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More is not better in the early care of acute myocardial infarction: a prospective cohort analysis on administrative databases

Hans Van Brabandt*, **Cécile Camberlin, France Vrijens, Yves Parmentier, Dirk Ramaekers, and Luc Bonneux**

Belgian Health Care Knowledge Centre (KCE), Wetstraat 155, B-1040, Brussels, Belgium

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Aims To assess the outcome and costs of patients with acute myocardial infarction (AMI) after initial admission to hospitals with or without catheterization facilities in Belgium.

Methods and results From a nationwide hospital register, we retrieved the data of 34 961 patients discharged during 1999–2001 with a principal diagnosis of AMI. They were initially admitted to hospitals without catheterization facilities (A), with diagnostic (B1) or interventional catheterization facilities (B2). Mortality has been recorded till the end of 2003 and re-admissions till the end of 2001.
The mortality hazard ratio and 95% CI of 5 years mortality of A vs. B2 was 1.01 (0.97, 1.06) and of B1 vs. B2 was 1.03 (0.98, 1.09). Re-admission rates and 95% CI for cardiovascular reason per 100 patient-years were 23.5 (22.7, 24.3) for A, 23.8 (22.5, 25.1) for B1, and 22.0 (21.2, 22.9) for B2. The mean cost in hospital of a patient at low risk with a single stay was in A €4072 (median: 3,861; IQR: 4467–3476), in B1 €5083 (median: 5153; IQR: 5769–4340), and in B2 €7741 (median: 7553; IQR: 8211–7298).

Conclusion Services with catheterization facilities compared with services without them showed no better health outcomes, but delivered more expensive care.

Introduction

Thrombolysis revolutionized emergency treatment of AMI.[1–4] Recent trial evidence has suggested that primary PCI might be a more effective treatment.[3,5–9] It is conceivable to expand the availability of PCI and to treat all patients eligible for reperfusion treatment preferentially with a PCI.

However, an issue often overlooked in the evaluation of randomized controlled trials and particularly in the evaluation of technologies is the external validity. PCI is not a drug, but a medical intervention requiring experience and equipment.[10,11] Trial results obtained in patients, carefully selected and treated by experienced cardiologists in well-equipped centres, may not be so easily obtained in the average patient in day-to-day practice of busy hospitals. This has been confirmed by the GRACE registry,[12] an international observational registry which prospectively studied and compared the outcome of patients with an AMI admitted to hospitals with and without catheterization facilities. After adjusting for baseline variables, medical history, and geographical region, patients admitted first to hospitals with catheterization facilities did not have a survival benefit over those first admitted to hospitals without such facilities.

Furthermore, PCI is more expensive, and the expansion of the number of catheterization laboratories per inhabitant will increase healthcare costs. If the added benefit of PCI is small compared with the added costs, policy makers should prefer the most cost-effective interventions from a societal perspective.

In Belgium, care for cardiac patients has been organized in three levels, depending on whether catheterization facilities, PCI, and/or cardiac surgery is available. Thrombolysis constitutes the only means of reperfusion in secondary hospitals (labelled A). PCI is available in tertiary hospitals (labelled B2), whereas intermediary hospitals, labelled B1, offer diagnostic coronary angiography only but no PCI. The policy question addressed was whether it was more efficient to convert the intermediary (B1) hospital services into tertiary (B2) ones or to revert B1 services into secondary (A) hospitals.

We evaluated the costs and effects of treatment, depending on the level of care (A, B1, or B2) to which AMI patients initially were referred.

Methods

Permission to use the linked individual records of the hospital register and of the reimbursed fees by unique double-encrypted patient identification number was obtained from the authorized body.

* Corresponding author. Tel: +32 2 287 33 01; fax: +32 2 287 33 85.
E-mail address: hans.vanbrabandt@kenniscentrum.fgov.be

Source data

We retrieved administrative data of all patients discharged during 1999–2001 from any Belgian hospital with a diagnosis of AMI. Data of 1997 and 1998 could be used to retrieve information on hospital admissions prior to the initial admission. A patient was considered as having an AMI when an ICD-9-CM (version 1997) code 410 was entered as a principal diagnosis. Two separate administrative hospital databases are at our disposal: one with clinical data and one with costs billed to insurance companies. Mortality data were obtained from health insurers until 2003. These three databases (hospital data, health insurance billing data, and mortality) are linked by a double-encrypted unique patient code (to ensure patient privacy protection), enabling us to reconstruct individual patient histories. For privacy reasons, the exact date of admission is not available, but only the month of admission.

A total of 115 secondary hospitals (A), 29 tertiary hospitals (B2), and 20 intermediary hospitals (B1) are covering the entire population of Belgium (10 million inhabitants). Because the treatment of AMI may involve interventional, diagnostic and therapeutic procedures which cannot be delivered in all facilities, patients often have to be transferred to a higher-level hospital. In order to take these transfers into account, we recorded any hospitalization with a cardiovascular principal diagnosis, during the month of the initial admission and the subsequent month, with a maximum of four admissions. This period was defined as the 'episode of care'. Re-admissions later on were designated as 'late re-admissions'. The level of care of the hospital of first arrival classified patients. The analysis and interpretation is based on the assumption of a natural experiment: the level of care of the hospital of admission is independent of the severity of the AMI, but is determined by the location where the acute event is taking place. Ambulances are required by law to drive to the nearest hospital. We excluded confounding by indication on available data. We assumed that this confounding by indication holds also for unavailable data, e.g. the presence or absence of ST-segment elevation.

We defined an urgent PCI as a PCI on the day of admission. A cardiovascular history was defined as an admission with a principal cardiovascular discharge diagnosis (ICD-9-CM codes 390–459) in the previous years since 1997. When any antidiabetic drug was prescribed or when they presented a diagnosis 250.xx during any admission during 1999, 2000, or 2001, patients were labelled as diabetic.

Cost assessment

Diagnostic and therapeutic variability by the level of care of initial admission was assessed, including all transfers within the episode. To compare the costs of different levels of cardiac care in comparable patients, we identified the costs of treating a group of patients arbitrarily considered as at low risk, with a single hospital stay during the episode of care. Low risk was defined as being <75 years, without diabetes and without a cardiovascular history, alive at the end of the episode and classified in APR-DRG major diagnostic category 5 (diseases and disorders of the circulatory system).[13] Costs considered are not true costs, but claims for medical acts, medical supplies (including implants and blood), and drugs as reimbursed by health insurance according to the legal tariffs published by the National Insurance Institute for Illness and Disability in Belgium.[14] Co-payments and supplements charged to the patients are not included. To assess whether expensive care led to better outcomes, we categorized hospitals within each level of care according to quartiles of average costs per patient (cheap: $<$ P25, intermediate: P25–P75, and expensive: $>$ P75) on the basis of treatment costs of single-stay episodes of the low-risk group of patients, as defined before.

Statistical analyses

The odds ratios (ORs) of short-term mortality after initial admission in different levels of care, defined as patients dying in the month of admission or the month thereafter, was calculated with a logistic regression model, adjusting for patient's age, gender, history of cardiovascular disease, and diabetes and taking into account clustering of patients within hospitals.[15] The hazard ratios of long-term mortality after initial admission in different levels of care, defined as patients dying in the month of admission or the years thereafter till a maximum of 5 years, was calculated with a Cox proportional hazards model, adjusted for the same baseline characteristics and adapted for data grouped by monthly interval. Effect estimates and two-sided 95% confidence intervals are presented. Survival curves over 5 years, stratified by levels of care of initial admission, were estimated in a life-table (censoring patients at the end of 2003). The effect of different hospital categories based on level of resource use on patient outcome (short term and long term) was assessed using the statistical models described before.

Re-admission rates were calculated by the number of hospital re-admissions over 3 years divided by the person-years of follow-up in all patients alive at the end of the initial episode of care. We considered re-admission for AMI (primary diagnosis ICD-9 410), all cardiovascular diseases (primary diagnosis ICD-9 390–459), and cardiac re-interventions (coronary angiography, PCI, or CABG). The cumulative probability of revascularization over 3 years was estimated for all patients, stratified by the level of care of the initial admission, with the life-table method (censoring patients at their time of death or at the end of 2001). The SAS software version 9.1 was used for all analyses.

Results

Baseline characteristics

A total of 34 961 AMI patients were identified; 66.4% of patients were male. Their mean age at initial admission was 67.8 years (64.7 years for males, 73.9 years for females). Of those patients, 20.3% had a cardiovascular history and 24.8% were diabetics. Baseline patient characteristics and transfers by cardiac care level of initial admission are presented in *Table 1*. There are small differences between patients initially admitted to a hospital of level A, B1, or B2. Patients in B2 level of care were slightly younger, 66.7 years vs. 67.9 (B1) and 68.8 (A), and more male, 67.8% in B2 vs. 65.8 in A and 65.1 in B1. Patients initially admitted to A and B1 hospitals, 38.4 and 33.4%, respectively, were transferred during their episode of care to a B2 hospital.

Treatment of AMI

The treatment offered by the care level of the initial admission and subsequently in the entire episode of care is presented in *Table 2*. The percentage of patients reperfused, i.e. receiving thrombolytics or treated by urgent PCI, is similar across the three levels of care of initial admission: 36.2% in A, 34.0% in B1, and 38.0% in B2. As expected, the mode of reperfusion differs: A and B1 hospitals use thrombolytics, B2 hospitals treat half of the reperfused patients with thrombolytics and half by means of urgent PCI. The overall probability of revascularization, i.e. the probability of having had a PCI or a surgical myocardial revascularization (CABG) at the end of the episode of care, is higher in patients initially admitted to B2 hospitals (53.7%) than in patients initially admitted to A and B1 hospitals (32.4 and 33.1%, respectively). This difference between revascularization probabilities persists after 3 years: 41.1% in level A, 41.9% in level B1, and 59.0% in level B2 (*Figure 1*). This suggests that supply induces demand independent of patient needs.

Table 1 Patient characteristics at initial admission for AMI, patients transferred to B2 hospitals and short-term mortality, by level of care of initial admission

	Level of care of initial admission			
	A, *n* (%)	B1, *n* (%)	B2, *n* (%)	All patients, *n* (%)
Total initial admissions (count)	15 205	6 367	13 389	34 961
Age, years [mean (SD)]	68.8 (13.3)	67.9 (13.8)	66.7 (13.7)	67.8 (13.6)
Male patients	10 001 (65.8)	4 142 (65.1)	9 073 (67.8)	23 216 (66.4)
Cardiovascular history	2 953 (19.4)	1 269 (19.9)	2 863 (21.4)	7 085 (20.3)
Diabetes	3 701 (24.3)	1 653 (26.0)	3 325 (24.8)	8 679 (24.8)
Transfer to B2 hospital	5 840 (38.4)	1 826 (33.4)	—	—
Short-term mortality	2 504 (16.5)	1 000 (15.7)	1 925 (14.4)	5 429 (15.5)

In A, only thrombolysis is available, in B1, thrombolysis and diagnostic coronary angiography are available, whereas B2 also has PCI facilities. A patient transferred from one care level to another is counted only once in the care level of admission.

Table 2 Emergency and elective treatment of AMI (taking into account transfers to other hospitals), by level of care of initial admission

	Level of care of initial admission			
	A, *n* (%)	B1, *n* (%)	B2, *n* (%)	All patients, *n* (%)
Number of initial admissions	15 205	6 367	13 389	34 961
During the initial admission (first stay)				
Conservative therapy	9 195 (60.5)	3 984 (62.6)	5 532 (41.3)	18 711 (53.5)
Reperfusion	5 507 (36.2)	2 165 (34.0)	5 093 (38.0)	12 765 (36.5)
Thrombolysis	5 476 (36.0)	2 161 (33.9)	2 756 (20.6)	10 393 (29.7)
Urgent PCI	43 (0.3)	14 (0.2)	2 635 (19.7)	2 692 (7.7)
Urgent CABG	0 (0.0)	0 (0.0)	63 (0.5)	63 (0.2)
Revascularization	1 047 (6.9)	431 (6.8)	6 469 (48.3)	7 947 (22.7)
PCI	1 040 (6.8)	431 (6.8)	5 870 (43.8)	7 341 (21.0)
CABG	7 (0.05)	0 (0.0)	662 (4.9)	669 (1.9)
CAG	1 430 (9.4)	1 144 (18.0)	7 389 (55.2)	9 963 (28.5)
During the episode of care				
Conservative therapy	7 100 (46.7)	3 040 (47.7)	5 021 (37.5)	15 161 (43.4)
Revascularization during episode	4 922 (32.4)	2 109 (33.1)	7 195 (53.7)	14 226 (40.7)
PCI	3 819 (25.1)	1 643 (25.8)	6 227 (46.5)	11 689 (33.4)
CABG	1 136 (7.5)	478 (7.5)	1 087 (8.1)	2 701 (7.7)
CAG	5 461 (35.9)	2 621 (41.2)	8 049 (60.1)	16 131 (46.1)

CAG, coronary angiography. Conservative therapy: neither reperfusion nor revascularization.

Mortality

Tables 1 and *3* present short-term and long-term mortality results by level of care of initial admission. A total of 5429 deaths (15.5% of patients) were observed during the month of initial admission or the subsequent month. Percentages were 16.5, 15.7, and 14.4, respectively, for patients initially admitted to A, B1, or B2 hospitals (*Table 1*). Increasing age, female gender, cardiovascular disease history, and diabetes increase the risk of death, but not the care level of the initial admission: ORs (95% CI) for short-term mortality of patients initially admitted to A or B1 compared with patients initially admitted to B2 was 1.05 (0.93, 1.19) and 1.03 (0.89, 1.19), respectively.

Figure 2 also presents the absolute 5 year survival of all patients in an actuarial life-table model, for a mean mortality follow-up of 31 months. The proportion of patients surviving 5 years was 61.5% (A), 62.9% (B1), and 65.1% (B2), respectively. The multivariable Cox proportional hazards model, adjusting for age, sex, cardiovascular history, and diabetes, shows that the cardiac care level of the initial admission has no statistically significant influence on the survival of patients (*Table 3*): the hazard ratio and 95% CI for patients initially admitted to A compared with patients initially admitted to B2 is 1.01 (0.97, 1.06), and B1 compared with B2 is 1.03 (0.98, 1.09).

Re-admissions (over 3 years)

Re-admission rates (95% CI) per 100 patient-years over 3 years of follow-up for a subsequent AMI was 2.8 (2.6, 3.1) for patients alive at the end of the episode of care and with initial admission in A, 2.5 (2.2, 2.9) for patients in B1, and 2.4 (2.2, 2.7) in B2. Rates of late re-admissions (after the episode of care) of all cardiovascular causes (23.0; 22.5, 23.5) and of re-interventions (coronary angiography, PCI, and CABG) (8.8; 8.5, 9.1) were also similar between the care levels (*Table 4*).

Costs

On a comparative basis, we identified the costs of treating patients at low risk with a single hospital stay only. The

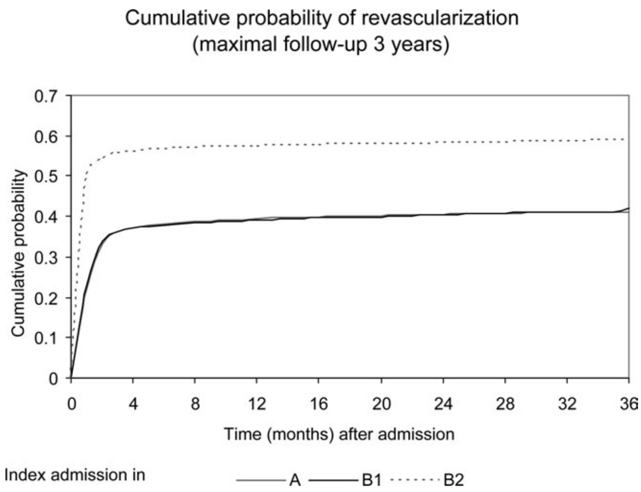

Figure 1 Cumulative probability of revascularization (PCI or CABG), stratified by care level of initial admission.

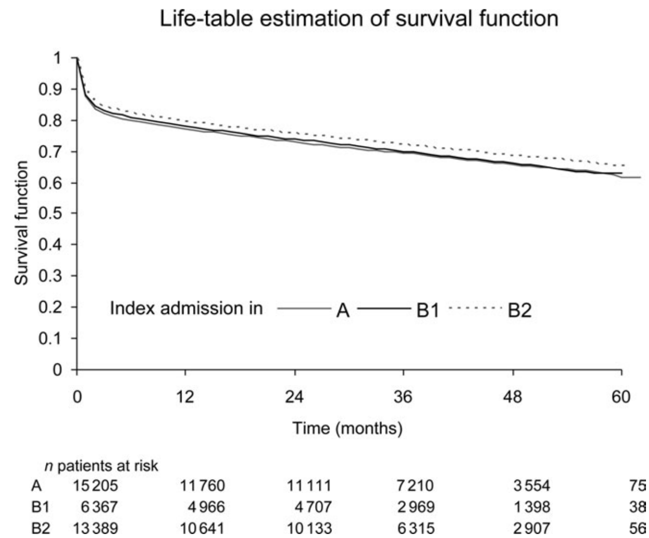

Figure 2 Survival curve over 5 years after admission for AMI, stratified on the basis of care level of initial admission.

Table 3 Short-term mortality (death within month of initial admission or within the month after) and long-term (over 5 years) mortality (results from regression models): comparisons of level of care of initial admissions

Short-term mortality (results from logistic regression)		
Factor	OR[a]	95% CI
Age (increase of 10 years)	2.13	(2.06, 2.19)
Gender (female vs. male)	1.12	(1.05, 1.19)
Cardiovascular history	1.22	(1.14, 1.31)
Diabetes	1.23	(1.15, 1.31)
Comparison of cardiac care levels		
A vs. B2	1.05	(0.93, 1.19)
B1 vs. B2	1.03	(0.89, 1.19)
Long-term mortality (results from Cox PH regression)		
Factor	Hazard ratio[a]	95% CI
Age (increase of 10 years)	2.15	(2.11, 2.20)
Gender (female vs. male)	1.00	(0.96, 1.04)
Cardiovascular history	1.42	(1.36, 1.48)
Diabetes	1.42	(1.37, 1.48)
Comparison of cardiac care levels		
A vs. B2	1.01	(0.97, 1.06)
B1 vs. B2	1.03	(0.98, 1.09)

[a]After adjustment for all factors included in the model.

Table 4 Rates (for 100 patient-years at risk) of rehospitalization for infarct, cardiovascular reason, and cardiovascular re-intervention over 3 years

Level of care of initial admission	Patients (*n*)	Events (*n*)	Patient-year at risk (*n*)	Rate	95% CI
Rates of re-admission for AMI					
All	29 720	1 004	38 393	2.6	(2.5, 2.8)
A	12 806	479	16 827	2.8	(2.6, 3.1)
B1	5 395	174	6 966	2.5	(2.2, 2.9)
B2	11 519	351	14 600	2.4	(2.2, 2.7)
Rates of re-admission for cardiovascular reason					
All	29 720	7 269	31 626	23.0	(22.5, 23.5)
A	12 806	3 223	13 720	23.5	(22.7, 24.3)
B1	5 395	1 357	5 707	23.8	(22.5, 25.1)
B2	11 519	2 689	12 198	22.0	(21.2, 22.9)
Rates of reinterventions (coronary angiography, PCI, or CABG)					
All	29 720	3 147	35 678	8.8	(8.5, 9.1)
A	12 806	1 401	15 567	9.0	(8.5, 9.5)
B1	5 395	564	6 484	8.7	(8.0, 9.4)
B2	11 519	1 182	13 627	8.7	(8.2, 9.2)

n patients at risk: patients alive at the end of their episode of care.

mean of A hospitals was €4072 (median: 3861; IQR: 4467–3476), of B1 hospital was €5083 (median: 5153; IQR: 5769–4340), and of B2 hospitals was €7741 (median: 7553; IQR: 8211–7298). Within each hospital level, there was no association between the category of resource use and prognosis of patients: in B2 hospitals, short-term mortality was 12.6, 15.2, and 14.5% in the low user, medium user, and high user hospitals, respectively [(OR and 95% CI: low user vs. high user 0.92 (0.75, 1.13), medium user vs. high user 1.11 (0.88, 1.40)]. Results for other hospital levels are available in the comprehensive web-based report.[16]

Discussion

This analysis of nationwide data on the emergency care of AMI indicates that the on-site availability of catheterization facilities induces a high use of invasive therapeutic strategies which does not lead to better outcomes. Initial admission in a secondary hospital is not disadvantageous to the patient, whereas costs are higher in patients initially admitted to intermediary (B1) or tertiary (B2) services, indicating a more efficient use of resources in secondary (A) hospitals.

In this study, we did not compare competing treatments or hospitals of initial admission, but we studied the performance of entire levels of care, i.e. the secondary level having only access to medical treatment, the tertiary level permitted to use PCI, and an intermediate level of Belgian hospitals that can use diagnostic coronarography but not PCI. By the unique identification number, all subsequent hospital admissions of a patient are tagged, and transfers and re-admissions in tertiary services are included in the patient history. Overall, probabilities of reperfusion and revascularization are comparable with those in other registries.[17,18] As expected, patients initially admitted to hospitals with catheterization facilities are treated more often by PCI than those initially admitted to secondary care hospitals. This applies to both acute reperfusion and elective revascularization strategies later on. In this nationwide register including all hospitals, we found no statistically significant or clinically relevant differences in mortality or re-admission rates for cardiovascular reason after adjustment for available baseline characteristics.

Our findings are in agreement with those of the GRACE registry.[12] In patients with acute coronary syndromes and with an elevated troponin level, early invasive strategy was not superior to a selective invasive strategy.[19] In selected patients with ST-segment elevation AMI, primary angioplasty is superior to thrombolytic therapy if executed timely by experienced operators.[20] However, patients recruited in randomized controlled trials do not necessarily represent those admitted to emergency departments with an AMI. In the landmark PRAGUE-2 trial,[9] only 850 of 4853 patients (17.5%) with any AMI were randomized into one of two treatment arms. Treatment results obtained in randomized controlled trials that transport AMI patients immediately to selected tertiary centres of excellence might not be reproducible in real-life practice. Crucial time is lost by deferring thrombolysis and transferring patients to a tertiary centre for mechanical intervention.[21,22] Average tertiary care centres may have higher door-to-balloon times than the 60 min reported in trial centres and they may be less well organized outside normal working hours.[23–25] Studies have shown increased mortality in patients treated with PCI in low-volume centres, whereas there is no association between volume and mortality for thrombolytic therapy.[26] The difference between average cardiological practice in real life and the highly controlled setting of selected centres of excellence in experimental research may explain the lack of benefit observed in Belgian tertiary centres. The only tangible difference between secondary, intermediary, and tertiary care services was the higher costs of treatment, partly induced by the supply of more expensive technology.

Our data are observational and collected for administrative purposes. We found no evidence for a primary selection of patients by the severity of the disease. Patients are not randomized, but according to Belgian law, ambulances have to bring the patient to the nearest hospital. The hospital of initial admission depends on the place where the ambulance service is contacted. Apart from age and sex, we had to infer clinical characteristics from healthcare data (previous admissions for a cardiovascular reason and use of antidiabetic drugs). Administrative databases are cheap and convenient to use but show shortcomings.[27–30] Nevertheless, codification behaviour differences should be evenly distributed across hospitals, regardless of their level of care. We missed electrocardiographic data and we could not differentiate between STEMI and non-ST segment elevation AMI. We have no evidence that the hospital of initial admission was selected by indication, and that the lack of observable benefit of B2 compared with A hospitals was caused by better treatment results among a more severe patient mix (e.g. higher fractions of STEMI). On the contrary, patients admitted to secondary care hospitals were on average 2 years older and 2% more were females than those admitted to B2 centres. Slightly more patients admitted to tertiary hospitals had a cardiovascular history, as specifically defined by us, compared with patients admitted to secondary hospitals. Comparable reperfusion proportions between the three types of care levels suggest again comparable patient groups.

We could find no prognostic differences between levels of care. The lack of ECG data documenting the presence or absence of ST-segment elevations is a drawback. However, if allocation to care level is entirely dependent on the place where the AMI happened, this large database may be considered a natural experiment, the large numbers of patients excluding confounding by indication. If we accept this assumption of unconfounded allocation, treatment efficiency was highest at the secondary level (A). Secondary hospitals had the same patient outcomes at lower treatment costs. For health policy, it is an inefficient use of resources to multiply tertiary care hospitals beyond what is needed for electively referred interventions. Elective transfer of patients, after clinical evaluation by the attending cardiologist, performs equally well at low cost than a systematic use of interventional techniques. According to our data, the nearest hospital is the best. Additional studies are needed to better define those subgroups of AMI patients who present at the secondary level, for whom immediate transfer to the tertiary level is beneficial. Improving compliance to guidelines and shortening the time interval between onset of symptoms and starting thrombolytic treatment when appropriate will likely result in a more efficient use of resources than the multiplication of expensive tertiary services for primary invasive treatment of AMI patients.

Conflict of interest: none declared.

References

1. Second International Study of Infarct Survival (ISIS-2) Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction. *Lancet* 1988;**2**:349–360.
2. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality major morbidity results from all randomised trials of more than 1000 patients. *Lancet* 1994;**343**:311–322.
3. Andersen HR, Nielsen TT, Rasmussen K, Thuesen L, Kelbaek H, Thayssen P, Abildgaard U, Pedersen F, Madsen JK, Grande P, Villadsen AB, Krusell LR, Haghfelt T, Lomholt P, Husted SE, Vigholt E, Kjaergard HK, Mortensen LS. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. *N Engl J Med* 2003;**349**:733–742.
4. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, Hochman JS, Krumholz HM, Kushner FG, Lamas GA, Mullany CJ, Ornato JP, Pearle DL, Sloan MA, Smith SC Jr, Alpert JS, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Gregoratos G, Halperin JL, Hiratzka LF, Hunt SA, Jacobs AK. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1999 guidelines for the management of patients with acute myocardial infarction). *J Am Coll Cardiol* 2004;**44**:E1–E211.
5. Boersma E, Harrington RA, Moliterno DJ, White H, Theroux P, Van de Werf F, de Torbal A, Armstrong PW, Wallentin LC, Wilcox RG, Simes J, Califf RM, Topol EJ, Simoons ML. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. *Lancet* 2002;**359**:189–198.

6. Bonnefoy E, Lapostolle F, Leizorovicz A, Steg G, McFadden EP, Dubien PY, Cattan S, Boullenger E, Machecourt J, Lacroute JM, Cassagnes J, Dissait F, Touboul P. Primary angioplasty vs. prehospital fibrinolysis in acute myocardial infarction: a randomised study. *Lancet* 2002;**360**:825–829.
7. Ribichini F, Wijns W. Acute myocardial infarction: reperfusion treatment. *Heart* 2002;**88**:298–305.
8. Silber S, Albertsson P, Aviles FF, Camici PG, Colombo A, Hamm C, Jorgensen E, Marco J, Nordrehaug JE, Ruzyllo W, Urban P, Stone GW, Wijns W. Guidelines for percutaneous coronary interventions: the task force for percutaneous coronary interventions of the European Society of Cardiology. *Eur Heart J* 2005;**26**:804–847.
9. Widimsky P, Budesinsky T, Vorac D, Groch L, Zelizko M, Aschermann M, Branny M, St'asek J, Formanek P. Long distance transport for primary angioplasty vs. immediate thrombolysis in acute myocardial infarction. Final results of the randomized national multicentre trial—PRAGUE-2. *Eur Heart J* 2003;**24**:94–104.
10. Forrester JS, Topol EJ, Abele JE, Holmes DR Jr, Skorton DJ. 28th Bethesda Conference. Task Force 5: Assessment, approval, and regulation of new technology. *J Am Coll Cardiol* 1997;**29**:1171–1179.
11. Rothwell PM. External validity of randomised controlled trials: 'to whom do the results of this trial apply?'. *Lancet* 2005;**365**:82–93.
12. Van de Werf F, Gore JM, Avezum A, Gulba DC, Goodman SG, Budaj A, Brieger D, White K, Fox KA, Eagle KA, Kennelly BM. Access to catheterisation facilities in patients admitted with acute coronary syndrome: multinational registry study. *BMJ* 2005;**330**:441.
13. Averill RF, Goldfield N, Steinbeck BA, Grant T. *All Patient Refined Diagnosis Related Groups (APR-DRGs): Definitions Manual*. **Vol. 1**. Wallingford: 3M Health Information Systems; 1998.
14. INAMI. Taux des honoraires, des prix et des remboursements des soins de santé. **http://riziv.fgov.be/insurer/fr/rate/index.htm (10 April 2006)**.
15. Burton P, Gurrin L, Sly P. Extending the simple linear regression model to account for correlated responses: an introduction to generalized estimating equations and multi-level mixed modelling. *Stat Med* 1998;**17**: 1261–1291.
16. Van Brabandt H, Camberlin C, Vrijens F, Parmentier Y, Ramaekers D, Bonneux L. Variaties in de ziekenhuispraktijk bij acuut myocardinfarct in België (Hospital practice variability in the treatment of acute myocardial infarction in Belgium). Belgian Health Care Knowledge Centre. KCE Reports 14A. **http://kce.fgov.be/index_nl.aspx?ID=0&SGREF=5270&CREF=5599 (22 July 2006)**.
17. Hasdai D, Behar S, Wallentin L, Danchin N, Gitt AK, Boersma E, Fioretti PM, Simoons ML, Battler A. A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin; the Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS). *Eur Heart J* 2002;**23**:1190–1201.
18. Simoons ML. The quality of care in acute coronary syndromes. *Eur Heart J* 2002;**23**:1141–1142.
19. de Winter RJ, Windhausen F, Cornel JH, Dunselman PHJM, Janus CL, Bendermacher PEF, Michels HR, Sanders GT, Tijssen JGP, Verheugt FWA, Invasive vs. Conservative Treatment in Unstable Coronary Syndromes Investigators. Early invasive vs. selectively invasive management for acute coronary syndromes. *N Engl J Med* 2005;**353**: 1095–1104.
20. Keeley EC, Boura JA, Grines CL. Primary angioplasty vs. intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 2003;**361**:13–20.
21. De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. *Circulation* 2004;**109**: 1223–1225.
22. Stone GW, Gersh BJ. Facilitated angioplasty: paradise lost. *Lancet* 2006;**367**:543–546.
23. Brophy JM, Bogaty P. Primary angioplasty and thrombolysis are both reasonable options in acute myocardial infarction. *Ann Intern Med* 2004;**141**:292–297.
24. Channer KS. Primary angioplasty should be first line treatment for acute myocardial infarction: AGAINST. *BMJ* 2004;**328**:1256–1257.
25. Henriques JPS, Haasdijk AP, Zijlstra F, Zwolle Myocardial Infarction Study Group. Outcome of primary angioplasty for acute myocardial infarction during routine duty hours vs. during off-hours. *J Am Coll Cardiol* 2003;**41**:2138–2142.
26. Canto JG, Every NR, Magid DJ, Rogers WJ, Malmgren JA, Frederick PD, French WJ, Tiefenbrunn AJ, Misra VK, Kiefe CI, Barron HV. The volume of primary angioplasty procedures and survival after acute myocardial infarction. National Registry of Myocardial Infarction 2 Investigators. *N Engl J Med* 2000;**342**:1573–1580.
27. Glance LG, Dick AW, Osler TM, Mukamel DB. Does date stamping ICD-9-CM codes increase the value of clinical information in administrative data? *Health Serv Res* 2006;**41**:231–251.
28. Iezzoni LI, Daley J, Heeren T, Foley SM, Fisher ES, Duncan C, Hughes JS, Coffman GA. Identifying complications of care using administrative data. *Med Care* 1994;**32**:700–715.
29. Lee DS, Donovan L, Austin PC, Gong Y, Liu PP, Rouleau JL, Tu JV. Comparison of coding of heart failure and comorbidities in administrative and clinical data for use in outcomes research. *Med Care* 2005;**43**:182–188.
30. Petersen LA, Wright S, Normand SL, Daley J. Positive predictive value of the diagnosis of acute myocardial infarction in an administrative database. *J Gen Intern Med* 1999;**14**:555–558.