Review Article

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Outcomes Of Intervention Treatment For Concurrent Cardio-Cerebral Infarction: Meta-Analysis

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1. Abstract

1.1. Background: The concurrent occurrence of acute ischemic stroke and acute myocardial infarction (concurrent Cardio-cerebral infarction) is an extremely rare emergency condition that can be lethal. The causes, prognosis and optimal treatment in these cases is still unclear.

1.2. Methods: We conducted a comprehensive review of five databases, PubMed, Embase, Scopus, Research Gate and Google Scholar on concurrent or simulations and synchronous cardio-cerebral infarction to locate all case reports or case series done on this topic, we analyzed clinical presentations, risk factors, type of myocardial infarction, site of stroke, modified ranking scale at discharge and at 90 days after discharge and treatment options.

1.3. Results: we identified 94 cases of concurrent cardio-cerebral infarction from case reports and series with mean age 62.5±12.6 years. Female 36 patients (38.3%), male 58 patients (61.7%). Median hospital duration 24 hours (0-792 hours). Median admission NIHSS 15 (range 1–30). 29 patients (30.8%) were treated using percutaneous coronary intervention (PCI): PCI with balloon only 9 (9.6%), PCI with aspiration only 1 (3.2%), PCI with Bare metal stent 3 (3.2%), PCI with Drug eluting stent 16 (17%). Treated via Mechanical thrombectomy of cerebral vessels in 24 patients (25.5%). Only 21 (22.3%) were treated combination by both PCI and Mechanical thrombectomy of cerebral vessels.

The outcome of 94 patients, the mortality rate at hospital discharge were in 24 patients from 72 patients with mortality rate (33.3%), the mortality rate at 90 days we recorded in 29 patients from 59 patients with mortality rate (49.2%). In patients with combination intervention treatment group: hospital mortality rate was 13.3% and 90-days mortality rate was:23.5% compared with mortality rate in medical treatment (23.5% and 59.5% respectively (P value 0.038 and 0.012 respectively)

1.4. Conclusion: despite its rarity, concurrent cardio-cerebral infarction prognosis is very poor, about third of patients died before discharge and half of patients died at 90 days after stroke. Only 22 % of patients treated by combination of both percutaneous coronary intervention and mechanical thrombectomy. Thus, further studies would be important to outline new possibilities in the management of this emergency condition.

2. Keywords:
Acute stroke, myocardial infarction, percutaneous coronary intervention (PCI), mechanical thrombectomy (MTE), modified ranking scale (mRS).

3. Introduction

Concurrent occurrence of Acute ischemic stroke (AIS) and acute myocardial infarction (AMI) are very rare medical emergency conditions and leading causes of morbidity and mortality worldwide [1]. Both conditions have a narrow therapeutic time-window and have high risk of mortality. The use of intravenous thrombolytics for acute myocardial infarction(AMI) increase the risk for intracranial hemorrhagic [2-3], and the use of a thrombolytic in acute ischemic stroke (AIS) increases the risk of cardiac wall rupture in the setting of early hours of AMI [4]. The association between cerebrovascular disease and coronary artery disease were reported in the Global Registry of Acute Coronary Event (GRACE) trial suggested the incidence of intra-hospital stroke 0.9% in patients presenting with acute coronary syndrome, and the incidence was much higher in patients with ST elevation myocardial infarction than the non-ST elevation myocardial infarction [5]

The definition of concurrent cardio-cerebral infarction according to Alshifa Hospital classification [6], Concurrent cardio-cerebral infarction syndrome can be diagnosed by the presence of simultaneous onset of a focal neurological deficit, indicating acute stroke and a chest pain with evidence of elevation of cardiac enzymes and electrocardiogram changes to confirm myocardial infarction. The prevalence rate of concurrent CCI were between 0.009 to 0.29 % [7-9]. The present review examines that we analyzed clinical presentations, risk factors, type of myocardial infarction, site of stroke, modified ranking scale at discharge and at 90 days after discharge hemorrhage and treatment options.

4. Methods

4.1. Study Design and Patient Selection

In this metanalysis, we screened retrospective a comprehensive review of five databases, PubMed, Embase, Scopus, Research Gate and Google

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Scholar on concurrent or simulations and synchronous Cardio-cerebral infarction to locate all case report or case series done on this topic. Based on the literature review, we analyzed all the cases of concurrent cardiocerebral infarction. Figure 1

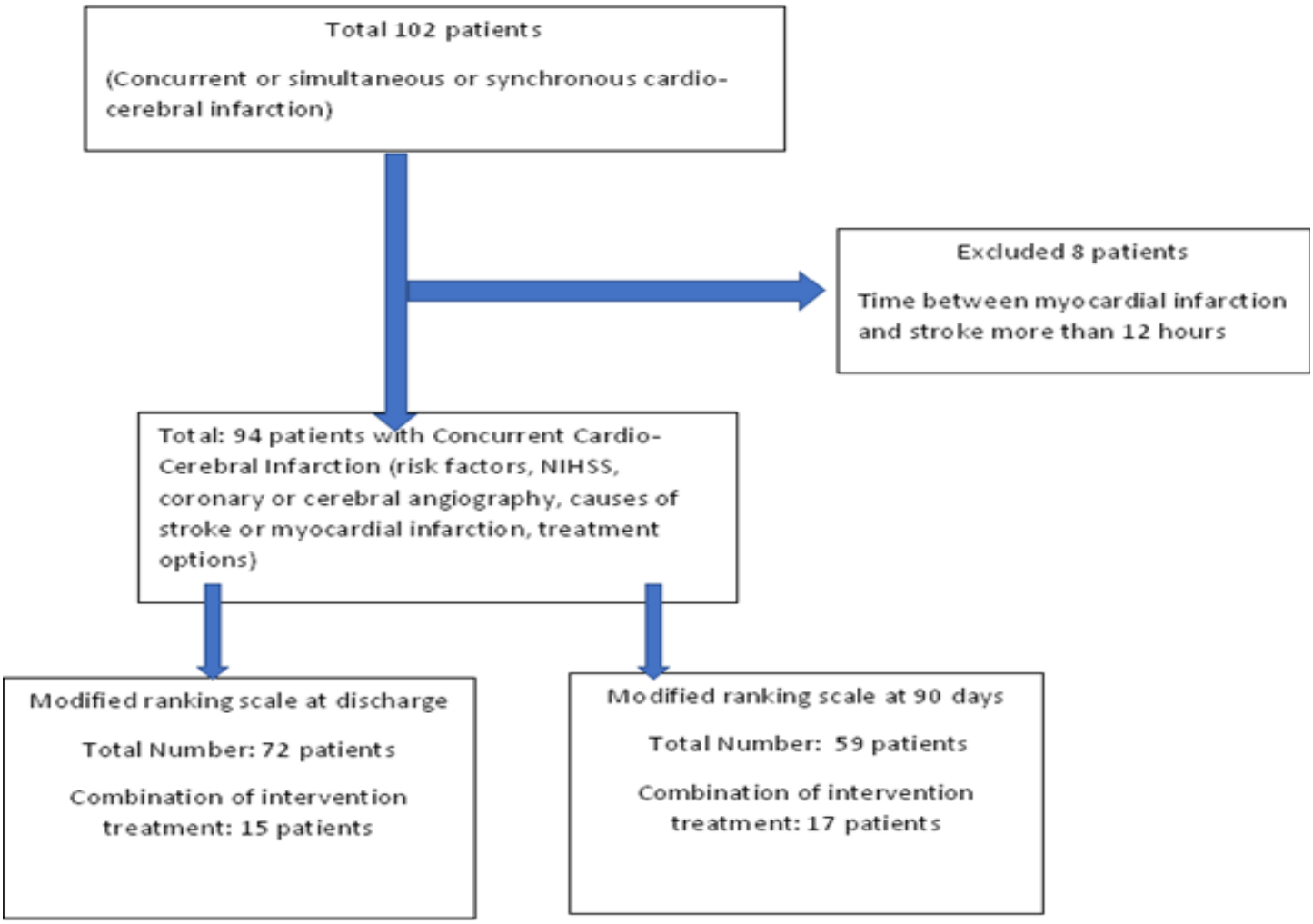

Figure 1 flowchart summarizing case report selection

4.2. Definitions Of Concurrent Cardio-Cerebral Infarction

The occurrence of acute ischemic stroke (onset of a focal neurological deficit) and acute myocardial infarction (elevation of cardiac enzymes plus ischemic symptoms and/or ECG changes and/or loss of viable myocardium on noninvasive test and/or coronary artery thrombus on angiography) either at the same time or one after the other within 12 hours

4.3. Data Collection

The following variables were collected: age and sex ,vascular risk factors (hypertension, diabetes mellitus, atrial fibrillation, history of coronary heart disease, dyslipidemia, smoking and previous stroke), stroke location (anterior vs posterior circulation; in anterior circulation strokes, right or left), stroke severity at admission evaluated by the National Institutes of Health Stroke Scale (NIHSS), first symptoms of cardio cerebral infarction (chest pain: Myocardial infarction or neurological deficit: acute ischemic stroke or synchronous symptoms chest pain and neurological deficit at same time) stroke etiology, presence of large vessel occlusion, myocardial infarction electrocardiographic subtype (ST elevation myocardial infarction: STEMI vs Non ST elevation myocardial infarction: NSTEMI), in STEMI Cases localization: anterior, inferior and lateral, coronary angiography findings and infarcted related artery (culprit lesion) , AMI treatment namely percutaneous coronary intervention (PCI) and AIS treatment by mechanical thrombectomy (MTE). antithrombotic medication. Outcomes according to modified Rankin Scale (mRS) in-hospital and the 3-months were registered. Table 1

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Table 1: concurrent CCI cases (age, sex, culprit lesion, treatment options, mRS in hospital and at 90 days) Results

No -	Name/REF	age	Sex	Culprit	Culprit	Treatment			MRS	MRS	1st event
				heart	Brain	tPA	PCI	MTE	discharg	90 d	
1	Bao C-h [10]	75	M	LCX	NS	Y	DES	N	0	6	MI
2	Bao C-h [10]	84	M	RCA	NS	Y	A,DES	N	4	NR	CVA
3	Habib M[11]	61	M	LAD	LMCA	Y	B,DES	Y	1	0	MI
4	Nakajima H[12]	86	F	RCA	LMCA	N	A	Y	4	NR	SYN
5	Chong CZ[13]	45	M	LAD	RICA	N	DES	Y	NR	3	SYN
6	Chong CZ[13]	53	M	LAD	LMCA	N	DES	Y	NR	5	SYN
7	Chong CZ[13]	71	F	LAD	PCA	N	DES	Y	NR	6	SYN
8	Chong CZ[13]	55	M	NR	LMCA	Y	NO	N	NR	1	SYN
9	Chong CZ[13]	57	M	NR	LMCA	Y	NO	N	NR	1	SYN
10	Chong CZ[13]	51	M	LAD	LMCA	Y	DES	N	0	0	SYN
11	Chong CZ[13]	70	M	NR	PCA	N	NO	N	NR	6	SYN
12	Chong CZ[13]	45	M	LAD	LMCA	Y	DES	N	NR	1	SYN
13	Chong CZ[13]	67	M	LAD	NS	N	DES	N	NR	1	SYN
14	Chong CZ[13]	76	M	NR	RMCA	N	NO	N	NR	6	SYN
15	Ibekwe E[14]	43	M	LAD	LMCA	N	NO	N	6	6	CVA
16	Ibekwe E[14]	80	F	NR	LMCA	Y	NO	N	5	6	CVA
17	Ibekwe E[14]	72	M	NR	LMCA	N	NO	N	6	6	CVA
18	Eskandarani R[15]	62	M	NR	LCCA	N	NO	N	6	6	CVA
19	Eskandarani R[15]	50	M	NR	NR	N	NO	N	5	NR	CVA
20	Eskandarani R[15]	50	M	NR	LMCA	N	NO	N	2	NR	CVA
21	Eskandarani R[15]	67	F	NR	RICA	NR	NO	N	6	6	SYN
22	Eskandarani R[15]	56	M	NR	RICA	N	NO	N	5	NR	MI
23	Iqbal P[16]	65	M	NR	LMCA	Y	NO	N	NR	NR	CVA
24	Abe S[17]	73	F	RCA	LMCA	Y	NO	Y	2	2	CVA
25	Katsuki M[18]	72	M	RCA	PCA	N	NO	N	5	NR	MI
26	Gungoren F[19]	69	M	LAD	LMCA	Y	DES	N	2	NR	SYN
27	Obaid O[12]	41	F	LAD	LMCA	Y	A,DES	N	5	NR	CVA

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28	Sakuta K[21]	55	F	RCA	LMCA	N	B	Y	3	3	CVA
29	Wan Asyraf WZ[22]	33	M	NR	LMCA	Y	NO	N	1	NR	CVA
30	Chen KW[23]	76	M	LAD	RICA	Y	A	Y	1	NR	CVA
31	Nardai S[24]	67	F	LAD	LMCA	N	DES	Y	1	NR	CVA
32	Seiya Nagao[25]	86	F	LCX	LMCA	Y	DES	Y	3	NR	CVA
33	Cabral M[26]	46	F	RCA	LICA	N	B,A,DES	N	NR	NR	MI
34	Plata-Corona JC[27]	46	M	LAD	RMCA	Y	DES	Y	2	0	CVA
35	Yeo LL[28]	45	M	LAD	RICA	N	DES	Y	NR	3	MI
36	Yeo LL[28]	53	M	LAD	LMCA	N	BMS	Y	NR	5	CVA
37	Yeo LL[28]	71	F	LAD	PCA	N	DES	Y	6	6	CVA
38	Yeo LL[28]	55	M	NR	LMCA	Y	NO	N	1	1	CVA
39	Yeo LL[28]	57	M	NR	LMCA	Y	NO	N	1	1	CVA
40	Kijpaisalratana N[29]	65	M	LCX	RMCA	Y	DES	N	NR	NR	CVA
41	Kijpaisalratana N[29]	64	M	LAD	RMCA	N	B	N	6	6	SYN
42	Hosoya H[30]	50	M	NR	NR	N	NO	N	NR	NR	MI
43	Maciel R[31]	44	M	NR	RMCA	Y	NO	N	3	2	MI
44	Wee CK[32]	49	M	RCA	PCA	N	A	N	5	2	CVA
45	Tokuda K[33]	87	F	RCA	RMCA	N	A	Y	NR	3	CVA
46	González- H[34]	66	F	RCA	NR	Y	B	N	NR	NR	SYN
47	Hashimoto O[35]	84	M	LAD	NR	N	A	N	2	NR	SYN
48	Kim HL[36]	58	M	LAD	LMCA	N	A,DES	N	NR	NR	CVA
49	Kleczyński P[37]	62	M	LAD	NR	N	A,B	N	NR	NR	MI
50	Omar HR[38]	48	M	NR	PCA	N	NO	N	6	6	SYN
51	Khairy M[39]	70	F	NR	NR	Y	NO	N	6	6	SYN
52	Lee Kijeong[40]	54	M	RCA	RMCA	Y	DES	Y	6	6	CVA
53	Yusuf M[41]	56	M	RCA	NR	N	DES	N	NR	1	MI
54	Bhandari M[42]	38	M	NR	LMCA	N	NO	N	6	6	MI
55	Mai Duy T[43]	79	M	RCA	NS	Y	A	N	2	NR	CVA
56	Bersano A[44]	70	F	NR	RMCA	N	NO	N	4	1	SYN
57	T. NISHIMURA[45]	50	F	RCA	RMCA	N	NO	N	2	NR	MI

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58	Grogono J[46]	39	F	LAD	NR	N	NO	N	1	NR	SYN
59	Almasi M[47]	78	F	RCA	ACA	Y	A,BMS	N	NR	NR	CVA
60	Karunathilake P[48]	59	F	NR	NR	N	NO	N	3	3	MI
61	Polo Taborda[49]	64	F	NR	RMCA	Y	NO	N	NR	NR	CVA
62	Nguyen TL[50]	60	M	RCA	LCCA	N	NO	N	NR	NR	SYN
63	Loffi M[51]	69	F	LCX	LICA	Y	A	N	6	6	CVA
64	Yong TH[52]	53	M	RCA	RMCA	N	DES	N	1	1	SYN
65	Yong TH[52]	61	M	LCX	LICA	N	DES	N	5	4	CVA
66	Yong TH[52]	80	M	RCA	NR	N	DES	N	2	1	CVA
67	Kawano H[53]	49	M	NS	RMCA	N	NO	N	6	6	SYN
68	Wang X[54]	72	F	NR	RICA	N	NO	N	6	6	CVA
69	Chlapoutakis GN[55]	50	F	NS	NS	N	NO	N	1	1	CVA
70	Koneru S[56]	50	M	NR	LICA	N	NO	N	1	1	CVA
71	Wallace EL[57]	70	M	RCA	LICA	Y	A,BMS	N	NR	NR	CVA
72	Meissner W[58]	62	F	LAD	RMCA	Y	B	N	6	6	CVA
73	Sweta A[59]	78	M	NR	RMCA	Y	NO	N	6	6	CVA
74	Sweta A[59]	58	F	NR	LMCA	Y	NO	N	6	6	CVA
75	Yang CJ[60]	79	M	RCA	LMCA	Y	B,DES	N	2	NR	CVA
76	Brz¸eczekM[61]	62	M	RCA	LMCA	NR	A,DES	N	1	NR	MI
77	Manea MM[62]	87	F	RCA	RMCA	Y	A,DES	N	6	6	CVA
78	Cai X-Q[63]	59	M	LAD	RICA	Y	DES	Y	1	1	MI
79	Fitzek S[64]	88	F	NR	RMCA	Y	NO	N	6	6	CVA
80	Mehdiratta M[65]	65	F	NR	RMCA	Y	NO	N	6	6	CVA
81	Mehdiratta M[65]	81	F	LAD	LMCA	Y	B,DES	N	6	6	CVA
82	Mehdiratta M[65]	75	F	NS	RMCA	Y	NO	N	NR	NR	CVA
83	Y-Hassan S[66]	67	F	NS	PCA	N	NO	Y	2	2	SYN
84	Wang B[67]	84	M	LAD	PCA	Y	DES	N	1	NR	CVA
85	Stafford P J[68]	69	F	NR	NR	Y	NO	N	6	6	MI
86	Stafford P J[68]	57	M	NR	NR	Y	NO	N	6	6	MI

87	Peng H[69]	60	M	RCA	NR	Y	DES	N	1	1	SYN
88	Chang GY[70]	56	M	NR	LMCA	Y	NO	N	NR	NR	MI
89	O. Kawarada[71]	64	F	LAD	RMCA	N	A,DES	Y	1	1	MI
90	Sihite T A[72]	69	M	LAD	NR	N	DES	N	1	NR	MI
91	ABUHEIT E[73]	49	M	RCA	RMCA	N	DES	Y	4	1	MI
92	Abdi IA[74]	51	M	NR	RMCA	Y	NO	N	2	1	MI
93	de Castillo LLC[75]	56	M	NR	PCA	Y	DES	y	2	1	CVA
94	de Castillo LLC[75]	56	M	NR	PCA	N	NO	N	2	2	CVA
95	de Castillo LLC[75]	56	M	NR	PCA	N	NO	N	6	6	CVA
96	de Castillo LLC[75]	56	M	NR	NR	N	NO	N	6	6	CVA
97	de Castillo LLC[75]	56	F	NR	NR	N	NO	N	6	6	CVA
98	de Castillo LLC[75]	56	F	NR	NR	N	NO	N	4	2	CVA
99	de Castillo LLC[75]	56	F	NR	NR	N	NO	N	4	NR	CVA
100	de Castillo LLC[75]	56	F	NR	NR	N	NO	N	4	NR	CVA
101	de Castillo LLC[75]	56	F	NR	NR	N	NO	N	4	NR	MI
102	M. Habib[76]	72	M	RCA	RMCA	Y	DES	Y	1	6	MI

N: not done, NR: not reported, NS: non-significant lesion, Y: yes- done, M: male, F: female, LAD: left anterior descending artery, RCA: right coronary artery, LCX: left circumflex, RMCA: right middle cerebral artery, LMCA: left middle cerebral artery, PCA: posterior cerebral artery, ACA: anterior cerebral artery, RICA: right internal carotid artery, LICA: left internal carotid artery, LCCA: left common carotid artery, RVA; right vertebral artery. A: thrombus aspiration, B: balloon angioplasty, DES: drug eluting stent, BMS: bare-metal stent, SYN: synchronized.

4.4. Intervention Treatment

Combination of treatment by: AMI treatment namely percutaneous coronary intervention (PCI) and AIS treatment by mechanical thrombectomy (MTE) from cerebral arteries.

4.5. Statistical Analysis

Baseline variables Continuous data are reported as means ± SD. Categorical data are presented as absolute values and percentages. NIHSS, hospitalization time, and time between acute ischemic stroke and acute myocardial infarction calculated as median (lower-upper value). Using the x2, Fisher for calculation mortality rate between female and male, and between patient treated with combination treatment with PCI plus MTE and medical treatment . Significance level was set at P value < 0.05. Statistical analysis was performed with SPSS Statistics, Version 23.0.

5. Results

5.1. Patient Characteristics

Total 102 cases were collected from literature; 8 cases were excluded due to the time between stroke and myocardial infarction were more than 12 hours. Total 94 cases were analyzed, the mean age 62.5±12.6 years. Female 36 patients (38.3%), male 58 patients (61.7%). Median hospital duration 24 hours (0-792 hours). Time between stroke and myocardial infarction 0.5 hour (0-12 hours). The most common risk factors of concurrent CCI was hypertension (46.8%) followed by diabetes mellitus and atrial fibrillation. The median NIHSS was 15 (range: 1-30) and the most type of myocardial infarction type was anterior ST segment elevation myocardial infarction (38.3%), the most culprit lesion in coronary arteries was left anterior descending artery (28.7%), the most common culprit artery in brain was left middle cerebral artery (30.9%). Cardiac and neurological investigations were performed on 94 patients by both ECG and computed tomography (CT) or magnetic resonance imaging. Table 2

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Table 2: Baseline characterizes in patients with cardio-cerebral infarction

Risk factors:	
Hypertension	44 (46.8%)
Diabetes mellitus	26 (27.7%)
Atrial fibrillation	19 (20.2%)
Previous stroke	11 (11.7%)
Smoker	16 (17%)
History of Coronary artery disease	11(11.7)
Dyslipidemia	19 (20.2%)
Stroke severity NIHSS (median	15(1-30)
The type of myocardial infarction:	
Anterior ST segment elevation	36 (38.3%)
Inferior wall St segment elevation	26 (27.7%)
Non-ST elevation myocardial infarction	20 (21.3%)
Inferior ST elevation and Right ventricle infarction	5 (5.3%)
High Lateral ST elevation Myocardial infarction	2 (2.1%)
Non-Reported	5 (5.3%)
Infarcted related artery (IRA)	
Left anterior descending artery	27 (28.7%)
Right coronary artery	22 (23.4%)
Left circumflex artery	4 (4.3%)
No significant stenosis	3 (3.2)
Non reported	38 (40.4%)
Culprit stenosis in cranial arteries	
Middle cerebral artery	Right 18 (19.1%), Left 29 (30.9%)
Basilar artery	10 (10.6%)
Internal carotid artery	Right 7(7.4%), Left 5 (5.3%)
Non reported	17 (18.1%)
No stenosis	4 (4.3%)
Anterior cerebral artery	1 (1.1%)
Left common carotid artery	2(2.1%)
Right vertebral artery	1(1.1%)

5.2. Treatments in concurrent Cardio-cerebral Infarction Patients

Medication: Alteplase forty-one patients were treated with intravenous t-PA (43.6%), for antiplatelet and anticoagulation 69 (73%) patients were reported and 25 (27%) patients not reported, Dual antiplatelet 27 (39 %) patients, single antiplatelet 7 (10%) patients, combination of dual antiplatelet and anticoagulation 26 (37.7%) patients (5 NOAC and 21 warfarin), combination of single antiplatelet and anticoagulation 5 (7%) patients (3 warfarin and 2 NOAC), anticoagulation alone 4 (6%) patients (1 NOAC and 3 warfarin) .

Interventions procedures: percutaneous coronary intervention (PCI) was used to treat 29 patients (30.8%): PCI with balloon only 9 (9.6%), PCI with aspiration only 1 (3.2%), PCI with Bare metal stent 3 (3.2%), PCI with Drug eluting stent 16 (17%). Treated via Mechanical thrombectomy of cerebral vessels in 24 patients (25.5%). Only 21 (22.3%) were treated combination by both PCI and Mechanical thrombectomy of cerebral vessels.

5.3. Causes of Cardio Cerebral Infarction:

the most common cause of cardio cerebral infarction was cardiogenic shock. Hypotension (37.2%), and heart failure (37.2%), then by atrial fibrillation (25.5%) and left ventricle thrombus (21.3%). Table 3

Cardiogenic shock/hypotension	35 (37.2%)
Atrial fibrillation	24 (25.5%)
Left ventricle thrombus	20 (21.3%)
Atherosclerosis	32 (34%)
COVID-19 infection	6(6.4%)
Heart failure	35 (37.2%)
Aortic dissection	4 (4.3%)
Malignancy	2(2.1%)
Patent foramen ovale	1 (1.1)

Table 3. Modified ranking scale (mRS) outcomes at hospital discharge and at 90 days after cardio-cerebral infarction:

5.4. Causes of Death

We identified confirm causes of death in only 23 patients. The most causes of patient were cardiac causes 18 (78%) such as ventricle tachyarrhythmias, cardiac Tamponade, aortic dissection, ventricle septal rupture or sudden death. Noncardiac causes 5 (22%): sepsis, infections and multi organ failure.

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5.5. Outcomes

We calculated outcome according to modified ranking scale which 0-2: mild disability, 3-5: moderate to severe disability and 6: death. The modified Rankin Score (mRS) was measured in 72 patients at hospital and in 59 patients at 90 days.

The mortality rate was 33.3% at hospital discharge measured from 72 (76.6%) patients and at 90 days the mortality rate was (49.2%) measured from 59 (62.8%) patients. Table 3

Modified ranking scale at hospital discharge (number: 72 patients)	
mRS 0-2 (mild disability)	32 (44.4%)
mRS 3-5 (moderate to severe disability)	16 (22.3%)
mRS 6 (death)	24 (33.3%)
Modified ranking scale at 90 days (number 59 patients)	
mRS 0-2 (mild disability)	22 (37.3%)
mRS 3-5 (moderate to severe disability)	8 (13.5%)
mRS 6 (death)	29 (49.2%)

5.6. Sex and in-hospital mortality

The hospital mortality rate in male was 11 from 58 patients (18.9%) and in female 13 from 36 patients (35%) the p value is 0.063.

5.7. Hospital and 90 days outcomes according to combination of intervention (PCI plus MTE)

we identified 21 cases of concurrent cardio-cerebral infarction. Female 8 patients (38.1%), male 13 patients (61.9%). Interventions procedures: percutaneous coronary intervention (PCI) was used to treat 21 patients: PCI with balloon only 3 (14%), PCI with aspiration only 1 (5%), PCI with Bare metal stent 1 (5%), PCI with Drug eluting stent 16 (76%). treated via Mechanical thrombectomy of cerebral vessels in 21 patients (100%). The outcome of 21 patients, we can calculate modified ranking scale (mRS) at discharge from 15 patients: mRS 0-2: 8 (53.3%) patients, mRS 3-5: 7 (46.7%) patients, mRS 6: 2 (13.3%), the mRS at 90 days we reached from 17 patients, the mRS was 0-2: 7 (41% %) patients, 3-5: 6 (35 %) patients and 6: 4 (23.5%) Patients.

5.8. Difference of mortality rate between combination intervention treatment and medical treatment.

The mortality rate was significantly lower in patient with combination intervention group than medical treatment). In medical group patients: 8 patients were treated with PCI plus medications and 3 treated with MTE plus medications and other patients treated with medication alone) Table 4

	Intervention (PCI and MTE)	Medical treatment	P value
Hospital mortality	13.30% (2/15)	38.60% (22/57)	0.038
90 days mortality	23.50% (4/17)	59.50% (25/42)	0.012

Table 4: Mortality rate between combination intervention treatment and medical treatment

5.9. Outcome according to first presentation symptoms

First presentation myocardial infarction symptoms followed by acute ischemic stroke symptoms were reported in 18 (19.1%) patients. In those patients the most common stroke type (total: 18 cases, 14 cases were reported and 4 cases non reported) anterior circulation (86 %) with right middle cerebral artery and right internal carotid artery occlusion (RMCA: 4 patients, LMCA: 2 patients, Basilar artery 2 patients, RICA:2), and this group had the highest mortality rate 33.3%.

The first acute ischemic stroke symptoms followed by acute myocardial infarction symptoms 50 (53.2%) patients. The type of MI: inferior STEMI 19 patients, anterior STEMI 17 patients, Non-STEMI 13 patients and 1 patient high lateral STEMI. Coronary angiography to confirm culprit lesion were reported in 28 patients (13 patients RCA and 2 Patients LCX, 11 patients LAD and 2 patients' nonsignificant stenosis), the mortality rate in this patient was reported in 13 patients 26%.

The same time presentation of myocardial infarction and acute ischemic stroke symptoms in 26(27.7%) patients. the mortality rate in this patient was reported in 5 (19%).

6. Discussion

We present a total of 94 patients with concurrent cardio-cerebral infarction and we reported multiple causes which can be categorized into five types: 1-Embolic (left ventricle thrombus in patients with previous myocardial infarction or dilated cardiomyopathy, left atrial appendage thrombus in patients with atrial fibrillation).

2-Hypotensive (patients with cardiogenic shock and heart failure).
3-Atherosclerotic (patient with hypertension, smoking, diabetes mellitus and previous coronary artery disease).
4-Hyper coagulant states (COVID 19 infection, Polycythemia, malignancy and patent foramen ovale).

5-Mechanical complication (aortic dissection).

The left ventricle systolic dysfunction and atrial fibrillation are increasing the likelihood of embolic stroke due to thrombus formation in the left ventricle and left atrial appendage. These two phenomena have been commonly reported in this analysis.

About half of the patients were presented with acute ischemic stroke symptoms followed by acute myocardial infarction symptoms 50 (53.2%). In this patient the most common MI type was inferior MI. First presentation myocardial infarction symptoms followed by acute ischemic stroke symptoms were reported in 18 (19.1%) patients. In this patient the most common stroke type anterior circulation with right middle cerebral artery or right internal carotid artery occlusion. The same time presentation of myocardial infarction and acute ischemic stroke symptoms in 26(27.7%) patients.

For alteplase medication forty-one patients were treated with intravenous alteplase (43.6%), percutaneous coronary intervention (PCI) was used to treat 29 patients (30.8%). Mechanical thrombectomy of cerebral vessels in 24 patients (25.5%). only 21 (22.3%) were treated combination by both PCI and Mechanical thrombectomy of cerebral vessels. The main concerns about giving alteplase to patients with AIS and history of recent MI are (Beyond the bleeding): 1. Thrombolysis-induced myocardial hemorrhage predisposing to myocardial wall rupture 2. Possible ventricular thrombus that could be embolize because of thrombolysis. 3. Post-myocardial infarction pericarditis that may become hemopericardium. According to the 2018 scientific statement guideline from the American Heart Association/American Stroke Association (AHA/ASA), For patients presenting with synchronous AIS and AMI, treatment with intravenous alteplase at the dose appropriate for acute ischemic stroke, followed by percutaneous coronary intervention (PCI) and stenting if indicated, is reasonable. (77). The new recommendation according to 2021 guidelines of European Stroke Organization (ESO) on intravenous thrombolysis for acute ischemic stroke suggested that (78): Contraindication of alteplase for patients with acute ischemic stroke of < 4.5 h duration and with history of subacute (> 6 h) ST segment elevation myocardial infarction during the last seven days. The intravenous alteplase also contraindications in patients with acute STEMI with recent acute ischemic stroke if stroke duration more than 4.5 hours from onset symptoms (79). So that if AIS after 6 hours from STEMI onset, or STEMI after 4.5 hours from AIS intravenous alteplase is contraindication. In these conditions we recommended intervention treatment with PCI and/or MTE.

Our metanalysis showed that concurrent CCI had high in-hospital mortality rate 33.3%, and 3-month mortality rate 49.2%. In-hospital mortality rate was higher in male (35%) than female (18.9%) and 78% of death related to cardiovascular causes. Lennie Lynn C. de Castillo et al, in case series involved 9 patients with concurrent CCI reported mortality rate 45% and cardiovascular death was 69% (8), In another metanalysis of 44 patients, ten patients died (23%), and nine (90%) of those were due to cardiac causes, (80). The use of combination of intervention reduce hospital mortality to 13.3% and 90-days mortality to 25.3%. (P value: 0.038 and 0.012 respectively) the most common co-morbidities that patients presented with included hypertension, smoking, atrial fibrillation and diabetes mellitus. A greater number of male patients were noted but the mortality rate was higher in female patient. The combination intervention (PCI and MTE) treatment was significantly reduce mortality.

7. Conclusion

The occurrence of concurrent cardio cerebral infarction is To the best of our knowledge, this is the largest meta-analysis on the concurrent cardio cerebral infarctions, encompassing of 94 patients. rare with high risk of mortality rate especially in female patients. The intervention with PCI and MTE was significantly reduces the mortality rate. Further studies will need to examine the optimum treatment strategies.

References

1. White H, Boden-Albala B, Wang C et al (2005) Ischemic stroke subtype incidence among whites, blacks, and Hispanics: the Northern Manhattan Study. Circulation 111:1327.
2. Zinkstok SM, Roos YB. Early administration of aspirin in patients treated with alteplase for acute ischaemic stroke: A randomised controlled trial. Lancet 2012; 380: 731-7.
3. Sandercock PA, Counsell C, Kane EJ. Anticoagulants for acute ischaemic stroke. Cochrane Database Syst Rev 2015.CD000024.
4. Patel MR, Meine TJ, Lindblad L, et al. Cardiac tamponade in the fibrinolytic era: analysis of >100,000 patients with ST-segment elevation myocardial infarction. Am Heart J 2006; 151: 316-22.
5. Budaj A, Flasinska K, Gore JM, et al. Magnitude of and risk factors for in-hospital and postdischarge stroke in patients with acute coronary syndromes: Findings from a global registry of acute coronary events. Circulation 2005; 111: 3242-7.
6. Mohammed Habib. Cardio-Cerebral Infarction Syndrome (CCIS): Definition, Diagnosis, Pathophysiology and Treatment. Cardiology and Cardiovascular Research. Vol. 5, No. 2, 2021, pp. 84-93.
7. Chong, Cheryl Zhiya MBBS; Tan, Benjamin Yong-Qiang MBBS; Sia, Ching-Hui MBBS; Khaing, Thet MBBS[3]; Yeo, Leonard Leong Litt MBBS[1]Simultaneous cardiocerebral infarctions: a five-year retrospective case series reviewing natural history. Singapore Medical Journal 63(11):p 686-690, November 2022.
8. de Castillo LLC, Diestro JDB, Tuazon CAM, Sy MCC, Añonuevo JC, San Jose MCZ. Cardiocerebral Infarction: A Single Institutional Series. J Stroke Cerebrovasc Dis. 2021 Jul; 30(7): 105831.
9. Yeo LLL, Andersson T, Yee KW, Tan BYQ, Paliwal P, et al. Synchronous cardiocerebral infarction in the era of endovascular therapy: which to treat first? J Thromb Thrombolysis. 2017; 44: 104-111
10. Bao C-h, Zhang C, Wang X-m and Pan Y-b. Concurrent acute myocardial infarction and acute ischemic stroke: Case reports and literature review. Front. Cardiovasc. Med. 2022; 9:1012345. doi: 10.3389/fcvm.2022.1012345.
11. Mohammed H Habib, “Synchronous Cardio-Cerebral Infarction

Syndrome with Cardiogenic Shock. Is it Safe to Perform Rescue Percutaneous Coronary Intervention and Mechanical Thrombectomy for Middle Cerebral Artery?". EC Neurology 2022: 14: 12 .

12. Nakajima H, Tsuchiya T, Shimizu S, Watanabe K, Kitamura T, Suzuki H. Endovascular therapy for cardiocerebral infarction associated with atrial fibrillation: A case report and literature review. Surg Neurol Int. 2022 Oct 21; 13: 479.
13. Chong CZ, Tan BY, Sia CH, Khaing T, Yeo LL. Simultaneous cardiocerebral infarctions: a five-year retrospective case series reviewing natural history. Singapore Med J. 2021 Apr 19. doi: 10.11622/smedj.2021043. Epub ahead of print. PMID: 33866711.
14. Ibekwe E, Kamdar HA, Strohm T. Cardio-cerebral infarction in left MCA strokes: a case series and literature review. Neurol Sci. 2022 Apr; 43(4): 2413-2422. doi: 10.1007/s10072-021-05628-x. Epub 2021 Sep 29. PMID: 34590206; PMCID: PMC8480750.
15. Eskandarani R, Sahli S, Sawan S, Alsaeed A. Simultaneous cardio-cerebral infarction in the coronavirus disease pandemic era: a case series. Medicine (Baltimore). 2021; 100(4): e24496.
16. Iqbal P. The role of anticoagulation in post-COVID-19 concomitant stroke, myocardial infarction, and left ventricular thrombus: a case report. Am J Case Rep. 2021; 22(1): 1-6.
17. Abe S, Tanaka K, Yamagami H, Sonoda K, Hayashi H, Yoneda S, Toyoda K, Koga M. Simultaneous cardio-cerebral embolization associated with atrial fibrillation: a case report. BMC Neurol. 2019; 19(1): 152.
18. Katsuki M, Katsuki S. A case of cardiac tamponade during the treatment of simultaneous cardio-cerebral infarction associated with atrial fibrillation - case report. Surg Neurol Int. 2019; 10: 241.
19. Gungoren F, Besli F, Tanriverdi Z, Kocaturk O. Optimal treatment modality for coexisting acute myocardial infarction and ischemic stroke. Am J Emerg Med. 2019 Apr; 37(4): 795.e1-795.e4.
20. Obaid O, Smith HR, Brancheau D. Simultaneous Acute Anterior ST-Elevation Myocardial Infarction and Acute Ischemic Stroke of Left Middle Cerebral Artery: A Case Report. Am J Case Rep. 2019 Jun 2; 20: 776-779.
21. Sakuta K, Mukai T, Fujii A, Makita Kand Yaguchi H. Endovascular Therapy for Concurrent Cardio-Cerebral Infarction in a Patient With Trousseau Syndrome. Front. Neurol. 2019; 10: 965.
22. Wan Asyraf WZ, Elengoe S, Che Hassan HH, Abu Bakar A, Remli R. Concurrent stroke and ST-elevation myocardial infarction: is it a contraindication for intravenous tenecteplase? Med J Malaysia 2020; 75(2): 169-170.
23. Chen KW, Tsai KC, Hsu JY, Fan TS, Yang TF, Hsieh MY. One-step endovascular salvage revascularization for concurrent coronary and cerebral embolism. Acta Cardiol Sin 2022; 38: 217-20.
24. Nardai S, Vorobcsuk A, Nagy F, Vajda Z. Successful endovascular treatment of simultaneous acute ischaemic stroke and hyperacute ST-elevation myocardial infarction: The first case report of a single-operator cardio-cerebral intervention. Eur Heart J Case Rep 2021; 5: ytab419.
25. Seiya Nagao, Yasuhide Tsuda, Michihisa Narikiyo, Gota Nagayama, Hirokazu Nagasaki, Yoshifumi Tsuboi, Noritoshi Itou, Chisaku Kambayashi, A case of a patient with endovascular treatment after intravenous t-PA therapy for the acute cerebral infarction and acute myocardial infarction, Japanese Journal of Stroke, 2019, Volume 41, Issue 1, Pages 7-12, Released on J-STAGE January 25, 2019, Advance online publication May 07, 2018, Online ISSN 1883-1923, Print ISSN 0912-0726.
26. Cabral M, Ponciano A, Santos B, Morais J. Cardiocerebral Infarction: A Combination to Prevent. Int J Cardiovasc Sci 2022; 01 Aug 2022 • https://doi.org/10.36660/ijcs.20210276.
27. Plata-Corona JC, Cerón-Morales JA, Lara-Solís B. Nonhyperacute synchronous cardio-cerebral infarction treated by double intervensionist therapy. Cardiovasc Metab Sci. 2019; 30(2): 66-75.
28. Yeo LL, Andersson T, Yee KW et al. Synchronous cardiocerebral infarction in the era of endovascular therapy: which to treat first? J Thromb Thrombolysis. 2017; 44: 104-111.
29. Kijpaisalratana N, Chutinet A, Suwanwela NC. Hyperacute simultaneous cardiocerebral infarction: rescuing the brain or the heart first? Front Neurol. 2017; 8: 664.
30. Hosoya H, Levine JJ, Henry DH, Goldberg S. Double the trouble: acute coronary syndrome and ischemic stroke in polycythemia vera. Am J Med. 2017; 130(6): e237-e240.
31. Maciel R, Palma R, Sousa P et al. Acute stroke with concomitant acute myocardial infarction: Will you thrombolyse? J Stroke. 2015; 17: 84-86.
32. Wee CK, DivakarGosavi T, Huang W. The clot strikes thrice: case report of a patient with 3 concurrent embolic events. Acta Neurol Taiwan. 2015; 24(3): 92-6.
33. K, Shindo S, Yamada K, Shirakawa M, Uchida K, Horimatsu T, Ishihara M, Yoshimura S. Acute embolic cerebral infarction and coronary artery embolism in a patient with atrial fibrillation caused by similar thrombi. J Stroke Cerebrovasc Dis. 2016; 25(7): 1797-1799.
34. González-Pacheco H, Méndez-Domínguez A, Vieyra-Herrera G, Azar-Manzur F, Meave-González A, Rodríguez-Zanella H, Martínez-Sánchez C. Reperfusion strategy for simultaneous ST-segment elevation myocardial infarction and acute ischemic stroke within a time window. Am J Emerg Med. 2014; 32(9): 1157. e1-4.
35. Hashimoto O, Sato K, Numasawa Y, Hosokawa J, Endo M. Simultaneous onset of myocardial infarction and ischemic stroke in a patient with atrial fibrillation: multiple territory injury revealed on angiography and magnetic resonance. Int J Cardiol. 2014; 172(2): e338-e340.
36. Kim HL, Seo JB, Chung WY, Zo JH, Kim MA, Kim SH. Simultaneously presented acute ischemic stroke and non-st elevation myocardial infarction in a patient with paroxysmal atrial fibrillation. Korean Circ J. 2013; 43(11): 766-769.
37. Kleczyński P, Dziewierz A, Rakowski T, Rzeszutko L, Sorysz D, Legutko J, Dudek D. Cardioembolic acute myocardial infarction and stroke in a patient with persistent atrial fibrillation. Int J Cardiol. 2012; 161(3): e46-e47.
38. Omar HR, Fathy A, Rashad R, et al. Concomitant acute right ventricular infarction and ischemic cerebrovascular stroke; possible

explanations. Int Arch Med 2010; 3: 25.

39. Khairy M, Lu V, Ranasinghe N, Ranasinghe L. A Case Report on Concurrent Stroke and Myocardial Infarction. Asp Biomed Clin Case Rep. 2021 Jan 23; 4(1): 42-49.
40. Lee Kijeong, Park Woohyun, Seo Kwon-Duk and Kim Hyeongsoo. Which one to do first?: a case report of simultaneous acute ischemic stroke and myocardial infarction. Journal of Neurocritical Care. 2021; 14(2): 109-112.
41. Yusuf M, Pratama IS, Gunadi R, Sani AF. Hemodynamic Stroke in Simultaneous Cardio Cerebral Infarction: A New Term for Cardiologist. Open Access Maced J Med Sci. 2021 Aug 05; 9(C): 114-117.
42. Bhandari M, Pradhan AK, Vishwakarma P, Sethi R. Concurrent Coronary, Left Ventricle, and Cerebral Thrombosis - A Trilogy. Int J Appl Basic Med Res. 2022 Apr-Jun; 12(2): 130-133.
43. Mai Duy T, DaoViet P, Nguyen Tien D, Nguyen QA, Nguyen Tat T, Hoang VA, Le Hong T, Nguyen Van H, Anh Nguyen D, Nguyen Van C, Thai Lien NV, Nga VT, Chu DT. Coronary aspiration thrombectomy after using intravenous recombinant tissue plasminogen activator in a patient with acute ischemic stroke: a case report. J Int Med Res. 2019 Sep; 47(9): 4551-4556.
44. Bersano A, Melchiorre P, Moschwitis G, Tavarini F, Cereda C, Micieli G, Parati E, Bassetti C. Tako-tsubo syndrome as a consequence and cause of stroke. Funct Neurol. 2014 Apr-Jun; 29(2): 135-7. PMID: 25306124; PMCID: PMC4198162.
45. Tomoya NISHIMURA, Daisuke KOBASHI, Mitsunobu NAKAMURA, Yoshihiko TAKAHASHI, Jun MARUYAMA, Takashi SASAKI, Cardio-cerebral infarction with splenic infarction, Journal of Japanese Society for Emergency Medicine, 2022, Volume 25, Issue 1, Pages 84-88, Released on J-STAGE February 28, 2022, Online ISSN 2187-9001, Print ISSN 1345-0581, https://doi.org/10.11240/jsem.25.84.
46. Grogono J, Fitzsimmons SJ, Shah BN, Rakhit DJ, Gray HH. Simultaneous myocardial infarction and ischaemic stroke secondary to paradoxical emboli through a patent foramen ovale. Clin Med (Lond). 2012 Aug; 12(4): 391-2.
47. Almasi M, Razmeh S, Habibi AH, Rezaee AH. Does Intravenous Administration of Recombinant Tissue Plasminogen Activator for Ischemic Stroke can Cause Inferior Myocardial Infarction? Neurol Int. 2016 Jun 29; 8(2): 6617.
48. Parackrama Karunathilake, Arun Rajaratnam, WKS Kularatne et al. Lessons learned from the management of a case of acute synchronous cardio cerebral infarction in a resource-poor setting, 09 June 2022, PREPRINT (Version 1).
49. Polo Taborda, Nelson; Besteiro, Guillermo; Pfirter, Flavia.Rev. Méd. Clín. Condes ; 31(5/6): 487-490, sept.-dic. 2020.
50. Nguyen TL, Rajaratnam R. Dissecting out the cause: a case of concurrent acute myocardial infarction and stroke. BMJ Case Rep. 2011 Jun 3; 2011: bcr0220113824.
51. Loffi M, Besana M, Regazzoni V, Enrico P, Giuli VD, et al. A masked ST-elevation myocardial infarction. J Clin Images Med Case Rep. 2021; 2(4): 1249.
52. Yong TH, See JHJ, Liew BW (2022) STEMI during Cardiocerebral Infarction (CCI): Is it Safe to Perform Primary Percutaneous Coronary Intervention?. Int J Clin Cardiol 8:251. doi.org/10.23937/23782951/1410251.
53. Kawano H, Tomichi Y, Fukae S, Koide Y, Toda G, Yano K. Aortic dissection associated with acute myocardial infarction and stroke found at autopsy. Intern Med. 2006; 45(16): 957-62.
54. Wang X, Li Q, Wang Y, Zhao Y, Zhou S, Luo Z, Gu M. A case report of acute simultaneous cardiocerebral infarction: possible pathophysiology. Ann Palliat Med. 2021 May; 10(5): 5887-5890.
55. Chlapoutakis GN, Kafkas NV, Katsanos SM, Kiriakou LG, Floros GV, Mpampalis DK. Acute myocardial infarction and transient ischemic attack in a patient with lone atrial fibrillation and normal coronary arteries. Int J Cardiol. 2010 Feb 18; 139(1): e1-4.
56. Koneru, S.; Jillella, D.V.; Nogueira, R.G. Cardio-Cerebral Infarction, Free-Floating Thrombosis and Hyperperfusion in COVID-19. Neurol. Int. 2021; 13: 266-268.
57. Wallace EL, Smyth SS. Spontaneous coronary thrombosis following thrombolytic therapy for acute cardiovascular accident and stroke: a case study. J Thromb Thrombolysis 2012; 34: 548–51.
58. Meissner W, Lempert T, Saeuberlich-Knigge S, Bocksch W, Pape UF. Fatal embolic myocardial infarction after systemic thrombolysis for stroke. Cerebrovasc Dis. 2006; 22: 213-214. [PubMed: 16766875].
59. Sweta A, Sejal S, Prakash S, Vinay C, Shirish H. Acute myocardial infarction following intravenous tissue plasminogen activator for acute ischemic stroke: An unknown danger. Ann Indian Acad Neurol. 2010; 13: 64-66. [PubMed: 20436751].
60. Yang CJ, Chen PC, Lin CS, Tsai CL, Tsai SH. Thrombolytic therapy-associated acute myocardial infarction in patients with acute ischemic stroke: A treatment dilemma. Am J Emerg Med. 2017 May; 35(5): 804.e1-804.e3.
61. Brz¸eczekM, KidawaM, Ledakowicz-Polak A, et al. Myocardial infarction with simultaneous acute stroke in a patient with prior aortic graft replacement - what is the origin of the embolic incident? Folia Cardiol 2019; 14(2): 166-168.
62. Manea MM, Drago¸sD, Stoica E, Buc¸sa A, MarinicaI, Tu¸ta S. Early ST-segment elevation acute myocardial infarction after thrombolytic therapy for acute ischemic stroke: a case report. Medicine (Baltimore) 2018; 97(50): e13347.
63. Cai X-Q, Wen J, Zhao Y, Wu Y-L, Zhang H-P, Zhang WZ. Acute ischemic stroke following acute myocardial infarction: adding insult to injury. Chin Med J (Engl). 2017; 130(9): 1129-1130.
64. Fitzek S, Fitzek C. A myocardial infarction during intravenous recombinant tissue plasminogen activator infusion for evolving ischemic stroke. Neurologist 2015; 20(3): 46-7.
65. Mehdiratta M, Murphy C, Al-Harthi A, Teal PA. Myocardial infarction following t-PA for acute stroke. Can J Neurol Sci. 2007; 34: 417-420. [PubMed: 18062448].
66. Y-Hassan S, Winter R, Henareh L. The causality quandary in a patient with stroke, Takotsubo syndrome and severe coronary artery disease. J Cardiovasc Med (Hagerstown). 2015 Jan;16 Suppl 2 :S118-21.
67. Wang B, Patel H, Snow T, et al. ST-elevation myocardial infarction

following thrombolysis for acute stroke: a case report. West Lond Med J 2011; 3: 7-13.

68. Stafford P J, Strachan C J, Vincent R, Chamberlain D A. Multiple microemboli after disintegration of clot during thrombolysis for acute myocardial infarction. British Medical Journal 1989; 299 :1310.
69. Peng H, Chen M, Li G, et al. Combination refusion therapy for a hemodynamically unstable patient with acute myocardial infarction complicated by acute ischemic stroke within a time window. Int J Cardiol 2015 Dec; 201: 152-153.
70. Chang GY. An ischemic stroke during IV tPA infusion for evolving myocardial infarction. Eur J Neurol 2001; 8: 267-8.
71. O. Kawarada, Y. Yokoi, Brain salvage for cardiac cerebral embolism following myocardial infarction, Catheter. Cardiovasc. Interv. 2010; 75: 679-683.
72. Teddy Arnold Sihite, Michi Astuti Rehmenda Mario Sitepu, Cut Azlina Effendi Review on Acute Cardio-Cerebral Infarction: a Case Report
73. IJIHS. 2021; 9(2): 84-88.
74. ABUHEIT E, Lu F, Liu S, et al. Mechanical thrombectomy for ischemic stroke during Percutaneous Coronary Intervention for Acute Myocardial Infarction in a three- vessel disease patient: a case report and literature review. Research Square; 2022. DOI: 10.21203/rs.3.rs-2044174/v1.
75. Abdi IA, Karataş M, Abdi AE, Hassan MS, Yusuf Mohamud MF. Simultaneous acute cardio-cerebral infarction associated with isolated left ventricle non-compaction cardiomyopathy. Ann Med Surg (Lond). 2022 Jul 16; 80: 104172.
76. de Castillo LLC, Diestro JDB, Tuazon CAM, Sy MCC, Añonuevo JC, San Jose MCZ. Cardiocerebral Infarction: A Single Institutional Series. J Stroke Cerebrovasc Dis. 2021 Jul; 30(7): 105831.
77. Mohammed Habib, Salama Awadallah. Acute Ischemic Stroke Followed by Acute Inferior Myocardial Infarction. Tech Neurosurg Neurol. 5(3). TNN. 000612. 2022.
78. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al; American Heart Association Stroke Council. 2018 Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2018; 49: e46-e110.
79. Eivind Berge et al. European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke. European Stroke Journal 2021 http://dx.doi.org/10.1177/2396987321989865.
80. Borja Ibanez et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. European Heart Journal. 2018; 39: 119-177.
81. Trina Priscilla Ng, Chloe Wong, Evangeline Li En Leong et al. Simultaneous Cardio-Cerebral Infarction — A Meta-Analysis. QJM. 2022 Jun 7; 115(6): 374-380.