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

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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 €4,072 (median: 3,861; IQR: 4,467–3,476), in B1 €5,083 (median: 5,153; IQR: 7,579–4,340), and in B2 €7,741 (median: 7,553; IQR: 8,211–7,298).

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

KEYWORDS
Myocardial infarction; Reperfusion therapy; Clinical practice variation; Cost-of-illness; Administrative databases

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.
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 previous years since 1997. When any antidiabetic drug was prescribed category 5 (diseases and disorders of the circulatory system).13

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 thrombolysis 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. 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.

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 thrombolitics 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 thrombolitics, B2 hospitals treat half of the reperfused patients with thrombolitics and half by means of urgent PCI. The overall probability of revascularization, i.e. the probability of having 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.
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
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 coronaryography 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.19 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.

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