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Variation in the use of coronary angiography in patients with unstable angina is related to differences in patient population and availability of angiography facilities, without affecting prognosis

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Objectives Examination of the difference in management strategies with respect to coronary angiography in patients with unstable angina pectoris, and the consequences of this difference on prognosis.

Design Prospective registration of consecutive patients admitted to two different hospitals.

Setting University and a large community hospital in Rotterdam, the Netherlands.

Subjects Patients under 80 years, without recent (<4 weeks) infarction or recent (<6 months) coronary revascularization procedure, admitted for chest pain suspected to indicate unstable angina pectoris.

Main outcome measures Decision to initiate coronary angiography or to continue on medical treatment. At 6 months the occurrence of death and myocardial infarction was measured.

Results Clinical variables associated with the decision to initiate angiography were young age, male gender, progression of angina, multiple pain episodes and use of β-blocker or calcium antagonists before admission, abnormal ST-T segment on baseline ECG, recurrent pain in hospital, and ECG changes during pain. These associations did not differ between hospitals. Nevertheless, angiography was performed more often in the presence of angiography facilities (university hospital), independent of the variable case-mix. Survival and infarct-free survival were similar in both hospitals, 96% and 90% respectively.

Conclusion The difference in angiography rate for unstable angina can be explained in part by differences in patient population and hospital facilities, but no difference was observed in physicians' assessment of patient characteristics. The observed practice variation did not affect prognosis.
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Key Words: Unstable angina, coronary angiography, practice variation.

Introduction

Delivery of health care services varies considerably among countries and regions[1,2]. For example, rates for coronary angiography and coronary angioplasty differed two- to four-fold among regions in recent studies from The Netherlands and the U.S.A.[3–6]. Variation between practices can be explained by differences in patient populations[5,7], by the lack of consensus on indications for particular services[8], and by limited availability of resources[3,9]. However, the relative contribution of these factors is often unclear.

Treatment of unstable angina is directed to the relief of symptoms and to prevent recurrent ischaemic episodes or progression to infarction or death. Initially, hospitalisation and medical treatment is recommended for these patients[10], and the unstable situation can be stabilised by combination therapy with various

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drugs in 80–90% of patients[11–13]. In case of failure of medical therapy, patients are referred for (urgent) angiography followed by angioplasty or bypass surgery, if feasible[14,15]. In addition, coronary angiography is often recommended for patients who stabilize on medical therapy, either to confirm the diagnosis or to assess whether the patient may benefit from angioplasty or bypass surgery[11,13,16]. In spite of apparent agreement on these issues, considerable differences were observed in treatment of patients with unstable angina between two hospitals in Rotterdam[17].

In order to examine the differences in management strategy in patients with unstable angina, data were analysed from 341 patients admitted to either of these two Rotterdam hospitals, one with and one without facilities for angiography and coronary interventions. Special attention was paid to the decision to initiate coronary angiography, because this is the key decision to prepare for subsequent interventions. The analysis was directed to investigate: (1) which clinical variables influence doctors to make a decision about angiography and interventions; (2) whether doctors in the two hospitals respond differently to clinical variables; and (3) how much practice variation is explained by the difference in the patients' characteristics, by differences in doctors' response to those characteristics, or by other factors, such as the availability of angiography facilities.

In addition, mortality and morbidity were compared 6 months after admission to verify whether the difference in management strategy resulted in a difference in prognosis.

Patients and methods

Study site

Two hospitals in Rotterdam, the Netherlands, participated in 1988/89 in a prospective registry of patients with unstable angina: the university hospital with teaching responsibilities and in-house facilities for coronary angiography, angioplasty and cardiac surgery, and a large community hospital, without in-house angiography facilities. If required, patients at the latter site are referred for diagnostic angiography procedures to other hospitals in the city.

Patient selection and definitions

All consecutive patients admitted for chest pain, suspected of unstable angina, without electrocardiographic signs of acute infarction, were followed prospectively throughout their hospital stay. Follow-up data up to 6 months after admission were extracted from clinical charts. Patients who were referred to the university hospital for coronary angiography and/or subsequent intervention (tertiary referrals), were not included in the registry.

The admission diagnosis, suspected unstable angina, was made by the physician on duty. The presenting symptoms were classified as pain of recent onset (within the last 4 weeks), pain progressive in frequency or duration, and pain at rest. Type of onset of the present episode was described as 'sudden' (without previous acceleration, with or without pre-existing stable angina) or 'progressive' (gradual acceleration of pre-existing angina). At the time of admission no distinction was made with respect to the last pain episode, since all patients had had symptoms within the previous 24 h before presentation. ST-T changes or other ECG abnormalities were not required for inclusion. During the hospital stay, clinical observations such as recurrent pain, ECG changes, or myocardial infarction, as well as drug treatment and interventions were recorded. A final diagnosis was made after evaluation of the in-hospital course: myocardial infarction, unstable angina and other causes of chest pain.

Myocardial infarction was defined by serum creatine kinase levels above twice the upper normal limit, in addition to typical chest pain, and/or compatible ECG changes. Other causes included non-cardiac illnesses or chest pain of uncertain aetiology.

The present analysis included all registry patients younger than 80 years, without previous infarction within the last 4 weeks or angioplasty or bypass surgery within the previous 6 months.

Analysis of the data

Univariate analysis

Univariate analysis of the baseline characteristics, the in-hospital course and the applied mode of treatment was used to compare patient characteristics and management strategies in both hospitals. Differences were tested by Student's t-test for continuous variables and by chi-square test for discrete variables.

Multivariable analysis

In order to correct statistically for the variable case-mix, proportional hazard models[18] were built to describe the association between clinical variables and the decision to initiate coronary angiography or to discharge and continue medical treatment. The selection of clinical variables was based on the result of the univariate analysis, or on assumed clinical relevance: age under 70 years, hypercholesterolaemia (cholesterol more than 6·5 mmol . l^{-1}), diabetes mellitus, smoking, gradual progression of angina (vs sudden onset or sudden increase of previously stable symptoms), multiple pain episodes during the 24 h before admission, use of β-blockers or calcium antagonists prior to admission, ST-T abnormalities on the baseline ECG, QRS abnormalities (pathological Q waves, signs of left ventricular hypertrophy or of intraventricular conduction disturbances), recurrent pain in hospital, ECG changes during pain.

Interaction terms of hospital and clinical characteristics were tested for significance, using the generalized likelihood ratio test statistic. If, for example,

Table 1 Baseline characteristics

	Total n=341 (%)	univ. n=118 (%)	comm. n=223 (%)
Age <70 years	248 (73)	98 (83)	150 (67)†
Male	126 (66)	77 (66)	149 (67)
Previous history of:			
Unstable angina	76 (22)	40 (34)	36 (16)†
Myocardial infarction	140 (41)	57 (49)	83 (37)*
Angiography	96 (28)	53 (45)	43 (19)†
Angioplasty	31 (9)	23 (20)	8 (4)†
Bypass surgery	53 (16)	29 (25)	24 (11)†
Hypertension‡	123 (36)	54 (46)	69 (31)†
Diabetes mellitus	40 (12)	16 (14)	24 (11)
Hypercholesterolaemia§	51 (15)	31 (27)	20 (9)†
Smoking•	120 (35)	40 (34)	80 (36)
Positive family history$	124 (36)	51 (44)	73 (33)*
Medication before admission			
Long acting nitrates	83 (24)	37 (32)	46 (21)*
β-blockers	128 (30)	52 (44)	76 (34)
Calcium antagonists	92 (27)	46 (39)	46 (21)†
Platelet inhibitors	55 (16)	15 (13)	40 (18)
Onset of angina before presentation			
Sudden	171 (50)	65 (56)	106 (47)
Progressive	170 (50)	53 (44)	117 (53)*
Baseline ECG			
QRS abnormalities	142 (42)	63 (53)	79 (35)†
STT abnormalities	196 (57)	77 (65)	119 (53)*
ECG during pain			
ECG recording during pain present	180 (53)	52 (45)	127 (57)
ST-T changes	108 (32)	33 (28)	75 (34)

*$P<0{\cdot}05$; †$P<0{\cdot}01$; univ.=university hospital; comm.=community hospital; ‡blood pressure >160/90 or current treatment; §serum cholesterol >6·5 mmol . l^{-1} or current treatment with cholesterol lowering drugs; •current smoking or smoking until less than a year ago; $infarct or cardiac death at age under 60 in first- or second-degree relative.

progression of angina had been selected in the first stage, it was tested to find out whether the coefficient for this term had significantly different values in one hospital compared to the other. Interaction terms were tested in a stepwise inclusion strategy, selecting the one with the largest contribution to the likelihood first. In the final step, the hospital was entered into the model as a main effect, to test the hypothesis of a different threshold for angiography in each hospital.

Kaplan–Meier analysis

Probability of survival and of survival without infarction was estimated using the Kaplan–Meier analysis.

Results

During the study period 417 patients were admitted with suspected unstable angina to the two hospitals. Seventy six patients were excluded from this analysis: 23 patients because of advanced age, 33 with post-infarction angina, and 20 because of recent revascularization procedures. Thus 341 patients were available for the present analysis: 118 patients in the university hospital and 223 patients in the community hospital.

Baseline characteristics

Patients in the university hospital were on average 2·3 years younger than in the community hospital, had a more severe history of coronary artery disease and a longer history of symptoms (Table 1). However, there was no difference in signs of acute ischaemia on the ECG at admission. Sixty percent of the patients in the university hospital and 43% in the community hospital ($P=0{\cdot}003$) had a history of either unstable angina, myocardial infarction or revascularization, which parallels the hospital differences in risk factors for coronary disease, and the extent of medication before admission.

In-hospital course and management

Despite the differences at admission, the clinical course in hospital was similar in both hospitals with respect to recurrent pain and ECG changes as well as the distribution of final diagnoses after observation (Table 2). Nevertheless, the management differed between hospitals, particularly with respect to medical therapy, the use of exercise testing, and the frequency of angiography and interventions.

Table 2 In-hospital course and management

	Total n=341 (%)	univ. n=118 (%)	comm. n=223 (%)
Clinical course			
Recurrent pain (any)	154 (45)	52 (44)	102 (46)
Multiple pain episodes	85 (25)	27 (23)	58 (26)
ECG changes during pain	104 (30)	32 (27)	72 (32)
Medication			
Oral nitrates	65 (19)	49 (42)	16 (7)†
Intravenous nitrates	198 (58)	45 (38)	153 (69)†
β-blockers	194 (57)	68 (58)	126 (57)
Calcium antagonists	106 (31)	47 (40)	59 (26)*
Platelet inhibitors	117 (34)	10 (8)	107 (48)†
Heparin	232 (68)	73 (62)	159 (71)
Exercise test	175 (51)	49 (42)	126 (57)†
Angiography	105 (31)	50 (43)	55 (25)
Number of stenoses >50%‡			
0	7	6	1
1	30	12	18
2	34	17	17
3	30	13	17
LM	3	2	1
PTCA	37 (11)	20 (17)	17 (8)*
CABG	39 (11)	17 (14)	22 (9)
Final (discharge) diagnosis			
AMI	34 (10)	13 (11)	21 (9)
UAP	211 (62)	78 (66)	133 (60)
Other	96 (28)	27 (23)	69 (31)

*$P<0.05$; †$P<0.01$; univ.=university hospital; comm.=community hospital; ‡missing for one patient; LM=left main stem disease; PTCA=percutaneous transluminal coronary angioplasty; CABG=coronary artery bypass grafting; AMI=acute myocardial infarction; UAP=unstable angina pectoris; Other=non-cardiac or non-specific chest pain.

Nitrates were predominantly administered intravenously in the community hospital, with supplementary β-blockers and both aspirin and heparin, while oral nitrates were prescribed more often by physicians in the university hospital. The number of antianginal drugs (nitrates, β-blockers and calcium antagonists) was similar.

The angiography rate was higher in the university hospital, especially for patients treated with multiple antianginal drugs. In addition, the decision for angiography was made earlier in the university hospital (Fig. 1). The median time until the decision for angiography was 1 day (range 0–8·5 days) in the university hospital, and 3 days (range 0–12 days) in the community hospital. However, the time until the decision to discharge was similar in both hospitals, with respective median times of 3·0 and 3·5 days.

Despite these differences, the findings during angiography were similar (Table 2, P=ns). Also the fraction of patients who underwent angioplasty or bypass surgery after angiography was not significantly different between the two hospitals.

The angiography decision

The decision to perform angiography was made more often for patients who were less than 70 years old, of male gender, who had progressive onset of angina, multiple pain episodes before admission, antianginal medication before admission, ST-T deviations on the baseline ECG — in the absence of QRS abnormalities — recurrent pain in hospital, and ST-T changes during pain (Table 3). No interaction terms of clinical variables and hospital were selected. The hospital variable, as the main factor, was included in the model, indicating an increased inclination for angiography in the university hospital, even after correction for the patient characteristics mentioned above.

A previous history of myocardial infarction or revascularization was not selected in the statistical models as independent factors. Instead, the presentation of symptoms and the level of medication were selected, even when previous infarction was forced into the model. Being the strongest variable, the level of medication was kept in the model, with the appreciation that it may be interpreted as indicating a previous history of ischaemic cardiac disease.

Mortality and morbidity

Overall survival and infarct-free survival were similar in the two hospitals over the 6 months follow-up period (Fig. 2).

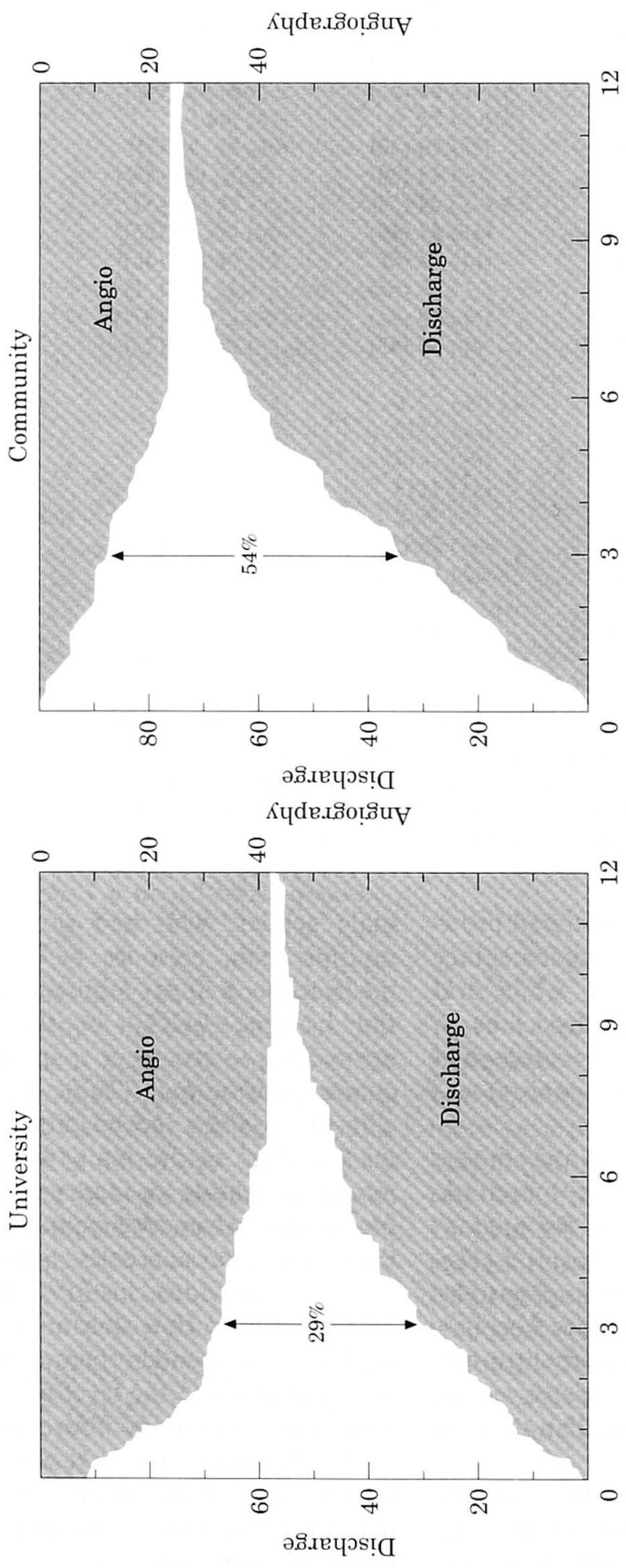

Figure 1 **Management in each hospital expressed as the decision 'angiography' (angio) or 'discharge without angiography' (discharge) in relation to the time since hospital admission. The white area represents the proportion of patients for whom no decision had yet been made at each moment in time. The upper and lower grey areas represent the proportion of patients for whom the decision 'angiography' or 'no angiography' had been made. More patients are referred for angiography in the university hospital (43 vs 25%. After 3 days, no decision had been made for 29% of patients in the university hospital, and 54% in the community hospital.**

Table 3 Association between clinical characteristics and hospital with the decision for angiography

	Angio		Crude		Adjusted	
	n	(%)	RR	(95% CI)	RR	(95% CI)
Age						
≥70 years	93	(20)	—		—	
<70 years	248	(35)	1·8	1·2–2·8	1·6	1·0–2·8
Male						
No	114	(26)	—		—	
Yes	227	(33)	1·1	0·9–1·3	1·5	1·0–2·4
Onset of angina before presentation						
Sudden	171	(19)	—		—	
Progressive	170	(43)	2·3	1·6–3·3	2·7	1·7–4·2
>2 pain episodes during last 24 h						
No	193	(23)	—		—	
Yes	145	(41)	1·8	1·3–2·6	1·4	1·0–2·2
Use of β-blockers or calcium antagonists before admission						
No	171	(19)	—		—	
Yes	170	(42)	2·2	1·5–3·1	2·3	1·5–3·6
Abnormal ST-T and normal QRS						
No	256	(26)	—		—	
Yes	85	(45)	1·7	1·3–2·3	1·9	1·2–3·0
Abnormal ST-T and QRS on baseline ECG						
No	230	(33)	—		—	
Yes	111	(26)	0·8	0·6–1·1	0·3	0·2–0·6
Pain in hospital						
No	187	(21)	—		—	
Yes	154	(43)	2·1	1·5–2·9	1·8	1·1–2·9
ECG changes during pain						
No	237	(18)	—		—	
Yes	104	(61)	3·4	2·5–4·7	4·9	3·0–8·0
Hospital						
Comm.	223	(25)	—		—	
Univ.	118	(43)	1·7	1·3–2·6	3·1	2·0–4·8

Clinical variables retained in the model independently associated with angiography. Age and gender were forced into the model. After selection of the clinical variables the hospital term was added and served as a significant determinant for angiography after adjustment for clinical characteristics. Crude risk ratios (RR) were estimated by univariate analysis; adjusted RR were calculated with multivariate proportional hazard regression; 95% CI=95% confidence interval, test-based.

Discussion

The management strategy applied to patients with unstable angina was studied in two hospitals in Rotterdam, which differed with respect to the patient population served, facilities, and teaching responsibilities. Statistical analysis revealed a basic difference in management strategy between the two hospitals, especially with respect to the use of coronary angiography.

Several clinical characteristics could be identified as independent predictors for subsequent decisions. People of younger age were referred to angiography earlier than more often[19]. Progressive onset of angina, the presence of multiple pain episodes, the level of medication and the presence of ST deviations on the baseline ECG were interpreted as indications of severe angina[20,21], and increased the hazard for angiography. Separately, recurrent pain and ECG changes during in-hospital observation independently raised this hazard.

None of the interaction terms was included into either model, suggesting that clinical variables were judged similarly by physicians in both hospitals. The hospital site remained an independent predictor for coronary angiography, even after adjustment for differences in clinical characteristics, indicating a difference in threshold for ordering angiography.

Our data are in contrast with some authors on practice variation, who say that there is little difference in important patient characteristics between geographic sites, and that physicians pay little attention to such characteristics when making decisions[9,22,23]. Age and gender, as well as other specific patient characteristics were independently related to the decision for angiography. Thus, although we found a difference in threshold for angiography between the two hospitals, physicians did attend to clinical variables when making decisions.

Comparison with other studies

Variability in the use of diagnostic and therapeutic measures has been described in different regions[2],

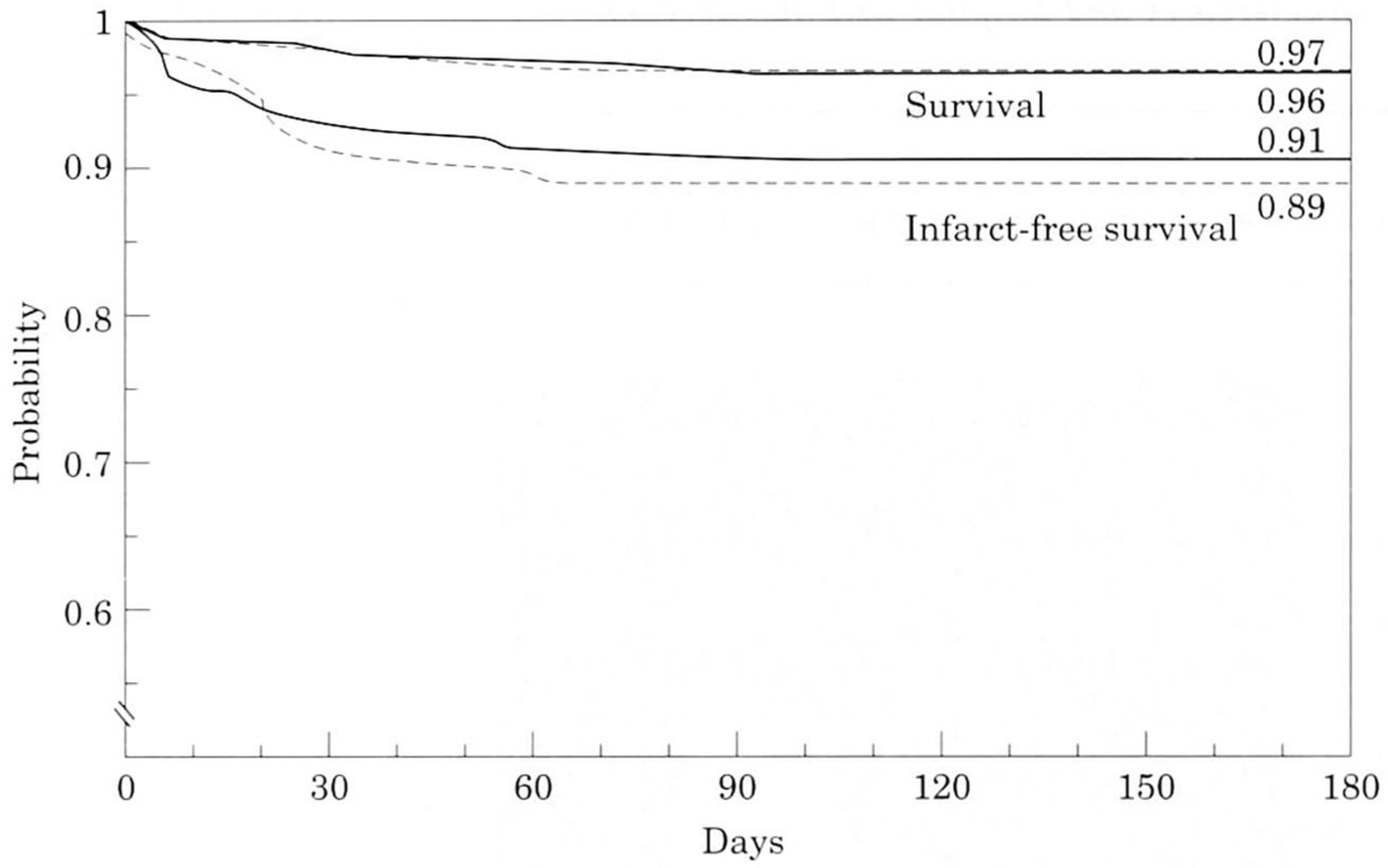

Figure 2 **Kaplan–Meier survival curves in patients with suspected unstable angina for both hospitals. ——=community-based hospital; – – –=university-based hospital.**

within one region[4], among different specialities[9] as well as in different practice settings[7,12]. Conti *et al.*[12] compared data of 111 patients admitted for unstable angina in a university hospital and interviews with cardiologists in a community hospital, which revealed a higher angiography rate in the latter. Similarly, Hlatky *et al.*[7] reported a higher rating of the 'need' for coronary angiography by community cardiologists when reviewing case summaries. These studies had different designs, but they showed similar though opposite differences between various hospital settings.

Limitations of this investigation

Data were collected prospectively in order to achieve a complete database with consistent information for all patients. The decisions of the physician on duty at the time of admission and those of the hospital staff during admission were accepted at face value and no attempt was made to re-classify in an objective manner whether the symptoms were typical angina or not. It was appreciated that the history was sometimes interpreted differently by the various physicians who were involved with the decision making process. Nevertheless, this approach was chosen to study the factors which contributed to the medical decisions, and not the correctness (sensitivity and specificity) of the decisions per se.

The present analysis represents the average decisions of many physicians in each hospital, and does not supply information about individual clinical management, nor were differences considered in the weighting of patient characteristics among physicians. Statistical analysis of these data did not reveal a difference in judgment of the importance of clinical characteristics among groups of physicians at the two hospital settings.

Quality of care

Less frequent use of angiography and coronary interventions will reduce the number of complications due to performing an invasive procedure (although these are infrequent), but may also fail to identify patients with severe coronary artery disease who may benefit from subsequent revascularization. However, the findings during angiography and the decisions as regards interventions after angiography were similarly distributed (see Table 2). Thus the more restricted use of angiography in the community hospital did not result in selecting a subset of patients with more advanced coronary disease. Also, no difference in outcome was observed either with or without statistical correction for differences between the patient populations.

Recently the TIMI IIIB trial showed similar results[24]. In that study no difference could be observed between initial invasive and conservative treatment in patients with unstable angina or non-Q wave infarction. Both studies confirm that it is safe to start treatment with the presently available drugs, including nitrates, β-blockers, aspirin, heparin and calcium channel blockers, and that invasive procedures should be reserved for patients whose symptoms persist despite intensive medical treatment.

Conclusion

The observed difference in angiography rate between two hospitals can be attributed to differences in patient populations and in availability of facilities for angiography and interventions, but not by different judgment of patients' characteristics. Angiography is performed more often in younger patients, who present with a

progressive onset of angina under treatment with β-blockers or calcium antagonists, and with recurrent pain episodes with concomitant ECG changes. After adjustment for patient characteristics the hospital site remains an important factor, associated with the decision for angiography. This effect is most prominent early after admission. Thus the decision to perform angiography is made rapidly early after admission in the presence of angiography facilities. The observed difference in policy does not affect prognosis.

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