LETTER TO THE EDITOR

The impact of statin therapy on survival for inhospital cardiac arrest

Introduction

We read with great interest the paper published by Hung et al describing the favorable impact of preceding statin therapy on survival following out-of-hospital cardiac arrest (OHCA).[1] Cardiac arrest remains a major cause of morbidity and mortality, despite improvement in resuscitation efforts. Statins have been shown to decrease the incidence of sudden cardiac death in ischemic heart disease.[2–4] We performed a retrospective study to examine the impact of statin pretreatment on in-hospital cardiac arrest (IHCA) survival.

Methods

This is a retrospective study conducted under the auspices of the Human Investigation Committee of the Research Institute of William Beaumont Hospital. All patients who suffered an IHCA and underwent cardiopulmonary resuscitation (CPR) at Beaumont hospital from April 2012 to December 2013 were included in the study. Exclusion criteria were for CPR in the setting of trauma, postoperatively, during pregnancy and postpartum. Out-of-the hospital cardiac arrest, patients who underwent hospice or palliative care approach were also excluded and patients with inadequate documentation were also excluded.

Survival was defined as survival to discharge. Patients were divided into two groups: survivors and non-survivors. CPR was performed by certified providers and the American Heart Association (AHA) guidelines for resuscitation were followed by all providers performing CPR.

Prearrest characteristics of the two groups were compared in a univariable analysis first, then we sought

Table 1 Patient characteristics

|	Non-survivors (n=80)	Survivors (n=44)	p Values	OR (95% CI)
Age Mean±SD (median)	68±18 (70)	69±14 (70)	0.88	0.97 (0.78 to 1.22) per increment of 10
Body mass index ≥30	33/78 (42.3%)	19/43 (44.2%)	0.84	1.08 (0.51 to 2.29)
Female	43 (53.8%)	16 (36.4%)	0.06	0.49 (0.23 to 1.05)
History of coronary artery disease	35/79 (44.3%)	24 (54.6%)	0.28	1.51 (0.72 to 3.17)
History of myocardial infarction	25/79 (31.7%)	17 (38.6%)	0.43	1.36 (0.63 to 2.94)
History of percutaneous coronary intervention	13/79 (16.5%)	16 (36.4%)	0.013	2.90 (1.23 to 6.82)
History of coronary artery bypass grafting	11 (13.8%)	7 (15.9%)	0.74	1.19 (0.42 to 3.32)
Hypertension	59 (73.8%)	39 (88.6%)	0.051	2.78 (0.97 to 7.98)
Hyperlipidemia	26 (32.5%)	30 (68.2%)	0.0001	4.45 (2.02 to 9.79)
Peripheral vascular disease	10 (12.5%)	7 (15.9%)	0.6	1.32 (0.47 to 3.76)
Stroke	16 (20.0%)	4 (9.1%)	0.11	0.40 (0.12 to 1.28)
Chronic kidney disease	26 (32.5%)	13 (29.6%)	0.73	0.87 (0.39 to 1.94)
Dialysis	11 (13.8%)	10 (22.7%)	0.2	1.84 (0.71 to 4.77)
Active cancer	13 (16.3%)	1 (2.3%)	0.018	0.12 (0.015 to 0.95)
Diabetes mellitus	33 (41.3%)	19 (43.2%)	0.83	1.08 (0.51 to 2.28)
Chronic obstructive pulmonary disease/emphysema	18 (22.5%)	12 (27.3%)	0.55	1.29 (0.55 to 3.01)
History of venous thromboembolism	12 (15.0%)	7 (15.9%)	0.89	1.07 (0.39 to 2.96)
Beta blockers	46 (57.5%)	31 (70.5%)	0.15	1.76 (0.80 to 3.86)
ACE inhibitors (ACE-I) or angiotensin receptors antagonists	29 (36.3%)	23 (52.3%)	0.08	1.93 (0.91 to 4.06)
Spironolactone	3 (3.8%)	3 (6.8%)	0.66	1.88 (0.36 to 9.73)
Aspirin	42 (52.5%)	31 (72.1%)	0.035	2.34 (1.05 to 5.19)
Anti-P2Y12 ADP antiplatelets	11 (13.8%)	4 (9.1%)	0.45	0.63 (0.19 to 2.10)
Anticoagulation	12 (15.0%)	11 (25.0%)	0.17	1.89 (0.75 to 4.73)
Statins	34/79 (43.0%)	33/43 (76.7%)	0.0004	4.37 (1.89 to 10.1)
Ejection fraction (EF) Mean±SD (median)	n=61 50±17 (55)	n=42 47±19 (55)	0.40	N/A
Moderate/severe mitral disease None Mitral Regurgitation (MR)	n=60 53 (88.3%) 7 (11.7%)	n=42 35 (83.3%) 7 (16.7%)	0.47	1.51 (0.49 to 4.69)
Moderate/severe aortic disease None Aortic Regurgitation (AR) Aortic Stenosis (AS) AR and AS	n=60 54 (90.0%) 1 (1.7%) 4 (6.7%) 1 (1.7%)	n=42 39 (92.9%) 2 (4.8%) 1 (2.4%) 0	0.66	N/A
Initial rhythm Ventricular fibrillation (Vfib) Ventricular tachycardia (VTach) Pulseless electrical arrest Asystole	n=77 3 (3.9%) 3 (3.9%) 46 (59.7%) 25 (32.5%)	n=44 5 (11.4%) 7 (15.9%) 23 (52.3%) 9 (20.5%)	0.031	N/A
Shockable rhythm (Vfib/VTach)	6/76 (7.9%)	12/43 (27.9%)	0.003	4.52 (1.55 to 13.1)
Length of CPR>15 min	61/74 (82.4%)	8/41 (19.5%)	<0.0001	0.05 (0.02 to 0.14)

CPR, cardiopulmonary resuscitation.

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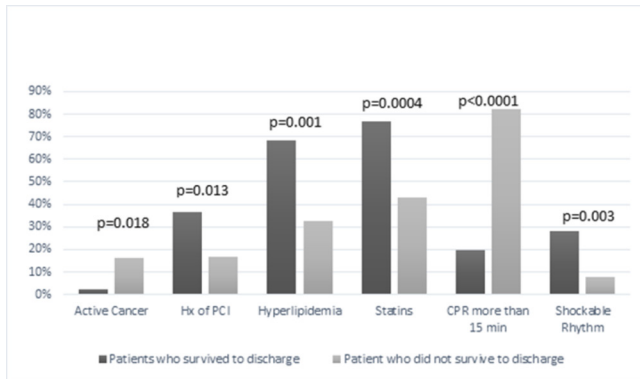
Figure 1 Univariable analysis of factors associated with survival.

to find the strongest associations of survival. We completed a step-down logistic regression analysis. The least significant variable was dropped at each step until only those with a p value of <0.05 remained in the final model.

Results

During the study period, we found 479 patients who suffered cardiac arrest. We excluded the following groups: 85 patients who suffered out of the hospital cardiac arrest, postoperative CPR in 170 patients, CPR in the setting of trauma in 43 patients, 14 patients who underwent hospice/palliative care following CPR, postpartum CPR in two patients and 41 patients were excluded due to inadequate documentation. One hundred and twenty-four patients satisfied the inclusion and exclusion criteria. Of those, return of spontaneous circulation was achieved on 47 patients, three of whom died later on during admission. Overall, 44 patients survived compared with 80 patients who did not survive. The characteristics of these patients are shown in table 1.

Survivors were more likely to have history of hyperlipidemia,to be on statin therapy prior to cardiac arrest and to have a history of percutaneous coronary intervention. Also, survivors were less likely to have an active cancer, as defined by newly diagnosed, progressing or metastatic disease (figure 1).

For CPR characteristics, non-survivors were more likely to have CPR duration of more than 15 min and less likely to have a shockable rhythm compared with the survivors (figure 1).

On multivariable step-down regression analysis, only two factors were associated with survival. Patients who did not survive were more likely to have CPR duration of more than 15 min (adjusted OR 18.1 with CI 95% (6.5 to 50.5) p<0.001) and to less likely be on statin therapy before CPR (adjusted OR 0.29 with CI 95% (0.10 to 0.83) p=0.021, C statistics of 0.86).

Discussion

This small retrospective study adds to the findings of Hung *et al* beyond OHCA[1] to show that statin pretherapy is associated with improved outcomes following IHCA. This study suggests that, on multivariable analysis, statin therapy is associated with improved survival post-IHCA regardless of age, gender, or other comorbidities.

The mechanism in which statin therapy was associated with improved survival following cardiac arrest is not studied. However, it has been shown that statins have a pleiotropic effects in coronary artery disease independent of cholesterol lowering effect including atherosclerotic plaque stability, anti-inflammatory effect, endothelial homeostasis, decreasing oxidase stress and thrombogenic response.[5 6] The effect of statins on survival post-IHCA may have similar mechanisms.

Limitations

This is a retrospective single center study of small sample size and therefore is subject to bias associated with such study. While our observation suggests a benefit of statin therapy on IHCA, larger studies are needed to confirm our results and to study the

biological mechanisms of statins that leads to improved survival following IHCA. Although the implication of our observation in clinical practice is not clear, further research is needed to address such implication. However, it is unlikely that a prospective, randomized trial that address the role of statins in IHCA will be permitted ethically as statins have a great benefit in primary prevention.

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