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ORIGINAL RESEARCH

Pharmacoinvasive strategy versus primary angioplasty in patients with acute ST-segment elevation myocardial infarction

Estrategia farmacoinvasiva versus angioplastia primaria en pacientes con infarto agudo al miocardio con elevación del segmento ST

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Palabras clave:
Infarto agudo al miocardio, trombólisis, angioplastia primaria, terapia farmacoinvasiva.

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ABSTRACT

Background: Primary percutaneous coronary intervention (PPCI) is the treatment of choice for acute ST-elevation myocardial infarction (STEMI). The delays associated with PPCI reduce the benefits of this therapy. To minimize these delays, the pharmacoinvasive strategy (PS) was developed, consisting of applying thrombolytic therapy followed by coronary angioplasty 2 to 24 hours after. **Objective:** To compare the safety and efficiency of PPCI vs PS in STEMI. **Methods:** We included patients with STEMI who had emergency PCI. The primary endpoint was combined major adverse cardiac events (MACE), death, reinfarction, stroke, target vessel revascularization (TVR) during hospitalization. The secondary endpoints were the individual components of MACE, and major bleeding (Bleeding Academic Research Consortium: BARC ≥ 3). **Results:** A total of 400 patients, 263 (65.8%) for PPCI group, 114 (28.5%) for PS group and 23 (5.75%) for diagnostic group. The PS group, 79 (69.3%) were then categorized as systematic angioplasty having had a successful thrombolysis, and 35 (30.7%) were rescue angioplasty because they had a failed thrombolysis. There were no differences in MACE: 13 (9.5%) patients in PS and 27 (10.3%) patients in the PPCI (p = 0.806), there were no differences in the individual components of MACE. The rate of major bleeding was the same, 5 (3.6%) and 4 (1.5%) respectively (p = 0.173). The multivariate analysis did not show a relationship between MACE and the reperfusion strategy. **Conclusions:** The pharmacoinvasive strategy when compared to PPCI has a similar rate of primary and secondary endpoints. There is no increase in major bleeding therefore, it is an important strategy that offers a reperfusion therapy for patients with STEMI in a non-PCI capable hospital.

RESUMEN

Antecedentes: *La intervención coronaria percutánea primaria (ICPP) es el tratamiento de elección en infarto agudo al miocardio con elevación del ST (IAMCEST). El retraso relacionado con ICPP disminuye el beneficio. Buscando una reperfusión oportuna se implementa la estrategia farmacoinvasiva (EFI), que consiste en realizar trombólisis seguido de ICP entre 2 a 24 horas después.* ***Objetivo:*** *Comparar la seguridad y eficacia en pacientes sometidos a ICPP contra EFI en IAMCEST.* ***Métodos:*** *Se incluyeron pacientes con IAMCEST sometidos a ICP emergente. El punto final primario son eventos cardiacos adversos mayores (ECAM), muerte, reinfarto, evento vascular cerebral y revascularización del vaso tratado, durante la hospitalización. Los puntos finales secundarios son la presencia de los componentes individuales del ECAM, y el sangrado mayor (BARC ≥ 3).* ***Resultados:*** *Se estudiaron 400 pacientes, 263 (65.8%) de ICPP, 114 (28.5%) a EFI y 23 (5.75%) angiografía diagnóstica. Del grupo EFI, 79 (69.3%) fueron angioplastia sistemática por trombólisis exitosa y 35 (30.7%) por angioplastia de rescate por trombólisis fallida. No se observó diferencia en la frecuencia de ECAM: EFI 13 (9.5%) contra ICPP 27 (10.3%) respectivamente (p = 0.806), tampoco hubo diferencia en los componentes individuales. No se observó diferencia en sangrado mayor, 5 (3.6%) vs 4 (1.5%), (p = 0.173). El análisis multivariado no relacionó la estrategia de reperfusión con los ECAM.* ***Conclusiones:*** *La EFI comparada con ICPP demuestra una tasa similar de ECAM, así como de sus componentes individuales. No se asocia con aumento de hemorragia mayor, concluyendo que ofrece el beneficio de una reperfusión oportuna sin aumento del riesgo en los hospitales que no tienen la capacidad para realizar ICPP.*

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BACKGROUND

Primary percutaneous coronary intervention (PPCI) is the treatment of choice for ST-elevation myocardial infarction (STEMI). Nevertheless, this treatment is not always the fastest option. This is mostly due to the transfer delays when patients arrive at a non-percutaneous coronary intervention (PCI) hospital. These delays can decrease the benefits of the PPCI.[1] The sooner that coronary flow is reestablished, the less myocardial necrosis, ventricular dysfunction and mortality.[2]

The chosen reperfusion treatment (thrombolysis or PPCI) should be established in the first 12 hours from symptom onset. In patients that are transferred to a PCI-capable hospital, the delay should be a maximum of 120 minutes after the diagnosis is made.[1] When the delay is greater than 120 minutes there is no benefit of PPCI over thrombolysis.[3] Many patients do not achieve these treatment objectives due to logistical and geographical issues.[4] There is also evidence that indicates that an early PCI after thrombolytic therapy improves outcomes especially in patients without reperfusion criteria.[5-7] The pharmacoinvasive strategy (PS) is defined as thrombolytic therapy combined with rescue PCI (in failed thrombolysis) or systematic PCI within the first 2 to 24 hours after thrombolysis (in successful thrombolysis). This strategy is particularly useful in patients who can't meet the 120-minute objective. This was shown in the STREAM trial, which suggested a benefit in patients who could not get PPCI done within 60 minutes.[8]

There is no evidence of the efficacy and safety of this strategy compared with PPCI in our population. This study focuses on the efficacy and safety of this strategy compared with PPCI in patients with STEMI during their hospitalization.

METHODS

This is an observational, descriptive, retrospective, single-center study done within the department of Interventional Cardiology in *Unidad Médica de Alta Especialidad, Hospital de Cardiología No. 34* (UMAE 34) from the *Instituto Mexicano del Seguro Social* (IMSS), in Monterrey, Nuevo León, Mexico. The patients included in the study were those treated between January 2016 to January 2017. Patients with cardiogenic shock, incomplete clinical file, and those treated after more than 24 hours from the onset of pain, were excluded from this study.

Patient selection. All patients were treated at UMAE 34 which is a reference center for the northeastern part of Mexico. This center receives patients from six different states, however acute STEMI patients are usually within the state. There were a few patients that were transferred from two neighboring states. Within the city and its metropolitan area we received patients from 1 tertiary-care hospital, six secondary-care hospitals, and 14 primary-care units. There were patients who arrived at UMAE 34 emergency department, however, most of the patients were transferred through an emergency protocol termed «*Código Infarto*» (Infarct Code) which is used as a direct reference implemented at the end of 2015. This protocol was started to offer a prompt reperfusion therapy with PPCI to a larger population of patients. UMAE 34 has an active PPCI program for more than 20 years, however, there were logistical issues that hindered its success. The «*Código Infarto*» protocol there has been over a 100% increase in the number of patients transferred for reperfusion therapy.

Definitions. It is considered an emergent PCI all angioplasties done in the context of an acute STEMI (PPCI, systematic PCI or rescue PCI). Primary PCI is defined as a percutaneous coronary intervention done within 12 hours after the onset of symptoms without a previous thrombolytic therapy. Systematic PCI is defined as an angioplasty done within 3 to 24 hours after a successful thrombolytic therapy. Rescue PCI is the term used for patients who receive thrombolytic therapy but without clinical or electrocardiographical evidence of reperfusion at 90 minutes post-thrombolysis. The pharmacoinvasive strategy is composed of systematic PCI and rescue PCI. Patients that had a greater than 50% decrease in ST-elevation, reperfusion arrhythmias, and resolution of symptoms at 90 minutes were considered a successful thrombolysis, whereas people who

didn't meet these criteria were considered failed thrombolysis.

Bleeding was classified according to the bleeding academic research consortium (BARC): type 0, no bleeding; type 1, bleeding that did not require any additional intervention in order to stop it; type 2, bleeding that required medical attention being larger than expected but without meeting criteria for type 3, 4, or 5. Type 3a, is significant bleeding which causes a decrease of 3 to 5 g/dL in hemoglobin or any bleeding that requires a transfusion; type 3b includes cardiac tamponade or any bleeding that requires surgical intervention or administration of vasoactive agents; type 3c is intracranial bleeding including intraspinal, or intraocular bleeding that compromises vision; type 4 is bleeding related to coronary artery bypass graft (CABG). Type 5 includes all fatal bleedings; type 5a is probable fatal bleeds; type 5b is definitive fatal bleeds. Total ischemia time was defined as the time from the onset of symptoms to the moment of reperfusion either by passage of guidewire or balloon dilatation. The door to balloon time is defined as the time between patient arrival at our hospital to the recovery of coronary flow after balloon dilatation. No-reflow phenomenon was defined as a loss of TIMI 3 (normal) flow or TIMI 0-2. Reinfarction was considered as the presence of chest pain for more than 30 minutes with new ST-segment elevation in the electrocardiogram (EKG) and/or new elevation in cardiac enzymes. Target vessel revascularization (TVR) was defined as a ≥ 70% stenosis that requires new intervention of a previously treated vessel. A stroke was defined as a new neurologic deficit that persists for more than 24 hours secondary to a intracranial bleed or a cerebral embolism, confirmed using computed axial tomography (CT scan), magnetic resonance imaging (MRI), or cerebral angiography.

End-points. The primary end-point for efficacy was the presence of major adverse cardiac events (MACE): death by any cause, reinfarction, hemorrhagic or ischemic strokes, and TVR during hospitalization. Secondary end-points were the individual components of MACE. To evaluate safety, bleeding ≥3 according the BARC classification during hospitalization.

Data collection was done using electronic files and databases from interventional cardiology department to retrieve information about adverse outcomes during their hospitalization.

Statistical analysis. The quantitative variables were expressed with a medium and standard deviation. The qualitative variables were expressed as frequency and percentage of the total value. The differences between the categorical variables were analyzed using χ^2 test or Fisher exact test in case their frequencies were < 5. The differences in quantitative variables were analyzed using t Student in variables with normal distribution and Mann-Whitney U in asymmetrical distribution. The values that were considered statistically significant were those with a $p \leq 0.05$ and a confidence interval of ≤ 95%.

RESULTS

Patient characteristics. A total of 400 patients were included, 310 male (77.5%) and 90 female (22.5%). Of these patients, 187 (46.8%) had diabetes mellitus, 224 (56%) had hypertension, and 112 (28%) dislipidemia. There were a total of 263 (65.8%) PPCI, 114 (28.5%) were treated with a pharmacoinvasive strategy, and 23 (5.75%) only had a diagnostic coronary angiography (8 patients with normal coronary arteries and the rest were sent for CABG). Of the 114 patients from the pharmacoinvasive strategy group, 79 (69.3%) had a successful thrombolysis and therefore had a systematic angioplasty, and 35 (30.7%) had a failed thrombolysis and required a Rescue Angioplasty. The patient's clinical characteristics are described in *Table 1*. The total ischemia time was 358 ± 221 minutes in the PS group and 309 ± 189 minutes in the PPCI group ($p = 0.081$). There was no significant difference in the total ischemia time in spite of the prolonged reperfusion time in patients who required Rescue PCI. The door-to-balloon time was 39 ± 22 minutes in the PS group and 39 ± 21 minutes in the PPCI group ($p = 0.876$).

Procedural techniques. The PS group had more radial access, more direct stenting and less usage of glycoprotein IIb/IIIa inhibitors with

statistical significance as shown in *Table 2*. In the PPCI group radial access was used in 50.2% and femoral access was 49.8%. Temporary pacemaker was used more frequently in PPCI (p = 0.002).

Angiographic results. Both groups had the same success rate obtaining TIMI 3 flow in 88.2% in the PS group and 88.6% in the PPCI group (p = 0.514). No-reflow phenomenon occurred in 4 patients (3.5%) in the PS group and 19 patients (7.2%) in the PPCI group (p = 0.166). In the PS, direct stenting technique was used in 25 patients (21.9%), whereas 18 patients (6.9%) in the PPCI group had direct stenting (p < 0.001), as shown in *Table 3*.

Primary and secondary end-points. The primary end-point was met in 13 patients (9.5%) in the PS group and 27 patients (10.3%) in the PPCI group without statistical significance (p = 0.806). The rate of secondary end-points were similar in both groups, as shown in *Table 4*.

Hemorrhagic and cerebrovascular complications. The rate of hemorrhagic stroke was similar between both groups, occurring in 1.5% of the PS group and 0.4% in the PPCI group (p = 0.235). The rate of major bleeding was similar between in both groups, occurring in 5 patients (3.6%) of the PS group and 4 patients (1.5%) of the PPCI group (p = 0.173).

Table 1: Clinical characteristics.

	Patients			
Clinical characteristics	Number (%)	Pharmacoinvasive (%)	Primary (%)	P value
Male	310 (77.5)	106 (77.4)	204 (77.6)	0.960
Female	90 (22.5)	31 (22.4)	59 (22.6)	
Smoking history	228 (57.0)	82 (59.9)	146 (55.5)	0.405
Diabetes mellitus	187 (46.8)	66 (48.2)	121 (46.0)	0.680
Hypertension	224 (56.0)	70 (51.1)	154 (58.6)	0.154
Dislipidemia	112 (28.0)	38 (27.7)	74 (28.1)	0.933
Killip Kimball I	358 (89.5)	122 (89.1)	236 (89.7)	0.956
Killip Kimball II	29 (7.2)	9 (6.6)	20 (7.6)	
Killip Kimball III	13 (3.3)	6 (4.4)	7 (2.7)	
Total ischemia time (min)	324 ± 201	358 ± 221	309 ± 189	0.081
Door-to-balloon time (min)	39 ± 20	39 ± 22	39 ± 21	0.876

Table 2: Procedural characteristics.

	Patients		
Procedural Characteristics	Pharmacoinvasive n = 137 (%)	Primary n = 263 (%)	P value
Radial access	86 (62.8)	132 (50.2)	0.016
Femoral access	51 (37.2)	131 (49.8)	
Direct stenting	25 (21.9)	18 (6.9)	< 0.001
GP IIb/IIIa inhibitors	30 (21.9)	156 (59.3)	< 0.001
Intra-aortic balloon pump	5 (3.6)	14 (5.3)	0.455
Temporary pacemaker	9 (6.6)	48 (18.3)	0.002
Successful angioplasty	101 (88.6)	232 (88.2)	0.915

DISCUSSION

The purpose of this study was to determine the efficacy and safety of the pharmacoinvasive strategy compared with PPCI. The results show a similar rate of MACE and bleeding in both the PS and PPCI group. These results suggest that the pharmacoinvasive strategy is non-inferior to the PPCI specially in patients that need to be transferred to a PCI-capable hospital with a more than 120-minute delay. In the multivariate analysis the only variables that showed a relationship with the rate of MACE were femoral access, history of diabetes mellitus, and age ≥ 75 years. This can be explained due to a greater risk of complications with femoral access and increased age, as well as an increase disease burden in patients with a history of Diabetes Mellitus.[8-10]

The rate of major bleeds was similar between both groups and in the multivariate analysis was related to the use of femoral access site. The rest of the variables were not related to the increase in major bleeding. These results also suggest that the use of thrombolytics did not statistically increase the rate of major bleeding.

In the pharmacoinvasive group there was a higher rate of radial access, increase in direct stenting technique, as well as an increase in the final TIMI 3 flow. There was less thrombus burden and less use of GP IIb/IIIa inhibitors.

There was no difference in the rate of normal coronary arteries between both groups, however there was an increase in the number of patients deferred for CABG. This is more likely explained because these patients had multivessel disease and the thrombolytic therapy had restored coronary blood-flow decreasing the need for mechanical reperfusion.

Table 3: Angiographic characteristics.

Angiographic characteristics	Patients		P value
	Pharmacoinvasive n = 137 (%)	Primary n = 263 (%)	
# Diseased vessels			
No lesions	8 (5.8)	0 (0.0)	0.001
1 Vessel disease	66 (48.2)	125 (47.5)	
2 Vessel disease	31 (22.6)	72 (27.4)	
3 Vessel disease	32 (23.4)	66 (25.1)	
Culprit vessel*			
Right coronary artery	49 (38.0)	104 (39.0)	0.654
Left anterior descending	66 (51.2)	138 (52.5)	
Circumflex	14 (10.9)	20 (7.6)	
Intermediate ramus	0 (0.0)	1 (0.4)	
# Of treated vessels*			
Non treated	15 (11.6)	0 (0.0)	0.000
1 Vessel	108 (38.7)	250 (38.7)	
2 Vessels	6 (4.7)	12 (4.6)	
3 Vessels	0 (0.0)	1 (0.4)	
Treatment of culprit vessel only§	108 (94.7)	250 (95.1)	0.890
Single vessel disease*	66 (51.2)	125 (47.5)	0.490
Calcified lesion	1 (0.7)	20 (7.6)	0.003
Thrombus burden	51 (37.2)	179 (68.1)	< 0.001

*Eight patients with normal coronary arteries were excluded from the analysis. §Fifteen patients were excluded due to differed angioplasty or because they were sent for CABG.

Table 4: Statistical analysis.

End-points	Patients: Pharmacoinvasive n = 137 (%)	Patients: Primary n = 263 (%)	P value
MACE	13 (9.5)	27 (10.3)	0.806
No-reflow	4 (3.5)	19 (7.2)	0.166
In-hospital myocardial infarction	1 (0.7)	5 (1.9)	0.360
Target vessel revascularization (TVR)	2 (1.8)	8 (3.0)	0.475
In-hospital death	7 (5.1)	14 (5.3)	0.928
Stroke	2 (1.5)	1 (0.4)	0.235
Major bleeding (BARC ≥ 3)	5 (3.6)	4 (1.5)	0.173
TIMI 3 post	122 (89.1)	236 (89.7)	0.833
Multivariate analysis for MACE	**Odds ratio**	**p value**	**95% CI**
Femoral access	2.27	0.043	1.02-5.0
Diabetes mellitus	2.21	0.046	1.01-4.8
Age ≥ 75 years	2.69	0.027	1.11-6.4
Primary PCI (vs PS)	0.77	0.610	0.29-2.0
Code STEMI	0.69	0.490	0.24-1.9
Multivariate analysis for bleeding BARC ≥ 3	**Odds ratio**	**p value**	**95% CI**
Femoral access	5.10	0.050	1.00-26.0
Diabetes mellitus	1.30	0.700	0.33-5.1
Age ≥ 75 years	1.40	0.680	0.26-7.7
Primary PCI (vs PS)	2.40	0.330	0.40-14.5
GP IIb/IIIa inhibitor use	1.80	0.400	0.44-7.6

In the setting of an acute STEMI, time is an important factor to improve the survival and outcomes. It is thus crucial to reestablish coronary blood-flow as soon as possible, using mechanical or pharmacological means. The treatment of choice is the use of mechanical reperfusion but there are certain hospitals that have logistical and geographical issues that don't allow the 120-minute to be met. The Action-GWTG registry shows that only 31.5% of patients achieve the 120-minute time goal. This hasn't changed in the last years.[4] This offers evidence that the goals for a prompt reperfusion technique are not being met in the real world.[11]

The total ischemia time was less in the PPCI group without statistical significance, and the door-to-balloon time was similar in both groups. The small delays in total ischemia time can be a consequence of the time required to determine if the thrombolysis was successful. The patients who required rescue PCI the delays to reperfusion weren't statistically significant and therefore, did not favor the PPCI group.

Treatment of acute STEMI has been in constant evolution. At first, the reperfusion strategy was either mechanical or pharmacological and they were rarely used in conjunction. The facilitated angioplasty was the only time when both were used together, however the results did not meet expectations and was later abandoned. The pharmacoinvasive strategy was first studied when comparing both reperfusion techniques. The DANAMI-2 trial compared the use of

thrombolytic therapy with PPCI in patients with acute STEMI and showed greater benefit in PPCI specially in reinfarction and recurrent ischemia.[3] The patients with failed thrombolysis have a greater benefit when transferred to rescue PCI as observed in the REACT trial.[12] There freedom of major cardiovascular events in 84.6% in the rescue PCI group, 70.1% in conservative treatment group and 68.7% in patients that received a second dose of thrombolytic therapy.[12] The NORIDSTEMI, GRACIA-2, and TRANSFER-AMI showed a decrease in major adverse cardiac events in patients that had early revascularization after a successful thrombolysis compared to those with deferred PCI and or ischemia driven PCI.[4-7] These trials can be considered as the foundation for the pharmacoinvasive strategy. The STREAM trial compared PS versus PPCI and was the first randomized trial of its kind. A total of 1,892 patients with acute STEMI who could not receive PPCI in the first two hours of symptom onset. They were randomized to pharmacoinvasive strategy within six hours after thrombolytic therapy or transfer for PPCI. There were no significant differences in the primary end-point between both groups.[8] There was a slight increase in the number of intracranial bleeds in the PS group compared with PPCI group (1.0% vs 0.2% $p = 0.04$).[8] This was later corrected by using half of the thrombolytic dose in patients 75 years or older. In the University of Ottawa trial showed similar results with a rate of MACE in 6.4% in the PS group and 7.0% in the PPCI group ($p = 0.71$).[9] The rate of intracranial bleeds was higher in the PS group than in the PPCI group (1.3% vs 0% respectively $p = 0.0004$).[10] In this study we had similar results without significant differences in the primary or secondary end-points.

Study limitations

The results obtained in this study represent real-world experience, yet they are not randomized, and are a single-center with a small number of patients. A high-volume population and a randomized trial should be done to consider these findings for accurate decision-making. This study excludes cardiogenic shock, which is a relatively frequent complication of acute STEMI, to determine the effect of thrombolytic therapy in hemodynamically stable patients. Nevertheless, evaluating the pharmacoinvasive strategy in patients with cardiogenic shock would give more information in this group of individuals.

CONCLUSIONS

The use of pharmacoinvasive strategy can be a safe and effective treatment option in patients that cannot achieve a reperfusion goal of 120 minutes with PPCI. There were no differences in the primary and secondary end-points and there were no significant differences in the delays to treatment including the rescue PCI group. As for safety, the use of thrombolytic therapy did not increase the rate of major bleeds. These results suggest a means to achieve a quicker reperfusion therapy while not increasing the rate of complications, especially in non-PCI capable hospitals.

REFERENCES

1. 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: 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.
2. Nallamothu BK, Bradley EH, Krumholz HM. Time to treatment in primary percutaneous coronary intervention. N Engl J Med. 2007; 357 (16): 1631-1638.
3. Andersen HR, Nielsen TT, Rasmussen K, Thuesen L, Kelbaek H, Thayssen P et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med. 2003; 349 (8): 733-742.
4. Vora AN, Holmes DN, Rokos I, Roe MT, Granger CB, French WJ et al. Fibrinolysis use among patients requiring interhospital transfer for ST-segment elevation myocardial infarction care: a report from the US National Cardiovascular Data Registry. JAMA Intern Med. 2015; 175 (2): 207-215.
5. Bøhmer 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 Coll Cardiol. 2010; 55 (2): 102-110.
6. Lavi S, Cantor WJ, Casanova A, Tan MK, Yan AT, Džavík V et al. Efficacy and safety of enoxaparin compared

with unfractionated heparin in the pharmacoinvasive management of acute ST-segment elevation myocardial infarction: Insights from the TRANSFER-AMI trial. Am Heart J. 2012; 163 (2): 176-81.e2.
7. Fernández-Avilés F, Alonso JJ, Peña G, Blanco J, Alonso-Briales J, López-Mesa J et al. 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 (8): 949-960.
8. Welsh RC, Van de Werf F, Westerhout CM, Goldstein P, Gershlick AH, Wilcox RG et al. Outcomes of a pharmacoinvasive strategy for successful versus failed fibrinolysis and primary percutaneous intervention in acute myocardial infarction (from the STrategic Reperfusion Early After Myocardial Infarction [STREAM] study). Am J Cardiol. 2014; 114 (6): 811-819.
9. Rashid MK, Guron N, Bernick J, Wells GA, Blondeau M, Chong AY et al. Safety and efficacy of a pharmacoinvasive strategy in ST-segment elevation myocardial infarction: a patient population study comparing a pharmacoinvasive strategy with a primary percutaneous coronary intervention strategy within a regional system. JACC Cardiovasc Interv. 2016; 9 (19): 2014-2020.
10. Sim DS, Jeong MH, Ahn Y, Kim YJ, Chae SC, Hong TJ et al. Pharmacoinvasive strategy versus primary percutaneous coronary intervention in patients with st-segment-elevation myocardial infarction: a propensity score-matched analysis. Circ Cardiovasc Interv. 2016; 9 (9). pii: e003508.
11. Danchin N, Dos Santos Teixeira N, Puymirat E. Weaknesses in regional primary coronary angioplasty programs: is there still a role for a pharmaco-invasive approach? Rev Esp Cardiol (Engl Ed). 2014; 67 (8): 659-665.
12. Gershlick AH, Stephens-Lloyd A, Hughes S, Abrams KR, Stevens SE, Uren NG et al. Rescue angioplasty after failed thrombolytic therapy for acute myocardial infarction. N Engl J Med. 2005; 353 (26): 2758-2768.

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