Access to catheterisation facilities in patients admitted with acute coronary syndrome: multinational registry study

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Abstract

Objective To investigate the relation between access to a cardiac catheterisation laboratory and clinical outcomes in patients admitted to hospital with suspected acute coronary syndrome.
Design Prospective, multinational, observational registry.
Setting Patients enrolled in 106 hospitals in 14 countries between April 1999 and March 2003.
Participants 28 825 patients aged ≥ 18 years.
Main outcome measures Use of percutaneous coronary intervention or coronary artery bypass graft surgery, death, infarction after discharge, stroke, or major bleeding.
Results Most patients (77%) across all regions (United States, Europe, Argentina and Brazil, Australia, New Zealand, and Canada) were admitted to hospitals with catheterisation facilities. As expected, the availability of a catheterisation laboratory was associated with more frequent use of percutaneous coronary intervention (41% *v* 3.9%, $P < 0.001$) and coronary artery bypass graft (7.1% *v* 0.7%, $P < 0.001$). After adjustment for baseline characteristics, medical history, and geographical region there were no significant differences in the risk of early death between patients in hospitals with or without catheterisation facilities (odds ratio 1.13, 95% confidence interval 0.98 to 1.30, for death in hospital; hazard ratio 1.05, 0.93 to 1.18, for death at 30 days). The risk of death at six months was significantly higher in patients first admitted to hospitals with catheterisation facilities (hazard ratio 1.14, 1.03 to 1.26), as was the risk of bleeding complications in hospital (odds ratio 1.94, 1.57 to 2.39) and stroke (odds ratio 1.53, 1.10 to 2.14).
Conclusions These findings support the current strategy of directing patients with suspected acute coronary syndrome to the nearest hospital with acute care facilities, irrespective of the availability of a catheterisation laboratory, and argue against early routine transfer of these patients to tertiary care hospitals with interventional facilities.

Introduction

Randomised trials and meta-analyses have shown better clinical outcomes in patients with acute coronary syndrome assigned to an early invasive strategy, including primary percutaneous coronary intervention for those with persistent ST segment elevation,[1] or early revascularisation with percutaneous coronary intervention or coronary artery bypass grafting in those with non-ST segment elevation acute coronary syndrome.[2–4] In these randomised trials a reduction in recurrent ischaemic events was consistently associated with the invasive strategy, while significant reductions in mortality were rarely observed.

In the "real world" the choice of a management strategy is often governed by the facilities available at the hospital where patients initially present. Only 20% of emergency care departments have access to a catheterisation laboratory, and still fewer hospitals can perform immediate percutaneous coronary intervention or coronary artery bypass grafting.[5] A positive association between the availability of a catheterisation laboratory and improved outcomes would argue for a change in the routing of patients with acute coronary syndrome from the nearest community hospital to a specialised hospital with immediate access to a catheterisation laboratory.

The global registry of acute coronary events (GRACE) is an ongoing, multinational, prospective registry of patients with the entire spectrum of acute coronary syndrome. The registry collects data on baseline characteristics, management, and clinical outcomes. We investigated the relation between access to a cardiac catheterisation laboratory and the use of percutaneous coronary intervention or coronary artery bypass grafting and clinical outcomes in patients admitted with suspected acute coronary syndrome.

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See bmj.com for three tables of additional data on baseline characteristics and use of revascularisation procedures in the three diagnostic subgroups and on regional differences in availability of catheterisation laboratories.

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Methods

Full details of the methods have been published previously.[6] The global registry is designed to reflect an unbiased population of patients with acute coronary syndrome, irrespective of geographical region. A total of 106 hospitals located in 14 countries contributed data to this analysis.

Patients entered in the registry had to be at least 18 years old, be admitted with a presumed diagnosis of acute coronary syndrome (that is, have symptoms consistent with acute ischaemia), and have at least one of the following: electrocardiographic changes consistent with acute coronary syndrome, serial increases in serum biochemical markers of myocardial necrosis, or documentation of coronary artery disease. At about six months after discharge from hospital, patients were followed up by telephone, clinical visits, or through calls to their primary care physician to ascertain the occurrence of selected long term study outcomes.

To ensure the enrolment of an unbiased population, each month we recruited the first 10 to 20 eligible consecutive patients from each site. We collected data on demographic characteristics, medical history, presenting symptoms, duration of prehospital delay, biochemical and electrocardiographic findings, treatment practices, and various hospital outcomes. All cases were assigned to ST segment elevation myocardial infarction, non-ST segment elevation myocardial infarction, or unstable angina.

We analysed regional differences according to the distribution of centres in four geographical regions: Australia/New Zealand/Canada; Argentina/Brazil; Europe; and the United States.

Key baseline characteristics and revascularisation procedures by type of hospital (n=28 825)

Characteristic	Catheterisation laboratory		P value
	Yes	No	
No (%) of patients	22 096 (77)	6729 (23)	
Median (interquartile range) age (years)	66 (55-75)	68 (57-76)	<0.001
No (%) of men	14 888 (68)	4232 (63)	<0.001
Killip class* (%):			
I	17 629 (82)	5254 (80)	<0.001 (4×2 comparison)
II	2745 (13)	995 (15)	
III	834 (3.9)	308 (4.7)	
IV	282 (1.3)	46 (0.7)	
Medical history (%):			
Stroke	1831 (8.4)	541 (8.1)	0.486
PCI	3818 (17)	557 (8.3)	<0.001
CABG	2947 (13)	577 (8.6)	<0.001
Coronary angiogram	6603 (31)	1154 (18)	<0.001
Positive stress test	2291 (11)	666 (10)	0.215
Myocardial infarction	6633 (30)	2102 (31)	0.07
Hypertension	13 069 (60)	3921 (59)	0.162
Diabetes mellitus	5487 (25)	1559 (23)	0.005
ACS subgroup (%):			
STEMI	7847 (36)	1986 (30)	<0.001 (3×2 comparison)
Non-STEMI	6991 (32)	2016 (30)	
Unstable angina	7258 (33)	2727 (41)	
Revascularisation (%):			
PCI	8941 (41)	253 (3.9)	<0.001
CABG	1554 (7.1)	46 (0.7)	<0.001

ACS=acute coronary syndrome; CABG=coronary artery bypass grafting; CAD=coronary artery disease; non-STEMI=non-ST segment elevation myocardial infarction; PCI=percutaneous coronary intervention; STEMI=ST segment elevation myocardial infarction.
*Clinical signs of worsening left ventricular function from class I to IV.

Statistical analysis

We assessed differences in demographics, clinical characteristics, and outcomes between patients who were admitted to hospitals with or without access to a catheterisation laboratory. Multiple logistic regression was used to examine the association between first admission to a hospital with catheterisation facilities or a hospital without such facilities and clinical outcomes of major bleeding, stroke, and mortality. Cox regression was used to examine the association between availability of catheterisation facilities at the hospital of first admission and mortality at 30 days and six months. We also examined reinfarction at six months after hospital discharge.

Results

Study population

We analysed data from 28 825 patients with acute coronary syndrome enrolled between April 1999 and March 2003. The crude model for death at 30 days and at six months was based on data from 28 371 (98%) patients, while the adjusted model was based on data from 25 402 (88%) patients. We collected data on myocardial infarction after discharge up to six months as of June 2000, from 15 205 patients.

Baseline clinical characteristics and revascularisation procedures

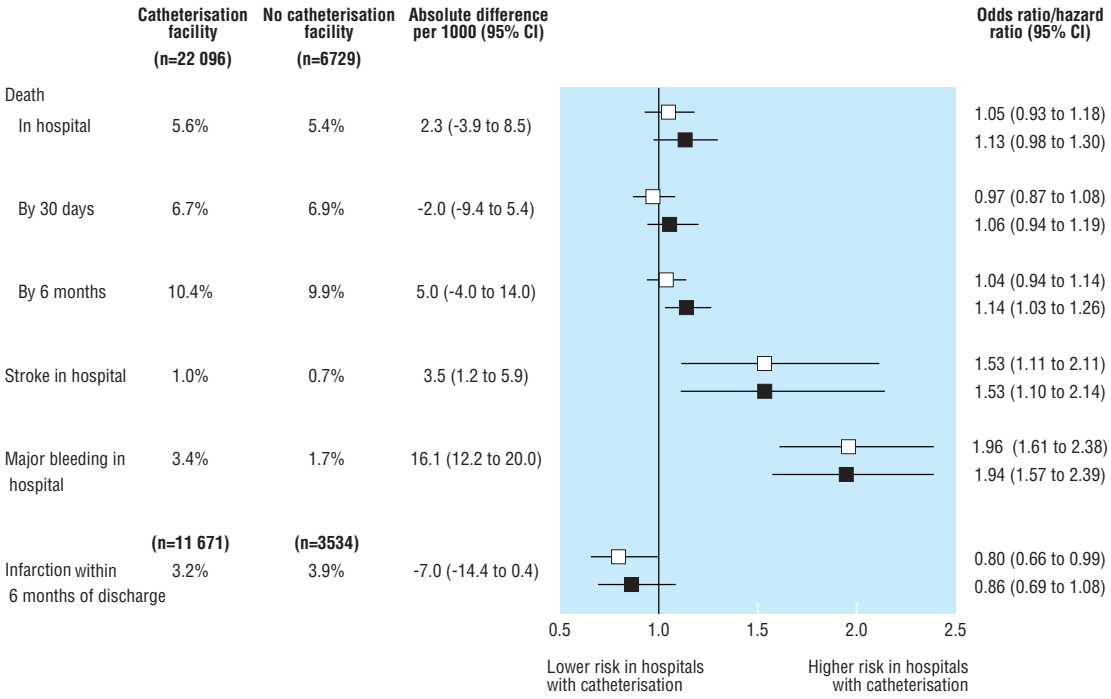
We analysed baseline characteristics of the patient cohort according to the capability of the admitting hospital to carry out cardiac catheterisation (table). Most patients (77%) were admitted to hospitals with catheterisation facilities with a consistent pattern across different regions (79% in the United States, 76% in Europe, 66% in Australia/New Zealand/Canada, and 83% in Argentina/Brazil).

In patients admitted to hospitals with catheterisation facilities, percutaneous coronary intervention procedures and coronary artery bypass graft during the index admission were significantly more common than in patients first admitted to hospitals without facilities: 41% *v* 4% and 7% *v* < 1% respectively (table). The largest difference in percutaneous coronary intervention was found in Europe, with 48% in hospitals with and 2% in hospitals without catheterisation facilities, respectively. For coronary artery bypass graft the largest differences between hospitals with and without facilities were found in the United States (11% *v* 1.6%) and Argentina/Brazil (10% *v* 1%).

Clinical outcomes

The figure shows the observed clinical outcomes, the absolute differences in outcome between patients first admitted to hospitals with or without catheterisation facilities, and the unadjusted and adjusted odds ratios/hazard ratios in the total acute coronary syndrome population.

In the total population of patients with acute coronary syndrome, and after adjustment for baseline characteristics, medical history, and geographical region, patients first admitted to hospitals with catheterisation facilities were at a 14% increased risk of death at six months. The risk of in hospital stroke or major bleeding was also higher (53% and 94% respectively). There was, however, a trend towards a lower risk of reinfarction after discharge in such patients.



Clinical outcomes for all patients with acute coronary syndrome, for patients admitted to hospitals with or without catheterisation laboratory (open squares are unadjusted ratios and closed squares are ratios adjusted for age, sex, Killip class (clinical estimate of severity of infarct), heart rate, systolic blood pressure, diastolic blood pressure, cardiac arrest at presentation, history of diabetes, previous myocardial infarction, stroke, positive stress test, percutaneous coronary intervention, coronary artery bypass graft, hypertension, and geographical region)

The pattern of increased risk of death at six months and increased risk of major bleeding or stroke in hospitals with catheterisation facilities remained consistent across the three subgroups (see bmj.com). There was a significant reduction in the risk of reinfarction after discharge in the patients with non-ST segment elevation myocardial infarction. In all hospitals, the highest rates of stroke were observed in patients with ST segment elevation myocardial infarction, while major bleeding complications were less common in patients with unstable angina.

Discussion

This analysis from a large multinational observational registry indicates that the availability of a catheterisation laboratory is associated with more use of percutaneous coronary intervention and coronary artery bypass graft in patients presenting with acute coronary syndrome. Despite this, after we adjusted for baseline variables, medical history, and geographical region, patients admitted first to hospitals with catheterisation facilities did not have a survival benefit but seemed to have higher rates of major bleeding and stroke in hospital than those first admitted to hospitals without such facilities.

Complications and mortality

Randomised studies of acute coronary syndrome have shown that an invasive approach is associated with an increase in bleeding complications (mainly puncture related).[1–4] In our analysis, rates of stroke were consistently higher across the three diagnostic groups in patients admitted to hospitals with catheterisation facilities. This excess could be attributed to the more frequent use of invasive procedures. The highest rates of stroke in patients first admitted to hospitals without catheterisation facilities were found in those with ST segment elevation myocardial infarction, in whom the difference with the patients admitted to hospitals with catheterisation facilities was also the smallest. These findings could be explained by additional haemorrhagic strokes due to the use of thrombolytic therapies.

Comparison with other studies

Our results support the findings of recent studies, that the use of intervention procedures in patients with ST segment elevation myocardial infarction is higher if the admitting hospital has a catheterisation laboratory.[5 7–9]

Meta-analyses of randomised trials have shown primary percutaneous coronary intervention to be associated with short and long term reductions in mortality when compared with thrombolytic therapy, regardless of whether the patient was transferred from a community hospital.[1] However, reduced time delays in these trials, selection of patients considered safe for transportation and, in some studies, the exclusion of procedure related reinfarctions from the primary end point, complicate interpretation.[10]

Recent randomised studies have reported a benefit of a routine invasive approach in patients with unstable angina and non-ST segment elevation myocardial infarction, mainly attributable to a reduction in the risk of reinfarction.[2–4] In our registry, early and late mortality in patients with unstable angina or non-ST segment

elevation myocardial infarction first admitted to hospitals without catheterisation facilities, were similar to those in patients first admitted to hospitals with facilities, despite a lower use of invasive procedures and a higher risk of reinfarction after discharge. Others report concordant results.[11–12]

The observed differences in mortality between patients first admitted to hospitals with or without catheterisation facilities were small, suggesting that an invasive approach does not result in a clear survival benefit. Although the lack of an early survival benefit could be attributed to mortality related to the procedure, the higher mortality at six months suggests that the much more frequent, and probably unselective, performance of revascularisation procedures in these patients is not beneficial.

Our results are supported by other registry data but are at variance with those of recent randomised trials. An important reason is the reluctance of investigators to include high risk patients in randomised studies. A more selective use of invasive procedures in the high risk patients of this registry may be partly responsible for the favourable outcomes observed in those first admitted to community hospitals without catheterisation facilities.

Study limitations

Though we performed multivariable adjustments, unmeasured variables may exist that we did not account for. In some centres, patients may have been discharged for subsequent readmission for cardiac catheterisation and percutaneous coronary intervention, and these data may not have been captured in our study. It was also not possible to account for the sampling fraction in the analysis. This may increase the uncertainty in the results beyond the reported confidence intervals, although the effect is probably small.

Clinical implications

This analysis supports the current strategy of admitting patients with acute coronary syndrome as rapidly as possible to the nearest hospital, irrespective of the availability of a catheterisation laboratory, and argues against the early routine transport of these patients to a specialised regional tertiary care hospital with interventional facilities.

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Ethical approval: Where required, local approval from institutional review boards was obtained.

What is already known on this topic

In patients with acute coronary syndrome evidence from randomised clinical trials has shown better outcomes in those who undergo an early invasive strategy

It is unclear whether access to interventional cardiology facilities in routine practice improves outcomes among these patients

What this study adds

Access to cardiac catheterisation is associated with more invasive intervention among patients with acute coronary syndrome

After adjustment for confounders there was no increase in survival at 30 days or six months and higher rates of major bleeding and stroke among patients with such access than among patients without such access

The results do not support the early routine transfer of these patients to specialist centres with interventional cardiology facilities

1 Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 2003;361:13-20.
2 Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. Fragmin and fast revascularization during instability in coronary artery disease investigators. *Lancet* 1999;354:708-15.
3 Cannon CP, Weintraub WS, Demopoulos LA, Vicari R, Frey MJ, Lakkis N, et al. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. *N Engl J Med* 2001;344:1879-87.
4 Fox KA, Poole-Wilson PA, Henderson RA, Clayton TC, Chamberlain DA, Shaw TR, et al. Interventional versus conservative treatment for patients with unstable angina or non-ST-elevation myocardial infarction: the British Heart Foundation RITA 3 randomised trial. Randomised intervention trial of unstable angina. *Lancet* 2002;360:743-51.
5 Rogers WJ, Canto JG, Barron HV, Boscarino JA, Shoultz DA, Every NR. Treatment and outcome of myocardial infarction in hospitals with and without invasive capability. Investigators in the national registry of myocardial infarction. *J Am Coll Cardiol* 2000;35:371-9.
6 GRACE Investigators. Rationale and design of the GRACE (global registry of acute coronary events) project: a multinational registry of patients hospitalized with acute coronary syndromes. *Am Heart J* 2001;141:190-9.
7 Marrugat J, Sanz G, Masia R, Valle V, Molina L, Cardona M, et al. Six-month outcome in patients with myocardial infarction initially admitted to tertiary and nontertiary hospitals. RESCATE investigators. Recursos Empleados en el Sindrome Coronario Agudo y Tiempos de Espera. *J Am Coll Cardiol* 1997;30:1187-92.
8 Feit F, Mueller HS, Braunwald E, Ross R, Hodges M, Herman MV, et al. Thrombolysis in Myocardial Infarction (TIMI) phase II trial: outcome comparison of a "conservative strategy" in community versus tertiary hospitals. The TIMI research group. *J Am Coll Cardiol* 1990;16:1529-34.
9 Gabriel Steg P, Lung B, Feldman LJ, Maggioni AP, Keil U, Deckers J, et al. Determinants of use and outcomes of invasive coronary procedures in acute coronary syndromes: results from ENACT. *Eur Heart J* 2003;24:613-22.
10 Andersen HR, Nielsen TT, Rasmussen K, Thuesen L, Kelbaek H, Thayssen P, et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. *N Engl J Med* 2003;349:733-42.
11 Yusuf S, Flather M, Pogue J, Hunt D, Varigos J, Piegas L, et al. Variations between countries in invasive cardiac procedures and outcomes in patients with suspected unstable angina or myocardial infarction without initial ST elevation. OASIS (organisation to assess strategies for ischaemic syndromes) registry investigators. *Lancet* 1998;352:507-14.
12 Lupon J, Valle V, Marrugat J, Elosua R, Seres L, Pavesi M, et al. Six-month outcome in unstable angina patients without previous myocardial infarction according to the use of tertiary cardiologic resources. RESCATE Investigators. Recursos Empleados en el Sindrome Coronario Agudo y Tiempos de Espera. *J Am Coll Cardiol* 1999;34:1947-53.

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