling 78,021 patients, mortality rates at hospital discharge and one-year follow-up compute to 91.9% and 92.9%, respectively. This means that, of all the OHCA patients in these three databases who were deceased by one-year post OHCA, 98.9% of the deaths occurred prior to hospital discharge. For this reason alone, it is impossible to consider predictors of long-term survival from OHCA without also considering predictors of survival to hospital discharge. Consistent with this, discharge from hospital has also been identified statistically as an independent predictor of longevity post OHCA (Andrew et al. 2017b).

For both survival to hospital discharge and long-term survival, several potential predictors that precede a patient's hospital admission have been studied, including baseline patient characteristics, factors pertaining to assessment and treatment administered prior to hospitalisation, and the patient's health status at the time of hospital admission.

Baseline Patient Characteristics

The baseline patient characteristic that has most consistently been found to predict both short- and long-term outcomes is patient age, with both in-hospital and long-term survival consistently reduced among those who are older (Andrew et al. 2017b; Brison et al. 1992; Bunch et al. 2004b; Chan et al. 2016; Herlitz et al. 2005; Hiemstra et al. 2018; Martinell et al. 2017; Rey et al. 2020; Wang et al. 2005). In one study, among 131 patients discharged from the hospital, five-year mortality rates were more than five times higher (6 versus 34%) among patients under versus ≥65 years old ($p<0.001$) (Bunch et al. 2004b). All three published combined-factor models predicting long-term survival from OHCA include age as a factor (Herlitz et al. 2005; Martinell et al. 2017; Rey et al. 2020). Older age also appears to predict long-term functional outcomes post OHCA (Andrew et al. 2018; Bunch et al. 2004b; Martinell et al. 2017). In one retrospective registry analysis of 20,103 patients ≥65 years old, each 10-year increase in age was associated with 41% and 66% reductions in the odds of good functional recovery and independent living, respectively (Andrew et al. 2018).

Comorbid illness is another baseline patient characteristic that has been consistently identified as a predictor of OHCA outcomes (Andrew et al. 2017a; Antonelli et al. 2017; Jang et al. 2016; Kang et al. 2017; Nehme et al. 2016;

Voruganti et al. 2018; Shuvy et al. 2017). Data show that comorbid illness in general (Andrew et al. 2017a), and specific comorbid illnesses like diabetes (Antonelli et al. 2017; Jang et al. 2016; Nehme et al. 2016; Voruganti et al. 2018), cancer (Kang et al. 2017; Shuvy et al. 2017), and renal failure (Antonelli et al. 2017), adversely affect both survival and functional outcomes in OHCA patients. In one Australian study of 15,953 patients, worse scores on the Charlson Comorbidity Index were associated with both an increased rate of dying after hospital discharge, and reduced likelihoods of good functional recovery and health-related quality of life at 12-month follow-up (Andrew et al. 2017a).

Other baseline patient characteristics that appear to influence survival and functional outcomes are gender and race. In terms of gender, women appear to have a higher rate of mortality post OHCA than men (Blom et al. 2019; Mahapatra et al. 2005; Safdar et al. 2014), but the data are conflicting, In one study, women were less likely to be resuscitated and to survive to hospitalisation and hospital discharge, but these differences all were explained by more women having non-shockable rhythms when first evaluated (Blom et al. 2019). In another study, women were more likely to survive than men up to age 47, but less likely afterwards (Safdar et al. 2014). And, in a third study, though less likely to survive to hospital discharge, women were more likely to survive to hospital admission, and there was no difference in survival at five-year follow-up (Mahapatra et al. 2005). With respect to race, in a meta-analysis of 15 American studies, relative to Caucasians, African-American patients were less likely to survive both from hospital admission (OR=0.59, 95% CI= 0.48-0.72) and discharge (0.74, 0.61-0.90), but also less likely to receive bystander cardiopulmonary resuscitation (0.66, 0.55-0.78), have a witnessed arrest (0.77, 0.72-0.83) and have an initially-shockable cardiac rhythm (0.66, 0.58-0.76) (Shah et al. 2014).

Pre-Hospital Care

Among factors pertaining to the initial, out-of-hospital assessment of OHCA patients, one factor consistently shown to impact both short and long-term survival is the type of cardiac rhythm identified; more specifically, was the original rhythm identified by the EMT is shockable or non-shockable. Shockable rhythms include ventricular fibrillation and ventricular tachycardia, while non-shockable rhythms are asystole and pulseless electrical activity (PEA) (Soar et al. 2012). Consistently, survival has been found to be better among patients whose initial cardiac rhythm was shockable than non-shockable (Andrew et al. 2014; Dumas and Rea 2012; Goto et al. 2013; Grimaldi et al. 2014; Herlitz et al. 2005; Luo et al. 2017; Martinell et al. 2017; Meaney et al. 2010; Rey et al. 2020; Sasson et al. 2010; Shuvy et al. 2017; Thomas et al. 2013). This link between shockable initial rhythms and enhanced survival extends as far out as five-years post-OHCA. In one study, among 1001 (17%) of 5958 successfully-resuscitated OHCA patients who survived to hospital discharge, five-year survival from the time of hospital discharge was 73% among those whose initial cardiac rhythm was either ventricular fibrillation or tachycardia, versus just 45% in patients with asystole or PEA (p<0.001) (Dumas and Rea 2012). As for patient age, the presence of a shockable cardiac rhythm when first assessed is retained in all three published models predicting long-term outcomes in OHCA patients (Herlitz et al. 2005; Martinell et al. 2017; Rey et al. 2020). This said, survival has not been shown to be enhanced by converting an initially non-shockable rhythm to a shockable one prior to hospital arrival (Thomas et al. 2013), suggesting that supportive management to sustain patient circulation and oxygenation plays a larger role.

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The initial cardiac rhythm identified, in turn, appears to be influenced by ambulance response time (Bunch et al. 2004a; Herlitz et al. 2005; Hollenberg et al. 2005; Hollenberg et al. 2007; Mathiesen et al. 2018) and time to initiating resuscitative efforts (Eisenberg et al. 1984; Rey et al. 2020). In one study comparing the two largest cities in Sweden, overall survival to hospital discharge was roughly 2½ times as common in Göteborg as in Stockholm (6.1 vs. 3.3%) (Hollenberg et al. 2005). Meanwhile, the average time between the cardiac arrest and ambulance arrival was 4.5 minutes less (8.5 vs. 13.0) and the likelihood of identifying ventricular tachycardia almost twice as high (31 vs. 18%) in Göteborg; otherwise, the two patient populations were similar.

Another factor that appears both to be linked to ambulance response time and to influence outcomes is whether a given patient is gasping when first evaluated by the EMT response team. For this potential outcome predictor, two meta-analyses have recently been published, encompassing 9822 and 10,797 patients, respectively (Zhang et al. 2018; Zhao et al. 2015). In the former analysis, gasping was associated with statistically-significant increases in rates for an initial shockable rhythm (RR=2.25; 95%CI=2.05-2.48), return of spontaneous circulation (ROSC: 1.87; 1.64-2.13), long-term survival (3.46; 1.70-7.07) and favourable neurological outcome (3.79; 1.86-7.73) (Zhang et al. 2018). The latter investigators generated a fixed effects model that identified gasping patients as 3.53 times (95% CI: 3.028-4.104; P<0.01) as likely to survive to discharge (Zhao et al. 2015).

Other factors associated with OHCA outcomes include whether a patient's collapse is witnessed by others (Herlitz et al. 2005; Lahmann et al. 2020; Sasson et al. 2010; Wang et al. 2005), whether it occurs at home or in public (Herlitz et al. 2005; Martinell et al. 2017), whether a bystander initiated cardiopulmonary resuscitation (CPR) (Herlitz et al. 2005; Mathiesen et al. 2018; Sasson et al. 2010), and whether a patient's OHCA occurs at night or daytime (Lin et al. 2019), with night-time OCHA associated with decreased survival up to 30 days post OHCA. Interestingly, despite consistent associations between patient outcomes and either ambulance response time or factors linked to ambulance response time (rhythm type, gasping), in a meta-analysis of 46,417 patients, no link was identified between outcomes and the time required to transport patients to a hospital (Geri et al. 2017).

Epinephrine

Numerous contradictory studies have been published on the potential effectiveness of epinephrine, administered either in the field or emergency room to assist in restoring a functional cardiac rhythm. These include the recent publication several meta-analyses (Atiksawedparit et al. 2014; Aves et al. 2020; Kempton et al. 2019; Lin et al. 2014; Ng and Teoh 2019), also yielding conflicting results. In two slightly older meta-analyses published in 2014 (Atiksawedparit et al. 2014; Lin et al. 2014), no benefit of epinephrine was detected, either for survival at any time point or for neurological outcomes. In a third, more-recently published meta-analysis, a greater percentage of patients survived to hospital admission; but no survival benefit was observed beyond this (Kempton et al. 2019). In a fourth meta-analysis, relative to receiving placebo or nothing, those who received epinephrine experienced an increased rate of ROSC, and increased survival at both hospital admission and discharge (Ng and Teoh 2019); while in the fifth, survival benefits were noted through three months (Aves et al. 2020), largely due to the inclusion of a recently-published randomised clinical trial (RCT) in which a slight increase in overall survival (3.2 vs. 2.4%) was observed at 30 days among those receiving epinephrine versus placebo (Perkins et al. 2018). In that same RCT, however, severe neurological impairment was more common (in 31 vs. 18%) among those receiving epinephrine. Consistent with this, no neurological benefit of epinephrine was detected in any of the five above-noted meta-analyses (Atiksawedparit et al. 2014; Aves et al. 2020; Kempton et al. 2019; Lin et al. 2014; Ng and Teoh 2019). Other studies assessing long-term outcomes among patients receiving versus not receiving epinephrine have generally identified decreased survival among epinephrine recipients (Grimaldi et al. 2014; Martinell et al. 2017; Reynolds et al. 2019; Wang et al. 2005). Epinephrine use also remains as one of ten predictors of poor long-term outcome post OHCA in a model with an area under the curve (AUC) of 0.842 (0.840-0.845), along with older age, OHCA at home, initial non-shockable rhythm, longer duration of no flow or low flow, bilateral absence of corneal and pupillary reflexes, Glasgow Coma Scale motor response=1, lower pH, and a partial pressure of carbon dioxide in arterial blood value <4.5 kPa at hospital admission (Martinell et al. 2017).

Patient Status at Hospital Presentation

An OHCA patient's clinical status upon hospital arrival also impacts the likelihood they will survive to hospital discharge and beyond. For example, as stated earlier, converting a non-shockable to a shockable rhythm by the time of a patient's arrival at the hospital does not appear to impact survival (Thomas et al. 2013), suggesting that other factors, other than the rhythm itself, are outcome determinants. This conjecture is supported by the association between indicators of oxygenation and tissue perfusion - like arterial pH (Martinell et al. 2017; Reynolds et al. 2019) and blood lactate level (Grimaldi et al. 2014) - and survival. Such factors were included in the predictive model of survival published by Martinelli et al. (2017), as was a longer duration of no flow or low flow, adrenaline administration, bilaterally absent corneal and pupillary reflexes, and a Glasgow Coma Scale (GCS) motor score=1 (Martinell et al. 2017). A higher overall GCS score at hospital admission has also been linked to better long-term neurological outcomes (Corrada et al. 2013; Hifumi et al. 2015).

Conclusions

Long-term survival with good cognitive outcomes remains very uncommon after an OHCA. Young patients who are otherwise in good health, accessed quickly by EMT services, are gasping, and having a shockable cardiac rhythm do best, as do those presenting to the emergency room with less-impaired cognitive function. Those whose OHCA occurs at home, limiting the likelihood of witnesses and bystanders to initiate CPR, do worse. Using all these criteria except gasping as part of the predictive model proposed by Herlitz et al (Abazi et al. 2019), survival likelihood among those for whom all six criteria are favourable is almost 60 times higher (23.8 vs. 0.4%) than among those with all six criteria unfavourable. Unfortunately, only one of the seven above-listed criteria (ambulance response time) is modifiable. Given that up to 50% of OHCA patients are alive when they reach emergency rooms, besides hastening ambulance arrival, further research is necessary to identify ways to modify the course of OHCA once patients arrive in hospital.

Conflict of Interest

The author of this paper has no conflicts of interest to report, and no funding of any kind was received for the preparation or submission of this manuscript. ■

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