RESUSCITATION 137 (2019) 52–60

Available online at www.sciencedirect.com

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Stenosis and revascularization of the coronary artery are associated with outcomes in presumed cardiogenic arrest survivors: A multi-center retrospective cohort study[☆]

Min-Shan Tsai[a], *Chih-Wei Sung*[b], *Wen-Jone Chen*[a,c,*], *Po-Ya Chuang*[d], *Chih-Hung Wang*[a], *Yen-Wen Wu*[e], *Wei-Tien Chang*[a], *Wei-Ting Chen*[a], *Chien-Hua Huang*[a,*]

[a] *Department of Emergency Medicine, National Taiwan University Medical College and Hospital, Taipei, Taiwan*
[b] *Department of Emergency Medicine, National Taiwan University Hospital Hsin-Chu Branch, Hsinchu, Taiwan*
[c] *Department of Internal Medicine (Cardiology division), National Taiwan University Medical College and Hospital, Taipei, Taiwan*
[d] *School of Health Care Administration, Taipei Medical University, Taipei, Taiwan*
[e] *Department of Nuclear Medicine, Cardiology Division of Cardiovascular Medical Center, Far Eastern Memorial Hospital, New Taipei City, Taiwan*

Abstract

Background: The emergent coronary angiography (CAG) is associated with better outcomes in CA survivors. However, the impact of severity and revascularization of coronary artery stenosis on outcomes in cardiac arrest (CA) survivors remains unclear.

Methods: A total of 273 non-traumatic adult CA survivors who underwent emergent CAG from January 2011 to July 2017 were retrospectively recruited. The stenosis and non-revascularization of an individual coronary artery ≥70% were defined as significant in any of the major coronary arteries based on an operator visual estimate.

Results: There were 201 patients (73.63%) had ≧1 significant coronary artery stenosis and 58 patients (21.25%) with ≧1 non-revascularized coronary artery. The increased number of stenosed coronary artery was associated with an increased risk for in-hospital mortality [1-vessel: adjusted hazard ration (HR) 2.27, 95% confidence interval (CI) = 1.43–4.04, $p = 0.021$; 2-vessel: adjusted HR 5.49, 95% CI=2.17–13.89, $p < 0.001$; 3-vessel: adjusted HR 11.05, 95% CI=4.20–29.04, $p < 0.001$)] and poor neurological recovery (cerebral performance category = 3–5) [(1-vessel: adjusted odds ration (OR) 1.66, 95% CI 0.67–4.15, =0.275; 2-vessel: adjusted OR 1.81, 95% CI 1.05–3.97, $p = 0.045$; 3-vessel: adjusted OR 3.19, 95% CI 1.25–8.15, $p = 0.001$)], which was positively correlated with the number of vessels. The incomplete revascularization were also associated with increased in-hospital mortality and poor neurological function in patients with ≧1vessel stenosis.

Conclusion: The severity and incomplete revascularization of coronary artery stenosis were associated with increased in-hospital mortality and poor neurological recovery in patients with presumed cardiogenic arrest.

Keywords: Cardiac arrest, Coronary angiography, Coronary artery stenosis, Neurological outcome, Percutaneous coronary intervention, Survival

☆ The study was performed in National Taiwan University Hospital.

* Corresponding authors at: Department of Emergency Medicine, National Taiwan University Hospital, No. 7, Chung-Shan S. Road, Taipei 100, Taiwan.
E-mail addresses: wjchen1955@ntu.edu.tw (W.-J. Chen), chhuang730@gmail.com (C.-H. Huang).

https://doi.org/10.1016/j.resuscitation.2019.01.040
Received 28 November 2018; Received in revised form 18 January 2019; Accepted 31 January 2019

Background

Post-cardiac arrest care has drawn more and more attention along with improvements in cardiopulmonary resuscitation (CPR) and the survival chain during recent decades.[1] As acute coronary syndrome is a frequent cause of sudden cardiac arrest, coronary angiography (CAG) and percutaneous coronary intervention (PCI) were suggested to be performed immediately in post-arrest patients with ST-elevation on electrocardiogram (ECG) to prevent arrest relapse and clinical deterioration.[1] Studies have shown the benefit of emergent CAG in survival and neurological recovery.[2–4] However, whether early PCI also benefits the outcome after cardiac arrest remains undetermined.[4–8] Casella et al. demonstrated that early CAG, but not PCI, is associated with improved survival in out-of-hospital cardiac arrest (OHCA) survivors.[5] PCI does not improve survival to hospital discharge in OHCA patients without ST-elevation.[6] In contrast, several OHCA studies have shown that early PCI is associated with improved survival and neurological outcome.[4,7–9]

Another interesting problem extending from this issue is whether complete revascularization is recommended for multivessel coronary artery disease (CAD) in OHCA survivors. Multivessel CAD occurs in 40–60% of patients with ST-elevation myocardial infarction (STEMI) and is associated with a worse prognosis in proportion to CAD severity.[10,11] Several observational studies have demonstrated conflicting results on the recommendation of complete revascularization for multivessel CAD management in patients with STEMI.[12–17] Acute multivessel complete revascularization is associated with increased short-term and long-term mortality compared to both culprit-only and staged PCI in these patients.[12–14] The 2013 American College of Cardiology/American Heart Association(AHA) STEMI guidelines recommend against routine non-infarct-related artery PCI.[18] However, several studies have shown contrary results. Two independent randomized clinical trials demonstrated a reduced risk of mortality and adverse cardiovascular events in patients with STEMI who underwent complete revascularization as compared to patients with PCI to the infarct-related artery only.[15,16] Smits et al. also showed that the reduced risk of adverse cardiovascular outcome in completely revascularized patients is mainly due to a reduction in subsequent revascularization.[17]

The prevalence of multivessel CAD in cardiac arrest survivors is 30–60%.[19,20] However, whether CAD severity is associated with worse outcome in this population and whether incomplete revascularization during the acute stage is associated with a poor prognosis has not been explored. Therefore, in the current study, we investigated whether CAD severity and the extent of revascularization are associated with outcomes in cardiac arrest survivors who received emergent CAG after return of spontaneous circulation (ROSC).

Materials and methods

This retrospective cohort study was approved by the Institutional Review Boards of National Taiwan University Hospital (tertiary-care medical center), National Taiwan University Hospital Hsin-Chu Branch, and Far Eastern Memorial Hospital (tertiary-care medical center). This study enrolled non-traumatic adult cardiac arrest survivors with a CPR attempt in the emergency department during 2011–July 2017 at National Taiwan University Hospital, from 2015 to 2017 at National Taiwan University Hospital Hsin-Chu Branch, and from 2011 to 2015 at Far Eastern Memorial Hospital. All three hospitals are competent to perform emergent CAG for 7 days a week, 24 h a day. A total of 3132 adult patients (≥18 years) who suffered a

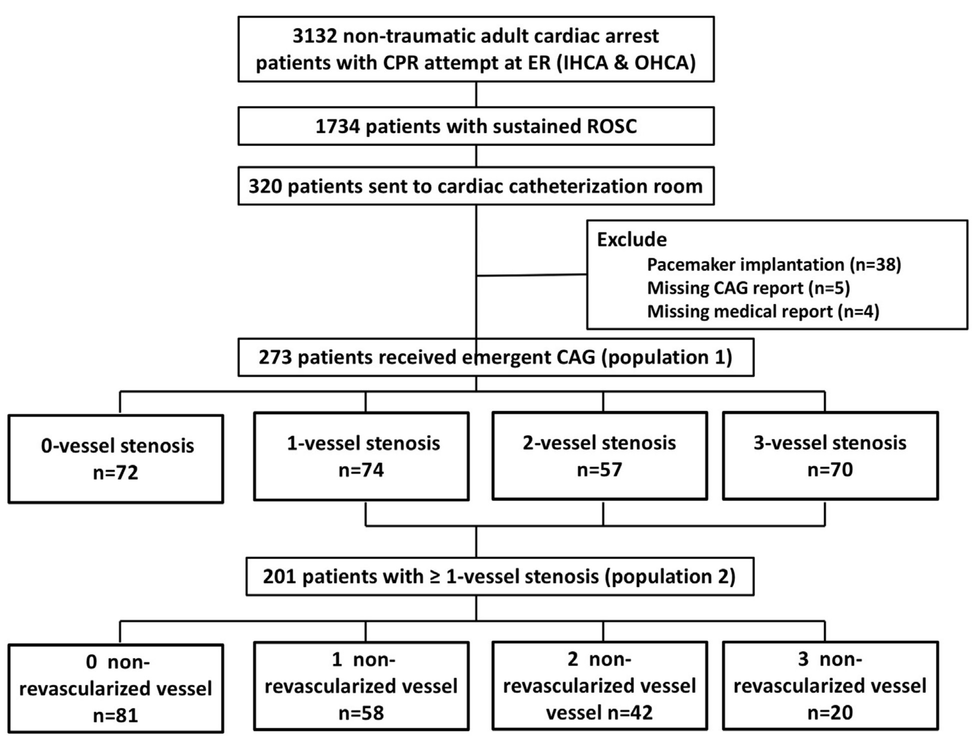

Fig. 1 – Process of selecting the study patients.
CAG = coronary angiography; CPR = cardiopulmonary resuscitation; IHCA = in-hospital cardiac arrest; OHCA = out-of-hospital cardiac arrest.

cardiac arrest with a CPR attempt were collected. A total of 1734 patients were successfully resuscitated from cardiac arrest and admitted to the intensive care unit. A total of 320 patients were sent to the cardiac catheterization room within 24 h following ROSC to receive further examination and treatment. After excluding 38 patients with an implanted pacemaker, five patients with a missing CAG report, and four patients without medical records, 273 patients receiving emergent CAG (within 24 h after ROSC) were finally enrolled in this study (population 1).

Coronary artery stenosis was defined as significant when emergent CAG showed the presence of ≥70% stenosis in a major epicardial coronary artery. The enrolled patients were classified into different groups according to the number of coronary artery vessels that were stenosed, such as 0-vessel stenosis, 1-vessel stenosis, 2-

Table 1 – Baseline characteristics between groups with different coronary artery stenosis.

		Vessel number of coronary artery stenosis				
	Total patients n (%) 273	0 n (%) 72 (26.37%)	1 n (%) 74 (27.16%)	2 n (%) 57 (20.88%)	3 n (%) 70 (25.64%)	*p*
Age (years)						
≤55	89 (32.60%)	31 (43.06%)	28 (37.84%)	16 (28.07%)	14 (20.00%)	0.023
55–65	85 (31.14%)	19 (26.39%)	19 (25.68%)	20 (35.09%)	27 (38.57%)	
≥65	99 (36.26%)	22 (30.51%)	27 (36.48%)	21 (36.84%)	29 (41.43%)	
Gender (male)	208 (76.19%)	41 (56.94%)	59 (79.73%)	46 (80.70%)	62 (88.57%)	<0.001
Body mass index (kg/m^2)	25.72 ± 4.79	25.19 ± 5.06	25.04 ± 4.96	26.25 ± 4.53	26.20 ± 4.49	0.078
Smoking	68 (24.91%)	21 (29.17%)	17 (22.97%)	10 (17.54%)	20 (28.57%)	0.417
Hospital						0.103
NTUH	197 (72.16%)	46 (63.89%)	55 (74.32%)	48 (84.21%)	48 (68.57%)	
HCH	49 (17.95%)	14 (19.44%)	14 (18.92%)	5 (8.77%)	16 (22.86%)	
FEMH	27 (9.89%)	12 (16.67%)	5 (5.76%)	4 (7.02%)	6 (8.57%)	
Pre-comorbidities						
Hypertension	154 (56.41%)	35 (48.61%)	38 (51.35%)	37 (64.91%)	44 (62.86%)	0.136
Diabetes mellitus	108 (39.56%)	23 (31.94%)	24 (32.43%)	23 (40.35%)	38 (54.29%)	0.021
Dyslipidemia	57 (20.88%)	13 (18.06%)	15 (20.27%)	13 (22.81%)	16 (22.86%)	0.869
Coronary artery disease	97 (35.53%)	14 (19.44%)	33 (44.95%)	22 (38.60%)	28 (40.00%)	0.006
Previous stent deployment	0.42 ± 0.97	0.15 ± 0.51	0.54 ± 1.02	0.47 ± 1.13	0.51 ± 1.10	0.049
Myocardial infarction	10 (3.66%)	3 (4.17%)	2 (2.70%)	0 (0.00%)	5 (7.14%)	0.188
Cardiac arrhythmia	21 (7.69%)	4 (5.56%)	7 (9.46%)	5 (8.77%)	5 (7.14%)	0.784
Heart failure	32 (11.72%)	17 (23.61%)	6 (8.11%)	6 (10.53%)	3 (4.29%)	0.003
Chronic kidney disease	49 (17.95%)	11 (15.28%)	8 (10.81%)	12 (21.05%)	18 (25.71%)	0.108
Malignancy	13 (4.76%)	4 (5.56%)	4 (5.41%)	2 (3.51%)	3 (4.29%)	0.941
Pre-arrest complaints						
Chest pain	115 (42.12%)	21 (29.17%)	28 (37.84%)	28 (49.12%)	38 (54.29%)	0.011
Palpitation	9 (3.30%)	4 (5.56%)	2 (2.70%)	2 (3.51%)	1 (1.43%)	0.586
Gastrointestinal upset	11 (4.03%)	4 (5.56%)	4 (5.41%)	0 (0.00%)	3 (4.29%)	0.362
Headache	4 (1.47%)	2 (2.78%)	1 (1.35%)	0 (0.00%)	1 (1.43%)	0.642
Others	103 (38.01%)	34 (47.22%)	29 (39.19%)	21 (36.84%)	19 (27.14%)	0.098
Resuscitation events						
Witnessed collapse	222 (81.92%)	61 (84.72%)	63 (85.14%)	44 (77.19%)	54 (79.41%)	0.526
Bystander CPR	199 (73.43%)	56 (77.78%)	52 (70.27%)	44 (77.19%)	47 (69.12%)	0.649
Initial shockable rhythm	114 (41.76%)	36 (50.00%)	26 (35.14%)	27 (47.37%)	25 (35.71%)	0.193
Shockable rhythm ever	169 (62.13%)	49 (68.06%)	45 (60.81%)	36 (63.16%)	39 (55.71%)	0.548
CPR duration						
CPR ≦ 10 min	116 (42.49%)	34 (47.22%)	29 (39.19%)	24 (42.11%)	29 (41.43%)	0.018
CPR > 10 min	157 (57.51%)	38 (52.78%)	45 (61.81%)	33 (57.89%)	41 (58.57%)	
Post-ROSC events						
Inotrope use	204 (75.56%)	50 (69.44%)	48 (64.86%)	46 (80.70%)	60 (85.71%)	0.034
Therapeutic hypothermia	98 (39.84%)	29 (40.28%)	22 (29.73%)	19 (38.00%)	28 (46.67%)	0.564
ECMO	102 (37.36%)	17 (23.61%)	27 (36.49%)	27 (47.37%)	31 (44.29%)	0.018
IABP	96 (35.29%)	6 (8.33%)	29 (39.19%)	27 (47.37%)	34 (48.57%)	<0.001
Vessel number of non-revascularized coronary artery						<0.001
0	153 (56.04%)	72 (100%)	51 (68.92%)	20 (35.09%)	10 (14.29%)	
1	58 (21.25%)	0 (0.00%)	23 (31.08%)	20 (35.09%)	15 (21.43%)	
2	42 (15.38%)	0 (0.00%)	0 (0.00%)	17 (29.82%)	25 (35.71%)	
3	20 (7.33%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	20 (28.57%)	
Emergent PCI after ROSC	149 (54.58%)	6 (8.33%)	51 (68.92%)	41 (71.93%)	51 (72.86%)	<0.001
Dual anti-platelet agents	199 (73.70%)	38 (52.78%)	60 (81.08%)	44 (77.19%)	57 (81.43%)	<0.001

CPR = cardiopulmonary resuscitation; ECMO = extracorporeal membrane oxygenation; IABP = intraaortic balloon pumping; PCI = percutaneous coronary intervention; ROSC = return of spontaneous circulation.

vessel stenosis, and 3-vessel stenosis. There were 72 patients in the 0-vessel stenosis group, 74 patients in the 1-vessel stenosis group, 57 patients in the 2-vessel stenosis group, and 70 patients in the 3-vessel stenosis group. The 201 patients with ≥1-vessel stenosis (population 2) were further divided into 0-non-revascularized vessels (NRV) (n = 81), 1-NRV (n = 58), 2-NRV (n = 42) and 3-NRV (n = 20), respectively, based on the number of NRV (Fig. 1). The non-revascularized stenosis of a coronary artery was defined as residual stenosis ≥70% in a major epicardial coronary artery after CAG. The primary outcome was in-hospital mortality during index hospitalization, and the secondary outcome measured functional outcome presenting as poor neurological recovery at hospital discharge (cerebral performance category (CPC) score = 3–5). We collected the following information from the individual medical records: age, gender, body mass index (BMI), smoking status, preexisting comorbidities, pre-arrest complaint (documented in the medical records), resuscitation events (presence of a witnessed collapse and bystander CPR, initial shockable rhythm or not, shockable rhythm ever during cardiac arrest and CPR duration) and post-ROSC events [use of an inotrope, therapeutic hypothermia, extracorporeal membrane oxygenation (ECMO) and iIABP, emergent PCI, and dual anti-platelet agents]. The use of an inotrope, ECMO, IABP, emergent PCI, and dual anti-platelet agents was defined as application of these therapies within 7 days following ROSC.

Table 2 – Baseline characteristics between groups with different non-revascularized coronary artery.

		Vessel number of non-revascularized coronary artery				
	Total patients n (%) 201	0 n (%) 81 (40.30)	1 n (%) 58 (28.85)	2 n (%) 42 (20.90)	3 n (%) 20 (9.95)	*p*
Age (years)						
≤55	58 (28.86)	31 (38.27)	16 (27.59)	10 (23.81)	1 (5.00)	0.023
55–65	65 (32.34)	19 (23.46)	20 (34.48)	18 (42.86)	8 (40.00)	
≥65	77 (38.31)	31 (38.27)	21 (36.21)	14 (33.33)	11 (55.00)	
Gender (male)	167 (83.08)	69 (85.19)	45 (77.59)	36 (85.71)	17 (85.00)	0.751
Body mass index (kg/m^2)	25.78 ± 4.63	25.14 ± 4.42	25.50 ± 4.84	27.47 ± 4.59	25.78 ± 5.01	0.049
Smoking	47 (23.38)	20 (24.69)	11 (18.97)	11 (26.19)	5 (25.00)	0.845
Hospital						0.194
NTUH	151 (75.12)	63 (77.78)	46 (79.31)	30 (71.43)	12 (60.00)	
HCH	34 (16.92)	12 (14.81)	10 (17.24)	6 (14.29)	6 (30.00)	
FEMH	15 (7.46)	6 (7.41)	1 (1.72)	6 (14.29)	2 (10.00)	
Pre-comorbidities						
Hypertension	119 (59.20)	51 (62.96)	29 (50.00)	27 (64.29)	12 (60.00)	0.464
Diabetes mellitus	85 (42.29)	33 (40.74)	18 (31.03)	26 (61.90)	8 (40.00)	0.024
Dyslipidemia	44 (21.89)	18 (22.22)	13 (22.41)	9 (21.43)	4 (20.00)	0.994
Coronary artery disease	83 (41.29)	34 (41.98)	23 (39.66)	18 (42.86)	8 (40.00)	0.993
Previous stent deployment	0.52 ± 1.08	0.58 ± 1.17	0.51 ± 1.08	0.54 ± 1.04	0.20 ± 0.69	0.567
Myocardial infarction	7 (3.48)	2 (2.47)	1 (1.72)	1 (2.38)	3 (15.00)	0.033
Cardiac arrhythmia	15 (7.46)	3 (3.70)	5 (8.62)	4 (9.52)	3 (15.00)	0.012
Heart failure	15 (7.46)	8 (9.88)	4 (6.90)	2 (4.76)	1 (5.00)	0.726
Chronic kidney disease	38 (18.91)	12 (14.81)	9 (15.52)	12 (28.57)	5 (25.00)	0.223
Malignancy	9 (4.48)	3 (3.70)	3 (5.17)	3 (7.14)	0 (0.00)	0.611
Pre-arrest complaints						
Chest pain	94 (46.77)	41 (50.62)	22 (37.93)	20 (47.62)	11 (55.00)	0.464
Palpitation	5 (2.49)	1 (1.23)	2 (3.45)	1 (2.38)	1 (5.00)	0.733
Gastrointestinal upset	7 (3.48)	3 (3.70)	2 (3.45)	1 (2.38)	1 (5.00)	0.961
Headache	2 (0.99)	2 (2.47)	0 (0.00)	0 (0.00)	0 (0.00)	0.396
Others	69 (34.33)	26 (32.10)	23 (39.66)	16 (38.10)	4 (20.00)	0.338
Resuscitation events						
Witnessed collapse	161 (80.10)	70 (86.42)	41 (70.69)	31 (77.50)	19 (95.00)	0.056
Bystander CPR	143 (71.14)	60 (74.07)	41 (70.69)	28 (70.00)	14 (70.00)	0.962
Initial shockable rhythm	108 (53.73)	65 (80.27)	16 (27.59)	18 (42.86)	9 (45.00)	0.283
Shockable rhythm ever	120 (59.70)	50 (62.50)	32 (55.17)	25 (59.52)	13 (65.00)	0.857
CPR duration						
CPR ≦ 10 min	82 (40.80)	36 (44.44)	24 (41.38)	14 (33.33)	8 (40.00)	0.039
CPR > 10 min	118 (58.71)	45 (55.56)	33 (56.90)	28 (66.67)	12 (60.00)	
Post-ROSC events						
Inotrope use	154 (76.62)	52 (65.00)	46 (79.31)	38 (90.48)	18 (90.00)	0.003
Therapeutic hypothermia	69 (34.32)	29 (29.82)	17 (29.31)	18 (42.86)	5 (25.00)	0.581
ECMO	85 (42.29)	29 (35.80)	23 (39.66)	22 (52.38)	11 (55.00)	0.023
IABP	90 (44.78)	38 (46.91)	25 (43.10)	16 (38.10)	11 (55.00)	0.629

CPR = cardiopulmonary resuscitation; ECMO = extracorporeal membrane oxygenation; IABP = intraaortic balloon pumping; PCI = percutaneous coronary intervention; ROSC = return of spontaneous circulation.

Categorical variables are expressed as percentages, and continuous variables are expressed as mean ± standard deviation (SD). Either the chi-square test (for categorical variables) or ANOVA test (for continuous variables) was used to delineate the demographic and clinical characteristics of the study subjects. A Cox regression analysis was performed to evaluate predictors of in-hospital mortality, and a logistic regression analysis was performed for a poor neurological outcome. Statistically significant variables identified with $p < 0.1$ were entered into a multivariate Cox proportional hazard regression model to determine the impact of coronary artery stenosis and non-revascularized coronary artery stenosis on in-hospital mortality. Similar criteria were applied to identify variables for the multivariate logistic regression analysis to evaluate the effect of coronary artery stenosis and non-revascularized stenosis on poor neurological outcome. The cumulative risk for in-hospital mortality was plotted vs. the cumulative incidence function, and the log-rank test was applied to evaluate the difference between the groups. A two-tailed p-value <0.05 was considered significant. All computations were performed using software (SAS/Stat v9.4 for Windows; SAS Institute, Cary, NC, USA). The components of a retrospective review were checked using the Strengthening the Reporting of Observational Studies in Epidemiology checklist for a cohort study.

Results

In patients grouped by the number of stenosed coronary artery vessels, patients with more stenosed vessels were older and more were male. The incidence of diabetes and CAD increased as the number of stenosed vessels increased. However, the incidence of heart failure showed a reverse distribution. A higher percentage of patients with stenosed vessels had pre-arrest chest pain. The groups with a higher number of stenosed vessels had an increased CPR duration and a higher incidence of applying an inotrope, ECMO, or IABP. No surprisingly, the group with 3-vessel stenosis had more patients with non-revascularized vessels (n = 60, 85.71%), received emergent PCI more frequently (n = 51, 72.86%), and were administered dual anti-platelet agents (n = 57, 81.43%) (Table 1).

Table 2 shows the demographic and clinical characteristics of patients with ≥1-vessel stenosis who were grouped by vessel number of non-revascularized coronary arteries. The groups with more non-revascularized vessels had a higher incidence of older age, previous myocardial infarction and cardiac arrhythmia. However, BMI and the incidence of diabetes did not increase linearly as the number of non-revascularized coronary arteries increased. Patients with more NRV had a longer CPR duration. The 3-NVR group had a higher percentage of patients using an inotrope or ECMO (Table 2).

Forty-five patients (64.29%) in the 3-vessel stenosis group failed to survive to hospital discharge compared to 13 patients (18.06%) in the 0-vessel stenosis group, 20 patients (27.03%) in the 1-vessel stenosis group, and 27 patients (47.37%) in the 2-vessel stenosis group (1-vessel: adjusted HR 2.27, 95% CI = 1.43–4.04, $p = 0.021$; 2-vessel: adjusted HR 5.49, 95% CI = 2.17–13.89, $p < 0.001$; 3-vessel: adjusted HR 11.05, 95% CI = 4.20–29.04, $p < 0.001$)(Table 3). The 2-vessel and 3-vessel stenosis groups had a significantly increased risk for in-hospital mortality compared with the one-vessel stenosis group (two-vessel: adjusted HR 2.33, 95% CI = 1.10–5.15, $p = 0.04$; 3-vessel: adjusted HR 5.19, 95% CI = 2.37–11.36, $p < 0.001$). The 3-vessel stenosis group also had a significantly higher risk for in-hospital mortality compared to the 2-vessel stenosis group (adjusted HR 2.68,

Table 3 – The association between in-hospital mortality and coronary artery stenosis and revascularization.[a]

	In-hospital mortality	Unadjusted HR (95% CI)	*p*	Adjusted HR (95% CI)	*p*
Vessel number of coronary artery stenosis					
0	13/72 (18.06%)	Reference		Reference	
1	20/74 (27.03%)	1.74 (0.79, 3.84)	0.016	2.27 (1.43, 4.04)	0.021
2	27/57 (47.37%)	4.15 (1.88, 9.19)	<0.001	5.49 (2.17, 13.89)	<0.001
3	45/70 (64.29%)	8.31 (3.83, 18.01)	<0.001	11.05 (4.20, 29.04)	<0.001
1		Reference		Reference	
2		2.39 (1.15, 4.95)	0.02	2.33 (1.10, 5.15)	0.04
3		4.77 (2.35, 9.69)	<0.001	5.19 (2.37, 11.36)	<0.001
2		Reference		Reference	
3		2.01 (1.08, 4.08)	0.04	2.68 (1.17, 6.17)	0.02
Vessel number of non-revascularized coronary artery					
0	13/81 (16.05%)	Reference		Reference	
1	32/58 (55.17%)	6.69 (3.04, 14.77)	<0.001	7.39 (3.13, 17.47)	<0.001
2	32/42 (76.19%)	12.74 (6.64, 29.87)	<0.001	16.95 (8.36, 36.98)	<0.001
3	15/20 (75.00%)	15.69 (4.85, 30.71)	<0.001	20.14 (4.92, 40.37)	<0.001
1		Reference		Reference	
2		2.60 (1.08, 6.26)	0.03	2.64 (1.03, 6.81)	0.04
3		2.44 (1.78, 6.59)	0.01	2.24 (1.67, 7.38)	0.009
2		Reference		Reference	
3		1.13 (1.02, 3.23)	0.04	1.78 (1.19, 3.29)	0.03

CPR = cardiopulmonary resuscitation; ECMO = extracorporeal membrane oxygenation; IABP = intraaortic balloon pumping; PCI = percutaneous coronary intervention; ROSC = return of spontaneous circulation.
CI = confidence interval; HR = hazard ratio.
[a] Adjusted for age gender, body mass index, diabetes mellitus, hypertension, coronary artery disease, chronic kidney disease, witnessed collapse, bystander CPR, CPR duration, post-arrest inotrope use, ECMO, IABP, vessel number of coronary artery stenosis (for non-revascularized coronary artery), vessel number of non-revascularized coronary artery (for coronary artery stenosis), emergent PCI after ROSC.

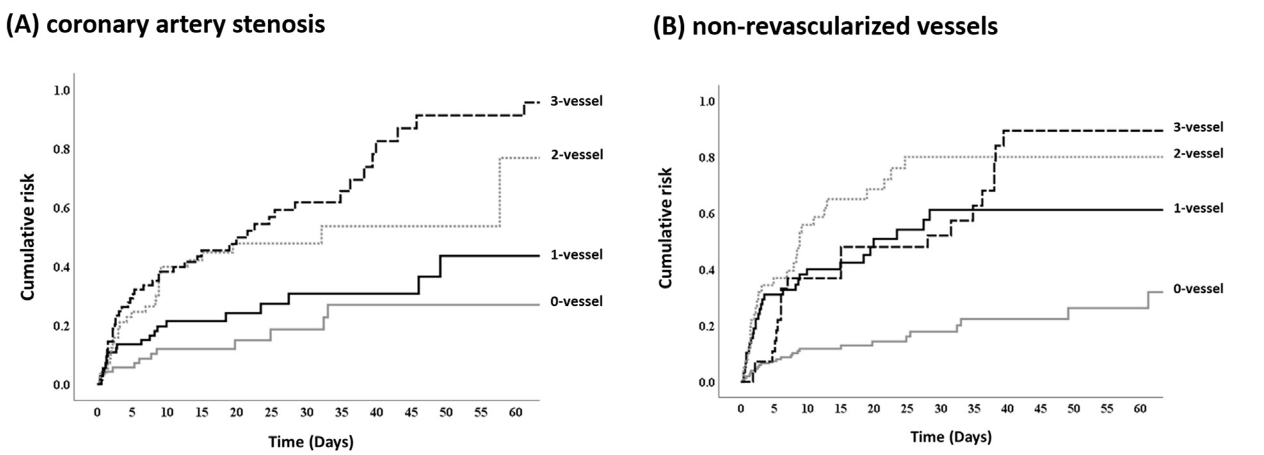

Fig. 2 – The cumulative risk of in-hospital mortality between groups with different (A) coronary artery stenosis (B) non-revascularized vessels in patients with ≥1-vessel stenosis.
Log-rank test $p < 0.001$.

95% CI = 1.17–6.17, $p = 0.02$). Fig. 2A shows the cumulative risk of in-hospital mortality between the groups. The patients with more NRV had a significantly increased risk for in-hospital mortality compared to patients without a NRV (1-NRV: adjusted HR 7.39, 95% CI = 3.13–17.47, $p < 0.001$; 2-NRV: adjusted HR 16.69, 95% CI = 8.36–36.98, $p < 0.001$; 3-NRV: adjusted HR 20.14, 95% CI = 4.92-40.37, $p < 0.001$) (Table 3). The 2- and 3-NRV groups had a higher risk for in-hospital mortality than the 1-NRV group (2-NRV: adjusted HR 2.64, 95% CI = 1.03–6.81, $p = 0.04$; 3-NRV: adjusted HR 2.24, 95% CI = 1.67–7.38, $p = 0.009$). The risk for in-hospital mortality in the 3-NRV group was also higher than that in the 2-NRV group (adjusted HR 1.78, 95% CI = 1.19–3.29, $p = 0.03$). The cumulative risk for in-hospital mortality between the different NRV groups is demonstrated in the Fig. 2B.

Twenty-five patients (34.72%) in the 0-vessel stenosis group, 28 patients (37.84%) in the 1-vessel stenosis group, 32 patients (56.14%) in the 2-vessel stenosis group and 50 patients (71.43%) in the 3-vessel stenosis group, respectively, were discharged with a poor neurological outcome (1-vessel: adjusted OR = 1.66, 95% CI 0.67–4.15, $p = 0.275$; 2-vessel: adjusted OR 1.81, 95% CI = 1.05-3.97, $p = 0.045$; 3-vessel: adjusted OR 3.19, 95% CI = 1.25-8.15, $p = 0.001$) (Table 4). The 2- and 3-vessel stenosis groups had a significantly increased risk for poor neurological outcome compared to the 1-vessel stenosis group (2-vessel: adjusted OR 1.82, 95% CI = 1.08–4.40, $p = 0.046$; 3-vessel: adjusted OR 4.25, 95% CI = 1.70–10.61, $p = 0.001$). The 3-vessel stenosis group also had a higher risk for poor neurological outcome than the 2-vessel stenosis group (adjusted OR 2.02, 95% CI = 0.97-7.04, $p = 0.054$). All 3 groups with NRV had a significantly higher incidence of poor neurological outcome compared with patients without NRV (1-NRV: adjusted OR 3.52, 95% CI = 1.43–8.66, $p = 0.006$; 2-NRV: adjusted OR 7.02, 95% CI = 2.37–20.80, $p < 0.001$; 3-NRV: adjusted OR 5.73, 95% CI = 1.44–19.89, $p = 0.001$) (Table 4). The risk for poor neurological outcome in the 2- and 3-NRV groups was higher than that in the 1-NRV group (2-NRV: adjusted OR 1.80, 95% CI = 0.63–4.87, p=0.345; 3-NRV: adjusted OR 1.67, 95% CI = 0.36–7.59, $p = 0.510$). No difference was detected between the 2- and 3-NRV groups (adjusted OR 1.45, 95% CI = 0.16–13.39, $p = 0.743$). Early PCI was significantly associated with less in-hospital mortality (adjusted HR 0.126, 95% CI = 0.035-0.457, $p = 0.002$) and less poor neurological recovery (adjusted OR 0.330, 95% CI = 0.118-0.919, $p = 0.034$).

Discussion

In this retrospective multicenter observational study, the increased number of coronary arteries with severe stenosis and the extent of incomplete revascularization (number of NRVs) after the index PCI were associated with a higher risk of in-hospital mortality and unfavorable neurological outcomes in cardiac arrest survivors who received emergent CAG after ROSC. Although several studies have evaluated whether complete revascularization benefits STEMI patients with multivessel CAD, this is the first study to investigate whether the severity of coronary artery stenosis and incomplete revascularization are associated with poor outcome in cardiac arrest survivors.

Up to 60% of patients with STEMI have multivessel CAD and the prognosis is proportional to the severity of the coronary artery stenosis.[10,11] In patients with acute transmural myocardial infarction, Goldstein et al. demonstrated that multiple complex coronary plaques are associated with a lower left ventricular ejection fraction, a higher incidence of recurrent angina, and an increased requirement for repeated catheterization or coronary bypass surgery within 1 year.[10] In another study enrolling patients with acute myocardial infarction receiving PCI, multivessel CAD was associated with an increased incidence of 1-year mortality and major adverse cardiac events (MACE) in proportion to the number of stenosed vessels.[11] Keeley et al. also reported that multiple complex plaques are an independent predictor of short- and long-term MACE.[21] A few studies have addressed the incidence of multivessel disease and prognosis in cardiac arrest survivors.[19,20] The incidence of multivessel CAD in patients resuscitated from sudden cardiac death is reported to be about 30% in those with STEMI and 54% in those with NSTEMI with no mention of their influence on outcome.[19] Mylotte et al. reported an incidence of 63.5% for multivessel CAD in STEMI patients resuscitated from cardiac arrest and suffered from cardiogenic shock. Although patients with multivessel CAD had a significantly lower 6-month survival, significance disappeared after a multivariate

Table 4 – The poor neurological outcome among different coronary artery stenosis and non-revascularization groups.[a]

	Poor neurological outcome	Unadjusted OR (95% CI)	*p*	Adjusted OR (95% CI)	*p*
Vessel number of coronary artery stenosis					
0	25/72 (34.72%)	Reference		Reference	
1	28/74 (37.84%)	1.14 (0.58, 2.25)	0.696	1.66 (0.67, 4.15)	0.275
2	32/57 (56.14%)	2.41 (1.18, 4.91)	0.016	1.81 (1.05, 3.97)	0.045
3	50/70 (71.43%)	4.70 (2.31, 9.56)	<0.001	3.19 (1.25, 8.15)	0.001
1		Reference		Reference	
2		2.10 (1.04, 4.25)	0.038	1.82 (1.08, 4.40)	0.046
3		4.11 (2.04, 8.27)	<0.001	4.25 (1.70, 10.61)	0.001
2		Reference		Reference	
3		1.95 (0.94, 4.08)	0.075	2.02 (0.97, 7.04)	0.054
Vessel number of non-revascularized coronary artery					
0	24/81 (29.63%)	Reference		Reference	
1	37/58 (63.79%)	4.19 (2.04, 8.57)	<0.001	3.52 (1.43, 8.66)	0.006
2	32/42 (76.19%)	7.60 (3.23, 17.88)	<0.001	7.02 (2.37, 20.80)	<0.001
3	15/20 (75.00%)	7.12 (2.33, 21.81)	<0.001	5.73 (1.44,19.89)	0.001
1		Reference		Reference	
2		1.82 (0.75, 4.42)	0.189	1.80 (0.63, 4.87)	0.345
3		1.70 (0.54, 5.35)	0.363	1.67 (0.36, 7.59)	0.510
2		Reference		Reference	
3		0.94 (0.27, 3.23)	0.919	1.45 (0.16, 13.39)	0.743

CPR = cardiopulmonary resuscitation; ECMO = extracorporeal membrane oxygenation; IABP = intraaortic balloon pumping; PCI = percutaneous coronary intervention; ROSC = return of spontaneous circulation.
CI = confidence interval; OR = odds ratio.
[a] Adjusted for age gender, body mass index, diabetes mellitus, hypertension, coronary artery disease, chronic kidney disease, witnessed collapse, bystander CPR, CPR duration, post-arrest inotrope use, ECMO, IABP, vessel number of coronary artery stenosis (for non-revascularized coronary artery), vessel number of non-revascularized coronary artery (for coronary artery stenosis), emergent PCI after ROSC.

analysis.[20] In our study, 46.5% of enrolled patients had more than one-vessel stenosis. After adjusting for baseline characteristics, pre-existing comorbidities, CPR events, and post-arrest care, multivessel CAD was still associated with survival and neurological recovery at discharge in proportion to the number of stenosed vessels.

Several studies have demonstrated that emergent CAG after ROSC is associated with improved outcomes in OHCA survivors.[2–4] The 2015 AHA guidelines suggest that emergent CAG be performed in OHCA patients with suspected cardiac origin and ST elevation on ECG or evidence of haemodynamic or electrical instability.[1] However, the influence of early PCI during the index catheterization on prognosis of cardiac arrest survivors remains controversial.[5–8] Early PCI does not always provide an additional benefit, while emergent CAG has been demonstrated to increase survival.[5,6] Recent studies have reported that early PCI is associated with improved survival and neurological recovery in OHCA survivors.[4,7–9] Moreover, Jentzer et al. demonstrated that only early PCI remains associated with a significant benefit after multivariate adjustment and propensity matching in OHCA survivors with presumed cardiac origin. These results suggest that the observed benefit of CAG might be primarily driven by PCI.[8] Our study showed that early PCI was significantly associated with less in-hospital mortality and poor neurological outcomes, which supports early PCI in selected patients after ROSC. However, the reason why early CAG and PCI improve neurological outcome has not be clarified yet. Early GAG was found to be associated with higher intensity of monitoring and care, more mechanical support with intra-aortic balloon pump (IABP) and prompt diagnosis making,[22] which might in turn improve survival and neurological outcomes. Besides, patients receiving early PCI were less likely to suffer from brain death and withdrawal of life-sustaining therapy as compared to those receiving early CAG without PCI.[8]

Studies investigating the benefit of complete revascularization in STEMI patients with multivessel CAD have shown inconsistent results on the prognosis.[12–18] Staged PCI for multivessel CAD is considered to be safe and associated with a lower mortality rate compared to culprit-only PCI.[13,14] In contrast, acute multivessel PCI is associated with increased mortality and MACE.[23–26] A more critical condition or a more complex procedure was proposed to explain the disadvantage when performing acute multivessel PCI. However, recent clinical trials revealed contrasting results. Wald et al. demonstrated that acute multivessel PCI significantly reduces the risk of adverse cardiovascular events when compared to culprit-only PCI.[15] In another clinical trial, Gershlick et al. also showed improved survival in patients receiving multivessel PCI compared to culprit-only PCI.[16] The benefit was primarily driven by decreased subsequent revascularization.[17] A few studies have addressed management of multivessel CAD in cardiac arrest survivors. In a study enrolling 169 STEMI patients with cardiac arrest and cardiogenic shock, multivessel primary PCI was associated with a significantly lower 6-month mortality rate compared with culprit-only intervention. Recurrent cardiac arrest/shock death was significantly reduced in patients receiving multivessel primary PCI.[20] In our current study, incomplete revascularization was associated with increased in-hospital mortality and poor functional outcome, and the risk of a poor outcome was positively correlated with the number of NRVs. The better outcome in completely revascularized patients may be attributed from the reduction in myocardial ischaemic burden in such a critical illness.

Limitation

Several limitations in the current study should be discussed. Selection bias was unavoidable due to the nature of a retrospective observational analysis. The decision to perform complete or incomplete revascularization during emergent CAG was based on the physicians' preference. We tried to eliminate bias by adjusting several CPR events and post-arrest care, such as CPR duration, inotrope use, IABP, and ECMO use. Unrecognized confounding variables also have the potential to influence the results. The small number of enrolled patients may have resulted in the lack of a statistical difference between groups for some variables. The limited ability of angiography to measure the severity and complexity of CAD and to determine whether a given complex lesion is acute or chronic should be recognized.[27] Last, as described above, we cannot clarify the causal relationship between emergent CAG/PCI and neurological recovery in the current study.

Conclusion

In conclusion, among cardiac arrest survivors receiving emergent CAG, multivessel CAD and incomplete revascularization were both associated with increased in-hospital mortality and poor neurological recovery.

Conflicts of interest

The authors declared that they have no conflict of interest, including relevant financial interests, activities, relationships, and affiliations.

Acknowledgements

None.

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