

Future directions include an effectiveness study that is adequately powered to evaluate safety. Such a study may well show that, with close monitoring, patients could continue taking opioids while tolerance develops to the nausea and sedation. Dose ranging studies in opioid tolerant and naive participants are also planned.

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Ethical approval: The study was approved by the local institutional research and ethics committee, and the trial was registered with the Australian therapeutic goods administration.

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Prognosis for South Asian and white patients newly admitted to hospital with heart failure in the United Kingdom: historical cohort study

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Abstract

Objectives To compare patterns of admission to hospital and prognosis in white and South Asian patients newly admitted with heart failure, and to evaluate the effect of personal characteristics and comorbidity on outcome.

Design Historical cohort study.

Setting UK district health authority (population 960 000).

Participants 5789 consecutive patients newly admitted with heart failure.

Main outcome measures Population admission rates, incidence rates for first admission with heart failure, survival, and readmission rates.

Results When compared with the white population, South Asian patients had significantly higher age adjusted admission rates (rate ratio 3.8 for men and 5.2 for women) and hospital incidence rates (2.2 and 2.9). Among 5789 incident cases of heart failure, South Asian patients were younger and more often male than white patients (70 (SD 0.6) v 78 (SD 0.1) years and 56.5% (190/336) v 49.3% (2494/5057)). South Asian patients were also more likely to have previous myocardial infarction (10.1% (n = 34) v 5.5% (n = 278)) or concomitant myocardial infarction

(18.8% (n = 63) v 10.7% (n = 539)) or diabetes (45.8% (n = 154) v 16.2% (n = 817), all P < 0.001). A trend was shown to longer unadjusted survival for both sexes among South Asian patients. After adjustment for covariables, South Asian patients had a significantly lower risk of death (hazard ratio 0.82, 95% confidence interval 0.68 to 0.99) and a similar probability of death or readmission (0.96, 0.81 to 1.09) compared with white patients.

Conclusions Population admission rates for heart failure are higher among South Asian patients than white patients in Leicestershire. At first admission South Asian patients were younger and more often had concomitant diabetes or acute ischaemic heart disease than white patients. Despite major differences in personal characteristics and risk factors between white and South Asian patients, outcome was similar, if not better, in South Asian patients.

Introduction

People of South Asian origin (Indian (subcontinent) origin) comprise the largest ethnic minority group in the United Kingdom—4.1% of the population in 2001. The incidence of coronary heart disease is around 40% higher among this group than among the indigenous

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white population.^{1,2} Moreover, the onset of coronary heart disease has been suggested to be earlier and mortality higher in South Asian patients.²⁻⁴ Some studies have shown a similar prognosis in South Asian and white patients after myocardial infarction.⁵ A high prevalence of coronary heart disease in South Asian people might be expected to result in a higher prevalence of heart failure, a major sequela of coronary heart disease. We compared population admission rates for heart failure and outcomes after first admission for heart failure in South Asian and white patients.

Methods

Data on admissions for heart failure were obtained from Leicestershire health information service. Our denominator was from 1991 census data for the local ethnic population. Data were obtained for patients aged 40 or over. Our principal measure was the ratio of standardised admission rates (South Asian patients to white patients) for men and women.

We obtained data on all Leicestershire residents, aged 40 or over, admitted with heart failure for the first time between 1 April 1998 and 31 March 2001. First admissions were defined as those where patients had no previous admission related to heart failure in these five years as a minimum. Ethnicity was that reported in the hospital discharge data.

Mortality was identified through the Office for National Statistics, and follow up hospital events were obtained from Leicestershire Health Authority data. Survival was measured from the date of first admission to the date of death, of readmission, or the end of follow up (30 September 2001). The main outcome measures were death from any cause (all cause survival) and all cause survival or emergency readmission for a cardiovascular event (event free survival).

Statistical analysis

Crude survival was estimated with the Kaplan-Meier method, and Cox proportional hazards modelling was used to investigate the influence of covariates on outcome. Potential modifiers of outcome included in the multivariate analysis were age, sex, ethnicity and social deprivation, and hospital comorbidity, such as

diabetes, hypertension, renal insufficiency, stroke, and myocardial infarction.

Our proxy measure of social deprivation was from the index of multiple deprivation 2000 at electoral ward level expressed in fifths (lowest fifth being most deprived), matched using the domicile postcode of the patient at admission. As a proxy of general comorbidity we took the average hospital stay in each of the five years before the index admission. From these same five years we obtained information on conditions associated with heart failure, including acute myocardial infarction, other coronary heart disease, other than coronary heart disease, hypertension, heart valve disease, diabetes, stroke, renal failure, and atrial fibrillation or flutter.

Results

Between 1 April 1998 and 31 March 2001, 5789 patients were newly admitted with heart failure; 5057 (87.4%) of these were white patients and 336 (5.8%) South Asian patients. Follow up ranged from 183 to 1279 days, a minimum of six months for those alive at the end of the observation period. Ethnicity was recorded as not given for 347 (5.9%) patients, but personal characteristics suggested this group to be predominantly white.

Patients in the South Asian cohort were on average eight years younger than those in the white cohort. The South Asian cohort also had a higher proportion of men (190; 56.5%) than the white cohort (2494; 49.3%). Less than 10% (519) of patients were treated within a cardiological setting within seven days before or after the index admission. No difference was found between cohorts in this respect.

Acute myocardial infarction, both before and concomitant with the first admission for heart failure, was more prevalent in South Asian than white patients (before, 10.1% *v* 5.5%; concomitant, 18.8% *v* 10.7%). Similarly, diabetes mellitus and hypertension were more commonly recorded among South Asian patients. In contrast, white patients were more likely to have atrial arrhythmias, both before or concomitant with the admission for heart failure (table 1).

Over half of all patients (51.4%; 2974) died before the end of follow up. Two thirds of all mortality (65.5%;

Table 1 Patterns of in-hospital comorbidity in five years before or concomitant with diagnosis of heart failure among white and south Asian patients. Values are numbers (percentages) of patients, with 95% confidence intervals, unless stated otherwise

Comorbidity	White patients (n=5057)	South Asian patients (n=336)	P value*
Acute myocardial infarction:	769 (15.2, 14.2 to 16.2)	91 (27.1, 22.4 to 32.2)	<0.001
Before admission with heart failure†	278 (5.5, 4.9 to 6.1)	34 (10.1, 6.9 to 13.3)	<0.001
Concomitant with heart failure	539 (10.7, 9.8 to 11.5)	63 (18.8, 14.6 to 22.9)	<0.001
Other coronary heart disease‡	1264 (25.0, 23.8 to 26.2)	98 (29.2, 24.4 to 34.3)	0.1
Other heart disease§	3024 (59.8, 58.4 to 61.2)	147 (43.8, 38.4 to 49.2)	<0.001
Hypertension	1484 (29.3, 28.1 to 30.6)	147 (43.8, 38.4 to 49.2)	<0.001
Valve disease	250 (4.9, 4.4 to 5.6)	6 (1.8, 0.7 to 3.8)	0.01
Diabetes	817 (16.2, 15.2 to 17.2)	154 (45.8, 40.4 to 51.3)	<0.001
Stroke	393 (7.8, 7.0 to 8.5)	26 (7.7, 4.9 to 10.6)	0.98
Renal failure	756 (14.9, 14.0 to 15.9)	56 (16.7, 12.7 to 20.7)	0.39
Atrial fibrillation or flutter:	174 (434.5, 33.2 to 35.8)	46 (13.7, 10.0 to 17.4)	<0.001
Before admission with heart failure†	646 (12.8, 11.9 to 13.7)	15 (4.5, 2.3 to 6.7)	<0.001
Concomitant with heart failure	148 (729.4, 28.1 to 30.7)	37 (11.0, 7.7 to 14.4)	<0.001

*Derived with χ^2 statistic.

†Diagnosed in hospital at any time within five years before, and excluding, first admission with heart failure.

‡No acute myocardial infarction.

§No acute myocardial infarction or coronary heart disease.

Table 2 Results of Cox proportional hazards modelling for all cause and cardiovascular mortality and for unplanned readmissions to hospital. Values are hazard ratios (95% confidence intervals)

Variable	All cause survival		Event free survival*	
	Univariate	Multivariate	Univariate	Multivariate
Sex (female v male)	1.01 (0.94 to 1.09)	0.88 (0.82 to 0.96)	0.99 (0.93 to 1.06)	0.92 (0.85 to 0.98)
Age (per 10 year increase)	1.44 (1.38 to 1.50)	1.42 (1.36 to 1.48)	1.24 (1.20 to 1.28)	1.24 (1.20 to 1.28)
Ethnicity:				
White	1.00	1.00	1.00	1.00
South Asian	0.62 (0.51 to 0.75)	0.82 (0.68 to 0.99)	0.83 (0.72 to 0.95)	0.94 (0.81 to 1.09)
Other	0.69 (0.43 to 1.10)	0.80 (0.50 to 1.27)	0.71 (0.47 to 1.04)	0.78 (0.52 to 1.13)
Not known	1.46 (1.27 to 1.69)	1.62 (1.39 to 1.87)	1.02 (0.89 to 1.18)	1.15 (0.99 to 1.31)
Gross comorbidity:				
None	1.00	1.00	1.00	1.00
<7 days	1.03 (0.95 to 1.12)	1.07 (0.98 to 1.17)	1.15 (1.07 to 1.23)	1.14 (1.06 to 1.22)
7-29 days	1.60 (1.40 to 1.75)	1.46 (1.30 to 1.64)	1.60 (1.45 to 1.76)	1.44 (1.30 to 1.59)
≥30 days	1.75 (1.32 to 2.30)	1.55 (1.17 to 2.05)	1.77 (1.39 to 2.26)	1.59 (1.24 to 2.03)
Deprivation†:				
Q1	1.00		1.00	1.00
Q2	0.94 (0.81 to 1.08)	0.96 (0.83 to 1.12)	0.99 (0.87 to 1.13)	1.01 (0.89 to 1.15)
Q3	0.90 (0.78 to 1.04)	0.94 (0.81 to 1.07)	1.01 (0.89 to 1.13)	1.04 (0.92 to 1.17)
Q4	0.90 (0.78 to 1.02)	0.95 (0.83 to 1.08)	0.99 (0.88 to 1.11)	1.02 (0.91 to 1.15)
Q5	0.81 (0.71 to 0.91)	0.88 (0.77 to 0.99)	0.94 (0.84 to 1.04)	0.98 (0.88 to 1.08)
Diabetes (yes v no)	0.85 (0.77 to 0.94)	0.98 (0.88 to 1.09)	1.06 (0.97 to 1.14)	1.11 (1.02 to 1.21)
Concomitant acute myocardial infarction (yes v no)	0.96 (0.85 to 1.08)	1.07 (0.94 to 1.17)	1.04 (0.94 to 1.14)	1.13 (1.02 to 1.24)
Hypertension (yes v no)	0.76 (0.70 to 0.83)	0.77 (0.71 to 0.84)	0.91 (0.85 to 0.97)	0.88 (0.82 to 0.94)
Stroke (yes v no)	1.57 (1.38 to 1.77)	1.46 (1.28 to 1.65)	1.34 (1.22 to 1.53)	1.26 (1.12 to 1.41)
Renal insufficiency (yes v no)	1.88 (1.70 to 2.06)	1.85 (1.68 to 2.03)	1.65 (1.51 to 1.80)	1.57 (1.44 to 1.72)
Atrial fibrillation or flutter (yes v no)	0.93 (0.86 to 1.00)	0.86 (0.79 to 0.92)	0.99 (0.92 to 1.06)	0.94 (0.88 to 1.00)
Year of diagnosis:				
1998-9	1.00	1.00	1.00	1.00
1999-2000	0.89 (0.81 to 0.97)	0.89 (0.81 to 0.97)	1.06 (0.98 to 1.15)	1.06 (0.98 to 1.14)
2000-1	0.89 (0.80 to 0.97)	0.88 (0.78 to 0.96)	1.17 (1.07 to 1.27)	1.14 (1.05 to 1.24)

*Survival to death from any cause or emergency readmission for cardiovascular event.
† Q1=least deprived, Q5=most deprived.

1948) was due to cardiovascular events. Crude survival analysis gave all cause case fatality rates at 30 days and one year of 21% and 42%, respectively, for the whole cohort and a median survival of 21 months (95% confidence interval 20 to 22).

Unadjusted in-hospital case fatality rates were lower in South Asian patients than in white patients (13% v 19%). Estimates of survival at 30 days, one year, and two years (both to death and to combined event) were consistently higher for South Asian patients (see *bmj.com*). Univariate Cox regression showed a 38% lower risk of death and a 17% lower risk of readmission or death among South Asian patients.

On multivariate analysis the risk of death remained lower (18%) for South Asian patients whereas the risk

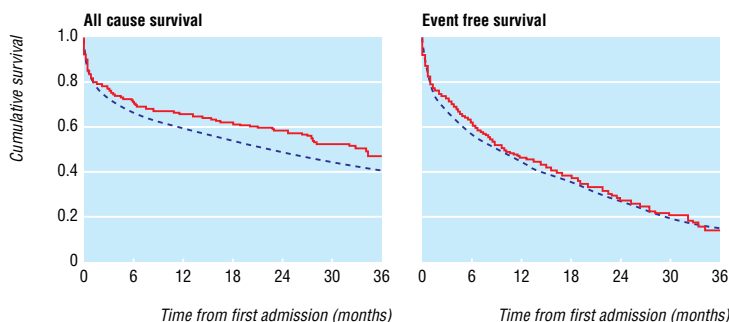
of readmission was similar to white patients (table 2). Among the factors influencing outcome were age (44% increase in the risk of death per decade of life) and comorbidity, particularly stroke and renal failure. Adjusted outcomes were better for women. A diagnosis of diabetes or concomitant acute myocardial infarction was associated with poorer event free survival. A lower risk was found in patients with hypertension (hazard ratio for death and event free survival 0.77 and 0.88, respectively) or atrial arrhythmias (0.86 and 0.94). No clear relation was found between deprivation and outcome. Indeed patients living in the most disadvantaged areas (lower fifth) had lower mortality.

After correction for covariates, the hazard ratio for all cause mortality was lower in South Asian patients than in white patients and similar for combined events (all cause, 0.82, 0.68 to 0.99; combined events, 0.94, 0.81 to 1.09; see table 2 and figure).

In the five years before the admission with heart failure, 3.3% (n=11) of South Asian patients had undergone a revascularisation procedure compared with 2.1% (n=105) of white patients (P<0.2). For procedures in the follow up period, values were 6.5% (n=22) and 3.1% (n=158), respectively (P=0.001).

Discussion

Our study has the advantage of a homogeneous South Asian cohort (94% of the South Asian population in Leicestershire is of Indian descent), but we cannot assume that our observations apply to other ethnic



Survival model for South Asian and white patients in cohort of new cases diagnosed with heart failure in hospital between 1 April 1998 and 31 March 2001

groups, among whom cardiovascular risk profiles differ.⁶ Similar results were, however, shown in another study, where South Asian people of Pakistani or Bangladeshi descent were in the majority.⁷

Our study is limited by lack of information on disease severity, non-invasive investigations, and pharmacological treatment before and after admission, all potential modifiers of outcome. We are confident about the robustness of the record linkage system, which allowed identification of all mortality and in-hospital events. Although the limitations of hospital discharge data cannot be ignored, such caveats apply equally to both ethnic cohorts and are unlikely to have introduced bias.⁷ In identifying incident cases we included all admissions with heart failure diagnosed in any position. Although this may cause some overestimate, excluding cases with a diagnosis of secondary heart failure may have led to more underestimation.

Coronary heart disease, the commonest cause of heart failure, is around 40% more common in patients from South Asian ethnic minorities in the United Kingdom and other countries compared with indigenous populations.^{1,2,8} Moreover, coronary heart disease has been reported to have earlier onset, to be more extensive, and to have a worse prognosis in South Asian people.^{2-4,9} Our data are compatible with a greater prevalence of coronary heart disease in South Asian people, with concomitant or previous myocardial infarction being nearly twice as common than in white patients. The younger age of the South Asian patients also supports earlier onset of disease. As might be expected, age adjusted rates for admission and incidence of heart failure were higher for South Asian patients.

Our study concurs with recent reports of an annual case fatality rate of 40% after a first admission for heart failure.^{10,11} A small proportion of our cohort was treated in a cardiological setting at the time of the index admission. In the context of previous reports from UK centres, indicating similar outcomes in South Asian and white patients after myocardial infarction and after coronary artery surgery, the lower mortality for South Asian patient newly admitted with heart failure is of note.^{5,12} This phenomenon is likely to be multifactorial and could be explained by heart failure being less advanced at the point of first admission, by a differing cause of heart failure in ethnic minority populations, or by better family support after discharge. Better prognosis among South Asian patients remained after adjustment for other prognostic variables and despite higher rates of coronary heart disease and diabetes. The higher prevalence of hypertension and diabetes in South Asian patients perhaps suggests that this cohort may have a higher prevalence of heart failure with preserved left ventricular systolic function. The protective effect of hypertension in our cohort lends some support to this postulate.

In the United States, black patients show more rapid disease progression with heart failure and are readmitted more frequently than white patients.^{9,13} Poorer prognosis for black and Asian patients in the United States after myocardial infarction has been ascribed in part to inequities in access to invasive procedures.^{14,15} Our observations do not support such phenomena in South Asian patients in Leicestershire,

What is already known on this topic

Coronary heart disease is more prevalent among South Asian people than white people, with an earlier onset and higher mortality

Ethnic minority patients are under-represented in clinical trials

Little is known about the clinical features of heart failure and outcomes in South Asian patients in the United Kingdom

What this study adds

Admission and incidence rates for heart failure are higher in South Asian patients than in white patients

South Asian patients newly admitted with heart failure are younger (average eight years) and have a history of a higher prevalence of acute myocardial infarction, diabetes, and hypertension than white patients

Even after adjusting for age and in-hospital comorbidity factors, survival is similar, if not better, for South Asian patients

for whom coronary revascularisation rates were higher than in white patients. There is, however, a parallel to a large study from California where Asian patients (likely to be ethnically different to our South Asian population) had lower rates for admission to hospital, incidence, mortality, and readmission than white patients.¹⁶

Better outcome for patients from areas of high deprivation is puzzling. As with all such measures, the index of multiple deprivation is a sum of indicators more relevant to the working age population than to elderly patients, who primarily comprised our cohort. Only two of the six domains in the index—housing and access to services (contributing no more than 20% of the overall weight)—could feasibly reflect the level of social deprivation among elderly patients. This indicates that the index is a relatively inappropriate measure of deprivation in this type of population. However short of knowing the current income or housing conditions, it is difficult to measure social deprivation in elderly patients.

Conclusions

Age adjusted admission and incidence rates for heart failure are higher among the South Asian ethnic population of Leicestershire than they are among the white population. Survival data suggest better outcomes for South Asian patients compared with white patients, this on a background of markedly differing risk factor profiles. The observations are clinically important to the UK South Asian population, among whom coronary heart disease and diabetes are common, and in whom the proportion of patients of an age that puts them at risk of heart failure is increasing. The data indicate that ethnicity is a significant factor in the development and course of the disease. Further studies are required to delineate

the cause, clinical course, and prognosis of heart failure in different communities worldwide.

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Additional tables appear on bmj.com

Cohort study on effects of parathyroid surgery on multiple outcomes in primary hyperparathyroidism

Peter Vestergaard, Leif Mosekilde

Abstract

Objectives To assess the effects of surgery compared with conservative treatment (no surgery) for primary hyperparathyroidism.

Design Cohort study.

Setting Nationwide Danish cohort.

Participants 3213 patients, mean age 61 (SD 16) years, with a diagnosis of primary hyperparathyroidism between 1980 and 1999. 1934 (60%) underwent surgery and 1279 (40%) were treated conservatively.

Main outcome measures Occurrence of fractures, osteoporosis, kidney or urinary tract stones, acute myocardial infarction, angina pectoris, cardiac arrhythmias, arterial hypertension, heart failure, stroke, acute pancreatitis, stomach or duodenal ulcers, muscle pain, malignant diseases, psychiatric disorders, and mortality.

Results At diagnosis of primary hyperparathyroidism, patients who subsequently underwent surgery had a lower prevalence of previous fracture (odds ratio 0.64, 95% confidence interval 0.51 to 0.80), acute myocardial infarction (0.59, 0.42 to 0.83), stroke (0.57, 0.37 to 0.88), psychiatric disorders (0.54, 0.31 to 0.94), and painful muscle disorders (0.44, 0.26 to 0.76), whereas kidney stones (2.49, 1.93 to 3.23) and acute pancreatitis (2.77, 1.33 to 5.76) were more prevalent. After diagnosis, the risks of fractures (hazards ratio 0.69, 0.56 to 0.84) and gastric ulcers (0.59, 0.41 to 0.84) were lower in patients treated surgically than those treated conservatively. Events involving kidney or urinary tract stones were more prevalent in patients treated surgically than patients treated conservatively

(1.87, 1.30 to 2.68). Mortality was lower in patients treated surgically (0.65, 0.57 to 0.73).

Conclusions Patients treated surgically for primary hyperparathyroidism have a lower prevalence of fractures and gastric ulcers than patients treated conservatively. The type of treatment had no effect on the occurrence of cardiovascular events.

Introduction

Most intervention studies on the effect of surgery in primary hyperparathyroidism are uncontrolled cohort or before and after trials comparing changes in left ventricular size, fracture risk, bone mineral density, and incidence of kidney stones.¹⁻⁴ They therefore have not evaluated the difference between surgically and non-surgically (conservatively) treated patients. One small randomised study evaluated the effects of surgery and conservative treatment on bone mineral density and found an increase in bone mineral density and quality of life scores in surgically treated patients.^{5 6} We collected data on a large cohort of patients with primary hyperparathyroidism and evaluated the long term outcome of hard end points in surgically treated patients compared with conservatively treated patients.

Materials and methods

Data were obtained from the Danish hospital discharge database. This central national database contains information on patients admitted to hospital according to their unique identification number and type of disease. Any surgical procedures are also recorded.