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FASTTRACK
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Reperfusion strategy in Europe: temporal trends in performance measures for reperfusion therapy in ST-elevation myocardial infarction

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Aims The rate and type of reperfusion, as well as time delays to reperfusion are directly associated with mortality and are established as performance measures (PMs) in the treatment of ST elevation myocardial infarction (STEMI). To date, little information exists about PMs for reperfusion in clinical practice in Europe and their temporal changes.

Methods and results Using the Euro Heart Survey ACS-III data set (2 years of inclusions between 2006 and 2008, 138 centres in 21 countries), we selected patients with STEMI eligible for reperfusion therapy. Recorded variables corresponded to the CARDS data set. The rate and type of reperfusion, as well as door to needle and door to artery times were assessed and compared between periods. Timely reperfusion was defined as a door to needle time <30 min, or a door to artery time <90 min. We assessed changes in PMs for reperfusion over the 2 years of recruitment. Among 19 205 patients included in the registry, 7655 had STEMI, and 6481 were admitted within the first 12 h and eligible for reperfusion. The rate of patients who underwent reperfusion increased from 77.2 to 81.3%, with an increase in the use of primary percutaneous coronary intervention (P-PCI). The door to needle and door to artery times decreased significantly during the study period, from 20 to 15 min ($P = 0.0011$) and from 60 to 45 min ($P < 0.0001$) respectively. As a result, the number of eligible patients receiving reperfusion therapy in a timely manner increased from 53.1 to 63.5% ($P < 0.0001$). In parallel, over the 2-year period, in-hospital mortality decreased from 8.1 to 6.6% ($P = 0.047$).

Conclusion In centres participating in the Euro Heart Survey ACS III, PMs for reperfusion in STEMI improved significantly between 2006 and 2008, with greater use of PCI. Similarly, the rate of patients reperfused in a timely manner also increased, with a significant reduction in door to needle and door to artery times.

Keywords ST segment elevation myocardial infarction • Reperfusion • Quality of care • Temporal trend

Introduction

Assessment of the quality of care has become an integral part of modern health care, usually by means of performance measures (PMs) that are based on recommendations from clinical practice guidelines, and intended to improve the performance at the physician level.[1] In patients with acute ST elevation myocardial infarction (STEMI), PMs have been defined.[2,3] A cornerstone of PMs in STEMI is the use of reperfusion strategy, either by primary percutaneous coronary intervention (P-PCI) or fibrinolytic therapy (FL), among patients admitted within the first 12 h after onset of symptoms. The benefit of reperfusion therapy decreases rapidly with delays in its application[4] and shortening the time from onset of symptoms to reperfusion therapy contributes to

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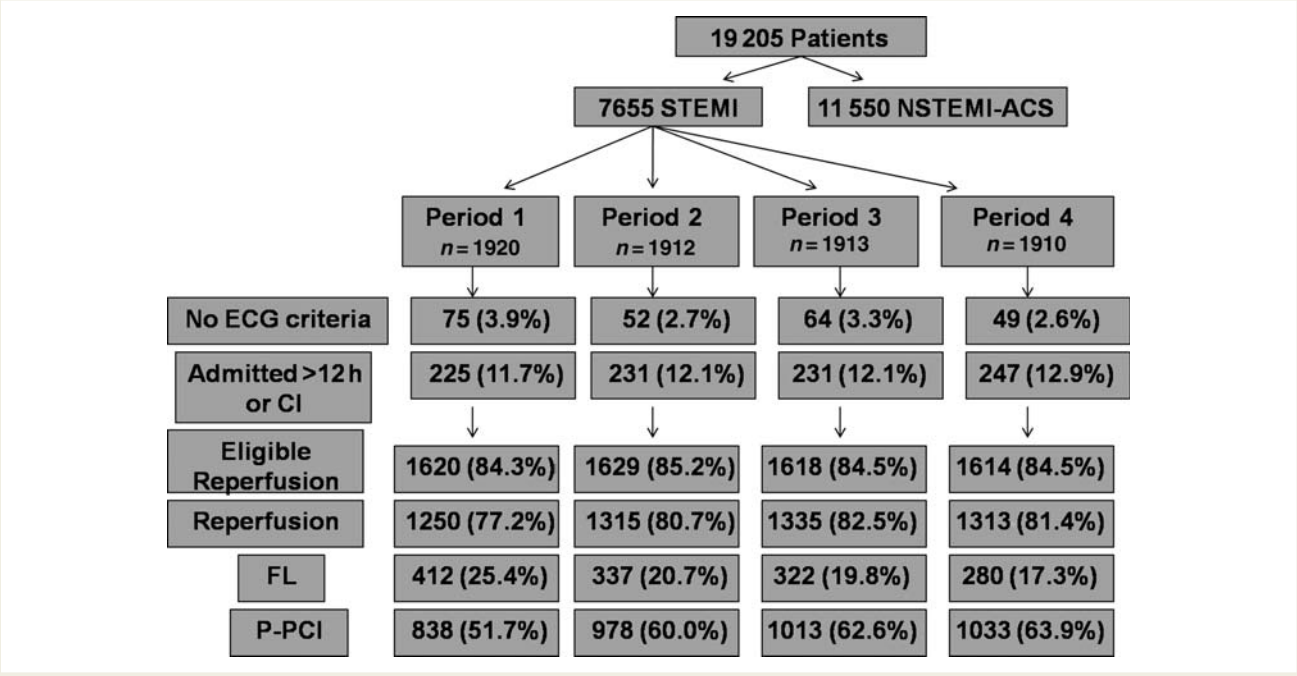

Figure 1 Flow chart of the study population.

decreased mortality.[5] Thus, specific PMs related to the timing of reperfusion therapy have been defined, namely the door to balloon and door to needle times, as well as the rate of patients receiving timely reperfusion (i.e. FL within 30 min or P-PCI within 90 min).[6] The Euro Heart Survey Acute Coronary Syndromes (EHS ACS) III registry collected data from patients admitted for ACS across 21 countries, and offers a unique opportunity to assess PMs for reperfusion therapy in Europe, and to examine temporal trends in PMs over a period of 2 years.

Methods

Data sources

The Euro Heart Survey Program is a cyclical program with surveys repeated every 2 years, launched to provide systematic information on the management of patients with suspected cardiovascular disease in Europe. As part of the EHS Program, the EHS ACS III was conducted by the European Society of Cardiology (ESC) from October 2006 to November 2008, including data from patients admitted for acute coronary syndromes in 138 centres across 21 countries in Europe. Three regions were defined: Central (Bulgaria, Croatia, Lithuania, Poland, Romania, Russian Federation, Serbia and Montenegro, Slovakia, and Ukraine), Mediterranean (Cyprus, Egypt, Greece, Israel, Italy, Portugal, Spain, and Turkey), and Western (Germany, Belgium and France). The study population was limited to first admittance for STEMI to a centre participating in the registry (patients coming from another centre were not included). The National Societies of Cardiology were invited to help in the recruitment of participating centres on a purely voluntary basis and without particular selection of the centres. A national coordinator was responsible for maintaining contact with the investigators in each of the centres, and information about the survey was posted on the website of the ESC. To enhance the generalizability of the results, it was suggested that patients who had been admitted during the first week of each month be included.

The population was divided into four groups (Periods 1–4) according to the quartiles of date of admission per region. Hospitals obtained approval for data collection by local ethics committees. Recorded variables corresponded to the CARDS data set[7] which was previously developed by the ESC. CARDS data included demographic characteristics, cardiovascular risk factors, previous diseases and medications, as well as clinical and biological status at admission. Acute, in-hospital, and discharge treatments and strategies were recorded.

Definitions and data management

Patients eligible for reperfusion were defined as those with chest pain and ECG criteria for diagnosis of STEMI, admitted within 12 h after onset of symptoms. We also recorded contra-indications for fibrinolysis. In patients submitted to reperfusion, four time variables were recorded: the time of onset of symptoms, the time of admission to the first hospital, the time to intravenous FL injection, and the time to artery puncture for P-PCI patients. According to these data, we calculated for each period: (i) the rate of patients eligible for reperfusion therapy. Among patients eligible for reperfusion, we also recorded (ii) the rate of use of P-PCI; (iii) the rate of use of FL; (iv) the rate and type of reperfusion among 'PCI-preferred' patients,[8–9] defined as patients with a contra-indication for fibrinolysis, admitted >4 h and <12 h after onset of symptoms, with cardiogenic shock or with Killip class >3; (v) the door to needle time (delay from admission to administration of FL); (vi) the symptoms to needle time (delay from onset of symptoms to administration of FL); (vii) the door to artery time (delay from admission to artery puncture); (viii) the symptoms to artery time (delay from onset of symptoms to artery puncture); and (ix) the rate of patients reperfused in a timely manner by primary PCI (i.e. door to artery time <90 min) or by FL (i.e. door to needle

Table 1 Baseline characteristics of the study population according to the period of admission

Variables	Period 1 ($n = 1920$)	Period 2 ($n = 1912$)	Period 3 ($n = 1913$)	Period 4 ($n = 1910$)	P_{trend}
Dates of admission					
West ($n = 2045$)	01/10/2006 28/03/2007	29/03/2007 18/09/2007	19/09/2007 28/02/2008	29/02/2008 31/10/2008	
Mediterranean ($n = 2425$)	01/10/2006 24/01/2007	25/01/2007 14/05/2007	15/05/2007 25/10/2007	26/10/2007 23/09/2008	
Central ($n = 3185$)	01/10/2006 06/08/2007	07/08/2007 04/12/2007	05/12/2007 07/04/2008	08/04/2008 07/10/2008	
Age	63(13)	64(13)	64(13)	64(13)	0.21[a]
Elderly (≥75 years)	434(22.6)	446(23.3)	455(23.8)	448(23.5)	0.29[b]
Male gender	1374(71.6)	1364(71.3)	1363(71.2)	1380(72.3)	0.67[b]
High blood pressure	1112(58.9)	1072(56.0)	1079(56.4)	1094(57.3)	0.44[b]
Diabetes	385(20.2)	416(22.0)	484(25.5)	438(23.1)	0.005[b]
Current smoker	761(40.8)	760(40.3)	733(38.6)	762(40.1)	0.46[b]
Hypercholesterolaemia	668(39.4)	744(41.8)	760(41.0)	717(38.1)	0.32[b]
Previous PCI	134(7.0)	166(8.7)	179(9.4)	161(8.4)	0.07[b]
Previous CABG	47(2.4)	44(2.3)	26(1.4)	31(1.6)	0.02[b]
History of stroke	117(6.1)	95(5.0)	85(4.5)	93(4.9)	0.06[b]
History of PAD	142(7.4)	124(6.5)	124(6.5)	91(4.8)	0.001[b]
History of renal dysfunction	88(4.6)	83(4.4)	80(4.2)	71(3.7)	0.16[b]
History of COPD	144(7.5)	91(4.8)	89(4.7)	84(4.4)	<0.001[b]
Killip class > 2	188(9.8)	157(8.2)	125(6.5)	135(7.1)	<0.001[b]
Admission heart rate	80(20)	80(20)	79(20)	79 (21)	0.03[a]
Admission systolic blood pressure (mmHg)	135(29)	133(28)	134(27)	133(28)	0.18[a]
Serum creatinine (μmol/L)	88[75;106]	88[76;106]	88[75;106]	88[75;106]	0.41[a]
Serum glucose (mmol/L)	8.4(4.1)	8.7(4.1)	8.7(4.0)	8.7(4.0)	<0.001[a]
Haemoglobin (g/dL)	14.1(2.1)	13.9(1.8)	14.2(2.1)	14.1(2.1)	0.18[a]
GRACE score	152(40)	154(39)	153(37)	156(39)	0.15[a]

PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; PAD, peripheral artery disease; COPD, chronic obstructive pulmonary disease.
[a]Wilcoxon's rank sum test.
[b]Cochran–Armitage test.

time <30 min). We also recorded where FL was administered (ambulance, emergency department, or cardiology unit).

Clinical outcome was assessed by a combined endpoint defined as occurrence of death (all causes), stroke, recurrent myocardial infarction, or major TIMI bleeding during hospitalization. The self-explanatory electronic case report form (CRF) was provided by the Euro Heart Survey Team at the European Society of Cardiology: the CARDS definitions of the documented parameters were available in the background and could be visualized to facilitate data entry. The list of the CARDS variables is available at the ESC website (http://www.escardio.org/Policy/Pages/data-standard-cards.aspx). Computerized checks were performed to verify the coherence of the data, and queries were generated in case of inconsistencies.

Statistics

Categorical variables are presented as number of cases (percentage), continuous unsymmetrically distributed variables as median [interquartile range (IQR)], and continuous symmetrically distributed variables as mean (standard deviation). Patient characteristics and management were compared by periods of 6 months, using Pearson's χ^2 and Wilcoxon's rank-sum tests, as appropriate. Temporal trends (by periods of 6 months) were tested, using the Cochran–Armitage test for binary and the Jonckheere–Terpstra test for continuous variables. Analyses were repeated for patients admitted in selected centres that had included a balanced number of patients over the 2 years of the survey (<50% variation in the number of patients included over the two years) and at least 10 patients during each period.

Interactions between the changes in rate of timely reperfusion in Periods 1 and 2 vs. 3 and 4, and gender, age (≥ or <75 years), diabetes and centre characteristics [University vs. Community, number of ACS patients admitted in 2005 (> or ≤500), off-hours presentation (admission between 6 pm and 8 am or during the weekend), presence of intensive cardiologic care unit, catheterization laboratory on site, cardiac surgery on site, presence of echocardiography in the admission unit, type of physician (specialist in cardiology or in internal medicine), and presence of a cardiologist on duty] were tested by the Breslow–Day test. To determine the variables associated with timely application of reperfusion among patients treated by reperfusion therapy, we performed a multivariable logistic regression analysis with 'timely reperfusion' as a dependent variable. A second logistic regression

Table 2 Reperfusion modalities according to the period of admission

Variables	Period 1 (*n* = 1920)	Period 2 (*n* = 1912)	Period 3 (*n* = 1913)	Period 4 (*n* = 1910)	P_{trend}
STEMI eligible for reperfusion	1620(84.4)	1629(85.2)	1618(84.6)	1614(84.5)	0.95
Among eligible					
Reperfused	1250(77.2)	1315(80.7)	1335(82.5)	1312(81.3)	0.0007
By FL	412(25.4)	337(20.7)	322(19.9)	280(17.3)	<0.0001
By P-PCI	838(51.7)	978(60.0)	1013(62.6)	1032(64.0)	<0.0001
Among all STEMI					
Admitted 12–24 h	156(8.1)	135(7.1)	148(7.7)	143(7.5)	
No reperfusion	81(51.9)	50(37.0)	46(31.1)	52(36.7)	0.0025
By FL	7(4.6)	4(3.0)	4(2.7)	10(7.0)	0.35
By P-PCI	68(43.6)	81(60.0)	98(66.4)	81(56.6)	0.0091
Among admitted <2 h	219(11.4)	234(12.2)	234(12.2)	218(11.4)	0.99
No reperfusion	59(26.9)	58(24.8)	47(21.1)	56(25.7)	0.49
By FL	49(22.4)	37(15.8)	50(21.4)	41(18.8)	0.70
By P-PCI	111(50.7)	139(59.4)	137(58.6)	121(55.5)	0.35
PCI-preferred patients[a]	1002(52.2)	1105(57.8)	1102(57.6)	1100(57.6)	0.0015
No reperfusion	147(14.7)	143(12.9)	132(12.0)	132(12.0)	0.005
By P-PCI	802(80.4)	912(82.5)	935(84.8)	937(85.2)	0.0006
By FL	53(5.3)	50(4.5)	35(3.2)	31(2.8)	0.0011
Fibrinolytic use[b]					
Pre-hospital	47(10.9)	63(18.4)	74(23.0)	73(25.0)	<0.0001
Emergency unit	89(21.6)	46(13.6)	39(12.1)	30(10.7)	<0.0001
Cardiology unit	256(62.1)	213(63.2)	205(63.7)	172(61.4)	0.68
FL and rescue PCI	95(5.9)	96(5.9)	75(4.6)	71(4.4)	0.0022
Facilitated PCI	38(2.7)	54(3.6)	31(2.1)	48(3.3)	0.13
Patients submitted to reperfusion with time information	1551(95.7)	1567(96.2)	1548(95.7)	1557(96.6)	0.44
Door to needle time[b]	20[10; 34]	20[−22; 31]	15[−21; 34]	15[−37; 30]	0.0011
Pre-hospital	−60[−90;-35]	−60[−85; −40]	−50[−70; −35]	−50[−80; −32]	
In-hospital	25[15; 35]	20[15; 35]	21[15; 42]	22[15; 40]	
Onset of pain to needle	150[90; 240]	150[90; 225]	125[85; 200]	130 [90; 210]	0.008
Pre-hospital	105[65; 185]	107[70; 165]	95[77; 130]	105[65; 185]	
In-hospital	150[90; 240]	160[105; 240]	140[90; 210]	150[95; 240]	
Door to artery time[c]	60[27; 119]	53[25; 110]	50[27; 95]	45[26; 84]	<0.0001
Onset of pain to artery time[c]	240[155; 390]	240[150; 405]	220[149; 365]	230[145; 386]	0.056
Fibrinolytics <30 min[b]	254(61.7)	219(65.0)	217(67.4)	199(71.1)	0.0081
P-PCI <90 min[c]	606(72.3)	707(72.3)	772(76.2)	826(80.4)	<0.0001
Timely reperfusion[d]					
Among eligible	860(53.1)	926(56.8)	989(61.1)	1025(63.5)	<0.0001
Among reperfused	860(68.8)	926(70.4)	989(74.1)	1025(78.1)	<0.0001
Centres including >10 patients/period	1111	1563	1689	1806	
Eligible for reperfusion	933(84.0)	1331(85.2)	1416(83.8)	1519(84.1)	0.71
Reperfused	770(82.7)	1089(81.9)	1173(82.9)	1240(81.6)	0.65
By FL	210(22.5)	212(15.9)	220(15.5)	239(15.7)	0.0004
By P-PCI	560(60.2)	877(65.9)	935(67.3)	1001(65.9)	0.012
Door to needle	20[0; 30]	15[-40; 30]	15[-40; 30]	15[-43; 28]	0.0033
Door to artery	67[30; 140]	53[25; 115]	49[26; 90]	44[25; 83]	<0.0001
FL <30 min[b]	149(70.9)	148(69.8)	158(71.8)	181(75.7)	0.21

Continued

Table 2 *Continued*

Variables	Period 1 ($n = 1920$)	Period 2 ($n = 1912$)	Period 3 ($n = 1913$)	Period 4 ($n = 1910$)	P_{trend}
P-PCI <90 min[c]	371(66.2)	620(70.7)	734(77.0)	798(79.7)	<0.0001
Timely reperfused[d]	520(55.8)	768(57.7)	892(63.0)	979(64.4)	<0.0001

[a]Patients admitted >4 h and <12 h after onset of symptoms, or with contra indication for fibrinolysis, cardiogenic shock or Killip Class 4.
[b]Among patients submitted to fibrinolytic therapy.
[c]Among patients submitted to primary PCI.
[d]Door to needle time <30 min or door to artery time <90 min.

Table 3 In-hospital treatments according to the period of admission

All STEMI patients	Period 1 ($n = 1920$)	Period 2 ($n = 1912$)	Period 3 ($n = 1913$)	Period 4 ($n = 1910$)	P_{trend}
Aspirin	1843(96.0)	1814(94.9)	1827(95.5)	1816(95.1)	0.33
Clopidogrel					
No loading dose	628(35.4)	373 (20.2)	328 (17.6)	257 (13.5)	
Loading 300 mg	518(29.2)	675(36.6)	637(34.1)	653(34.3)	<0.0001
Loading 600/900 mg	628(35.4)	794(43.1)	901(48.3)	995(52.2)	
Maintenance dose	1448(75.5)	1715(89.8)	1764(92.3)	1807(94.9)	<0.0001
Beta blocker	1544(80.4)	1511(79.0)	1526(79.8)	1485(77.8)	0.09
ACEI[a]	1426(74.3)	1439(75.3)	1417(74.1)	1379(72.2)	0.10
Coronary angiography	1335(69.9)	1491(78.0)	1537(80.6)	1513(79.5)	<0.0001
Patients eligible for reperfusion	$n = 1620$	$n = 1629$	$n = 1618$	$n = 1614$	
Aspirin	1555(96.0)	1548(95.0)	1547(95.6)	1544(95.7)	0.86
Clopidogrel					
No loading dose	511(34.3)	295(18.9)	264(16.7)	201(12.5)	
Loading 300 mg	434(29.1)	577(36.9)	540(34.2)	551(34.2)	<0.0001
Loading 600/900 mg	546(36.6)	690(44.2)	773(49.0)	854(53.3)	
Maintenance dose	1235(76.3)	1468(90.2)	1486(91.9)	1533(95.2)	<0.0001
Clopidogrel among FL patients[a]					
No loading dose	39(17.5)	33(12.9)	29(11.5)	28(10.2)	
Loading 300 mg	145(65.2)	176(69.0)	177(73.3)	209(76.0)	0.02
Loading 600/900 mg	39(17.5)	46(18.0)	36(14.9)	35(12.7)	
Clopidogrel among P-PCI patients[b]					
No loading dose	59(6.9)	70(6.5)	60(5.2)	48(4.1)	
Loading 300 mg	272(31.7)	350(32.7)	306(26.7)	275(23.7)	<0.0001
Loading 600/900 mg	527(61.3)	649(60.7)	780(68.1)	868(72.2)	
Beta blocker	1310(80.9)	1289(79.1)	1295(80.0)	1274(78.9)	0.28
ACEI	1202(74.2)	1231(75.6)	1202(74.3)	1180(73.1)	0.35
Coronary angiography	1158(71.8)	1298(79.7)	1321(81.9)	1301(81.0)	<0.0001

ACEI, angiotensin converting enzyme inhibitors.
[a]Data available for 74% of the patients.
[b]Data available for 91% of the patients

was performed with 'door to balloon in the first quartile' as dependent variable. Variables entered into the models were patient characteristics [age, gender, weight, cardiovascular risk factors, Killip class (>2), heart rate (≥100 bpm), systolic blood pressure (≥100 mmHg), anterior location of MI, previous infarction, percutaneous or surgical revascularization, stroke, peripheral artery disease, heart failure, admission haemoglobin, serum glucose and creatinine levels] and centre characteristics. Results were expressed as odds ratios with 95% confidence intervals. All analyses were performed using SAS software, version 9.2 (SAS Institute, Inc., Cary, NC, USA).

Results

Population

During the 2 years of inclusion, among the 19 205 patients included in the Euro Heart Survey ACS III registry, 7655 presenting with STEMI were included in this analysis (*Figure 1*). In total, 58% were admitted off-hours or during the weekend, 42% were admitted to a university centre, 25% to a high volume centre, and 73.6% to a centre with catheterization laboratory on site. The majority of patients (80.6%) were admitted to centres that included more than 10 patients per period and a balanced number of patients across the four periods. The clinical characteristics of the population are presented in *Table 1*, by period of admission. During the study period, there was a temporal trend towards more diabetic patients, fewer patients with peripheral artery disease, previous coronary artery bypass graft, chronic obstructive pulmonary disease and Killip Class >2, but the average Global Registry of Acute Coronary Events (GRACE) risk score remained stable.

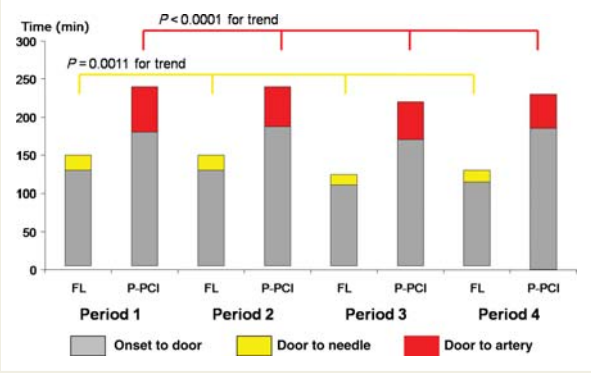

Figure 2 Temporal trends in delay times. Red bars, door to artery; yellow bars, door to needle; grey bars, onset of symptoms to door; *P*-value from Jonckheere–Terpstra test.

Reperfusion therapy

Table 2 presents the details of reperfusion therapy. Among eligible patients (84.7% of all STEMI patients), 5213 (80.4%) were submitted to reperfusion; 3862 (59.6%) by P-PCI and 1351 (20.8%) by FL. Although the rate of patients eligible for reperfusion was comparable across the four periods, the rate of patients treated by reperfusion increased from 77.2 to 81.3% ($P = 0.0007$). The strategy of reperfusion changed over the 2 years, with an increase in the use of P-PCI from 51.7 to 64.0% ($P < 0.0001$ for trend) and a significant decrease in the use of FL (from 25.4 to 17.3%, $P < 0.0001$ for trend). Almost two-thirds of FL were performed in cardiology units, although there was an increase in the use of pre-hospital FL (from 2.8 to 4.3%, $P < 0.0001$), representing 25% of all FL by the end of 2008. PCI-preferred patients represented two-thirds of the population eligible for reperfusion. In this group, P-PCI increased from 80.4 to 85.2% ($P = 0.0006$ for trend) and the rate of FL decreased from 5.3 to 2.8% ($P = 0.0011$ for trend). The rate of patients admitted between 12 and 24 h after onset of symptoms remained stable but, in this subgroup, the rate of reperfusion increased through an increase in P-PCI. In-hospital treatments are presented by period of admission in *Table 3* in the whole population and in patients eligible for reperfusion. In parallel to the changes in reperfusion strategy, the rate of use of clopidogrel and coronary angiography increased.

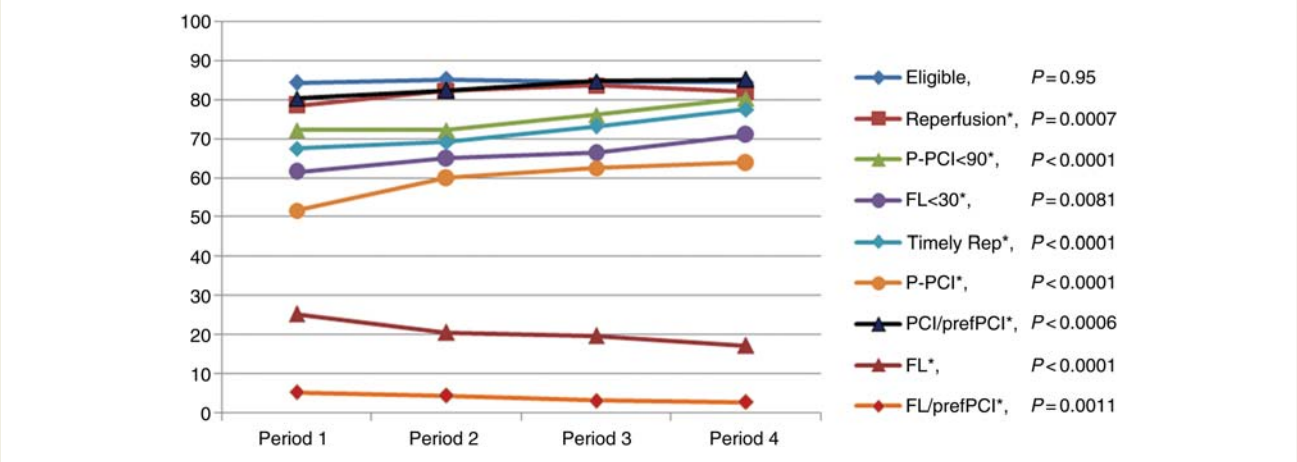

Figure 3 Temporal trends in performance measure for reperfusion. Eligible: patients admitted with ST-segment elevation MI, within 12 h after onset of symptoms. Reperfusion: patients eligible for reperfusion, actually treated with reperfusion. P-PCI: patients eligible for reperfusion, treated with primary PCI. FL: patients eligible for reperfusion, treated with fibrinolytics. P-PCI < 90: patients treated by PCI within 90 min after admission. FL < 30: patients treated with fibrinolytics within 30 min after admission. Timely Rep: patients treated by PCI within 90 min or by fibrinolysis within 30 min after admission. PCI/prefPCI: patients treated by PCI among group defined as 'PCI preferred'. FL/prefPCI: patients treated by fibrinolysis among group defined as 'PCI preferred'.

Temporal trends in time to reperfusion

Time information was available for 98% of the patients. The overall median door to needle time was 20 min [IQR −15; 31] and median door to artery time was 50 min [IQR 27; 100]. Accordingly, 58.6% of patients eligible for reperfusion received reperfusion therapy in a timely manner: 65.8% of FL was performed <30 min and 75.4% of P-PCI within <90 min. *Figure 2* presents the temporal trends in delay times in patients undergoing FL and P-PCI. Between Periods 1 and 4, there was a 25% reduction in both door to needle (20−15 min, $P = 0.0011$) and door to artery (60−45 min, $P < 0.0001$) times. Among patients treated with FL, the rate of FL <30 min increased from 61.7 to 71.1% ($P = 0.0081$). Among those treated by P-PCI, the rate of P-PCI <90 min increased from 72.3 to 80.4% ($P < 0.0001$). For all those eligible for reperfusion, the rate of patients treated in a timely manner increased from 53.1 to 63.5% ($P < 0.0001$). *Figure 3* displays the temporal trends in PMs for reperfusion. When analyses were restricted to patients admitted to centres that included a balanced number of patients over the 2 years of the survey and at least 10 patients per period, we observed similar increases in the rate of use of P-PCI and timely reperfusion; as well as similar reductions in door to artery and door to needle times (*Table 2*). The increase in the rate of patients with timely reperfusion between Periods 1−2 and 3−4 was significant in all subgroups, except in centres that included only a limited number of patients, where a significant interaction was observed ($P = 0.006$). Other centre or patient characteristics did not alter the improvement in time to reperfusion over the 2 years (*Figure 4*). Multivariable analysis showed that among patients eligible for reperfusion, the factors associated with timely application of reperfusion were: the period of admission (more in Period 4 than in Period 1 or 2), Killip class >2, and systolic blood pressure at admission, history of heart failure and the centre characteristics (high volume and university centre; *Figure 5*). For patients treated by P-PCI, Killip class, systolic blood pressure, and admission to a high volume or university centre or during work hours were associated with a door to artery time within the first quartile (i.e. <27 min).

Outcomes

Vital status (in-hospital mortality) was available for 100% of the patients: 546 (7.1%) of all STEMI patients and 443 (6.8%) of those eligible for reperfusion died. These rates are comparable with those observed in other large registries, including STEMI patients. This argues for a lack of patient selection and therefore for the representativeness of the patients admitted for STEMI. In-hospital mortality and adverse events are presented in *Table 4* for the whole population and among patients eligible for reperfusion. In-hospital mortality was 6.8% and the combined event rate was 11.5%. The rate of major bleeding was stable, but in-hospital re-infarction decreased (from 3.1 to 1.4%, $P < 0.0001$) as did mortality (from 8.1 to 6.6%, $P = 0.047$) and the rate of combined endpoint (from 13.1 to 10.4%, $P = 0.006$). Similar temporal trends were observed the whole STEMI population and among those eligible for reperfusion.

Discussion

This analysis from the Euro Heart Survey ACS III registry provides insights into the modalities of reperfusion in STEMI patients across Europe. On the basis of this assessment of PMs for reperfusion, we observed a significant and rapid

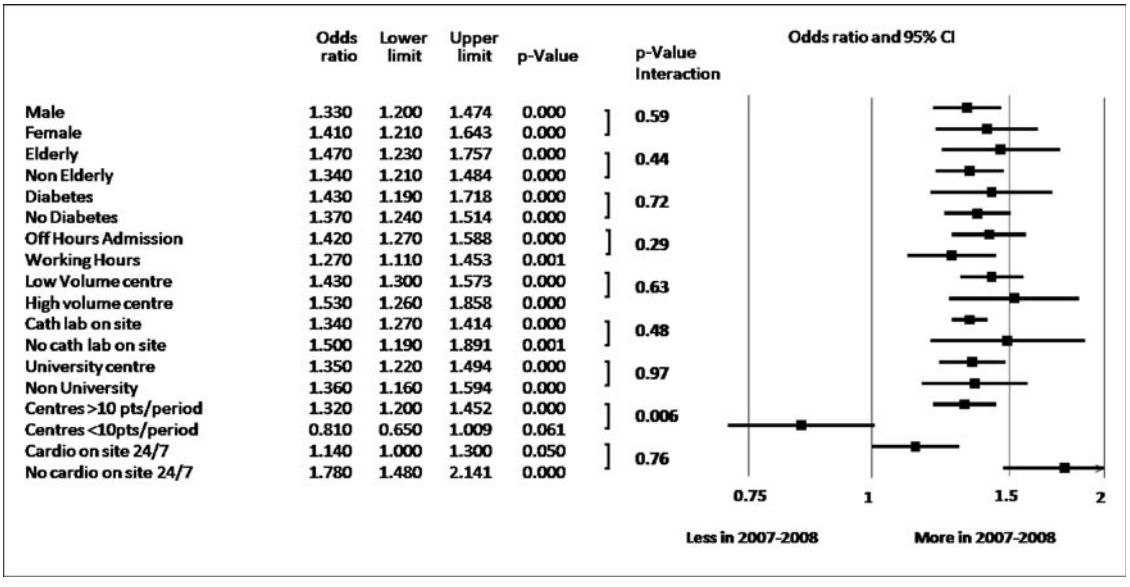

Figure 4 Changes in the rate of patients receiving timely reperfusion (i.e. fibrinolytics <30 min or by primary PCI <90 min), between 2006−2007 and 2007−2008, in subgroups.

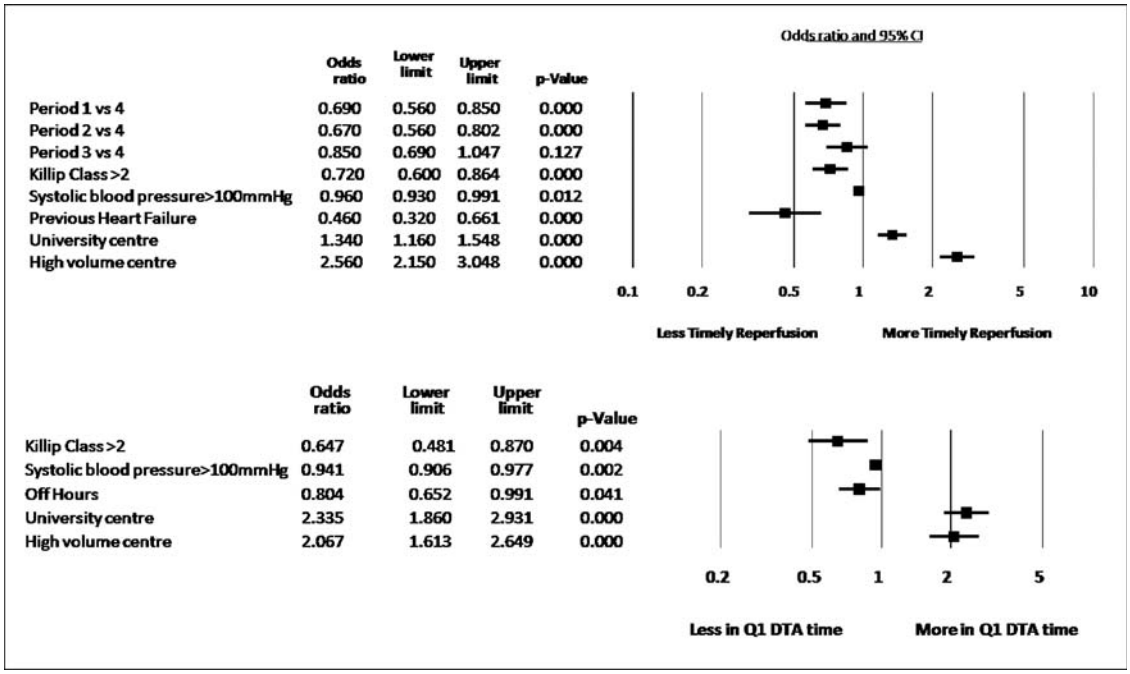

Figure 5 Upper panel: independent factors associated with timely reperfusion (fibrinolytics <30 min or primary PCI <90 min). Lower panel: independent factors associated with door to artery time in the first quartile (i.e. <27 min). Q1 DTA, first quartile of door to artery time.

Table 4 **In-hospital outcomes according to the period of admission**

All STEMI patients	Period 1 (n = 1920)	Period 2 (n = 1912)	Period 3 (n = 1913)	Period 4 (n = 1910)	P_{trend}
In-hospital major bleedings	72(3.8)	69(3.6)	74(3.9)	59(3.1)	0.36
In-hospital re-infarction	59(3.1)	35(1.8)	27(1.4)	26(1.4)	<0.0001
In-hospital stroke	20(1.0)	11(0.6)	14(0.7)	15(0.8)	0.49
In-hospital death	155(8.1)	140(7.3)	125(6.5)	126(6.6)	0.047
Combined endpoint	252(13.1)	222(11.6)	210(11.0)	198(10.4)	0.006
Patients eligible for reperfusion	n = 1620	n = 1629	n = 1618	n = 1614	
In-hospital major bleedings	66(4.1)	65(4.0)	63(3.9)	51(3.2)	0.18
In-hospital re-infarction	50(3.2)	29(1.8)	27(1.7)	25(1.5)	0.0025
In-hospital stroke	16(1.0)	10(0.6)	12(0.7)	13(0.8)	0.67
In-hospital death	131(8.1)	115(7.1)	101(6.2)	96(5.9)	0.0099
Combined endpoint	219(13.5)	190(11.6)	177(10.9)	160(9.9)	0.001

improvement in the quality of reperfusion strategies between October 2006 and November 2008, particularly as regards the delays to reperfusion.

Performance measures for reperfusion in the Euro Heart Survey Acute Coronary Syndromes III

Reperfusion therapy in eligible patients has been used as a quality indicator since 1994[10] and is still advocated by the ACC/AHA in the setting of STEMI.[11] As compared with the first Euro Heart Survey (EHS ACS I) conducted in 2000–2001[12] and the second (EHS ACS II)[13] in 2004, reperfusion rates have gradually increased over the course of the three Euro Heart Survey ACS programs. By the end of 2008, 81.3% of eligible patients received reperfusion therapy. This reperfusion rate is comparable with that reported in the National Registry of Myocardial Infarction (NRMI) in 2006[14] or in the GRACE registry in 2006[15] and 2007,[16] as are the relative proportions of FL and P-PCI. The median delays from onset of symptoms to door, from door to needle, and from door to artery were comparable with those reported in the GRACE registry in 2007. Door to needle time was shorter in EHS ACS III than that reported in other registries, probably because of the wider use

of pre-hospital FL. In these patients, the door to needle time presents a negative value, and pre-hospital FL represented up to 25% of the overall use of FL. Despite a similar time to P-PCI as in the European report from Widmisky *et al.*[17] and in the GRACE registry,[16] direct comparisons of the time to P-PCI, and subsequently of the rate of P-PCI < 90 min, are challenging, because in EHS ACS III, we did not record the door to balloon time, but rather the door to artery time. However, since we focused more on temporal changes rather than on absolute values, the use of door to artery instead of door to balloon time would likely not alter these results and we can assume that variations in the door to artery time correspond to comparable variations in the door to balloon time.

Temporal trends in reperfusion rate and modalities

One important finding in our study was the significant change over the 2-year study period in the rate and type of reperfusion. As reported in other registries,[14–15] the overall reperfusion rate increased, with a shift from FL to P-PCI. Despite a significant 32% relative decrease in the use of FL, the proportion of pre-hospital FL increased, representing 25% by the end of the study, in agreement with the ESC guidelines.[18]

The choice between FL and P-PCI is not considered as a PM,[11,19] but triage and decision for FL or for P-PCI are important issues in clinical practice. On the basis of meta regression analyses, it has been shown that the time delay that nullifies the survival benefit of P-PCI over FL differs according to the patient's baseline risk.[20] Thus, patients at higher risk, such as those defined as 'PCI-preferred', benefit more from P-PCI than from FL, even at the price of a longer delay.[4,20] The ACC/AHA guidelines for the management of STEMI[8,18] recommend P-PCI over FL when it can be performed within 120 min, but also in case of contra-indication for FL, high bleeding risk, in patients presenting late or in case of cardiogenic shock. In the PCI-preferred group, both the significant increase in P-PCI and decrease in FL can be considered as improvements in quality of care, as suggested in an analysis of the NRMI.[9] Although the rate of patients admitted between 12 and 24 h after onset of symptoms remained stable, the use of reperfusion by P-PCI in these patients increased. Since reperfusion by P-PCI for patients admitted late (12–24 h) corresponds to a Class IIb recommendation of the ESC guidelines,[18] it could also be considered in the future as a quality indicator.

Temporal trends in reperfusion delays

We report significant reductions in door to needle and door to artery times, explaining the increase in the rate of timely reperfusion. A reduction in door to balloon and door to needle times has been reported in the NRMI,[14] and the National Audit of Myocardial Infarction Project.[21] Conversely, in a recent analysis of the GRACE registry,[16] no significant reduction in time to reperfusion was found. Specific strategies and programs to improve reperfusion time, such as the Reperfusion of acute myocardial infarction in North Carolina emergency department (RACE) study,[22] the Door-to-Balloon (D2B) Campaign,[23] or the National Cardiovascular Data Registry-Acute Coronary Treatment and Intervention Outcomes Network (NCDR-ACTION), have succeeded in reducing time to reperfusion. These programs are based on organizational changes aiming to simplify and speed up access to FL or P-PCI: having emergency physicians and a central page operator to activate the catheterization laboratory while the patient is still en route, having a cardiologist on site at all times and staff who arrive within 20 min, and providing real-time feedback to staff have been shown to be effective.[24] In the RACE study, the quality program resulted in a 13% relative reduction in door to balloon time, and a 17% relative reduction in door to needle time. In the Get With the Guidelines program (GWTG), the door to balloon time decreased from 101 to 87 min.[25] In EHS ACS III, the relative reductions in door to needle and door to artery times were comparable with those reported in the RACE[22] and GWTG programs.[25] Timely application of reperfusion therapy was associated with patient characteristics (previous heart failure, Killip class, systolic blood pressure), type of centre (high volume, university), and the period of admission. It is possible that some strategies used in university or high volume centres coincide with those used in specific programs, but we did not record these centre-related characteristics in the EHS ACS III.

The increase in the rate of use of clopidogrel and coronary angiography, as well as the decrease in in-hospital mortality, observed in parallel to the changes in the PMs for reperfusion, suggest that the temporal changes observed between 2006 and 2008 in the EHS ACS III were not only related to reperfusion therapy and were beneficial for the patients.

Limitations

The present study has the usual limitations of observational studies: (i) despite a broad spectrum of centres participating in the EHS ACS III registry, covering 21 countries, including high and low volume, university and non-university centres, with and without catheterisation laboratory on site, we cannot exclude the possibility that participating centres were more motivated and more aware of the quality of care. (ii) To limit selection bias, enrolment of consecutive patients admitted during the first week of each month was strongly recommended, but we cannot rule out any selection of patients. Moreover, the rate of in-hospital mortality is typical of an unselected population. Furthermore, when analyses were restricted to patients enrolled in selected centres where inclusions were balanced over the 2 years, the results were not altered. (iii) Time of the first medical contact and time of the first device of PCI were not recorded as recently proposed by a 2008 ACC/AHA statement.[19] Finally, patients included in the reperfusion analyses were only those who were initially admitted for STEMI and treated at first site of admission and our results are not applicable for transferred patients.

Conclusions

In the Euro Heart Survey ACS III registry, among patients admitted for STEMI and eligible for reperfusion, all PMs for reperfusion improved significantly between 2006 and 2008. We observed a significant trend for an increase in reperfusion rate and in the use of P-PCI in the whole population, as well as in patients in whom this technique has been shown superior

to FL. The door to needle and door to artery times decreased and the rate of patients undergoing reperfusion therapy in a timely manner increased significantly.

Conflict of interest: none declared.

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