Incidence, recurrence, and case fatality rates for myocardial infarction in southwestern France, 1985 to 1993

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Abstract

Objective—To assess the impact of incidence, recurrence, and case fatality rates for myocardial infarction on coronary heart disease mortality in southwestern France between 1985 and 1993.
Design—Toulouse-MONICA myocardial infarction register.
Settings and patients—All subjects aged 35 to 64 years living in the French department of Haute-Garonne.
Interventions—All coronary artery disease events between 1985 and 1993.
Main outcome measures—7210 events collected by the register between 1985 and 1993.
Results—In men, adjusted attack, total, and out of hospital mortality decreased by 2% (95% confidence interval (CI), −3.8% to −0.1%), 6.2% (95% CI −8.4% to −4.0%), and 4.2% (95% CI −7.0% to −1.5%) a year, respectively ($p < 0.05$). Incidence and recurrence rates decreased by 2% (95% CI −4.1% to −0.1%, $p < 0.05$) and 1.9% (95% CI −5.9% to 2.2%) a year (NS). In women, attack, total, and out of hospital mortality decreased by 1.7% (95% CI −5.2% to 1.8%), 4.8% (95% CI −9.6% to 0.1%), and 2.6% (95% CI −9.4% to 4.1%) a year, respectively; incidence decreased by 2% (95% CI −6.5% to 2.5%) and recurrence increased by 1.4% (95% CI −9.8% to 12.6%) a year (all NS). In men, total, incident, and recurrent 28 day case fatality decreased by 3.8% (95% CI −4.8% to −2.8%), 3.2% (95% CI −4.1% to −2.3%), and 6.4% (95% CI −9.5% to −3.3%) a year, respectively ($p < 0.05$). For women, the corresponding decreases were 3.3% (95% CI −6.1% to −0.6%), 3.3% (95% CI −13.2% to 6.6%), and 11.7% (95% CI −24.6% to 1.3%) a year, but only the decrease in total 28 day case fatality reached significance. In both sexes, the reduction in case fatality contributed nearly 70% of the decrease in myocardial infarction mortality.
Conclusions—In southwestern France, the decrease in myocardial infarction mortality mainly reflects improvements in acute management rather than prevention.
(*Heart* 2000;**84**:171–175)

In recent years, coronary heart disease mortality has decreased considerably in western populations,[1–4] but whether this reflects a decline in cardiovascular risk factors (primary prevention), improvement in treatment (secondary prevention), or a combination of both remains to be assessed in France. Primary prevention would decrease the incidence of new coronary events, whereas secondary prevention would decrease recurrent events. More intensive treatment after the onset of acute myocardial infarction is also believed to decrease case fatality.[5 6]

Southwestern France is characterised by a low mortality from myocardial infarction[7] and by rapidly increasing invasive management of this condition.[8] Cardiovascular risk factors in southwestern France are similar to those in other regions with much higher myocardial infarction rates, such as Northern Ireland.[9] Although screening for the main cardiovascular risk factors has increased in this region, attempts to modify these factors have remained relatively stable.[10] Though dietary factors might partly explain the difference in attack rates between southwestern France and Northern Ireland,[9] the effect of primary and secondary prevention of myocardial infarction has not yet been studied. Thus we hypothesised that

any decrease in coronary heart disease mortality could reflect better treatment of cases of myocardial infarction and also improved secondary prevention. To test this hypothesis, we used the data collected between 1985 and 1993 by the Toulouse MONICA (monitoring trends and determinants in cardiovascular disease) myocardial infarction register to examine the evolution of attack, incidence, recurrence, and case fatality rates of myocardial infarction events.

Methods

POPULATIONS

The World Health Organization MONICA project is a study that monitors deaths from coronary heart disease, myocardial infarction, coronary care, and risk factors in men and women aged 35 to 64 years.[7 11–14] It consists of 39 MONICA collaborative centres in 26 countries. Each collaborative centre is in charge of a coronary event register for patients aged 35 to 64 years living in the geographical area of the centre. The details of the registration procedure have been described elsewhere.[7 14 15] Briefly, all private and public hospitals within the geographical area of the collaborative centre were screened by trained staff for suspected coronary heart disease events; death

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certificates, including those for sudden deaths, were also screened.

Diagnosis of myocardial infarction was based on five criteria: symptoms, ECG findings, cardiac enzymes, previous coronary artery disease history, and necropsy findings (if required). An event was considered "new" if its apparent date of onset was more than 28 days after any previous coronary heart disease event. Events were considered fatal if death occurred before midnight of the 27th day after the initial event. In this analysis, MONICA definition 1 for myocardial infarction was used (corresponding to non-fatal "definite" myocardial infarction, plus fatal "definite," "possible," and "unclassified" myocardial infarction).[7] During the whole survey period, no changes in the criteria for definition of myocardial infarction were made.

STATISTICAL ANALYSIS

Statistical analyses were performed using EPI-Info (WHO, Geneva, Switzerland) and STATA (Stata Corporation, College Station, Texas, USA) statistical software. Attack rates were calculated by dividing the total number of events by the number of subjects in the corresponding age group; incidence rates were calculated similarly, using the number of first events in the numerator; recurrence rates were calculated using the number of recurrent events in the numerator. Case fatality rates were calculated by dividing the number of fatal events by the total number of events (fatal + non-fatal). Coronary event rates were expressed per 100 000 inhabitants and age standardised by the direct method, using five year age groups and the world standard population as the reference.[16] The 28 day case fatality rate was age standardised, using the age distribution of pooled myocardial infarction patients in the WHO MONICA myocardial infarction registers as the reference,[7] and was expressed as the percentage of all events. Trends in event and case fatality rates were assessed as published, using linear regression analysis with the natural logarithm of age standardised rate as the dependent variable and year as the independent variable[17 18]; they were expressed as per cent/year.

The assessment of the impact of incidence, recurrence, and case fatality on coronary heart disease mortality was performed as described previously,[18] with slight modifications. Briefly, the reduction in age standardised mortality for the period 1985 to 1993 was calculated from a regression model using the natural logarithm of rate as the dependent variable and year as the independent variable. The incidence of first coronary events at the beginning and at the end of the study period was estimated using a similar regression model. The reduction in the number of deaths (per 100 000 inhabitants) resulting from the decrease in the incidence of first events was then obtained by calculating [estimated incidence rate for year 1985 − estimated incidence rate for year 1993] × 28 day case fatality rate for incident events. The reduction in the number of deaths resulting from the decrease in recurrent events was calculated similarly. In this study, mean 28 day case fatality rates for incident and recurrent events were used in the calculations.

Results

NUMBER OF EVENTS

In all, 7210 events were collected by the register during the period 1985 to 1993, of which 3839 fulfilled the criteria for inclusion in the analysis. Eighty five per cent of all the events occurred in men (3263 of 3839), and 29% of all the events in men were out of hospital deaths (964 of 3839); for women, 45% of all the events were out of hospital deaths (262 of 561).

ATTACK, INCIDENCE, AND RECURRENCE RATES

In men, adjusted attack, total mortality, and out of hospital mortality rates decreased significantly between 1985 and 1993 (table 1). Incidence, mortality from incident events, and out of hospital mortality for incident events also decreased significantly (table 1). Recurrence rates decreased by 1.9% a year, but this decrease was not significant. Conversely, total and out of hospital mortality rates from recurrent events decreased significantly during 1985 and 1993 (table 1), and most of the decreases in rates tended to be steeper in the first three years.

In women, similar decreases were found for attack, total mortality, and out of hospital mortality rates, but those decreases were not significant (table 2). Also, a non-significant decrease was found for incidence, total mortality, and out of hospital mortality from

Table 1　Age standardised attack, incidence, recurrence, total mortality, and out of hospital mortality rates (per 100 000) from myocardial infarction events in men, 1985 to 1993

Year	All events			First myocardial infarction			Recurrent myocardial infarction		
	Attack rates	Total mortality	Out of hosp mortality	Incidence rates	Total mortality	Out of hosp mortality	Recurrence rates	Total mortality	Out of hosp mortality
1985	258	119	80	211	90	62	47	28	18
1986	240	107	74	199	83	60	41	25	13
1987	225	92	65	180	71	54	45	21	11
1988	234	94	75	198	76	63	36	18	12
1989	224	88	70	191	73	57	33	15	13
1990	246	90	71	203	68	55	43	23	17
1991	245	90	69	205	74	59	40	16	10
1992	203	72	53	172	59	45	31	13	8
1993	206	65	53	162	50	45	44	14	8
Trend	−2.0	−6.2	−4.2	−2.0	−5.6	−3.4	−1.9	−8.2	−7.8
95% CI	−3.8 to −0.1	−8.4 to −4.0	−7.0 to −1.5	−4.1 to −0.1	−8.1 to −3.2	−5.9 to −0.9	−5.9 to 2.2	−12.6 to −3.8	−14.1 to −1.5

hosp, hospital.

Table 2   Age standardised attack, incidence, recurrence, total mortality, and out of hospital mortality rates (per 100 000) from myocardial infarction events in women, 1985 to 1993

Year	All events			First myocardial infarction			Recurrent myocardial infarction		
	Attack rates	Total mortality	Out of hosp mortality	Incidence rates	Total mortality	Out of hosp mortality	Recurrence rates	Total mortality	Out of hosp mortality
1985	33	24	15	27	20	14	5	3	2
1986	38	22	17	35	21	17	3	2	0
1987	39	25	19	37	24	18	2	2	1
1988	38	23	16	36	22	16	2	1	1
1989	42	28	24	39	25	22	3	2	1
1990	39	20	15	33	18	15	6	2	0
1991	29	14	10	24	11	10	4	3	1
1992	34	20	17	29	18	17	5	2	1
1993	32	18	14	29	16	14	3	1	1
Trend	−1.7	−4.8	−2.6	−2.0	−3.3	−2.3	1.4	−4.3	−10.0
95% CI	−5.2 to 1.8	−9.6 to 0.1	−9.4 to 4.1	−6.5 to 2.5	−13.2 to 6.6	−9.4 to 4.7	−9.8 to 12.6	−20.3 to 11.6	−20.7 to 0.7

Table 3   Age standardised 28 day case fatality (%) for all, incident, and recurrent myocardial infarction events: data from 1985 to 1993 in men and women aged 35 to 64 years from the Toulouse MONICA register

Year	Men			Women		
	First	Recurrent	All events	First	Recurrent	All events
1985	43.4	61.2	46.9	67.9	64.5	73.7
1986	42.0	60.9	45.7	40.9	38.2	57.7
1987	39.6	47.8	41.1	40.3	47.7	65.1
1988	38.6	48.1	40.3	41.0	15.9	61.7
1989	38.1	44.0	39.2	54.7	65.5	64.6
1990	36.0	52.1	38.8	45.5	31.8	50.2
1991	37.4	45.2	38.6	32.4	45.5	50.2
1992	35.7	41.2	36.5	55.9	23.9	58.0
1993	31.8	31.8	32.8	33.6	25.5	53.3
Trend	−3.2	−6.4	−3.8	−3.3	−11.7	−3.3
95% CI	−4.1 to −2.3	−9.5 to −3.3	−4.8 to −2.8	−13.2 to 6.6	−24.6 to 1.3	−6.1 to −0.6

incident cases (table 2). Finally, recurrence rates increased, while overall and out of hospital mortality from recurrent cases decreased, but again those trends did not reach significance (table 2).

TWENTY EIGHT DAY CASE FATALITY

In men, a significant decrease was found for overall 28 day case fatality, 28 day case fatality from incident events, and 28 day case fatality from recurrent events (table 3). In women, similar decreases were observed, but only the decrease in overall 28 day case fatality reached significance (table 3).

IMPACT OF INCIDENCE, RECURRENCE, AND CASE FATALITY FROM MYOCARDIAL INFARCTION ON CORONARY HEART DISEASE MORTALITY

The effect of incidence, recurrence, and case fatality on coronary heart disease mortality was assessed using the mean 28 day case fatality rates for incident and recurrent events separately for men and for women. Calculations showed that in both sexes most of the reduction in coronary heart disease mortality resulted from the decrease in case fatality rather than from a reduction in incident and recurrent events (table 4). In women, the decline in case fatality was almost entirely responsible for the decrease in coronary heart disease mortality, while the change in recurrent cases had a negative effect; this latter finding is in agreement with the slight increase of recurrent cases observed for women (table 3).

Discussion

Little is known about the evolution of cardiovascular morbidity and mortality, and about the impact of prevention and the medical man-

Table 4   Proportion (%) of observed reduction in mortality from myocardial infarction (change in age standardised rate/100 000 inhabitants), predicted by changes in incidence, recurrence, and case fatality rates

	Observed reduction	Incidence	Recurrence	Case fatality
Men	45	27%	6%	67%
Women	8	11%	−2%	91%

agement of myocardial infarction in France. Because of its well standardised methodology, data from the WHO MONICA project can be used to assess these issues.

Mortality from myocardial infarction decreased considerably in both men and women, but the decrease was significant only in men. Those findings are in agreement with other studies,[4] [18–22] and as the decrease in mortality exceeded the decrease in incidence, our data suggest that the decline in mortality from myocardial infarction mainly reflects improvements in the treatment of this condition rather than a decrease in new events.

The decrease in incidence was comparable for both men and women, but again the decrease in women did not reach significance. Those findings suggest that primary prevention is equally effective in both sexes.

Recurrence rates decreased in men, but only the decrease in mortality from recurrent myocardial infarction reached significance. As secondary prevention would decrease recurrence rates and medical care would decrease mortality, these findings indicate that acute medical care (thrombolysis, angioplasty, and emergency medicine facilities) takes precedence over secondary prevention in southwestern France. Nevertheless, in a previous report, patients living in France who survived a

myocardial infarct received significantly more medical treatment than their Northern Irish counterparts.[23] A possible explanation is that improvements in the acute medical care of myocardial infarction have outpaced improvements in secondary prevention in southwestern France. In women, recurrence rates decreased less than incidence rates; this suggests either a lower level of secondary prevention in this group[24 25] or more severe coronary disease in women than in men.[26 27] Nevertheless, this latter hypothesis would not apply to southwestern France, as the distribution of one, two, and three vessel disease was comparable in women and men (data not shown).

Out of hospital mortality decreased in both sexes, but the decrease was significant only in men. The decrease was more pronounced for recurrent cases than for incident cases, possibly indicating better management of patients with a history of myocardial infarction. These findings also suggest the need for a better education of subjects at risk of myocardial infarction, as patients who have already had an infarct tend to be admitted to hospital more rapidly than patients presenting with their initial event.[28]

The favourable trends observed in men are reflected in other data from the French MONICA centres,[8 29–31] and may be related in part to an increase in the acute treatment of myocardial infarction in southwestern France,[5 8 29 32 33] a region that has been at the forefront of the acute management of myocardial infarction.[5 32] The less favourable trends observed in women are most probably explained by the small number of events leading to a decrease in statistical power.

The relative part of medical treatment and of changes in cardiovascular risk factor levels on the decline in coronary heart disease mortality has been estimated at 60% and 40%, respectively.[34] However, it is unlikely that changes in cardiovascular risk factor levels of this degree are present in Haute-Garonne, as we found an *increase* in the prevalence of some cardiovascular risk factors in both sexes (Marques-Vidal P *et al*, unpublished observations). Thus it is possible that the impact of treatment on the decrease in myocardial infarction event rates may be greater in the Haute-Garonne region of France than in other countries, although this hypothesis awaits further investigation.

Another possible explanation for the decrease in 28 day mortality is that the severity of myocardial infarcts has decreased over the years. However, analysis of the angiographic data on all hospital inpatients between 1988 and 1993 indicates that the distribution of one, two, and three vessel disease has remained stable over that period in both men and women (data not shown). Although there are no data on left ventricular ejection fraction, the available angiographic data indicate that it is unlikely that the decrease in 28 day mortality can be explained by a decrease in the severity of myocardial infarction. Another possible explanation would be a change in the criteria which define myocardial infarction, but this hypothesis can be rejected as no alteration in these criteria was found when an external quality control was applied to our coronary event registration data (not shown).

The effect of incidence, recurrence, and case fatality on coronary heart disease mortality was assessed using the mean 28 day case fatality rates for incident and recurrent events in men and women separately. This was considered necessary so that the same model could be used for both sexes, while also taking into account the decrease in case fatality rates observed in men but not in women. It is of note that the use of different case fatality rates did not lead to significant changes in the results (data not shown).

Case fatality rates explained the decrease in coronary heart disease mortality in both sexes almost entirely. This supports our finding that there was a larger decrease in mortality than in incidence and recurrence rates. Thus, in contrast to other countries where the decrease in cardiovascular mortality has been attributed mainly to primary and secondary prevention[18 22 35 36] or to a combination of both prevention and medical treatment,[37] our findings indicate that in southwestern France, primary and secondary prevention seem to contribute little to the decline in coronary mortality, and improvements in medical management appear more important.

National vital statistics alone cannot provide information on the impact of new preventive measures or therapeutic strategies on mortality from coronary disease. Continuous monitoring is necessary to assess the effects of preventive measures such as lowering of cholesterol or blood pressure and of acute treatments such as thrombolysis and angioplasty. Our data indicate that primary and secondary prevention of myocardial infarction appear to contribute little to the decline in coronary heart disease mortality in southwestern France, and that efforts should be directed towards improving preventive measures and consolidating the existing medical management of myocardial infarction. For instance, better education of the general public about the importance of decreasing the delay between the onset of symptoms and admission to hospital would reduce the frequency of out of hospital deaths, which still account for three quarters of all infarct related deaths in men and women. Finally, as these results were obtained in subjects aged between 35 and 64 years, our conclusions may not be applicable to all patients suffering from myocardial infarction, particularly older patients.

CONCLUSIONS
Our results show that myocardial infarction events are decreasing in men aged 35 to 64 years living in southwestern France, and that the decline in coronary heart disease mortality has probably resulted from improved management of acute cases. The non-significant trends observed in women may either reflect the small number of events collected or a stabilisation of coronary heart disease in this group. Further

research is necessary to clarify this point. Finally, the decline in mortality from myocardial infarction appears to be almost entirely caused by improved medical management, and the effect of primary and secondary prevention remains modest.

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