ORIGINAL ARTICLE

Myocardial Infarction in the Daily Practice

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Abstract

Background: Guideline recommendations for the management of patients with ST-elevation myocardial infarction (STEMI) are mainly based on data from randomized clinical trials.

Objectives: We sought to assess temporal trends in characteristics, treatment and outcomes of patients with STEMI representative of the daily practice.

Methods: Prospective cohort study including all patients with STEMI who presented at our institution from 2010 to 2013. Clinical, angiographic, laboratory, treatment aspects and 30-day major cardiovascular events (MACEs) were assessed and compared over the years.

Results: The mean TIMI risk score, and most baseline clinical and angiographic characteristics of the 1973 patients included remained stable from 2010 to 2013, except for diabetes mellitus (whose frequency increased from 21% to 28%; $p < 0.01$). Primary PCI was performed in 95% of cases, and the door-to-balloon time decreased from 1.27 to 1.11 hours ($p < 0.01$). Regarding treatment, there were significant increases in the use of 600 mg boluses of clopidogrel (75% in 2010 vs 93% in 2013; $p < 0.001$), upstream anticoagulant (50% vs 91%; $p < 0.001$) and the radial approach in pPCI (9% vs 66%; $p < 0.001$), and lower use of beta-blockers (72% vs 63%; $p < 0.001$). MACE decreased from 17.4% to 9.5% ($p < 0.05$). Independent predictors of MACE were baseline characteristics, the radial approach, and use of beta-blockers and upstream anticoagulant.

Conclusions: The baseline characteristics of patients with STEMI remained stable over a four-year period, except for the incidence of diabetes mellitus, which increased significantly. Medical and interventional treatments significantly changed, and short-term adverse cardiovascular outcomes significantly decreased. Predictors of better outcomes were baseline characteristics, use of beta-blockers and upstream anticoagulant, and the radial approach. (Int J Cardiovasc Sci. 2016;29(4):253-261)

Keywords: Myocardial Infarction; Delivery of Health Care; Quality of Health Care; Percutaneous Coronary Intervention.

Introduction

Despite significant improvements in medical and interventional treatments that have occurred in recent years, ST-segment elevation myocardial infarction (STEMI) remains a leading cause of death in the world.[1] Most of the scientific evidence that supports the treatment of patients with STEMI comes from randomized clinical trials (RCT). However, patients included in RCTs are not representative of those seen in the daily practice, who are generally older, with more comorbidities and tend to present higher cardiovascular event rates.[2,3] The short-term mortality of STEMI patients included in recent RCTs has been reported to be below 5%.[4,5] However, contemporary real-world registries show higher rates even in developed countries in Europe.[6-10] In the present study, we sought to investigate temporal trends in the baseline characteristics, medical and invasive treatments

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and outcomes of patients with STEMI representative of the daily practice.

Methods

Patients

This was a prospective cohort study which consecutively included all patients with STEMI who presented at the *Instituto de Cardiologia do Rio Grande do Sul, Fundação Universitária de Cardiologia*, Porto Alegre, Brazil, from January 2010 to December 2013. Our facility is a tertiary referral center, and its catheterization laboratory works 24 hours a day, seven days a week, with at least one member of the health team at the facility.

The inclusion criterion was STEMI in the first 12 hours. STEMI was defined as typical chest pain at rest associated with ST-segment elevation of at least 1mm in two contiguous leads in the frontal plane or 2 mm in the horizontal plane, or typical pain at rest in patients with a new, or presumably new, left bundle-branch block. The exclusion criteria were time from onset of symptoms to hospital arrival above 12 hours, age less than 18 years or refusal to participate.

Primary Percutaneous Coronary Intervention Procedures

The medications used in the patient's initial care follow the routines of our institution: a bolus dose of acetylsalicylic acid (300 mg) and clopidogrel (300 to 600 mg) was administered in the emergency room immediately after patient arrival. Anticoagulant therapy (heparin 70-100 U/Kg) was administered in the emergency room at the discretion of the attending physician. For those not receiving heparin in the emergency room, it was given in the catheterization laboratory if the patient would undergo primary percutaneous coronary intervention (pPCI).

After conventional coronary angiography, pPCI was performed as described elsewhere.[1] Aspects related to the procedure were left at the operators' discretion. Coronary flow before and after the procedures was assessed and described according to the Thrombolysis in Myocardial Infarction (TIMI) criteria.[11] Myocardial blush was assessed as described elsewhere.[12]

Data Collection, Outcomes and Follow-up

All patients were interviewed on hospital admission, and visited daily during the in-hospital period by one of the investigators. All-cause mortality and major cardiovascular events (MACEs) were assessed and registered by one of the study investigators. MACEs were defined as a combination of all-cause mortality, new myocardial infarction (MI) or stroke. New MI was defined as recurrent chest pain with new elevation of serum biomarkers, after the initial decline of the natural curve, with ST-segment elevation or new Q waves. Stroke was defined as a new, sudden-onset focal neurological deficit, of presumably cerebrovascular cause, irreversible (or resulting in death) within 24 hours and not secondary to any other readily identifiable cause. Major bleeding was defined according to the TIMI criteria.[13]

Statistical Analysis

Statistical analysis was performed using SPSS for Windows 22.0. Results are expressed as mean ± SD or absolute and relative frequencies as appropriate. Variables with a non-normal distribution are presented as median and interquartile range. This was a consecutive cohort study, and a sample size calculation was not previously performed. Statistical significance was defined as a two-tailed p-value < 0.05.

For categorical variables, the chi square test for trend was used. For continuous variables, the ANOVA and Tukey test were used for multiple comparisons in the case of normal distribution and the Kruskal-Wallis´s test for non-normal variables. Multivariate logistic regression was used to assess independent predictors of 30-day MACE.

Results

Patients

In the study period, 1973 patients were included; pPCI was performed in 1884 of them (95.5%) and cardiac surgery in 4 (0.2%). The remaining 85 patients (4.3%) received medical treatment, either because there was no significant coronary stenosis or because only a minor branch was occluded and considered to be unsuitable for intervention. No thrombolysis was performed at our hospital, but 38 patients had received thrombolytics (2%) prior to transfer from another institution.

Clinical Characteristics

The percentage of patients diagnosed with diabetes mellitus significantly increased over the years, and the

median door-to-balloon time significantly decreased (Table 1). The baseline risk of the patients, as assessed by the TIMI risk score did not change significantly, nor did the percentage of patients undergoing pPCI, which remained relatively stable around 95%.

Angiographic and Procedural Features

The lesion length increased significantly over the years (Table 2). There was a significant increase in the use of the radial approach, which was 9% in 2010 and increased to 66% in 2013. The rates of adjunctive aspiration thrombectomy declined significantly, and the use of direct stenting remained stable. The percent of patients receiving post-dilatation and the size of the balloon used to post-dilate the stent increased significantly, but the maximal pressure and the percent residual stenosis did not show statistically significant differences. The rates of angiographic success remained around 94-97% over the study period. Regarding indices of coronary and microvascular perfusion, the rates of TIMI 3 flow and blush 3 grades before pPCI procedures decreased over time, while the rates of TIMI 3 flow post procedure remained stable and the rate of blush 3 grade significantly increased during the study period.

Table 1
Clinical and laboratory characteristics of the study population according to the year of STEMI

Characteristic		2010 (n = 560)	2011 (n = 494)	2012 (n = 458)	2013 (n = 461)	p
Age, years		60.4±11.8	60.8±12.2	60.3±11.5	60.0±12.6	0.79
Male, %		68	70	71	71	0.30
Hypertension, %		67	64	62	66	0.78
Diabetes mellitus, %		21	24	24	28	0.01
Dyslipidemia, %		37	32	35	40	0.28
Smoking, %		42	41	44	41	0.67
Family history of CAD, %		33	30	30	29	0.21
	PCI, %	16	15	18	18	0.25
Medical history	CABG, %	4	4	4	5	0.52
	Myocardial infarction, %	24	18	20	21	0.57
Anterior MI, %		42	44	43	45	0.32
Killip III/IV		7	8	11	6	0.80
Complete atrioventricular block		3	2	1	5	0.27
Duration of pain until hospital arrival, hours		3.75 [1.86-6.00]	3.96 [2.25-6.73]	3.99 [1.99-7.00]	3.99 [1.99-6.78]	0.20
Door-to-balloon time, hours		1.27 [0.95-1.75]	1.25 [0.92-1.68]	1.08 [0.83-1.41]	1.11 [0.86-1.45]	0.006
Primary PCI, %		95	94	90	95	0.17
TIMI risk score		3.37±2.14	3.45±2.20	3.25±2.19	3.46±2.02	0.66

CAD: coronary artery disease; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; MI: myocardial infarction; TIMI: thrombolysis in myocardial infarction.

Table 2
Angiographic and procedural aspects of the study population according to the year of STEMI

Characteristic		2010 (n = 542)	2011 (n = 476)	2012 (n = 424)	2013 (n = 442)	p
Three-vessel disease, %		19	17	21	18	0.94
LAD involvement, %		46	43	42	46	0.98
Reference vessel diameter, mm		3.15±0.49	3.17±0.48	3.22±1.5	3.22±0.82	0.54
Lesion length, mm		17±8.7	18±8.7	19±8.8	19±9.2	0.03
Radial approach,%		9	20	55	66	< 0.001
Drug-eluting stent, %		1	2	4	5	< 0.001
Direct stenting, %		31	35	34	34	0.22
Adjunctive aspiration thrombectomy,%		31	39	28	21	< 0.001
Post-dilatation, %		24	26	27	34	< 0.001
Final balloon diameter, mm		3.3±0.5	3.5±0.5	3.4±0.7	3.6±0.7	0.03
Maximal inflation pressure, ATM		14±2.6	14±2.5	14±2.3	14±2.6	0.25
% stenosis	Pre, %	98±6.1	97±9	97±9.2	97±9.2	0.21
	Post, %	3.5±16	5±19	5.8±21	3±14	0.07
Angiographic success, %		96	95	94	97	0.65
TIMI grade 3 flow	Pre, %	21	23	23	14	0.08
	Post, %	89	89	92	92	0.20
Blush grade 3	Pre, %	14	14	14	8	< 0.001
	Post, %	66	69	74	73	< 0.001

LAD: left anterior descending artery; ATM: atmospheres; TIMI: thrombolysis in myocardial infarction.

Medical Treatment

Table 3 shows aspects of the medical treatment in the first 24 hours of hospitalization according to the year of STEMI. Aspirin and clopidogrel were used in virtually all patients. The use of a 600 mg clopidogrel bolus increased over the years, with 93% of patients receiving this higher dosing scheme in 2013. The use of adjunctive IIb/IIIa glycoprotein in the catheterization laboratory also significantly increased, as well as that of an upstream heparin bolus (in the emergency room, before catheterization laboratory arrival). The use of statin remained stable in almost 4 out of 5 patients, but that of beta-blockers, angiotensin-converting enzyme inhibitors and nitrates significantly decreased. To better understand the reasons leading to the progressive lower use of beta-blockers over the years, we assessed the baseline risk profile of these patients. The mean TIMI risk score of patients receiving beta-blockers decreased significantly over the years (2010= 3.23±2.04; 2011=3.33±2.08; 2012=1.92±2.20 and 2013=1.86±2.02; p=.008).

Outcomes

The overall rates of combined and individual 30-day adverse cardiovascular events in this population were as follows: MACE=13%, death=8.5%, MI=4.2%, stroke=0.9%, stent thrombosis=2.3%, and major bleeding=2.4%. Figure 1 shows the rates of cardiovascular outcomes over the study period. Major cardiovascular events decreased significantly from 17.4% in 2010 to 9.5% in 2013 ($p < 0.05$). Mortality also decreased from 8.8% in 2010 to 7.1% in 2013, but this difference did not reach statistical significance. MI (7.3% vs 2.9%), urgent revascularization procedures (3.9% vs 2.4%) and stent thrombosis (3.8% vs 2.1%) also decreased from 2010 to 2013, but these differences were also not statistically significant. Stroke and bleeding rates remained relatively stable.

Table 3
Medical treatment in the first 24 hours of hospitalization according to the year of STEMI

Treatment		2010 (n = 560)	2011 (n = 494)	2012 (n = 458)	2013 (n = 461)	p
Aspirin, %		98	97	98	99	0.53
Clopidogrel	300 mg, %	23	12	5	4	< 0.001
	600 mg, %	75	87	92	93	< 0.001
Ticagrelor,%		0	0	1	2	< 0.001
GP IIb/IIIa inhibitor, %		29	27	36	34	0.007
Heparin upstream, %		50	72	84	91	< 0.001
Statin, %		85	87	85	86	0.68
Beta-blocker, %		72	73	66	63	0.001
ACE inhibitor, %		70	74	66	65	0.02
Nitrates, %		27	24	5	21	< 0.001

ACE: angiotensin-converting enzyme; GP: glycoprotein.

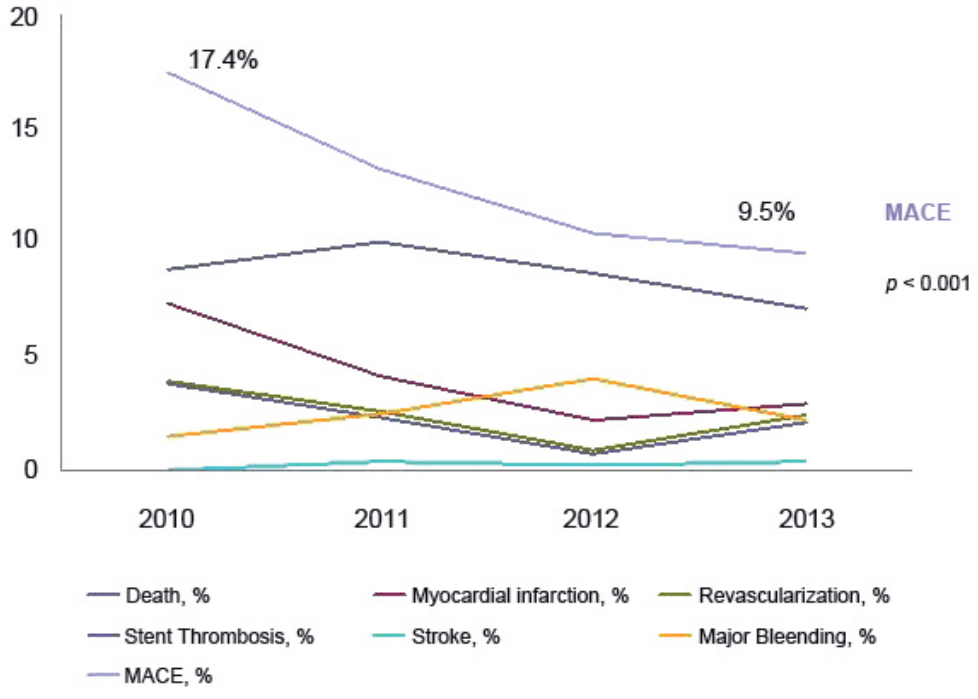

Figure 1
Rates of adverse cardiovascular events over the years
MACE: major adverse cardiovascular events.

The association between major bleeding and access site to perform pPCI was assessed. The rate of major bleeding in patients undergoing pPCI via the radial approach was 0.9%, and 3.3% when pPCI was performed via the femoral approach ($p < 0.001$). Patients who presented with major bleeding had significantly higher rates of 30-day MACE (42% vs 11%; $p < 0.001$) and mortality (29% vs 7%; $p < 0.001$) than those who did not bleed.

Patients who received upstream heparin had a better rate of blush-3 grades post procedure (72% vs 64%; $p < 0.01$), and lower rates of MACE (10.9% vs 17.3%; $p < 0.001$) and death (7.4% vs 11.5%; p=0.004) than those who received the first heparin bolus only in the catheterization laboratory.

Multivariate Analysis

Table 4 shows multivariate analysis for 30-day MACE. Several baseline variables such as age, Killip III/IV class and atrioventricular block were associated with MACE, as shown in previous studies. Interestingly, dyslipidemia was a protective factor for MACE. Regarding pharmacological treatment, the use of an upstream bolus of heparin in the emergency room and of beta-blockers were also significantly associated with lower MACE, but a 600 mg bolus of clopidogrel was not. In relation to interventional aspects, the radial approach to perform pPCI and less residual stenosis after stent implantation were associated with lower MACE rates.

Table 4
Multivariate analysis of candidate variables associated with30-day MACE

Variables	Chi-square	OddsRatio	Confidence Interval 95%		p
Age	8.90	1.02	1.01	1.04	0.003
Male	0.43	1.12	0 .79	1.60	0.51
Diabetes Mellitus	1.40	1.25	0.86	1.82	0.24
Dyslipidemia	4.70	0.66	0.46	0.96	0.03
Smoking	0.53	1.05	0.72	1.51	0.82
Hypertension	0.78	1.18	0.82	1.70	0.38
Door-to-Balloon time	2.96	1.09	0 .99	1.21	0.09
Killip III/IV	52.30	5.14	3.30	8.01	< 0.01
Atrioventricular block	5.85	2.51	1.19	5.30	0.02
Chronic renal failure	1.92	1.69	0.80	3.50	0.17
Heparin upstream	5.58	0.65	0.46	0.93	0.02
Radial approach	9.27	0.53	0.35	0.80	0.002
% Post stenosis	3.97	1.01	1.001	1.02	0.05
Clopidogrel 600 mg	1.28	0.78	0.50	1.20	0.26
Beta-blocker	9.28	0.58	0.41	0.83	0.002

Discussion

The decline in cardiovascular events reported in the present study can be considered clinically significant and meaningful, since 30-day MACE rates were almost halved in this four-year period. This important reduction cannot be explained by the selection of lower risk patients over the years, since all patients presenting to our institution with STEMI were consecutively included during the study. Additionally, the mean TIMI risk score for STEMI and other high-risk baseline characteristics remained relatively stable over time, and the frequency of diabetes mellitus increased. Instead, independent predictors of lower MACE rates were the use of the radial

approach, of beta-blockers, upstream heparin bolus, and several other baseline variables traditionally associated with cardiovascular events in previous studies. The rates of short-term cardiovascular events reported in the present study compare favorably with recent reports in patients representative of the daily clinical practice in developed countries.[6-10] However, the decline in MACE rates described in our study is in contrast to that of a large nationwide registry in Germany demonstrating no improvement in outcomes from 2005 to 2009.[6]

During the study period, we observed a remarkable increase in the use of the radial approach, which was 9% in 2010 and increased to 66% in 2013. The use of the radial approach was independently associated with a 47% lowering of 30-day MACE, as well as with significantly lower rates of major bleeding in comparison to the femoral approach. Patients who experienced a major bleeding had significantly higher rates of 30-day MACE, and this probably explains the benefit of the radial approach in this cohort.[14] Despite several studies demonstrating significant benefits of the radial approach in patients with STEMI,[14-16] it has been infrequently adopted in the clinical practice in some countries.[17] One of the reasons is the learning curve to perform pPCI through the arm,[18] and also concerns that it would increase the door-to-balloon time in patients with STEMI. In the present study, we report the opposite, i.e., the use of the radial approach increased over the years, and the door-to-balloon time significantly decreased.

Anticoagulant use immediately on patient arrival at the emergency room as compared to its use in the catheterization laboratory increased significantly over the study period, and 91% of the patients were treated with this approach in 2013. Bivalirudin is not approved for clinical use in Brazil, and heparin is the most frequently used anticoagulant in most centers. Among patients treated with a strategy of upstream heparin, there was a higher frequency of post-procedural grade-3 blush, lower mortality rate, and a 36% lower MACE rate by multivariate analysis. The recent European guidelines on STEMI recommend unfractionated heparin as one of the reasonable options for intravenous anticoagulant therapy in the setting of STEMI,[1] but there is no mention regarding the timing of administration, whether upstream or in the catheterization laboratory. The influence of upstream heparin on cardiovascular outcomes in STEMI patients has been evaluated by several studies,[19-23] which have shown different results. Like ours, other institutions have adopted the use of upstream heparin in STEMI patients.[24] Since a proper sized randomized clinical trial is not available, the observational data presented here should reinforce the notion that upstream heparin is at least safe, and probably beneficial, in contemporary STEMI patients treated mainly via the radial approach.

Finally, we believe that one important characteristic of the present study is the inclusion of all patients who presented with STEMI in our institution in the study period, with no exclusions. It has been shown that the exclusion of even a small number of patients from a registry in the setting of STEMI can cause a significant selection bias, since the patients excluded are generally those with more comorbidities and higher event rates.[25,26]

The limitations of this study include its observational nature, which preclude definitive conclusions regarding the effect of therapies on outcomes even after performance of a multivariate analysis. Most of the patients included in this cohort have received medical and interventional treatment according to the policies of the public health system in Brazil, which do not reimburse drug-eluting stents, prasugrel, ticagrelor or bivalirudin. This may limit extrapolation of the results, although patient characteristics and outcomes reported here are comparable to those of several others large reference centers over the world. This prospective registry started in 2010, and the collection of clinical data and the knowledge of the existence of an initiative to evaluate the clinical practice may have influenced medical decisions by the attending physicians. The angiographic results were not independently evaluated by a core angiographic laboratory, a limitation that is also shared by several other contemporary registries of pPCI patients. The 30-day follow-up evaluation is short and may be not enough to precisely identify the impact of the different studied factors on cardiovascular outcomes. However, 30-day outcomes have traditionally been considered as an important and relevant clinical outcome in STEMI patients by several previous studies.

In conclusion, we showed that baseline characteristics of patients with STEMI presenting to a tertiary referral center in interventional cardiology remained stable over a four-year period, except for the frequency of diabetes mellitus, which increased significantly. Medical and interventional treatments significantly improved, and short-term adverse cardiovascular outcomes significantly decreased. Predictors of better outcomes were baseline characteristics, upstream heparin use and the radial approach to perform primary PCI.

Impact On Daily Practice

Our study reinforces the safety and effectiveness of the radial approach to perform pPCI in the daily practice. Importantly, the adoption of the radial approach in our center experience did not translate into an increase in the door-to-balloon time, which significantly decreased over time. This finding should further encourage the adoption of the radial approach as the default access to perform pPCI by low-volume centers and operators.

Author Contributions

Conception and design of the research: Quadros AS, Schmidt MM. Acquisition of data: Quadros AS, Schmidt MM, Gazeta C, Melleu K, Azmus AD, Teixeira JV, Moraes CV, Gomes H, Sarmento-Leite R, Gottschall CA. Analysis and interpretation of the data: Quadros AS, Schmidt MM. Statistical analysis: Quadros AS, Schmidt MM. Writing of the manuscript: Quadros AS, Schmidt MM. Critical revision of the manuscript for intellectual content: Quadros AS, Gottschall CA.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

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