CARDIOVASCULAR MEDICINE

Trends in incidence and case fatality rates of acute myocardial infarction in Denmark and Sweden

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Objective: To compare the incidence and case fatality of acute myocardial infarction in Denmark and Sweden.
Design: A cohort study, linking the national registries of hospital admissions and causes of death in the two countries.
Patients: All admissions and deaths with acute myocardial infarction as primary or secondary diagnosis were extracted (Denmark, 1978 to 1998; Sweden, 1987 to 1999).
Main outcome measures: The incidence was estimated using the first acute myocardial infarct for each patient. Case fatality was estimated in the first 28 days after acute myocardial infarction, including prehospital deaths. All rates were adjusted for age.
Results: The incidence of myocardial infarction and the case fatality declined significantly among all subgroups of patients. Case fatality was higher in Denmark early in the study period (1987–1990) than in Sweden. The odds ratios (OR) ranged from 1.28 to 1.50 in the four age groups. In 1994–1999, the prognosis of patients younger than 75 years did not differ. Patients aged 75–94 years still fared worse in Denmark (OR 1.21, 95% confidence interval 1.17 to 1.27). Women aged 30–54 years had a worse prognosis than men in both Denmark and Sweden (OR associated with male sex 0.85 and 0.90, respectively). In contrast, for patients older than 65 years, women had a better prognosis than men. This difference in the effect of sex with age was significant ($p < 0.0001$) and did not change over time.
Conclusions: Case fatality after acute myocardial infarction was notably higher in Denmark than in Sweden in 1987–1991, but in the later periods the prognosis was comparable in the two countries.

Although cardiovascular mortality has been diminishing in all of western Europe and North America for the past decades, it is still one of the major contributors to mortality, and especially premature death. Most studies investigating the incidence of acute myocardial infarction have found a significant and unequivocal reduction over the years.[1–3] The trends in case fatality have been less clear and also less well studied. Most studies looking at survival after acute myocardial infarction have pooled data from several years and are thus unable to study the trend over time.[4–7] The World Health Organization MONICA (monitoring of trends and determinants in cardiovascular diseases) project focused especially on the trends in the rate and outcome of coronary events.[1] The researchers found a clear and significant reduction in the event rate but only a dispersed and modest decrease in case fatality. This led to the conclusion that most of the decrease in cardiovascular death was attributable to the decrease in the event rate.[1] Even though MONICA made an intense effort to define the event uniformly, the MONICA centres only covered a small part of the population at risk in each country. The selection of centres may have produced results that are not representative of the national trends. However, the MONICA study showed wide variation between centres in countries considered to be quite similar, and this highlights the need for comparison of nationwide data.

Several studies have compared the prognosis of men and women, with different results.[5 8] In recent studies it has been found that younger women have a higher risk of dying than men, whereas older women have a comparable or even lower risk than men.[5 6] Again, these studies have pooled data for several years, which rules out the possibility of studying the trends over time.

Very few studies have described the trends in case fatality in recent years, and ours is the first study to compare the results from national registries in two countries. To make the comparison meaningful it includes all patients, whether dying before hospital admission from acute myocardial infarction or admitted for treatment. Including the patients who die before admission also helps to illustrate the true burden of ischaemic heart disease in western societies.

Our study was designed to compare the trends in incidence and case fatality after acute myocardial infarction in Denmark and Sweden and to look for possible differences in the trends experienced by men and women in different age groups, with special focus on the poor prognosis of younger women compared with men.

METHODS

Material

This study relies on two separate national registries in Denmark and Sweden. Each registry was formed by linking the discharge registry to the registry of causes of death by the unique personal identification number assigned to every citizen in the two countries. The Danish registry covers the period from 1978 to 1998. All diagnoses and causes of death were classified using the *International classification of diseases* (ICD), version 8 until 1994, when ICD-10 was introduced. The Swedish registry covers the period from 1987 to 1999 and used ICD-9 up to 1997 and ICD-10 from 1997 onwards. The diagnosis of acute myocardial infarction in the registries has been validated by reclassification of a random sample (Sweden) and by comparison with the results from the MONICA database in Denmark.[9] The sensitivity and specificity were 90–95%.

Definition of acute myocardial infarction

The definition included death with acute myocardial infarction as the primary or secondary cause, and discharge from hospital alive or dead with acute myocardial infarction as a primary or secondary diagnosis. In the separate subanalyses

on incidence rate this definition was widened by inclusion of all deaths with any ischaemic heart disease as the primary cause of death. Finally all sudden deaths from unknown cause were also included.

The ICD codes used were as follows: *acute myocardial infarction*, ICD-8: 410; ICD-9: 410; ICD-10: I21–22; *ischaemic heart disease*, ICD-8: 410–414; ICD-9: 410–414; ICD10: I20–25; *sudden death from unknown causes*, ICD-8: 795–796; ICD-9: 798 + 427.5; ICD-10: R96 + R98 + I46. Because the length of the hospital stay varies over time and regions, the case fatality after acute myocardial infarction was defined as all cause death within a fixed period of 28 days after the infarct, including out of hospital death. The first event for each patient was recorded. A later event was only recorded if it occurred more than 28 days after the admission for the previous infarct. The incidence of acute myocardial infarction was analysed using all occurrences of acute myocardial infarction (attack rate) and only the first infarct, to ensure that a lower case fatality did not lead to an increase in the number of survivors more prone to having another infarct, which would result in an apparent increase in the incidence. To secure a similar definition of first acute myocardial infarction, identical periods of four years (4×365 days) free of any history of acute myocardial infarction were applied in the two registries. Because of this definition, the incidence of first acute myocardial infarction could only be estimated for 1982–1998 for the Danish registry and for 1991–1999 for the Swedish registry.

Statistical methods

The incidence and case fatality was expressed as age adjusted estimates of rates per year for each country. As one focus of the analyses was to demonstrate and describe a possible interaction between age, sex, and time period, each sex was divided into four age groups (30–54, 55–64, 65–74, and 75–94 years). The trends in case fatality were expected to be very different in the pre- and post-thrombolytic era, and hence the period was divided into 1978 to 1986 (Denmark only) and 1987 to 1999 (Denmark and Sweden). As the trends in each country differed, the latter period was further divided into 1987–1990, 1991–1993, 1994–1996, and 1997–1999. The incidence rates for men and women were age standardised using the Danish population in 1998, making the age standardised rates directly comparable between countries and sexes. The case fatality rates were age standardised using the Danish acute myocardial infarction population in 1998 as the reference. Trends in incidence rates were evaluated using Poisson regression analysis. Trends in case fatality were evaluated using multiple logistic regression analysis. Even if the analyses were undertaken within a selected age group, the specific age was entered into the model as a class covariate, each class covering five years.

RESULTS

The crude number of first acute myocardial infarcts in Denmark decreased from 18 161 in 1982 to 11 886 in 1998. In Sweden the crude number decreased from 33 450 in 1991 to 30 912 in 1999. The total number of patients with acute myocardial infarction in this study was 567 752.

Incidence rates

The age adjusted incidence rates of first acute myocardial infarction are plotted in fig 1 for each of the two countries and for men and women in the four age groups. Denmark and Sweden differed significantly with respect to the four age groups. Among patients aged 30–54 years the incidence was slightly higher in Denmark (rate ratio = 1.06 (95% confidence interval (CI) 1.03 to 1.09)). The rate ratio (Denmark *v* Sweden) for patients aged 55–64 years was 0.99 (95% CI 0.95 to 1.03); aged 65–74 years, 0.86 (95% CI 0.84 to 0.89); and aged 75–94 years, 0.74 (95% CI 0.72 to 0.76).

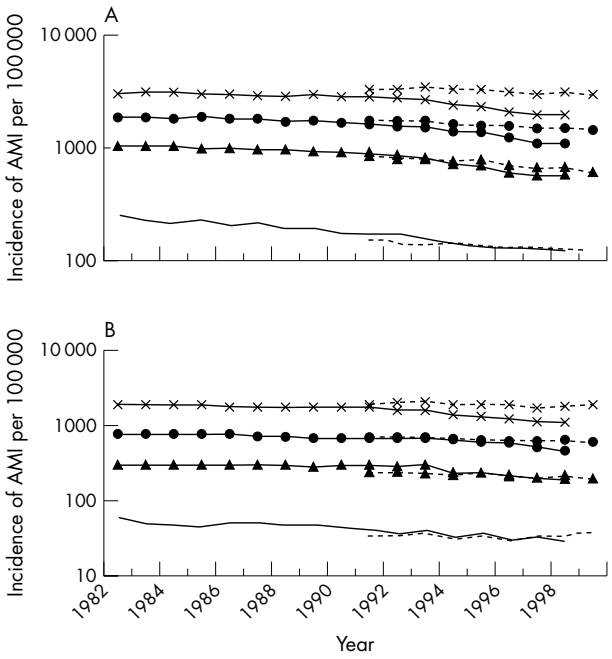

Figure 1 Age adjusted incidence rates of first acute myocardial infarct per 100 000 inhabitants according to sex (panel A, men; panel B, women), age group, and calendar year in Denmark and Sweden (y axis on log scale). Denmark: solid line; Sweden: dashed line. No symbol, 30–54 years; triangles, 55–64 years; circles, 65–74 years; crosses, 75–94 years.

Men had a significantly higher incidence of first acute myocardial infarction than women in both Denmark and Sweden. In Denmark the rate ratio was 2.28 and in Sweden it was 2.17 ($p < 0.0001$ for both countries). We found a significant interaction between age and sex in both Denmark and Sweden ($p < 0.0001$), such that the effect of male sex was smaller in the older age groups than in the younger ones. The rate ratios associated with male sex among patients aged 30–54 years were 4.29 in Denmark and 4.10 in Sweden; aged 55–64 years, 3.13 and 3.37; aged 65–74 years, 2.39 and 2.45; and aged 75–94 years, 1.74 and 1.75. This change with age in the risk associated with male sex did not alter over time ($p > 0.8$ in both countries). The incidence rate of first acute myocardial infarction declined continuously and distinctly among both men and women. Table 1 lists the change from 1991 to 1998 in the age adjusted incidence in Denmark and Sweden by sex and age group. The trends were comparable for men and women of all ages, but the decrease per year was significantly greater for both men and women of all ages in Denmark than in Sweden ($p < 0.0001$).

The incidence rates were also analysed after the addition of all patients who died from ischaemic heart disease before

Table 1 Average annual relative change (%) in the incidence of first acute myocardial infarct from 1991 to 1998, according to age and sex

		Age group (years)			
	Total	30–54	55–64	65–74	75–94
Denmark					
Men	–6.0	–4.8	–6.9	–6.3	–5.6
Women	–5.9	–4.2	–6.7	–5.4	–6.0
Sweden					
Men	–2.3	–2.0	–3.3	–2.8	–1.7
Women	–1.8	–0.6	–2.5	–2.1	–1.7

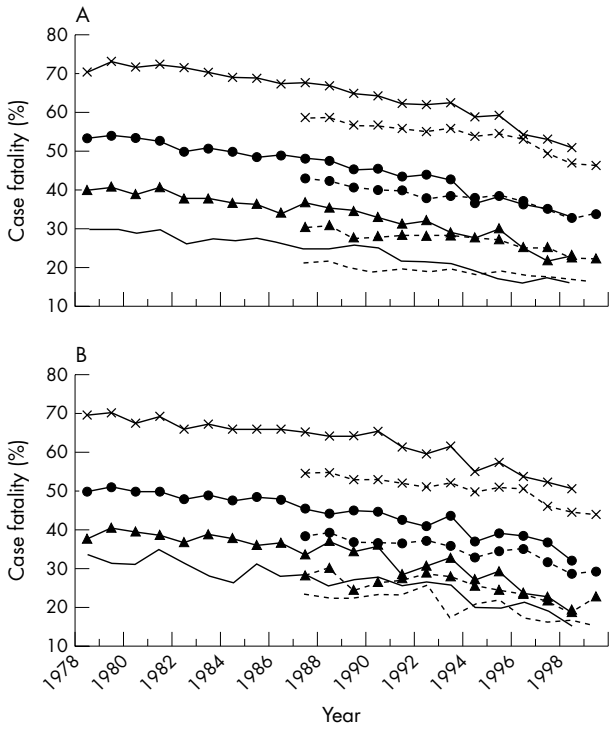

Figure 2 Age adjusted case fatality rate in per cent, 0–28 days after acute myocardial infarction according to sex (panel A, men; panel B, women), age group, and calendar year. Denmark: solid line; Sweden: dashed line. No symbol, 30–54 years; triangles, 55–64 years; circles, 65–74 years; crosses, 75–94 years.

hospital admission, and further after including all sudden deaths from unknown causes. The trends in incidence were less pronounced, but the difference in sex effect according to age group was present regardless of the definition used.

Case fatality rates

Figure 2 shows the age adjusted case fatality rate after any attack of acute myocardial infarction for both countries and for men and women in the four age groups. Case fatality did not differ significantly after the first acute myocardial infarction or after any attack. In Denmark, the case fatality declined more steeply after thrombolytic agents were introduced (1987–1998) than in the prethrombolytic era (1978–1986). The difference in prognosis after acute myocardial infarction in Denmark and Sweden changed significantly according to calendar year and age group. Table 2 lists the odds ratios for Denmark according to age group and the four time periods. The difference between Denmark and Sweden was highly significant in all age groups in the early period, but over time the differences declined. In the period 1997–1999, only the odds ratio for patients aged 75–94 years was significant, at 1.21 (95% CI, 1.17 to 1.27).

Denmark had a slightly higher age adjusted case fatality rate among men than among women in both periods ($p < 0.001$). The odds ratio in 1978–1986 was 1.09 (95% CI 1.07 to 1.12) and in 1987–1998, 1.03 (95% CI 1.01 to 1.06). In Sweden the increase in case fatality associated with male sex was notably higher (OR 1.15, 95% CI 1.12 to 1.17) in 1987–1999. Because of a significant interaction ($p < 0.0001$) between age and sex, the analyses were repeated in the four age groups for 1987–1999. This showed that the case fatality rate was higher among women aged 30–54 years than among men, whereas in the older age groups men had a higher case fatality rate than women. Table 3 presents the odds ratios associated with male sex in each of the four age groups for both Denmark and Sweden. A similar difference in the sex effect according to age was present in Denmark in the period 1978–1986. This higher case fatality among younger women compared with men was similar in degree during the entire study period ($p > 0.7$ in both Denmark and Sweden).

Table 2 Odds ratio for case fatality rate for Denmark compared with Sweden on days 0 to 28 after acute myocardial infarction, adjusted for age and sex within each age group and period

Age group (years)	Period	Odds ratio (95% CI)
30–54	1987 to 1990	1.31 (1.23 to 1.40)
	1991 to 1993	1.16 (1.07 to 1.25)
	1994 to 1996	0.94 (0.86 to 1.02)
	1997 to 1999	0.97 (0.87 to 1.08)
55–64	1987 to 1990	1.32 (1.25 to 1.40)
	1991 to 1993	1.13 (1.06 to 1.22)
	1994 to 1996	1.06 (0.99 to 1.14)
	1997 to 1999	0.94 (0.84 to 1.05)
65–74	1987 to 1990	1.28 (1.24 to 1.32)
	1991 to 1993	1.23 (1.19 to 1.28)
	1994 to 1996	1.03 (0.97 to 1.10)
	1997 to 1999	1.06 (0.97 to 1.15)
75–94	1987 to 1990	1.50 (1.44 to 1.56)
	1991 to 1993	1.39 (1.32 to 1.46)
	1994 to 1996	1.19 (1.14 to 1.25)
	1997 to 1999	1.21 (1.17 to 1.27)

CI, confidence interval.

Table 3 The odds ratio for male sex for case fatality 0 to 28 days after acute myocardial infarction, according to age and country from 1987 to 1996

Age group (years)	Odds ratio (95% CI)	
	Denmark	Sweden
30–54	0.85 (0.79 to 0.92)	0.90 (0.84 to 0.97)
55–64	0.99 (0.93 to 1.07)	1.07 (1.01 to 1.13)
65–74	1.03 (0.99 to 1.08)	1.17 (1.13 to 1.21)
75–94	1.07 (1.03 to 1.11)	1.16 (1.13 to 1.19)

Table 4 Average annual relative change (%) in case fatality after AMI according to age and sex in Denmark and Sweden from 1987 to 1999

	Sex	Age group (years)	Annual relative change (%)	95% CI
Denmark				
	Men	30–54	–5.82	(–6.82 to –4.80)
		55–64	–5.89	(–6.82 to –4.94)
		65–74	–5.58	(–6.32 to –4.83)
		75–94	–5.85	(–6.48 to –5.22)
	Women	30–54	–5.58	(–7.33 to –3.80)
		55–64	–6.12	(–7.88 to –4.31)
		65–74	–4.09	(–5.05 to –3.13)
		75–94	–5.75	(–6.59 to –4.91)
Sweden				
	Men	30–54	–2.35	(–3.17 to –1.52)
		55–64	–2.97	(–3.70 to –2.25)
		65–74	–3.12	(–3.62 to –2.62)
		75–94	–3.80	(–4.34 to –3.26)
	Women	30–54	–4.16	(–5.54 to –2.75)
		55–64	–3.41	(–4.60 to –2.20)
		65–74	–3.03	(–3.73 to –2.34)
		75–94	–3.44	(–3.94 to –2.94)

The case fatality rate declined more rapidly in Denmark than in Sweden ($p < 0.0001$). There was no difference in the trends among men *v* women. Further, the trends for different age groups did not differ significantly for either men or women in Denmark or Sweden. Table 4 lists the trends in case fatality after any acute myocardial infarction from 1987 to 1999 according to sex and the four age groups. Because both the use of the diagnosis "acute myocardial infarction" in deaths outside the hospital and the admission procedures may differ, case fatality was analysed again after all patients dying on the day of their infarct were excluded. The differences between countries, sexes, and age groups did not change significantly using this 1 to 28 day case fatality rate.

DISCUSSION

The main findings of this study are a pronounced decrease in the incidence and case fatality of acute myocardial infarction from 1978 to 1999 in both Denmark and Sweden. Sex influenced the incidence of acute myocardial infarction—this depended on age, such that the excess incidence among men became smaller with increasing age in both Denmark and Sweden. The impact of sex on case fatality also depended on age. Women younger than 55 years had a higher mortality than men of the same age, whereas women aged 55 or above had a comparable or lower risk than men. This interaction between age and sex for both incidence and case fatality did not change over time.

The incidence differed in Denmark and Sweden. Among the younger population, the incidence rate was slightly higher in Denmark than in Sweden. However, the incidence among the older population was notably higher in Sweden. The most likely explanation for this is the greater risk in the Danish population of dying from many competing diseases. Life expectancy in Denmark has been among the lowest in Europe for many years, especially for women. Life expectancy in Sweden is approximately three years longer than in Denmark for both men and women.

The case fatality rate declined clearly and significantly throughout the entire study period in both Denmark and Sweden. Case fatality was much higher in Denmark than in Sweden in the late 1980s and early 1990s. In the late 1990s, the excess mortality in Denmark was less striking and only clinically and statistically significant among patients aged 75–94 years.

There are several possible explanations for the difference in prognosis in the two countries. Differences in the treatment offered to patients and in the general health of the population may influence the probability of surviving an acute myocardial infarct. As mentioned previously, the life expectancy has been considerably higher in Sweden than in Denmark, but in this study we could not adjust for any differences in the severity of the infarct on an individual basis. However, significant differences in lifestyle have been demonstrated. Dietary habits are reported to be healthier in Sweden than in Denmark.[10] Further, the WHO MONICA project[11] showed differences in the levels of various risk factors. The proportion of daily smokers in Denmark was almost double that in Sweden, though the level of systolic blood pressure was higher in Sweden. The total risk score was similar in Denmark and Sweden. With regard to differences in treatment, Sweden has among the highest use of β blocker treatment in the whole of Europe for patients with acute myocardial infarction, whereas Denmark has been more restrictive in this regard.[12] Furthermore, invasive treatment was very infrequent in the early 1990s in Denmark compared with Sweden (and the rest of the world).[13] After the Danish Heart Plan was implemented in 1994, invasive treatment in Denmark rose to a level comparable with that of Sweden.[13] However, the proportion of patients with acute myocardial infarction treated with primary percutaneous coronary intervention is still very low in both Denmark and Sweden, and this development cannot account for much of the decrease in case fatality.

The decrease in case fatality over the years may be attributable to factors such as improved care and treatment, changes in lifestyle that modify the risk once heart disease is established, and a decrease in severity of cases of acute myocardial infarction.[14] This last factor can result from both profound changes in the presentation of the disease and changes in comorbidity, but changes over time in awareness of the disease, both among lay people and professionals, may also play a role.

Previous studies in USA[5 15] and Sweden[7] have reported differences in the effect of sex on case fatality depending on age, as in our study. Ours is the first to show that the interaction between sex and age has been present and unchanged in the past 20 years, which may indicate that this difference is inherent in biological factors. Vaccarino and colleagues termed younger women a high risk group in view of their relative risk.[5] However, the absolute crude risk of anyone younger than 55 years is less than half that of anyone older than 55 years, and this is true for both men and women.

The background for the difference in sex effect according to age is not well described. In Sweden, Rosengren and colleagues found a higher frequency of diabetes among women than among men who had had an acute myocardial infarct, and this difference in comorbidity accounted for most of the excess mortality in young women.[7] The study from the USA[5] found that, even after adjustment for several risk factors from the patient's history and the current course and treatment of the infarct, female sex was still associated with a poor outcome. An important difference between the two studies is that the one in Sweden also included death from acute myocardial infarction before hospital admission, as in the present study. This takes into account the higher risk of sudden death among men than among women, as demonstrated by the Framingham heart study.[16] Explanations other than comorbidity could be differences in treatment and awareness of the disease in men and women. Small differences have been found but cannot fully explain the differences in outcome.[5 6] Women tend to present with less characteristic symptoms; they also present later and are treated less aggressively than men.[17 18]

The problem of potential differences in the accuracy of the diagnosis of acute myocardial infarction in men and women is difficult to account for. We included all patients dying from ischaemic heart disease and also all sudden deaths from unknown causes, but analyses in these subgroups of patients did not alter the presence and magnitude of the interaction between age and sex. Furthermore, the fact that analyses of case fatality after exclusion of patients dying on the day of their infarct showed similar results indicates the robustness of these data.

Conclusions

The incidence and case fatality of acute myocardial infarction decreased significantly in both Denmark and Sweden over the period studied. Case fatality was notably higher in Denmark in 1987 to 1991, but in the later periods the prognosis after acute myocardial infarction was comparable in the two countries. The relatively poor prognosis among younger women was similar in degree throughout the entire study period.

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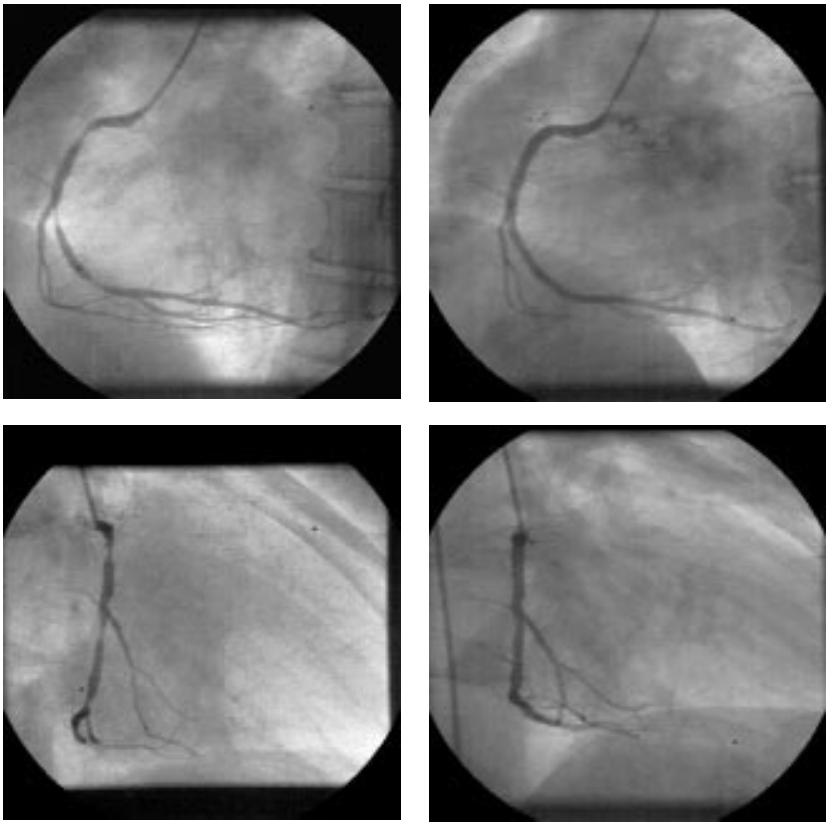
IMAGES IN CARDIOLOGY

Catheter induced spasm: a trap for the unwary

A 48 year old smoker with atypical chest pain and a positive exercise test was referred for percutaneous coronary intervention to the right coronary artery (RCA). Coronary angiography had shown an unobstructed left system and three discreet critical stenoses in the RCA (middle upper and lower panels). Pre-intervention angiography was performed via a Right Judkins 3.5 French guide catheter, following routine intracoronary injection of isosorbide dinitrate. Interestingly, the RCA was found to be unobstructed in multiple views (right upper and lower panels). The stenoses apparent at diagnostic angiography were likely to have been a manifestation of catheter induced spasm; the use of intracoronary nitrates at repeat angiography prevented an unwarranted interventional procedure. The patient was discharged on oral diltiazem and is well six months later.



Coronary spasm during selective angiography is the result of interplay between increased vasomotor tone and a myogenic reflex triggered by mechanical stimulation by the catheter tip. Spasm involving the coronary ostium may be suspected because of damping and ventricularisation of the pressure waveform, but more distal spasm is often indistinguishable from fixed obstructive coronary disease. The angiographic appearances of catheter induced spasm can mimic a wide spectrum of obstructive disease, including left main stem stenosis, two vessel disease or diffuse three vessel disease. Failure to identify and control for coronary spasm may lead to inappropriate revascularisation and medical treatment as well as potential medico-legal problems.

Routine use of intracoronary nitrates in all patients undergoing diagnostic angiography would minimise the confounding effects of vasospasm and enhance reproducibility of coronary measurements.

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