

Comparative Analysis of Early and Late Angiography Post - Fibrinolysis in ST - Segment Elevation Myocardial Infarction Patients

Dr. Sricharan Theja Nalisetty¹, Dr. Kannan Radhakrishnan MD DM², Dr. Raghothaman Sethumadhavan³,
Dr. Suresh Kumar Ponnusamy⁴, Dr. Velmariappan Esakkimuthu⁵

¹Senior Resident, Department of Cardiology, Government Chengalpattu Medical College and Hospital, Tamil Nadu, India
Corresponding Author Email: [drrsricharantheja\[at\]gmail.com](mailto:drrsricharantheja[at]gmail.com)

²Associate Professor, Department of Cardiology, Government Chengalpattu Medical College and Hospital, Tamil Nadu, India

³Assistant Professor, Department of Cardiology, Government Chengalpattu Medical College and Hospital, Tamil Nadu, India

⁴Assistant Professor, Department of Cardiology, Government Chengalpattu Medical College and Hospital, Tamil Nadu, India

⁵Assistant Professor, Department of Cardiology, Government Chengalpattu Medical College and Hospital, Tamil Nadu, India

Abstract: *Aims and objectives: To compare the major cardiovascular events (MACE) and other cardiac side effects during in hospital care and to compare clinical outcome profile. To study and compare the complications and functional improvement of heart. Methods: Data collected retrospectively from department records. This study included all patients presented with ST elevation Myocardial infarction who were successfully fibrinolysed. Patients with failed fibrinolysis, unstable angina and elective procedure patients were excluded. They were grouped into early angiography (n=49) and late angiography (n=64) based on time duration after fibrinolysis. Retrospective data analysis done by comparing objectives of the study between both the groups. Results: The mean age of population was 55±8.68. The baseline characteristics like demographics and comorbidities were comparable between both the groups. Physiological status, mechanical and electrical complications of acute myocardial infarction (AMI) at presentation were not significantly different. Laboratory parameters also comparable. Re - infarction occurred in 1 (2%) patient in group A and 2 (3%) patients in group B with P value 0.58. Death occurred in 1 (1.5%) patient in group B and none in group A with p value 0.61. Recurrent MI, readmission and cardiac function status at 30 days period was also statistically insignificant between two groups. Conclusions: In patients presented with STEMI after successful fibrinolysis, both early angiography (within 24hours) and late angiography has similar incidence of MACE. Improvement in cardiac function and complications during hospitalisation are comparable between late and early angiography following successful lysis.*

Keywords: Acute myocardial infarction, Early coronary angiography, Fibrinolysis, Late coronary angiography, ST elevation myocardial infarction

1. Introduction

Acute Myocardial infarction (AMI) is one of the most important cardiovascular events and is responsible for significant mortality and morbidity in India. India has a higher relative incidence of ST - segment elevation myocardial infarction (STEMI) compared to Western countries. The diagnosis of STEMI is based on symptoms, signs and 12 - lead electrocardiogram (ECG). A history of Coronary artery disease and radiating pain in the neck, jaw, or upper arm are the symptoms suggestive of AMI. Atypical symptoms are shortness of breath, nausea/vomiting, weakness, palpitations or fainting. Access to STEMI treatment in India has been delayed by several factors, including a lack of information on PCI facilities [1, 2]. The reperfusion strategies are primary PCI and timely thrombolysis. [2]

Thrombolysis is an effective method of treatment in patients diagnosed with STEMI and unable to undergo PCI on time. According to the latest ESC guidelines, it is recommended to be done within 12 hours of the onset of symptoms. If thrombolysis fails or symptoms persist or there is hemodynamic/electrical weakness, rescue PCI is performed

[1]. On the other hand, after successful treatment with fibrinolysis, early PCI within 3 - 24 hours of onset of symptoms is recommended [2].

There are many trials comparing pharmacolysis and primary PCI as primary revascularization strategy [3 - 9]. An ideal time interval from completion of fibrinolysis to PCI has not been established.

A meta - analysis of large trials found a time delay from 1.7 hours to 17 hours. A review of six RCTs found that delay to fibrinolysis was not a predictor of death/re - infarction at one year and recurrent ischemia at 30 days, but latency to symptom onset was death [8, 10 - 12]. In 2017, the European Society of Cardiology (ESC) recommended a delay of 2 - 24 hours from fibrinolysis to angiography [2]. However, in a place like India where there is limited access to medical care and many delays and less number of 24hours working cath lab facility, there is still a need to define the time from completion of fibrinolysis to angiography. There is less research in this area in the Indian subcontinent.

With this background, we designed a retrospective cross-sectional study to compare routine early angiography (2 - 24 hours) and late angiography (24 - 72 hours)

2. Material and Methods

A retrospective cross-sectional study was conducted among patients who presented in STEMI to emergency room in a tertiary care hospital in southern part of India during study period from Jan 2022 to June 2022. Institutional Ethical committee approval obtained.

Enrolment Criteria

Retrospective comparative study

Study period: 6 months (January 2022 to June 2022)

Study place: Department of cardiology, Chengalpattu government medical college

Study population: Patients aged above 18 years who had STEMI

Inclusion criteria:

Following successful fibrinolysis

All consecutive STEMI patients in whom fibrinolysis was successful and undergone angiography.

- 1) Early angiography group includes those patients who underwent angiography within 3 - 24 hours
- 2) Late angiography group includes STEMI patients who underwent angiography from 24 - 72 hours

Exclusion criteria:

- 1) Failed fibrinolysis, unstable angina and elective procedure patients
- 2) Patient who has not undergone angiography after pharmacolysis

Definitions

STEMI:

- 1) New onset J - point ST - elevation in two contiguous leads with the cut - point of ≥ 1 mm in all leads other than V2 - V3.
- 2) In V2 and V3 cut off point of ≥ 2 mm in men ≥ 40 years; ≥ 2.5 mm in men < 40 years, or ≥ 1.5 mm in women irrespective of age

Presence of LBBB (left bundle branch block): Based on Smith - Sgarbossa criteria

- Concordant ST elevation more than 1 mm in leads with positive QRS complex
- Concordant ST depression more than 1 mm in V1 - V3
- Discordant ST elevation more than 5 mm in leads with negative QRS complex [13]

Sample Size -

Based on a previously published study on timing of coronary angiography (CAG) following successful thrombolysis [14], the sample size was calculated

$$N = Z^2 p (1 - p) = 1.96 \times 1.96 \times 71.4 \times 28.6 = 38.47 + (10\%) = 38 + 4 = 42$$

$$l^2 7.14 \times 7.14$$

which yields a **sample of 42** which is similar to the past previous year's admissions in our hospital. Hence we have kept it as a sample for the study.

3. Study Methodology

Data from hospital records of all the patients aged above 18 years who were admitted to our emergency room with STEMI from Jan 2022 to June 2022 and were analyzed retrospectively after obtaining consent and enrolled in the study.

After enrollment, subjects were compared based on time delay from fibrinolysis to angiography as early CAG and late CAG. Primary and secondary objectives were compared between the two groups. Baseline variables were recorded. Primary objectives i. e. major adverse cardiovascular events (MACE) and other cardiac side effects during in hospital care and clinical outcome profile among both groups were compared. Secondary objectives are also compared in the form of re - admission within 30 days after discharge and improvement in cardiac function during follow up. All outcome measures were entered in the study proforma for all enrolled subjects.

History details, Clinical examination Details, Blood Examination Details, Electrocardiogram, Echocardiography, Coronary angiography, Treatment Details were also recorded

Each enrolled subject was followed until discharge and were advised about the compliance of medications and were taught to recognize symptoms early. Patients were followed at regular visits at cardiology OPD and enquired regarding any coronary artery disease symptoms. Those who did not come for follow up for 30 days, telephonic call was made, and the details recorded.

Statistical analysis

Microsoft excel spreadsheets for data entry and SPSS version 22 software for statistical analysis. Categorical information is presented in the form of frequency and proportion. Chi - square test or Fischer test (for 2x2 tables only) was used as statistical significance test for qualitative data. Continuous data are presented as mean and standard deviation. Independent t - test or Mann Whitney U - test were used as significance tests, respectively, to determine the difference between two variables in terms of quantity and quality. Graphical presentation by using bar and line charts. A p value of < 0.05 (probability of true result) was considered significant after considering all the rules of the test.

Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA)

4. Results

A total of 113 patients were included in the study. Among them, there are 49 patients underwent early angiography and 64 patients underwent late angiography.

Baseline Characteristics

Median age in both groups was 54 years. Male population constituted 75.51% in early CAG group and 70.31% in late CAG group. All base line characteristics like age, sex distribution, weight, duration of chest pain prior to ER visit, mean needle time (early CAG: 7.51 ± 3.22 h and late CAG: 7 ± 3.01 h; $p = 0.38$), type of STEMI, number of patients undergone PTCA, complications of MI at presentation and co - morbidities were comparable between both early and late angiography groups with no significant difference statistically (Table 1).

Comparison of outcome variables

Major Adverse Cardiovascular Events (MACE) in the form of all - cause mortality (2.08 vs.0; $p = 0.406$), re infarction (4.08% vs.3.13%; $p = 0.487$), and stroke were compared between both the groups (fig.1). No significant difference noticed between them. Secondary outcome measures like readmission within 30days of discharge (early CAG Group: 2.04% vs.3.13%; late CAG; $p = 0.48$) and left ventricular function (fig 2) at review were also not statistically different. (Table 2).

5. Discussion

Current study showed that following successful fibrinolysis performing CAG within 3 - 24 hours or 24 - 72 hours did not show any difference in the MACE rate and secondary outcome measures. Recent ESC guidelines recommended the time delay of 2 - 24hours for CAG after successful fibrinolysis [2]. In developing nations like India, multiple social factors influence the time delay for treatment of STEMI. S. Guha et al. researched many Indian trials and registries in their latest update [1]. The median time of presentation from symptom onset ranging from 4.5 hours to 13 hours [13 - 19]. In our study mean time of presentation 6.53 ± 3.1 hours. OAT trial revealed comparable long term adverse events of late angiography & PCI from 3 - 28 days and Optimal medical therapy alone in stable patients [20 - 21]. Brave - II study showed PCI from 12 - 48hours decreased infarct size significantly [6]. The recommendation of existing guidelines and previous studies have shown that a good number of patients did not perform CAG within 24 h. Costa C et al. showed coronary intervention done after 24 hours, which was outside the frame of recommended guidelines, did not show increased mortality [24].

NORDISTEMI, GRACIA - 2, TRANSFER - AMI, a few studies focused on pharmaco - invasive therapy compared to standard therapy. In these trials it was proved that transfer for PCI is better than conservative management [9, 10&12]. WEST, FAST - AMI, STREAM trials compared early routine PCI with Primary PCI [8&25 - 26]. However to the best of our knowledge, there is limited research on patients who were presented after 24 hours of fibrinolysis to the PCI facilitated health care unit.

Kilic S et al. in their prospective observational study, feizi B et al. in their cohort study and sharma et al. in their prospective observational studies tried to compare the relation of MACE rate and time delay from fibrinolysis [14, 29].

Our Study compared early angiography and revascularization (3h to 24h) with late angiography and revascularization (24h - 72 h). Time interval groups were comparable to study by sharma et al. even though ours is a retrospective comparative study where as Kilic S et al. grouped the study population into 24 - 72h and >72 h, Feizi et al. grouped the study population into CAG done less than 48h and more than 48hours. Similar to above studies in our study it was found out that time delay more than 24 hours did not result in increased MACE, re hospitalization or decrease in LV systolic function (table.3)

6. Conclusion

Our Study did not show any MACE, increased re - admission with delay of PCI more than 24 hours. We suggest to consider our study as a preliminary observation and supporting the need of conducting more qualitative and quantitative studies to re - define the time targets for routine PCI strategy in Indian population in the following settings as recommended in ESC guidelines in 2017.

- 1) Patients presenting late after symptom onset (12 - 48 h)
- 2) Patients presenting after 48 hours
- 3) Time delay for start of fibrinolysis to angiography

7. Limitations

Our study is a single centered, short duration and a retrospective design with limited supportive evidence

References

- [1] Guha S et al. Cardiological Society of India: Position statement for the management of ST elevation myocardial infarction in India. Indian Heart Journal 69 (2017) S63–S97. [doi: 10.1016/j.ijcha.2018.10.006](https://doi.org/10.1016/j.ijcha.2018.10.006)
- [2] Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli - Ducci C, Bueno H, Caforio ALP, et al. 2017 ESC Guide lines for the management of acute myocardial infarction in patients presenting with ST - segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST - segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018; 39 (2): 119 - 177
- [3] Helal AM, Shaheen SM, Elhammady WA, Ahmed MI, Abdel - Hakim AS, Allam LE. Primary PCI versus pharmacoinvasive strategy for ST elevation myocardial infarction. Int J Cardiol Heart Vasc. 2018 Oct 27; 21: 87 - 93. doi: 10.1016/j.ijcha.2018.10.006. PMID: 30402534; PMCID: PMC6205251
- [4] Baine KR, Armstrong PW, Zheng Y, Brass N, Tyrrell BD, Lueng R et al. Pharmacoinvasive Strategy Versus Primary Percutaneous Coronary Intervention in ST - Elevation Myocardial Infarction in Clinical Practice. Circulation: Cardiovascular Interventions. 2019; 12: e008059
- [5] Fazel R, Joseph TI, Sankardas MA, Pinto DS, Yeh RW, Kumbhani DJ et al. Comparison of Reperfusion Strategies for ST-Segment-Elevation Myocardial Infarction: A Multivariate Network Meta-analysis.

- [6] Kastrati A, Mehilli J, Schlotterbeck K, Dotzer F, Dirschinger J, Schmitt C, Nekolla SG, Seyfarth M, Martinoff S, Markwardt C, et al; Bavarian Reperfusion Alternatives Evaluation (BRAVE) Study Investigators. Early administration of reteplase plus abciximab vs abciximab alone in patients with acute myocardial infarction referred for percutaneous coronary intervention: a randomized controlled trial. *JAMA*.2004; 291: 947–95
- [7] Di Mario C, Dudek D, Piscione F, Mielecki W, Savonitto S, Murena E, Dimopoulos K, Manari A, Gasparone A, Ochala A, et al; CARESS-in-AMI (Combined Abciximab RE-teplase Stent Study in Acute Myocardial Infarction) Investigators. Immediate angioplasty versus standard therapy with rescue angioplasty after thrombolysis in the Combined AbciximabREteplase Stent Study in Acute Myocardial Infarction (CARESS-in-AMI): an open, prospective, randomised, multicentre trial. *Lancet*.2008; 371: 559–568
- [8] Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, et al; STREAM Investigative Team. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. *N Engl J Med*.2013; 368: 1379–1387
- [9] Fernández-Avilés F, Alonso JJ, Peña G, Blanco J, Alonso-Briales J, López-Mesa J, Fernández-Vázquez F, Moreu J, Hernández RA, Castro-Beiras A, et al; GRACIA-2 (Grupo de Análisis de CardiopatíaIsquémicaAguda) Investigators. Primary angioplasty vs. early routine post-fibrinolysis angioplasty for acute myocardial infarction with ST-segment elevation: the GRACIA-2 non-inferiority, randomized, controlled trial. *Eur Heart J*.2007; 28: 949–960
- [10] Cantor WJ, Fitchett D, Borgundvaag B, Ducas J, Heffernan M, Cohen EA, Morrison LJ, Langer A, Dzavik V, Mehta SR, Lazzam C, Schwartz B, Casanova A, Goodman SG, TRANSFER - AMI Trial Investigators. Routine early angioplasty after fibrinolysis for acute myocardial infarction. *N Engl J Med*2009; 360 (26): 2705–2718.
- [11] Di Mario C, Dudek D, Piscione F, Mielecki W, Savonitto S, Murena E, Dimopoulos K, Manari A, Gasparone A, Ochala A, Zmudka K, Bolognese L, Steg PG, Flather M, CARESS AMI Investigators. Immediate angioplasty versus standard therapy with rescue 3 angioplasty after thrombolysis in the CombinedAbciximabREteplase Stent Study in Acute Myocardial Infarction (CARESS - in - AMI): an open, prospective, randomised, multicentre trial. *Lancet* 2008; 371 (9612): 559–568.
- [12] 2008; 371 (9612): 559–568.
- [13] Bohmer E, Hoffmann P, Abdelnoor M, Arnesen H, Halvorsen S. Efficacy and safety of immediate angioplasty versus ischemia - guided management after thrombolysis in acute myocardial infarction in areas with very long transfer distances. Results of the NORDISTEMI (NORwegian study on DIstrict treatment of ST - Elevation Myocardial Infarction). *J Am CollCardiol* 2010; 55 (2): 102–110.
- [14] Hygesen K, Alpert JS, White HD, Jaffe AS, Katus HA, Apple FS et al. Third universal definition of myocardial infarction. *EurHeart J* 2012; 33 (20): 2551–2567
- [15] Kilic S and Turkoglu K. Timing of Coronary Angiography After Successful Fibrinolytic Therapy in ST - Segment Elevated Myocardial Infarction. *Cardiol Res*.2019 Feb; 10 (1): 34–39
- [16] Negi PC, Merwaha R, Paday D. Multicentre HP ACS registry. *Indian Heart J*. 2015; 07–027
- [17] Iqbal F, Barkataki JC. Spectrum of acute coronary syndrome in North Eastern India a study from a major center. *Indian Heart J*.2013; 68: 128–131.
- [18] Xavier D, Pais P, Devereaux PJ, Xie C, Prabhakaran D, Reddy KS, et al. CREATE registry investigators: treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. *Lancet*.2008; 371 (9622): 1435–1442.
- [19] Mohanan PP, Mathew R, Harikrishnan S, et al. Presentation, management, and outcomes of 25748 acute coronary syndrome admissions in Kerala, India: results from the Kerala ACS Registry. *Eur Heart J*.2013; 34 (2): 121–129
- [20] Prabhakaran D, Yusuf S, Mehta S, et al. Two - year outcomes in patients admitted with non - ST elevation acute coronary syndrome: results of the OASIS registry 1 and 2. *Indian Heart J*.2005; 57 (3): 217–225.
- [21] George E, Savitha D, Pais P. Pre - hospital issues in acute myocardial infarction. *J AssocPhys India*.2001; 49: 320–323.
- [22] Rajagopalan RE, Chandrasekaran S, Pai M, et al. Pre - hospital delay in acute myocardial infarction in an urban Indian hospital: a prospective study. *Natl Med J India*.2001; 14: 8
- [23] Menon V, Pearte CA, Buller CE, Steg PG, Forman SA, White HD, et al. Lack of benefit from percutaneous intervention of persistently occluded infarct arteries after the acute phase of myocardial infarction: time independent: insights from Occluded Artery Trial. *Eur Heart J*2009; 30 (2): 183–191
- [24] Hochman JS, Lamas GA, Buller CE, Dzavik V, Reynolds HR, Abramsky SJ, Forman S, Ruzyllo W, Maggioni AP, White H, Sadowski Z, Carvalho AC, Rankin JM, et al. Occluded Artery Trial Investigators. Coronary intervention for persistent occlusion after myocardial infarction. *N Engl J Med*2006; 355 (23): 2395–2407
- [25] Costa C, Durao D, Belo A, Domingues K, Santos B, Leal M, Investigators of the Portuguese Registry of Acute Coronary S. Coronary angiography after successful thrombolysis - Is the recommended time interval of 24h an important issue? *Int J Cardiol*.2016; 222: 515 - 52
- [26] Danchin N, Puymirat E, Steg PG, Goldstein P, Schiele F, Belle L, Cottin Y, Fajadet J, Khalife K, Coste P, Ferrières J, Simon T, on behalf of the FAST - MI 2005 investigators Five - year survival in patients with ST - segment - elevation myocardial infarction according to modalities of reperfusion therapy: the French Registry on Acute ST - Elevation and Non - ST - Elevation Myocardial Infarction (FAST - MI) 2005 Cohort. *Circulation*.2014; 129 (16): 1629–1636. doi: 10.1161/CIRCULATIONAHA.113.005874

- [27] WEST Steering Committee A comparison of pharmacologic therapy with/without timely coronary intervention vs primary percutaneous intervention early after ST - elevation myocardial infarction: the WEST (Which Early ST - elevation myocardial infarction Therapy) Study. *Eur Heart J.*2006 Jul; 27 (13): 1530 - 8. doi: 10.1093/eurheartj/ehl088
- [28] Estevez - Loureiro R, Lopez - Sainz A, Perez de Prado A, Cuellas C, Calvino Santos R, Alonso - Orcajo N, SalgadoFernandez J, et al. Timely reperfusion for ST – segment elevation myocardial infarction: Effect of direct transferto primary angioplasty on time delays and clinical outcomes. *World J Cardiol.*2014; 6 (6): 424 - 433
- [29] Sharma AK, Kumar V, Chaudhary GK, Saran M, Narain VS, Dwivedi SK et al. A comparison of outcomes with adjunctive and delayed routine pharmacoinvasive percutaneous coronary intervention strategy after thrombolysis in patients with ST - elevation myocardial infarction: Experience from a tertiary - care center in India. *Heart India* 2018 Mar; 6 (4): 141 - 147.
- [30] Feizi B, Taghdisil S, Etemadi J, Feizi AH, Asgarzadeh S, Kamal S. Early vs Late Coronary Angiography and Intervention Following Thrombolytic Therapy; a Cohort Study. *Emergency.*2017; 5 (1): e32.

Table 1: Comparison of baseline characteristics

Characteristics	Early CAG (N=49)	Late CAG (N=64)	P
Age (Mean ± SD)	54.53 ± 8.49	58.44 ± 5.5	0.06
Male Gender (percentage)	75.15	70.5	0.53
Duration of chest pain (Mean ± SD)	6.53 ± 3.1	6.27 ± 2.92	0.643
Time to Fibrinolytic therapy (Mean ± SD)	7.51 ± 3.22	7 ± 3.01	0.388
Types of STEMI (percentage)			
AWMI	61.22	51.56	0.305
IWMI	38.78	48.44	
Co morbidities (percentage)			
HTN	44.9	31.25	0.317
T2DM	26.53	31.25	
Hyperlipidemia	4.08	3.13	
HTN and T2DM	16.33	10.94	
Smoking (percentage)	51.02	42.19	0.351
Vessel involved			
Single Vessel Disease	41	50	0.28
Double vessel disease	2	8	
Triple vessel disease	6	6	
Recanalized Vessel	0	0	
PTCA done	81.63	78.13	0.646
LMCA disease	6.12	9.38	0.527
Complications of MI			
Mitral valve rupture	1 (2.04)	3 (4.69)	0.432
Ventricular Septal rupture	0 (0)	1 (1.56)	
Shock	6 (12.24)	7 (10.94)	
Electrical complications	2 (4.08)	1 (1.56)	

Table 2: Comparison of Outcome variables

Variables	Early CAG	Late CAG	P
MACE			0.406
All cause mortality	1 (2.04)	0 (0)	
Re infarction	2 (4.08)	2 (3.13)	
Stroke	0 (0)	2 (3.13)	
EF at follow up	47.49 ± 5.27	46.45 ± 5.35	0.37
Readmission with in 30days	1 (2.04)	2 (3.13)	0.489

Table 3: Comparison with previous studies

Study	Type of study	Place	Defining time	Outcome variables	Results
Sharma AK, <i>et al.</i> 2018	Prospective observational single center study	UP (India)	24 hours	Allcause mortality Reinfarction Hospitalisation	Statistically insignificant
Feizi B, <i>et al.</i> 2017	Cohort Study	Iran	48 hours	Recurrent MI Mortality Bleeding No reflow phenomenon	Statistically insignificant
Our study	Retrospective single center study	TN (India)	24 hours	Allcause mortality Mortality cardiac Stroke Re infarction Hospitalization	Statistically insignificant

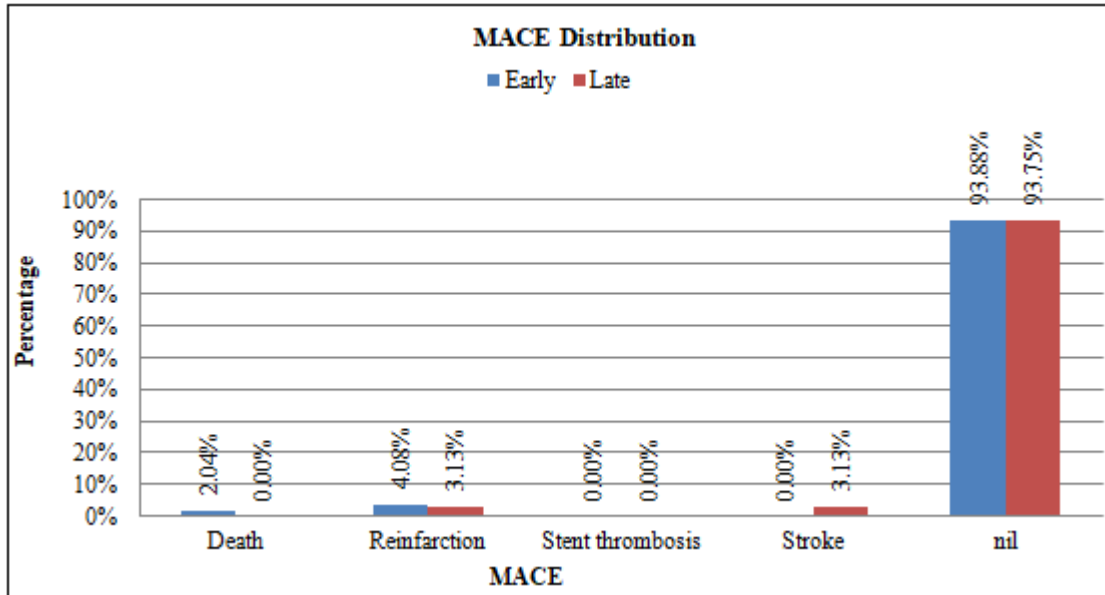


Figure 1

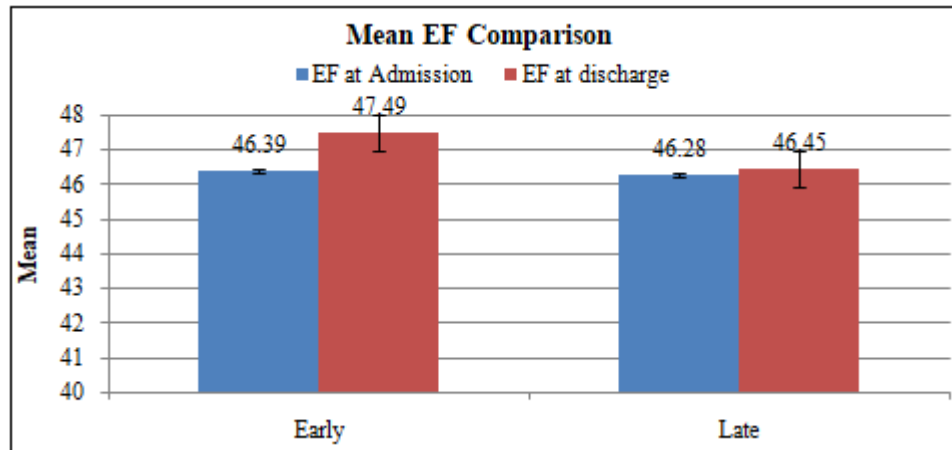


Figure 2