

Treatment Of Concurrent Cardio-Cerebral Infarction: Meta-Analysis

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ABSTRACT

Background: The synchronous occurrence of acute ischemic stroke and acute myocardial infarction is an extremely rare condition that can be lethal. The causes and optimal treatment in these cases is still unclear.

Methods: We conducted on the literature review, we analyzed clinical presentations, causes, type of myocardial infarction, site of stroke, modified ranking scale at discharge and treatment options. We compare mortality rate at hospital discharge and 90 days after discharge between patients with combination intervention treatment (both percutaneous coronary intervention for coronary arteries and mechanical thrombectomy for cerebral vessel) and medical treatment.

Results: We identified 94 cases of concurrent cardio-cerebral infarction from case reports and case series. The mean age was 62.5 ± 12.6 years. Male 58 patients (61.7%). 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% at hospital and 59.5% at 90 days (P value 0.038 and 0.012 respectively)

Conclusion: Concurrent cardio-cerebral infarction prognosis is very poor, without intervention about 25% of patients died before discharge 60% of patients died at 90 days after stroke. Despite only one quarter of patients treated by combination intervention treatment, this treatment modality significantly reduces mortality rate compared medical treatment.

Keywords: *acute stroke, myocardial infarction, percutaneous coronary intervention*

¹ Makale geliş tarihi: 02/03/2024

Makale kabul tarihi: 13/06/2024

Eş Zamanlı Kardiyο-Serebral Enfarktüsün Tedavisi: Meta-Analiz

ÖZET

Amaç: Akut iskemik inme ve akut miyokard enfarktüsünün eş zamanlı ortaya çıkması son derece nadir görülen bir durumdur. Bu vakalarda nedenler ve optimal tedavi hala belirsizdir.

Yöntemler: Literatür taraması yaparak klinik tabloları, nedenlerini, miyokard enfarktüsünün tipini, inme bölgesini, taburculukta değiştirilmiş sıralama ölçeğini ve tedavi seçeneklerini analiz ettik. Kombinasyon müdahale tedavisi (koroner arterler için perkütan koroner girişim ve serebral damar için mekanik trombektomi) ve tıbbi tedavi uygulanan hastalar arasında hastaneden taburcu olurken ve taburcu olduktan 90 gün sonra ölüm oranlarını karşılaştırıyoruz.

Bulgular : Vaka raporlarından ve vaka serilerinden 94 eş zamanlı kardiyο-serebral enfarktüs vakasını belirledik. Ortalama yaş 62, 5±12, 6 yıl idi. 58 hasta (%61,7) erkek. Kombinasyon müdahaleli tedavi grubundaki hastalarda: hastane mortalite oranı %13, 3 ve 90 günlük mortalite oranı: tıbbi tedavide ki mortalite oranıyla karşılaştırıldığında %23,5 (hastane de %23,5 ve 90 gün de %59,5 (sırasıyla P değeri 0,038 ve 0,012)

Sonuç: Eş zamanlı kardiyο-serebral enfarktüs prognozu çok kötü olup, müdahale edilmezse hastaların yaklaşık %25'i taburcu olmadan kaybedilmiştir. Hastaların %60'ı inmeden 90 gün sonra ölmüştür. Hastaların yalnızca dörtte birinin kombinasyon müdahale tedavisi ile tedavi edilmesine rağmen, bu tedavi yöntemi, tıbbi tedaviye kıyasla mortalite oranını önemli ölçüde azaltmaktadır.

Anahtar Kelimeler: Akut inme, miyokard infarktüsü, perkütan koroner girişim (PKG), mekanik trombektomi (MTE), modifiye sıralama ölçeği (mRS)

INTRODUCTION

Synchronous occurrence of Acute ischemic stroke (AIS) and ST elevation or non-ST elevation acute myocardial infarction (AMI) are very rare medical emergency conditions and may be lethal (1). Both conditions have a narrow treatment time-window. The use of intravenous thrombolytics for acute myocardial infarction(AMI) can be increase the risk for intracranial bleeding (2-3), also the use of a thrombolytic in patients with history of recent ST elevation myocardial infarction (after 6 hours of stating AMI) for treatment of acute ischemic stroke (AIS) increases the risk of cardiac wall rupture and mortality (4).

Global Registry of Acute Coronary Event (GRACE) trial suggested that, the incidence of intra-hospital acute ischemic stroke was 0.9% in patients presenting with acute coronary syndrome, and the incidence was much higher among patients with ST elevation myocardial infarction than the non-ST elevation myocardial infarction (5).

Multiple metanalysis suggested primary PCI reduce mortality compared with thrombolytic treatment among patients with ST elevation myocardial infarction. (6)

Also the shorter time of reperfusion was directly associated with a higher probability of functional independence after Mechanical thrombectomy (MTE) for patients with acute ischemic stroke (7). In 2015 several randomized trials showed the superiority of MTE combined with thrombolytics for stroke patients with a large vessel occlusion.

Until now no trial was found to compare the benefit of PCI and MTE over medical treatment for patient with co-incidence of AMI and AIS. The present Review analyzed the comparison between combination intervention strategy versus medical treatment in these cases.

METHODS

Study design and Patient selection

In this Review, we screened retrospective a comprehensive analysis of five databases, PubMed, Embase, Scopus, Research Gate and Google Scholar on concurrent or simulations and synchronous Cardio-cerebral infarction to locate all case report or case series done on this topic (Figure 1).

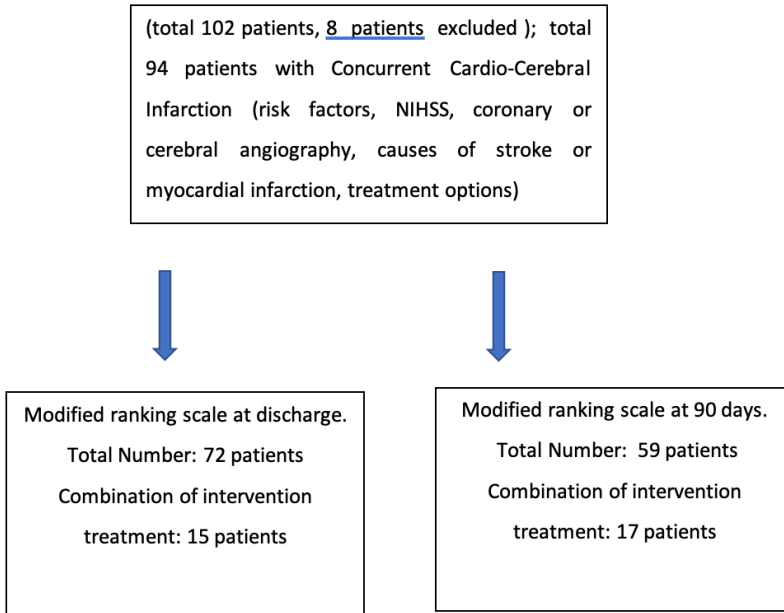


Figure 1 flowchart summarizing case report selection

Inclusion criteria

We analyzed all the cases of concurrent or synchronous cardiocerebral infarction (The occurrence of acute ischemic stroke and acute myocardial infarction either at the same time or one after the other within 12 hours) from first symptoms to first medical contact.(8-76)

Exclusion criteria

The occurrence of two conditions of acute ischemic stroke and acute myocardial infarction one after the other more than 12 hours

Definitions of concurrent cardio-cerebral infarction:

The occurrence of first sign of acute ischemic stroke and first sign of acute myocardial infarction either at the same time or one after the other within 12 hours

Data collection

The following variables were collected: age and sex, medical treatment such as thrombolytics, anticoagulant and antiplatele. Intervention treatment of AMI by percutaneous coronary intervention (PCI) and AIS treatment by mechanical thrombectomy (MTE). antithrombotic medication.

Combination intervention treatment

Combination of intervention treatment for both percutaneous coronary intervention (PCI) for coronary arteries and for mechanical thrombectomy (MTE) for cerebral arteries.

Outcome

1. Calculated the outcome according to modified ranking scale which 0-2: mild disability, 3-5: moderate to severe disability and 6: death at hospital discharge and 90 days after discharge.
2. Comparison of mortality rate during hospital stay and 90 days after discharge between patients with combination intervention treatment and medical treatment.

Statistical analysis

Baseline variables continuous data are reported as means \pm SD. Categorical data are presented as absolute values and percentages. Using the χ^2 , Fisher for calculation mortality rate between patient who treated with combination intervention treatment and medical treatment. Significance level was set at P value < 0.05 . Statistical analysis was performed with SPSS Statistics, Version 23.0.

RESULTS:

Patient Characteristics

Total 94 cases were analyzed, the mean age 62.5 ± 12.6 years. Female 36 patients (38.3%), male 58 patients (61.7%). The median time between stroke and myocardial infarction was 0.5 hour (0-12 hours).

Table 1- Baseline characterizes of patients

Risk factors:	N (%)
Hypertension	45 (46.8%)
Diabetes mellitus	26 (27.7%)
Previous stroke	11 (11.5%)
Smoker	19 (19.8%)
History of Coronary artery disease	13 (13.5%)
Dyslipidemia	22 (22.9%)
Stroke severity NIHSS (median)	15 (1-30)

The resting ECG findings were reported in table 2

Table 2 -Resting ECG findings in the patients:

Resting ECG findings	N (%)
Anterior ST segment elevation	37 (38.5%)
Inferior wall St segment elevation	27 (28.1%)
Non-ST elevation myocardial infarction	20 (20.8%)
Inferior ST elevation and Right ventricle infarction	5 (5.2 %)
High Lateral ST elevation Myocardial infarction	2 (2.0%)
Non-Reported	5 (5.2%)
Atrial fibrillation	21 (21.9%)

Culprit stenosis in cranial arteries in angiography findings suggested culprit intracranial artery in (Table 3).

Table 3 - Culprit stenosis in cranial arteries

Target cranial artery	N (%)
Middle cerebral artery	Right 19 (19.8%), Left 30 (31.2%)
Basilar artery	10 (10.4%)
Internal carotid artery	Right 7(7.3%), Left 5 (5.2%)
Non reported	17 (17.8%)
No stenosis	4 (4.2 %)
Anterior cerebral artery	1 (1 %)
Left common carotid artery	2 (2.1%)
Right vertebral artery	1(1%)

Treatments in concurrent cardio-cerebral Infarction Patients

1-Drug Medication:

1. Thrombolytics: intravenous t-PA 42 patients (44.7%) and one patient Tenecteplase.
2. Antiplatelet treatment was reported in 69 (73%) patients and not reported in 25 (27%) patients.
3. Anticoagulation; 4 (4.2%) patients (1 Novel oral anticoagulation and 3 warfarin) .
4. Combination of dual antiplatelet and anticoagulation: 26 (27.7%) patients (5 patients; Novel oral anticoagulation and 21 patients' warfarin),

5. combination of single antiplatelet and anticoagulation: 5 (5.3%) patients (3 warfarin and 2 Novel oral anticoagulation).

2-Interventions of procedures:

1. 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%).
2. Mechanical thrombectomy of cerebral vessels in 24 patients (25.5%).

3- Combination of intervention treatment.

Only 21 (22.3%) were treated by both PCI for coronary arteries and Mechanical thrombectomy of cerebral vessels.

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. (Table4)

Table 4 - Modified ranking scale (mRS) outcomes at hospital discharge and at 90 days after cardio-cerebral infarction:

Modified ranking scale	At hospital discharge 72 patients (%)
Mild disability	32 (44.4%)
Moderate – severe disability	16 (22.3%)
Death	24 (33.3%)
Modified ranking scale	At 90 days after discharge 59 patients (%)
Mild disability	22 (37.3%)
Moderate – severe disability	8 (13.5%)
Death	29 (49.2%)

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 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%). Treatment with mechanical thrombectomy of cerebral vessels in 21 patients (100%). (Table 5).

Table 5 - The outcome of patients with combination intervention treatment

Modified ranking scale	At hospital discharge 15 patients (%)
Mild disability	6 (40%)
Moderate – severe disability	7 (46.7%)
Death	2 (13.3%)
Modified ranking scale	At 90 days after discharge 17 patients (%)
Mild disability	7(41%)
Moderate – severe disability	6 (35 %)
Death	4 (23.5%)

Comparison 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 during hospital stay (P:038) and at 90 days after discharge (P:0.012). 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 6).

Table 6 - Mortality rate between combination intervention treatment and medical treatment

	Combination intervention (Death/total patient), %	Medical treatment (Death/total patient), %	P value
Mortality during hospital stay	(2/15),13.3%	(22/57) 38.6%	0.038
Mortality 90 days after discharge	(4/17), 23.5%	(25/42)59.5%	0.012

DISCUSSION

The mortality rate was 33.3% at hospital discharge and at 90 days the mortality rate was (49.2%). Only 21 (22.3%) were treated combination by both PCI for coronary arteries and Mechanical thrombectomy of cerebral vessels. The main concerns about giving alteplase to patients with AIS and history of recent MI are divided into 3 items.

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%. Lennie Lynn C. de Castillo et al, in case series involved 9 patients with concurrent CCI reported mortality rate 45% (8), In another metanalysis of 44 patients, ten patients (23%) died (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). To the best of our knowledge, this is the largest meta-analysis, on the concurrent cardio cerebral infarctions, encompassing of

94 patients. The combination intervention (PCI and MTE) treatment was significantly reduce mortality.

CONCLUSION

The occurrence of concurrent cardio cerebral infarction is rare with high risk of mortality and disability rate especially. The intervention with PCI and MTE was significantly reduces the mortality rate. Further studies will need to examine the optimum treatment strategies

Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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