

ST ELEVATION MYOCARDIAL INFARCTION: THROMBOLYSIS IN ANY LOCATION WITH AVAILABLE MEDICATION

INFARTO AGUDO DO MIOCÁRDIO COM SUPRA DE ST: TROMBÓLISE EM QUALQUER LOCAL QUE A MEDICAÇÃO ESTEJA DISPONÍVEL

ABSTRACT

Antonio Cláudio do Amaral
Baruzzi¹
Edson Stefanini^{2,3}
Agnaldo Pispico⁴

1. TotalCor Hospital. São Paulo,
SP, Brazil.
2. Sírio-Libanês Hospital, São Paulo,
SP, Brazil.
3. Paulista School of Medicine (EPM)/
Federal University of São Paulo.
São Paulo, SP, Brazil.
4. Santa Casa de Araras. Araras,
SP, Brazil.

Corresponding Author:
Antonio Baruzzi. TotalCor Hospital.
Al. Santos, 764, São Paulo, SP, Brazil.
abaruzzi@totalcor.com.br

Received on 10/16/2018,
Accepted on 11/20/2018

Cardiovascular events, especially acute myocardial infarction, are the main cause of death in our country. In addition to its physiopathogenesis and the involved risk factors, the 30-day mortality rates vary from 3% to 5% in advanced centers and 30% in those where care does not apply the recommended guidelines. Such change will depend on organizational improvement, as well as patient education, professionals in the emergency department, and harmony with agents in the public or private health system. Primary angioplasty is the gold standard treatment for myocardial reperfusion, but is only available in 15% of hospitals. If it is not available in the public sector, a pharmacoinvasive strategy – fibrinolytic therapy followed by patient transfer for angioplasty – has been recommended. Diagnosis is based on ECG criteria, but there is a shortage of physicians qualified for such confirmation. This delays the treatment and compromises the results. Telemedicine or teleECG allows distant professionals to corroborate with the diagnosis, guide the treatment, and obtain quality and mortality metrics. The rapid identification of patients with signs and symptoms of acute myocardial infarction, immediate diagnosis on ECG, and fibrinolytic administration should not exceed 20 min. They are life-saving minutes dependent on prior organization. Fibrinolytic treatment is the reality for a country with continental dimensions and transport logistic limitations. It is the responsibility of health managers to make them available to the care of patients with infarction.

Keywords: Fibrinolytics; Acute Myocardial Infarction, Reperfusion.

RESUMO

As doenças cardiovasculares, especialmente, o infarto agudo do miocárdio, são responsáveis pela primeira causa de óbito em nosso país. Baseando-se em sua fisiopatogenia e nos fatores de risco envolvidos, a taxa de mortalidade, em 30 dias, varia de 3-5% em centros avançados e quase 30% naqueles cujo atendimento não aplicam as diretrizes recomendadas. Tal mudança dependerá de um aprimoramento organizacional com ações educativas para o paciente, profissionais do setor de emergência e plena sintonia com os gestores do sistema de saúde público ou privado. A angioplastia primária é o tratamento padrão-ouro da reperfusão miocárdica, porém, disponível apenas em 15% dos hospitais. Em geral, o setor público carece dessa disponibilidade, sendo a estratégia fármaco-invasivo - terapia fibrinolítica seguida da transferência precoce para angioplastia – a recomendada. O diagnóstico baseia-se em critérios eletrocardiográficos, porém, nem sempre há médicos habilitados para tal confirmação. Isso retarda o tratamento e compromete bastante os resultados. A disponibilidade da telemedicina ou teleECG permite que profissionais mesmo à distância possam corroborar com o diagnóstico, orientar o tratamento e obter métricas de qualidade e mortalidade. A rápida identificação do paciente com sinais e sintomas de infarto agudo, diagnóstico imediato no ECG e administração do fibrinolítico não devem ultrapassar 20 minutos. São minutos dependentes da prévia organização que salvam vidas! O tratamento fibrinolítico é a realidade para um país com dimensões continentais e sérias limitações logísticas de transporte. Compete aos gestores de saúde disponibilizá-lo a qualquer hora ou momento para o atendimento do paciente infartado.

Descritores: Fibrinolíticos; Infarto Agudo do Miocárdio; Reperusão.

INTRODUCTION

Reperfusion therapy is the main objective in the treatment of ST-segment elevation myocardial infarction (STEMI), based on findings in recent decades.^{1,2}

Fissures in atherosclerotic plaques trigger a series of events that culminate in coronary occlusion. Exposure of thrombogenic substances such as collagen and tissue factors, activates the coagulation cascade, beginning with platelet adhesion and aggregation leading to thrombus formation. This process occurs in seconds and is a primarily vascular event, which has repercussions on the heart muscle.

The wave of necrosis originates from the subendocardial layer, which consumes an elevated amount of energy and spreads to the epicardial region, thus characterizing a transmural myocardial infarction. It usually occurs within a hours of the infarction, depending on factors such as the presence of collateral circulation and the supply/consumption ratio of oxygen through the myocardium.³

The earlier reperfusion therapy (mechanical or pharmacoinvasive procedure) is performed, the smaller the necrotic area and thus the better the prognosis. This disease is the leading cause of death in developed or developing countries.^{4,5} Sudden death observed within the first hour of symptoms is secondary to electrical instability and cardiac arrest due to ventricular fibrillation. Other complications include cardiogenic shock, mechanical dysfunction, heart failure, and complex ventricular arrhythmias.⁶

In some European countries (e.g., France, Portugal, Italy), mortality rates due to infarction have declined in recent decades to as low as 3% to 5%. This reflects the organization of healthcare logistics including pre-hospital care, unified protocols, training, central regulation, and commitment to care.⁷

In our country, the National Association of Private Hospitals, which includes almost 90 hospitals with international quality certification (JOINT Commission), also demonstrates mortality rates between 3% and 5%.⁸ Unlike the nation's reality, the public healthcare system, with some exceptions, lacks diagnostic flowcharts, institutional protocols, central regulation, or professionals who are able to interpret the diagnosis for infarction using electrocardiogram (ECG). In some regions, death rates are at 30%, which is comparable to rates prior to the advent of thrombolysis.⁹ In our context, training for doctors and nurses working in public hospitals that do not have the resources for primary angioplasty but have an organized system to transfer patients to a tertiary hospital after administration of thrombolytic drugs, results in a significant decrease in mortality due to acute myocardial infarction (AMI) and a shorter hospitalization period.¹⁰

In spite of evidence surrounding high quality healthcare, we find that many centers lack equipment in emergency sectors (defibrillator, intubation materials, ventilators, electrocardiographs, vasoactive drugs, cardiac monitors, temporary pacemakers, and fibrinolytic drugs) and coronary units and have a lack of qualified professionals to provide the best treatment.

REPERFUSION TREATMENT

Although primary angioplasty represents the gold standard of reperfusion therapy, due to limited human resources,

there are estimates that only 15% of Brazilian hospitals have a hemodynamic laboratory that is fully available for 24 hours a day, 7 days a week.

If the primary healthcare center has such a facility, it is best to recanalize the artery within 60 minutes of infarction. Compared to fibrinolytic therapy, this procedure results in high recanalization rates (nearly 100%), plaque stabilization with a drug-eluting stent implant, low hemorrhage risk, risk stratification, and safe radial access. Otherwise, considering that the transfer time for primary angioplasty is less than 120 minutes, healthcare professionals should administer fibrinolytic therapy immediately.¹¹

When the fibrinolytic agent is infused within the first 3 hours of the onset of symptoms, mortality rates are similar to that for primary angioplasty. This is particularly relevant for tenecteplase (TNK), a third-generation thrombolytic agent with a high specificity to fibrin linked to thrombus with a long half-life (20 min), and low central hemorrhage risk (0.5%), when doses are non-antigenic, adjusted by weight and age (≥ 75 years), and administered as bolus.¹²

Although the rate of artery recanalization varies from 60 to 70% (TIMI (thrombolysis in myocardial infarction) 3 flow) and is easily accessible and universally practiced, there is a 10% – 20% risk of reocclusion. This means that this strategy is not definitive, as there are limitations concerning recanalization and reocclusion rates.

Given these variables, a combined treatment (pharmacoinvasive procedure) is currently recommended considering fibrinolytic and associated with subsequent percutaneous intervention in centers which not have the resources for primary angioplasty.

Ideally, at the end of fibrinolytic therapy, the patient should be transferred to a hemodynamic center. It is not possible to predict which patients will have positive results or present with reocclusion, or how the state of their conditions will evolve within the next few hours following reperfusion therapy.

One of the main reperfusion criteria is resolution of ST-segment elevation of over 50% within 60 min to 90 min from the onset of infusion. The patient is then referred for angioplasty with a drug-eluting stent implant within two to twenty-four hours.¹³

For patients with little or no resolution of ST-segment elevation who present with persistent pain, signs of hemodynamic or electrical instability, or suspected reocclusion, rescue angioplasty must be immediately performed.

Patients with STEMI require attention and forward planning. Twenty minutes is enough to save lives! The first ten are needed to complete ECG and confirm diagnosis, and the other ten for fibrinolytic infusion. The initial first aid treatment and administration of adjuvant medication for reperfusion therapy are crucial.

TWENTY MINUTES CAN SAVE LIVES!

Treatment for infarction is time-sensitive. Patients must recognize symptoms and seek medical attention immediately at a specialized unit in their area. This requires action by healthcare administrators to generate awareness. The slogan is "The right patient in the right place."

With the right information, there is quicker access to care. The ideal situation is artery recanalization within the first hour

of symptom onset (the golden hour).¹⁴ The benefit of this treatment in reducing mortality declines over the first 12 hours and is borderline between 12 and 24 hours.¹⁵ Based on coronary angiography, if TIMI 3 flow is fully achieved (full artery recanalization), the mortality rate varies from 3% to 4% in 30 days and 7% to 8% for TIMI 0, 1 or 2 flow. In addition to epicardial coronary flow, we should also consider the myocardial flow, which is measured as the time taken for the contrast of the ventricular muscle to clear and is also a prognostic factor. Less time means better epicardial and myocardial perfusion. Therefore, when epicardial flow is equal to TIMI 3 and myocardial flow is equal to TMP 3, the mortality rate in 30 days is less than 3% percent.¹⁶

The dose of tenecteplase is adjusted for weight and age, while the dose of alteplase is adjusted for weight. Along with fibrinolytic therapy, 2 antiplatelet drugs (aspirin and clopidogrel) are given, along with enoxaparin. Clopidogrel and enoxaparin are also adjusted for weight and age. In patients who are 75 years or older, there is an increased risk for hemorrhage, which is the reason for this adjustment.

The double dose of antiplatelet drugs and enoxaparin reduce mortality in fibrinolytic therapy, as observed by improved recanalization rates and fewer incidences of reocclusion. There are not enough studies to support the recommendation of more potent antiplatelet agents when fibrinolytic therapy is applied.

Thus, there is no time to lose. We have 20 minutes between diagnosis and fibrinolytic infusion. Remember: Time is muscle, flow is life. Get organized! (Figure 1)

WHAT IS NECESSARY FOR APPROPRIATE TREATMENT?

Organization, activities to raise patients' awareness, and a multi-professional team in the emergency sector. A health-care system in synchronization with each center's needs is fundamental. (Table 1)

Table 1. Components for treating ST-segment elevation myocardial infarction (STEMI).

Patient
Recognize signs and symptoms (awareness campaigns)
Call for emergency services (in Brazil, SAMU - 192 or)
Head quickly to the Emergency Department in your region
Emergency Department
Immediately identify and attend to the patient with thoracic pain
Perform and interpret ECG in up to 10 min
Administer aspirin, clopidogrel, and enoxaparin
Administer fibrinolytic agent (rule out contraindications) in 10 min
Transfer patient to referral center after fibrinolytic treatment
Verify resolution (reduction ≥ 50 of ST-segment elevation) 60'-90 min after beginning fibrinolytic treatment
- If $\geq 50\%$: transfer for angioplasty within 2-24 hours
- If $< 50\%$ or reocclusion: rescue angioplasty (urgent care)
Fill out the Checklist Form
Fill out the Transfer Form
Previously contacted Referral Center
Ensure transfer safety
Healthcare System
Raise patients' awareness to recognize symptoms of infarction through media
Population aware of location for specialized care
Ensure human resources and equipment work properly
Disclose and post healthcare and treatment flow charts
Provide ICU ambulance
Periodically train professionals in the emergency sector
Collect healthcare quality markers/indicators
Facilitate counter-referral (patient returns to originating center after angioplasty)

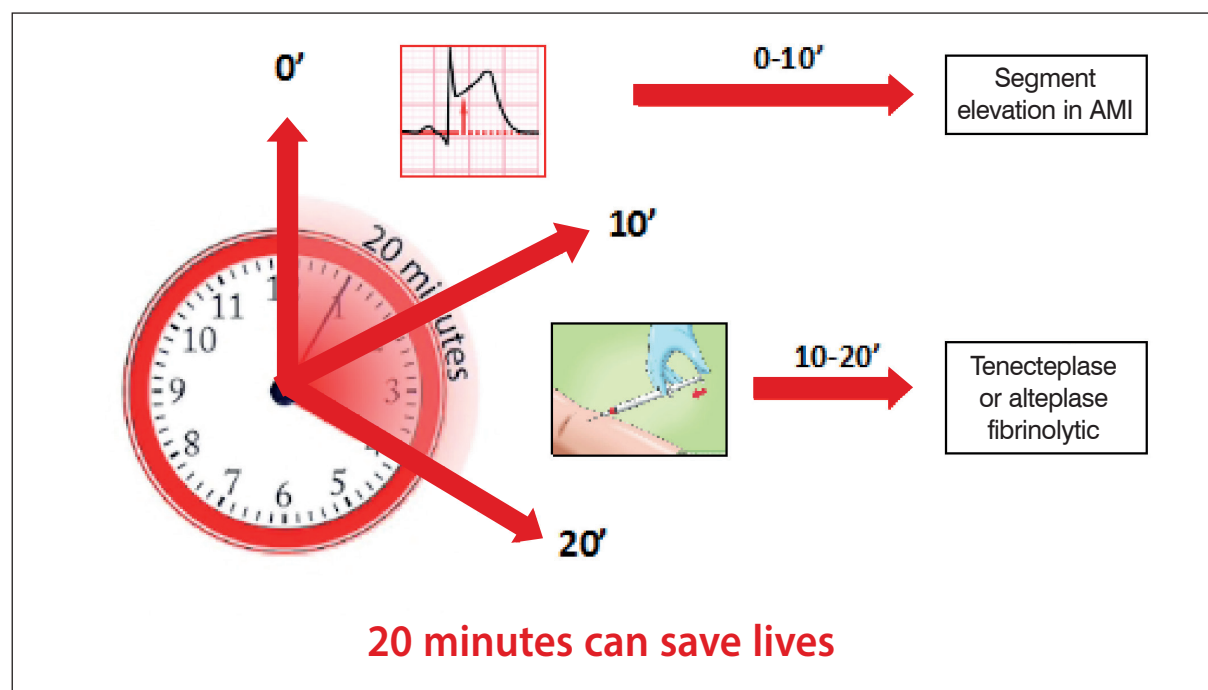


Figure 1. Fibrinolytic therapy in STEMI. Ten minutes for electrocardiographic diagnosis and another ten to administer fibrinolytic agent.

Flow charts (Annexes 1 and 2)

- A. Centers without a hemodynamic laboratory or with a transfer time ≥ 120 min:
1. Immediate care for patient with thoracic pain, electrocardiographic diagnosis within 10 min of admission.
 2. Administer "Fibrinolysis kit": aspirin, clopidogrel, enoxaparin, fibrinolytic agent (tenecteplase or alteplase) in the subsequent 10 min. Respect their contraindications.
 3. Transfer the patient for angioplasty within 2 to 24 hours after diagnosis if resolution of ST-segment elevation is $\geq 50\%$ (ECG taken 60-90 min after beginning fibrinolytic infusion)
 4. Rescue angioplasty (urgent care) when there is no resolution $\geq 50\%$ for ST-segment elevation and the patient presents with persistent pain, and electrical or hemodynamic instability.
 5. Fill out the Checklist and Transfer Forms (Annexes 3 and 4).
 6. Ensure patient safety in the ambulance and in the ICU.
 7. Facilitate counter-referral (patient returns to originating hospital).
- B. Centers with a hemodynamic laboratory or transfer time < 120 min:
1. Administer double antiplatelet therapy: aspirin + clopidogrel or aspirin + ticagrelor or aspirin + prasugrel.
 2. Transfer the patient for angioplasty in 120 min. Avoid passage through emergency department once diagnosis is made.
 3. Primary angioplasty < 60 min in centers with a hemodynamic laboratory
 4. Administer unfractionated heparin in the hemodynamic room.
 5. Prefer radial access, drug-eluting stent.
 6. Fill out the Checklist Form.

Fibrinolysis kit

It aims to expedite care for the patient with STEMI. It is administered within 10 min of electrocardiographic confirmation and is available for immediate administration. (Table 2)

Tenecteplase is a molecule derived from alteplase and comes with the advantage of bolus administration, a longer half-life, lower hemorrhage risk, and greater fibrin specificity, according to next article.

Table 2. Fibrinolysis kit.

Medication	Dose
100 mg Aspirin	2 chewable tablets
75 mg Clopidogrel	< 75 years – 4 tablets ≥ 75 years – 1 tablet
Enoxaparin	< 75 years – 30 mg IV + 1 mg/Kg SC 12/12h ≥ 75 years – 0.75 mg/Kg SC 12/12h
Tenecteplase 40 mg or 50 mg bottles	Rapid infusion (1-2 min.) Total dose = 0.53 mg/kg (bolus) < 60 kg = 30mg, ≥ 60 a 70 kg = 35mg ≥ 71 a 80 kg = 40mg ≥ 81 a 90 kg= 45mg ≥ 91 kg = 50mg For patients ≥ 75 years: administer half the total dose
Alteplase 50 mg bottles	Accelerated infusion (90min.) 15 mg (bolus) + 0,75 mg/kg (30') (maximum 50mg) + 0,5 mg/kg (60') (maximum 35mg) Do not exceed 100 mg

Primary angioplasty kit

Two antiplatelet agents are administered, based on institutional protocol:

1. 200 mg aspirin + 600 mg clopidogrel;
2. 200 mg aspirin + 180 mg ticagrelor; or
3. 200 mg aspirin + 60 mg prasugrel.

In general, the artery affected by infarction is recanalized within 48 hours of its evolved state and extended to 3 days for patients who still present with symptoms, hemodynamic instability, and complex ventricular arrhythmias. In multi-artery cases, the strategy is to offer staged treatment, depending each case's analysis.

Figure 2 illustrates examples of different STEMI scenarios and recommendations according to the European Society of Cardiology's recent guidelines and quality standards.^{17,18}

As for the concomitant use of other medications, the following are recommended:

1. Oxygen – digital O₂ saturation $< 90\%$ or PaO₂ < 60 mmHg;
2. Nitrates - sublingual or systemic if patient presents with precordial pain, pulmonary congestion, if SBP (systolic blood pressure) > 90 mmHg;
3. IV Morphine - 2 mg doses to control pain, pulmonary congestion, and anxiety;
4. Statins - high-potency (atorvastatin or rosuvastatin) to reduce LDL < 70 mg/dL, administered within the first 24 hours of infarction;
5. Angiotensin-converting enzyme inhibitor or angiotensin I receptor blocker—in cases with ventricular dysfunction (EF $< 40\%$), they reduce risk of death and hospitalization;
6. Beta blocker: indicated for patients with LVEF (left ventricular ejection fraction) $< 40\%$, reduces risk of death, recurrence of infarction, and hospitalization;
7. Spironolactone - indicated when LVEF $< 40\%$, reduces risk of hospitalization and death. Avoid in patients with renal dysfunction and hyperkalemia;
8. Change habits, quit smoking.

After treatment, the patient remains under cardiac monitoring in the coronary unit for the first 24 hours. Patients without complications receive early hospital discharge.

CONCLUSION

Reperfusion therapy is the main objective in treating ST-segment elevation myocardial infarction. The gold standard of treatment is primary angioplasty, but it is not always available, especially in the public healthcare system. In these cases, pharmacoinvasive treatment is recommended, wherein the administration of the fibrinolytic agent is quick, and the patient is transferred to a center with a hemodynamic laboratory.

An electrocardiographic diagnosis should be performed within 10 minutes, and two antiplatelet agents, enoxaparin and a fibrinolytic agent, should be administered within the subsequent 10 minutes; this results in two-thirds of artery recanalization.

Twenty minutes can save lives!

The fibrinolytic agent must be administered irrespective of the location or time when a hemodynamic laboratory is not available.

CONFLICTS OF INTEREST

The author declares that he has no conflicts of interest in this work.

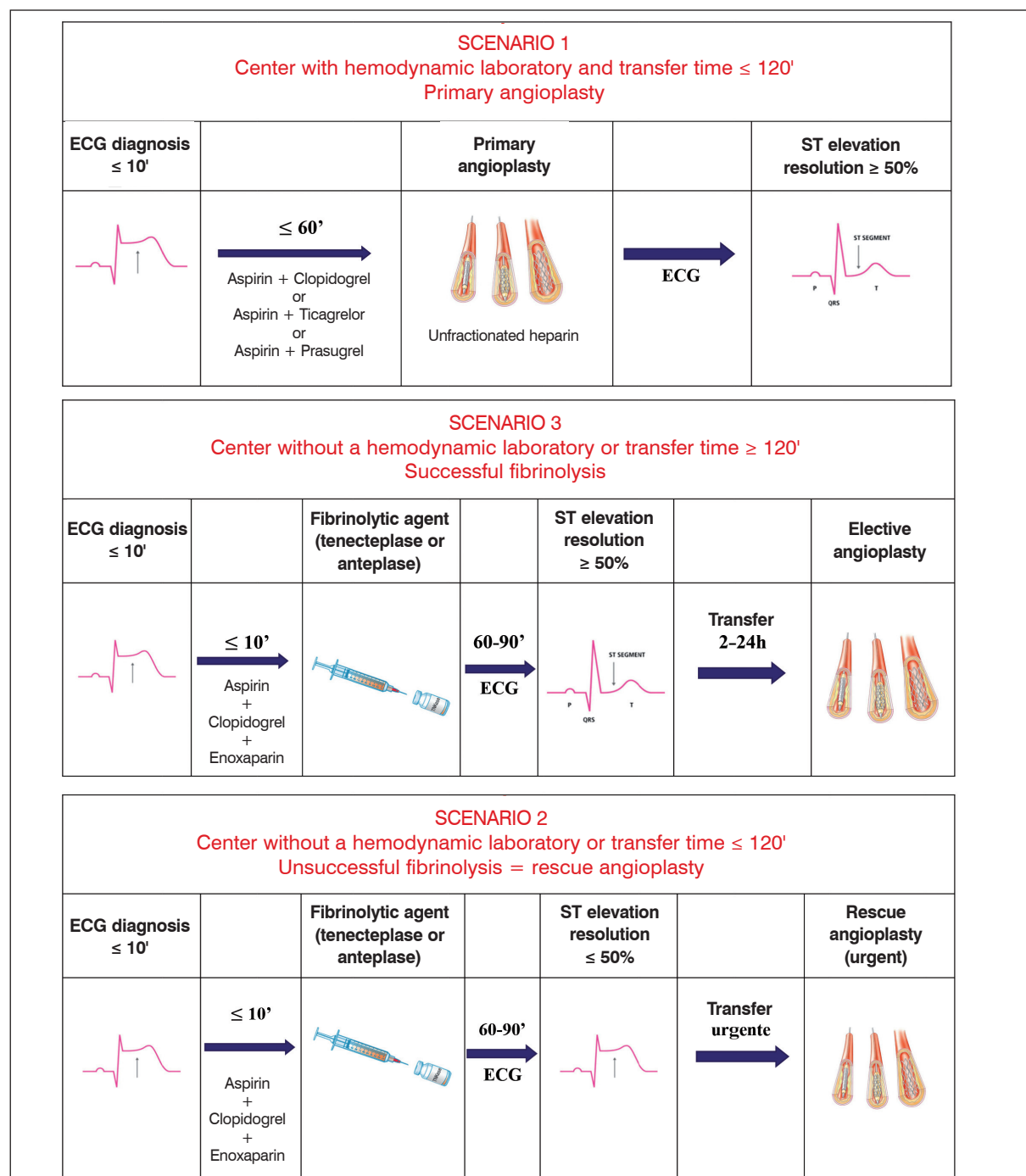


Figure 2.

REFERENCES

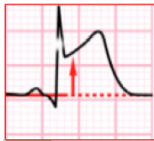
- Van de Werf F. The history of coronary reperfusion. Eur Heart J. 2014;35(37):2510-15.
- Bagai A. Reperfusion strategies in acute coronary syndromes. Cir Res. 2014;114(12):1918-28.
- Crea F, Liuzzo G. Pathogenesis of acute coronary syndromes. J Am Coll Cardiol. 2013;61(1):1-11.
- Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. Circulation. 2015;131(4):e29-322.
- Roth GA, Huffman MD, Moran AE, Feigin V, Mensah GA, et al. Global and regional patterns in cardiovascular mortality from 1990 to 2013. Circulation. 2015;132(17):1667-78.
- Scirica MB, Libby P, Marrow DA. ST-Elevation myocardial infarction: Pathophysiology and Clinical Evaluation. In: Braunwald E. Heart Disease. New York: Elsevier; 2019. p.1055-1120
- Eurostat 2017. Statistics explained. www.ec.europa.eu
- Associação Nacional dos Hospitais Privados – Observatório Anual 2018. www.anap.com.br
- Nabel EG, Braunwald E. A tale of coronary artery disease and myocardial infarction. N Engl J Med. 2012;366(1):54-63.

-
10. Matos LN, Carvalho AC, Gonçalves Jr I e col. Pharmacoinvasive therapy in STEMI patients in emerging countries, different from the developed world, could decrease mortality compared to usual treatment. *JACC*. 2013;61
 11. Feres F, Costa RA, Siqueira D, Costa JR Jr, Chamié D, Staico R, et al. Diretriz da sociedade brasileira de Cardiologia e da Sociedade Brasileira de Hemodinâmica e Cardiologia Intervencionista sobre Intervenção coronária percutânea. *Arq Bras Cardiol*. 2017;109(1 Suppl1):1-81.
 12. Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert y, et al. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. *N Engl J Med*. 2013;368(15):1379-87.
 13. Anderson JL, Morrow DA. Acute myocardial infarction. *N Engl J Med*. 2017;376(21):2053-64.
 14. Boersma E, Maas AC, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *Lancet*. 1996;348(9030):771-5.
 15. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of mortality and major morbidity from all randomized trials of more 1000 patients. Fibrinolytic Therapy Trialists (FTT) Collaborative Group. *Lancet*. 1994;343(8893):311-22.
 16. Bohula E, Morrow DA. ST-Elevation myocardial infarction: Management. In: Braunwald E, Heart Disease. New York: Elsevier; 2019.p.1123-72.
 17. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J*. 2018;39(2):119-77.
 18. Jneid H, Addison D, Bhatt DL, Fonarow GC, Gokak KL, et al. 2017 AHA/ACC Clinical Performance and Quality Measures for Adults with ST-Elevation and Non-ST Elevation Myocardial Infarction: A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. *J Am Coll Cardiol*. 2017;70(16):2048-90.

Annex 1.



- PROJECT INFARCTION -



ACUTE CORONARY SYNDROME WITH ST-SEGMENT ELEVATION PHARMACOAISIVATIVE TREATMENT TENECTEPLASE

INCLUSION CRITERIA

- Beginning of symptoms ≤ 12 hours
- Transfer time for primary angioplasty > 120 min.
- ECG: ST elevation (J point) ≥ 1.0 mm (≥ 2 contiguous derivations)
- In V_2-V_3 derivations, consider ST elevation:
 - Men: ≥ 2.5 mm < 40 years
 - ≥ 2.0 mm < 40 years
 - Women: ≥ 1.5 mm
- LBBB or new RBBB
- ST elevation $V_3R-V_4R = RV$ infarction
- ST elevation $V_7-V_9 \geq 0.5$ mm = dorsal infarction (generally ST depression V_1-V_2)

EXCLUSION CRITERIA

- Any contraindication absolute to tenecteplase

SPECIAL SITUATIONS

(indicate primary angioplasty)

- Symptoms ≥ 12 hours (pain or signs of persistent ischemia)
- Hemodynamic instability (hypotension, shock, pulmonary congestion)
- Complex ventricular arrhythmias
- High hemorrhage risk

TENECTEPLASE INFUSION*

(10 min. after ECG)

< 75 years
200 mg aspirin +
300 mg clopidogrel +
enoxaparin:
(30 mg IV + 1mg/Kg SC
12/12h)

≥ 75 years
200 mg aspirin +
75 mg clopidogrel +
enoxaparin:
(0.75 mg/Kg SC 12/12h)

Tenecteplase
Complete dose

Tenecteplase
50% dose

TENECTEPLASE DOSE (IV bolus)

< 60 Kg = 30mg = 6 ml	80-89 Kg = 45mg = 9 ml
60-69 Kg = 35mg = 7 ml	> 90 Kg = 50mg = 10 ml
70-79 Kg = 40mg = 8 ml	

ST ELEVATION RESOLUTION $> 50\%$ at 60-90 min.?
(after beginning infusion)

Yes

No

ANGIOPLASTY in 2-24h

URGENT ANGIOPLASTY
"RESCUE"



*Ideally, after tenecteplase, refer patient immediately
to Referral Center

FIBRINOLYTIC THERAPY: CONTRAINDICATIONS

ABSOLUTE

- Hemorrhage via CNS
- CNS neoplasm (primary or metastatic)
- Vascular structural lesion in CNS
- Ischemic CVA < 6 months
- Aortic dissection (suspected or confirmed)
- Active bleeding (except menstruation)
- Gastrointestinal bleeding < 30 days
- Puncture or biopsy in non-compressible site (ex.: liver, kidneys, lower back < 24 h)
- Coagulopathies
- TBI and/or face trauma < 30 days
- CNS surgery < 2 months

RELATIVE

- SBP ≥ 180 mmHg or DBP ≥ 110 mmHg - refractory
- Prolonged or traumatic CPR
- Transient ischemic attack ≤ 6 months
- Active peptic ulcer
- Major surgery ≤ 3 weeks
- Pregnancy, abortion, or recent delivery < 7 days
- Oral anticoagulants
- Cocaine: prefer clinical treatment and/or angioplasty
- Endocarditis

HEMORRHAGE RISK FACTORS

- Age ≥ 75 years
- Low body weight (men < 80 Kg, women < 67 Kg)
- Female

INVASIVE PROCEDURE PRIMARY ANGIOPLASTY

- Time ≤ 60 min. in center with hemodynamic lab or
- Transfer time < 120 min.

(200 mg aspirin + 600 mg clopidogrel) or
(200 mg aspirin + 180 mg ticagrelor) or
(200 mg aspirin + 60 mg prasugrel)
+
unfractionated heparin (hemodynamic room)
70-100 IU/Kg IV (maximum 5,000 IU)

CLINICAL

STENT

SURGICAL

AFTER TENECTEPLASE AND TRANSFER DELAY, MAINTAIN

- 100 mg/day aspirin + 75 mg/day clopidogrel + 1mg/kg enoxaparin 12/12h (1 mg/kg/day if $Cl_{Cr} < 30$ ml/min.) until Coronary Angiography or until hospital discharge or until the 8th day if still hospitalized.
- Prasugrel: contraindicated: previous CVA/TIA > 75 years.
Weight ≤ 60 kg = 5 mg/day (special cases)



ACUTE CORONARY SYNDROME WITH ST-SEGMENT ELEVATION PHARMACOAISVATIVE PROCEDURE ALTEPLASE

INCLUSION CRITERIA

- Beginning of symptoms ≤ 12 hours
- Transfer time for primary angioplasty > 120 min.
- ECG: ST elevation (J point) ≥ 1.0 mm (≥ 2 contiguous derivations)
- In V_2-V_3 derivations, consider ST elevation:
 - Men: ≥ 2.5 mm < 40 years
 ≥ 2.0 mm ≥ 40 years
 - Women: ≥ 1.5 mm
- LBBB or new RBBB
- ST elevation V_3R-V_4R = RV infarction
- ST elevation $V_7-V_9 \geq 0.5$ mm = dorsal infarction (generally ST depression V_1-V_2)

EXCLUSION CRITERIA

- Any contraindication absolute to tenecteplase

SPECIAL SITUATIONS

(indicate primary angioplasty)

- Symptoms ≥ 12 hours (pain or signs of persistent ischemia)
- Hemodynamic instability (hypotension, shock, pulmonary congestion)
- Complex ventricular arrhythmias
- High hemorrhage risk

TENECTEPLASE INFUSION*

(10 min. after ECG)

< 75 years
200 mg aspirin +
300 mg clopidogrel +
enoxaparin:
(30 mg IV + 1mg/Kg SC
12/12h)

+

≥ 75 years
200 mg aspirin +
75 mg clopidogrel +
enoxaparin:
(0.75 mg/Kg SC 12/12h)

+

ALTEPLASE

15 mg IV bolus +
0.75 mg/Kg IV 30 min. (at 50 mg) +
0.50 mg/Kg IV 60 min. (at 35 mg)

ST ELEVATION RESOLUTION $> 50\%$ at 60-90 min.?
(after beginning infusion)

Yes



ANGIOPLASTY in 2-24h

No



**URGENT ANGIOPLASTY
"RESCUE"**



*Ideally, after tenecteplase, refer patient immediately to Referral Center

FIBRINOLYTIC THERAPY: CONTRAINDICATIONS

ABSOLUTE

- Hemorrhage via CNS
- CNS neoplasm (primary or metastatic)
- Vascular structural lesion in CNS
- Ischemic CVA < 6 months
- Aortic dissection (suspected or confirmed)
- Active bleeding (except menstruation)
- Gastrointestinal bleeding < 30 days
- Puncture or biopsy in non-compressible site (ex.: liver, kidneys, lower back < 24 h)
- Coagulopathies
- TBI and/or face trauma < 30 days
- CNS surgery < 2 months

RELATIVE

- SBP ≥ 180 mmHg or DBP ≥ 110 mmHg - refractory
- Prolonged or traumatic CPR
- Transient ischemic attack ≤ 6 months
- Active peptic ulcer
- Major surgery ≤ 3 weeks
- Pregnancy, abortion, or recent delivery < 7 days
- Oral anticoagulants
- Cocaine: prefer clinical treatment and/or angioplasty
- Endocarditis

HEMORRHAGE RISK FACTORS

- Age ≥ 75 years
- Low body weight (men < 80 Kg, women < 67 Kg)
- Female

INVASIVE PROCEDURE PRIMARY ANGIOPLASTY

- Time ≤ 60 min. in center with hemodynamic lab or
- Transfer time < 120 min.

(200 mg aspirin + 600 mg clopidogrel) or
(200 mg aspirin + 180 mg ticagrelor) or
(200 mg aspirin + 60 mg prasugrel)
+
unfractionated heparin (hemodynamic room)
70-100 IU/Kg IV (maximum 5,000 IU)

CLINICAL

STENT

SURGICAL

AFTER TENECTEPLASE AND TRANSFER DELAY, MAINTAIN

- 100 mg/day aspirin + 75 mg/day clopidogrel + 1mg/kg enoxaparin 12/12h (1 mg/kg/day if $ClCr < 30$ ml/min.) until Coronary Angiography or until hospital discharge or until the 8th day if still hospitalized.
- Prasugrel: contraindicated: previous CVA/TIA > 75 years.
Weight ≤ 60 kg = 5 mg/day (special cases)

Annex 3.



ACUTE CORONARY SYNDROME WITH ST-SEGMENT ELEVATION

PROJECT INFARCTION
SOCESP

CHECKLIST FORM

IDENTIFICATION			
Name:		Age:	
Weight (kg):		Height (cm):	
Admission:	Date:	Time:	
Onset of symptoms:	Date:	Time:	

REPERFUSION THERAPY

INCLUSION CRITERIA			
<input type="checkbox"/> Onset symptoms ≤ 12 h			
<input type="checkbox"/> Onset symptoms > 12 h (if pain or signs of ischemia persist)			
<input type="checkbox"/> ST elevation (J point) ≥ 1 mm (≥ 2 contiguous derivations)			
<input type="checkbox"/> In V_2 - V_3 derivations, consider ST elevation: - Men: $\geq 2,5$ mm < 40 anos $\geq 2,0$ mm ≥ 40 anos - Women: $\geq 1,5$ mm		<input type="checkbox"/> ST elevation V_7 - $V_9 \geq 0,5$ mm = dorsal infarction (verify ST depression V_1 - V_2) <input type="checkbox"/> ST elevation V_2R - V_4R = RV infarction <input type="checkbox"/> LBBB or new RBBB	
ECG DIAGNOSIS			
<input type="checkbox"/> Anterior (V_1 - V_4)		<input type="checkbox"/> Dorsal (V_7 - V_9)	
<input type="checkbox"/> Extended anterior (V_1 - V_6)		<input type="checkbox"/> RV (V_3R - V_4R)	
<input type="checkbox"/> Inferior (D_2 , D_3 , aV_F)		<input type="checkbox"/> Inferior-dorsal (D_2 , D_3 , aV_F) + (V_7 - V_9)	
<input type="checkbox"/> Lateral (D_1 - aV_L) (V_5 - V_6)		<input type="checkbox"/> Inferior-lateral-dorsal	

A. CENTER WITHOUT HEMODYNAMIC LAB AND WITH TRANSFER TIME > 120 min. = FIBRINOLYTIC AGENT

CONTRAINDICATIONS			
ABSOLUTE		RELATIVE	
Prior hemorrhage CNS		SBP > 180 and/or DBP 11 mmHg*	
CNS neoplasm (primary or metastatic)		Prolonged or traumatic CPR	
CNS structural lesion		Transient ischemic attack < 6 months	
Ischemic cerebrovascular accident < 6 months		Major surgery < 21 days	
CNS surgery < 2 months		Endocarditis	
Craniocerebral and/or face trauma < 30 days		Pregnancy, abortion, postpartum < 7 days	
Active bleeding (except menstruation)		Cocaine: prefer primary angioplasty	
Coagulopathies		Oral anticoagulants	
Aortic dissection		Advanced liver disease	
Gastrointestinal bleeding < 30 days		Active peptic ulcer	
Non-compressible puncture site < 24 h (liver, kidneys, lower back)		*No response to antihypertensive drugs	

ADMINISTER FIBRINOLYSIS KIT (up to 10 min. after ECG)			
MEDICATION (only one fibrinolytic option)	Date	Time	
1. 200 mg aspirin oral route (chewable)			
2. clopidogrel oral route (adjusted for age) <ul style="list-style-type: none"> < 75 years = 300 mg ≥ 75 years = 75 mg 			
3. enoxaparin (adjusted for age) <ul style="list-style-type: none"> < 75 years = 30 mg IV + 1 mg/kg 12/12h SC ≥ 75 years = 0.75 mg SC 12/12h 			
4. ALTEPLASE IV (adjusted for weight) 15 mg bolus + 0.75 mg/kg (up to 50 mg) in 30 min. + 0.50 mg/kg (up to 35 mg) in 60 min.			
5. tenecteplase IV bolus (adjusted for weight and age) Attention: ≥ 75 years – administer half the total dose <ul style="list-style-type: none"> < 50 Kg = 30mg = 6mL 60 - 69Kg = 35mg = 7mL 70 - 79Kg = 40mg = 8mL 80 - 89Kg = 45mg = 9mL ≥ 90Kg = 50mg = 10mL 			

TRANSFER PATIENT IMMEDIATELY TO REFERRAL CENTER			
ECG 60-90 min. after beginning fibrinolytic treatment	Date	Time	
• ST elevation resolution ≥ 50%? (perform angioplasty in 2-24h)			
• ST elevation resolution > 50%? (immediate angioplasty = rescue = URGENT CARE)			

B. CENTER WITH HEMODYNAMIC LAB OR TRANSFER TIME ≤ 120 min. = PRIMARY ANGIOPLASTY

ADMINISTER THERAPY KIT (up to 10 min. after ECG)			
TWO ANTIPLATELET AGENTS + UNFRACTIONATED HEPARIN	Date	Time	
1. 200 mg aspirin + 600 mg clopidogrel or			
2. 200 mg aspirin + 180 mg ticagrelor or			
3. 200 mg aspirin + 60 mg prasugrel*			
4. unfractionated heparin (hemodynamic room) 70-100 IU/Kg IV (maximum 5000 IU)			
<ul style="list-style-type: none"> Patient with elevated hemorrhage risk: prefer clopidogrel * Prasugrel – contraindicated: ≥ 75 years, progress. ICVA/TIA. Weight ≤ 60kg = 5 mg (whenever necessary) 			



IMMEDIATE ANGIOPLASTY

Date:

Doctor

Nurse

Annex 5.



ACUTE CORONARY SYNDROME WITH ST-SEGMENT ELEVATION

PROJECT INFARCTION
SOCESP

CHECKLIST FORM

IDENTIFICATION			
Name:		Age:	
Weight (kg):		Height (cm):	
Admission:	Date:	Time:	
Onset of symptoms:	Date:	Time:	

TRANSFER INDICATION	
1. PRIMARY ANGIOPLASTY (symptoms < 12h)	
2. PRIMARY ANGIOPLASTY (symptoms ≥ 12h, persistent pain or persistent signs of ischemia)	
3. ANGIOPLASTY AFTER THROMBOLYSIS (resolution ≥ 50%) – perform in 2-24h	
4. ANGIOPLASTY AFTER THROMBOLYSIS (resolution < 50%) = rescue = URGENT CARE	
5. ANGIOPLASTY SPECIAL SITUATIONS (cardiogenic shock, pulmonary congestion, acute mitral regurgitation, complex ventricular arrhythmias, fibrinolytic contraindication)	
6. ELECTIVE CORONARY ANGIOGRAPHY (evolving infarction)	

ECG DIAGNOSIS – ST ELEVATION			
		Date	Time
1. Anterior (V ₁ - V ₄)			
2. Extended anterior (V ₁ -V ₆)			
3. Inferior (D ₂ , D ₃ , aV _F)			
4. Lateral (D ₁ - aV _L) (V ₅ - V ₆)			
5. Dorsal (V ₇ - V ₉)			
6. Right ventricle (V _{3R} -V _{4R})			

CLINICAL CONDITIONS			
BP (mmHg):	HR (beats/min.)	RR (breaths/min.)	T(°C):
KILLIP-KIMBALL Class:	I	II	III
			IV

ADMINISTERED DRUGS

A. FIBRINOLYSIS KIT					
			Date	Time	
1. 200 mg aspirin oral route (chewable)					
2. clopidogrel oral route					
< 75 years = 300 mg = 4 tablets					
≥ 75 years = 75 mg = 1 tablet					
3. Enoxaparin					
< 75 years = 30 mg IV + 1mg/kg 12/12h SC					
≥ 75 years = 0.75 mg SC 12/12h					
4. tenecteplase* IV bolus (adjusted for weight and age)					
< 50 Kg	30mg	6 ml			
60 – 69 Kg	35mg	7 ml			
70 – 79 Kg	40mg	8 ml			
80 – 89 Kg	45mg	9 ml			
≥ 90 Kg	50mg	10 ml			
*tenecteplase – (syringe = 40 mg or 50 mg = 8 or 10 ml)					
Attention: ≥ 75 years = administer half of total dose					
5. alteplase IV (adjusted for weight)					
15 mg bolus + 0.75 mg/kg (up to 50 mg) in 30 min. + 0.50 mg/kg (up to 35 mg) in 60 min.					
B. PRIMARY ANGIOPLASTY KIT					
			Date	Time	
1. 200 mg aspirin + 600 mg clopidogrel or					
2. 200 mg aspirin + 180 mg ticagrelor or					
3. 200 mg aspirin + 60 mg prasugrel +					
4. unfractionated heparin (hemodynamic room): 70-100 IU/kg IV (maximum 5000 IU)					

DRUGS-DEVICES			
		Date	Time
<ul style="list-style-type: none"> dopamine, dobutamine, norepinephrine, amiodarone, lidocaine CPR, temporary pacemaker, invasive mechanical ventilation 			

Date:

Doctor

Nurse