



Clinical research

Changes in hospitalization rate and mortality after acute myocardial infarction in Denmark after diagnostic criteria and methods changed

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KEYWORDS

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Aims To analyse the effect of the change in diagnostic criteria for acute myocardial infarction (AMI) and the use of troponin as a diagnostic marker on the hospitalization rate and mortality of hospitalized AMI patients from 1994 to 2001.

Methods and results Patients (≥ 30 years) admitted for their first AMI were identified using the National Patient Registry in Denmark. We registered when each hospital introduced troponin as a diagnostic marker. The reported hospitalization rate decreased until 1998 and then increased substantially from 1999 to 2001 from 3472 to 4163 per million inhabitants (19.9%) for men and from 1648 to 2020 per million inhabitants (22.6%) for women. Troponin use was associated with a significant 14% increase in hospitalization rate in this period [rate ratio 1.14, 95% confidence interval (CI) 1.11–1.18]. The effect of troponin was greatest among patients 70 years and older (rate ratio 1.19, 95% CI 1.14–1.23). The 28 day mortality decreased steadily from 25.9% in 1994 to 17.5% in 2002 (32.4%) and was not affected by troponin use.

Conclusion The reported hospitalization rate for AMI increased significantly after the new diagnostic criteria for AMI were introduced. The measurement of cardiac troponins further increased the hospitalization rate. The mortality among hospitalized patients with AMI declined steadily and was not affected by the use of troponins.

Introduction

Many surveys have demonstrated a declining incidence of acute myocardial infarction (AMI) over the past 20 years.^{1–4} During the same period, the risk factor profile has changed in a complex manner. The frequency of smoking and levels of serum cholesterol have decreased, whereas the occurrence of overweight, non-insulin-dependent diabetes mellitus, and the proportion of elderly have increased. During recent years the reported hospitalization rate of AMI has been affected by new definitions and the use of more sensitive markers of

myocardial necrosis. Guidelines for the definition of AMI in Europe and the United States, issued in 2000,⁵ recommend that any certain increase in cardiac troponin or creatinine kinase MB isoenzyme should be regarded as an AMI if it is assumed to be caused by ischaemia. The introduction of these new guidelines, together with the increased sensitivity provided by cardiac troponin,^{6–8} would most likely increase the reported hospitalization rate of AMI. Accordingly, we examined changes in the hospitalization rate and mortality among patients hospitalized with AMI in Denmark from 1994 to 2001. We further registered when troponin was introduced as a diagnostic marker in individual coronary care units to study how the increased sensitivity of this marker has influenced both hospitalization rate and mortality.

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Methods

Material

This study used data from the National Patient Registry in Denmark. This Registry assigns all patients admitted to hospital a primary diagnosis and any number of secondary diagnoses at the time of discharge. The Registry covers the period since 1978. A specific patient can be identified by the unique civil registration number assigned to every permanent resident of Denmark. The survival of each hospitalized patient was followed for 1 year using the Civil Registration System. Mortality at 28 days and 1 year was defined as death from any cause within 28 days or 1 year after admission. The study covered the period from 1 January 1994 until 31 December 2001. Only patients aged 30 years or older were included.

Definition of AMI

An AMI was defined as a hospital admission in which the primary or secondary diagnosis was AMI (International Classification of Diseases, ICD-8: 410; ICD-10: I21–I22). The cases from 1978 to 1993 were used to ensure that the patients with AMI from 1994 to 2001 had no previous admission for AMI. To ensure a similar period of history, each case was included if the patient had not been recorded with the same diagnosis in the preceding 16 years. Patients who died before reaching hospital or in the emergency room were not included.

The diagnosis of AMI in the National Patient Registry has previously been validated using the WHO MONICA Project as a reference.⁹ For 5002 admissions with AMI as the primary or secondary diagnosis in the National Patient Registry, 85% were verified as definite or possible AMI in the MONICA database (79% as definite).

Definition of other heart disease diagnoses

The annual numbers of first admissions for unstable angina (ICD-10: I20.0), congestive heart failure (ICD-10: I50.0), and all cardiovascular diseases (ICD-10: I20–I25 and I30–I52) were retrieved from the National Patient Registry. The annual age-adjusted hospitalization rates were estimated.

Use of troponin

In June 2002, a questionnaire was sent to all 77 hospital departments in Denmark that received AMI patients from 1994 to 2001 or any part thereof. Each department was asked whether and when they had introduced troponin in the routine diagnosis of AMI. If they only used troponin in selected cases, they were asked to describe this. Sixty-nine (90%) returned a completed questionnaire. Four of the eight non-responding hospitals no longer received AMI patients. The use of troponin could not be determined for 1714 patients (2% of those eligible for this study).

Statistical methods

The hospitalization rates were expressed as age-adjusted rates per 100 000 population per year. The study included only patients aged 30 years or older, and rates were standardized for age based on the general population over the age of 30 years in 2001 as the reference. Trends in hospitalization rates were evaluated using Poisson regression analysis, with the natural logarithm as the link function. All tests were two-sided, and *P*-values <0.05 were considered statistically significant.

In 2001, Denmark had 275 municipalities and a total population aged 30 years or older of 3 354 374. A catchment area for each of the 69 hospitals was defined by aggregating the municipalities into catchment areas for which the exact population was known. The hospitalization rate for each hospital was based on the population living in the catchment area as the population at risk, which was recalculated each year. The gender and age of each person in the population at risk was obtained from the Civil Registration System. The data were stratified using these same variables to adjust for age, gender, period, and use of troponin.

The mortality rates were age-adjusted using the patient population in 2001 as the reference. Trends in case-fatality rates were evaluated using multiple logistic regression analysis with logit as the link function. Age was entered in the model as 10 year age bands (30–39, 40–49, . . . , 90–99 years).

In the logistic and Poisson regression analyses, the use of troponin was entered as a binary variable (yes or no) depending on whether the patient was admitted before or after troponin was introduced as a diagnostic marker. We used generalized estimating equations to account for the effects of clustering within each hospital. Since the trends were not linear and thus violated the assumptions of the regression model, the effect of troponin

Table 1 Crude numbers of patients and mortality within the first 28 days after admission for first AMI in Denmark according to use of troponin in diagnosis and calendar year, 1994–2001

Year	Use of troponin measurement in AMI diagnosis					
	Yes			No		
	<i>n</i>	28 day mortality %	95% CI	<i>n</i>	28 day mortality %	95% CI
1994	0	–	–	9623	25.7	24.9–26.6
1995	138	25.4	18.1–32.6	9064	24.3	23.4–25.2
1996	363	19.6	15.5–23.6	8217	23.8	22.8–24.7
1997	528	19.3	16.0–22.7	7635	22.2	21.3–23.1
1998	1051	21.2	18.7–23.7	7202	20.1	19.2–21.1
1999	1803	21.4	19.5–23.3	6277	20.3	19.3–21.3
2000	3694	18.8	17.5–20.0	5158	18.5	17.4–19.6
2001	7784	17.0	16.2–17.8	1944	19.7	17.9–21.4

measurement was analysed with the use of splines, assuming a piecewise linear effect in the periods 1994–98 and 1999–2001.

Results

We analysed 70 481 patients admitted with AMI. Of these, 15 361 were diagnosed at hospital departments that had introduced troponin measurement as a diagnostic marker. The mean age of the AMI population was 66.7 years for men and 73.6 years for women. The proportion of women was 38.8%. Within the first 28 days after admission, 15 120 patients died. A further 6617 died during the remainder of the first year after admission.

Dissemination of troponin in AMI diagnosis

The use of troponin in diagnosing AMI started slowly in 1995; by 1998, 12 of the 69 hospitals used troponin. Use accelerated in 1999, and by the end of 2001, 56 hospitals used troponin and 13 did not. *Table 1* lists the number of AMI patients admitted according to whether the hospital used troponin, along with the crude 28 day mortality for each calendar year.

Trends in rate of hospitalization for first AMI

The age-adjusted hospitalization rate declined significantly from 1994 to 1999 and then increased in 2000 and further in 2001 for both men and women (*Figure 1*). From 1999 to 2001, the rate increased by 19.9% for men and 22.6% for women. Although men and women had similar trends, the relative (and absolute) increase for both men and women was highest among those 70 years or older (*Figure 1, Table 2*).

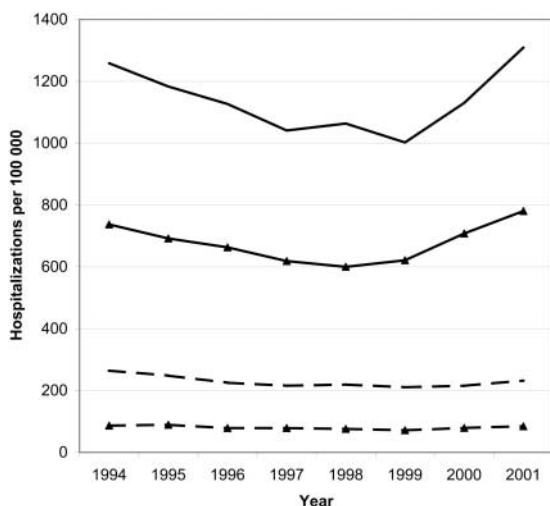


Figure 1 Age-adjusted hospitalization rates for first AMI per 100 000 population according to gender and calendar year among the population of Denmark 30 years or older, 1994–2001. Plain line without triangles: men 70 years or older; plain line with triangles: women 70 years or older; dashed line without triangles: men 30–69 years; dashed line with triangles: women 30–69 years.

Figure 2 shows the annual age-adjusted hospitalization rates according to when troponin was introduced as a diagnostic marker. All three categories of hospital had similar hospitalization rates in 1994 ($P = 0.09$). Troponin measurement was associated with a statistically significant increase in hospitalization rate independently of age and gender. The increase was present in the entire period, but it was significantly higher in the later years. The rate ratio of hospitalization associated with hospital use of troponin as a diagnostic marker was 1.07 (95% CI 1.03–1.12) in 1994–98 and 1.14 (95% CI 1.11–1.18) in 1999–2001. Further, the effect of troponin measurement on the hospitalization rate was more pronounced among older versus younger patients. *Table 3* shows the rate ratios associated with troponin measurement in 1994–98 and 1999–2001 for patients younger and older than 70 years. Troponin measurement affected the hospitalization rates of women and men similarly.

Trends in mortality after first AMI

The 28 day and 1 year mortality declined steadily through the study period (*Figure 3*). The 28 day mortality decreased steadily from 25.9% in 1994 to 17.5% in 2002 and was not affected by the use of troponin measurement. The odds ratio associated with the use of troponin measurement adjusted for age, gender, and calendar year was 1.05 (95% CI 0.98–1.11, $P = 0.14$). The odds ratio for 1 year mortality was 1.03 (95% CI 0.97–1.08, $P = 0.35$).

Trends in hospitalization rate for other heart diseases

The age-adjusted hospitalization rates for unstable angina and congestive heart failure declined significantly from 2000 to 2001 after the new diagnostic criteria were introduced (*Figure 4*). The hospitalization rate for all cardiovascular diseases increased steadily but only slightly.

Table 2 Trends in the annual increase in hospitalization rate for first AMI in Denmark from 1994 to 1999 and 1999 to 2001 according to gender and age group.

Period	Age (years)	Relative increase per year, % (95% CI)	
		Men	Women
1994–99	30–69	–5.0 (–3.9 to –6.1)	–3.9 (–2.0 to –5.7)
	70+	–5.1 (–3.9 to –6.2)	–4.9 (–3.6 to –6.1)
1999–2001	30–69	5.1 (2.4–7.8)	8.6 (4.1–13.3)
	70+	13.3 (10.2–16.6)	12.3 (9.2–15.5)

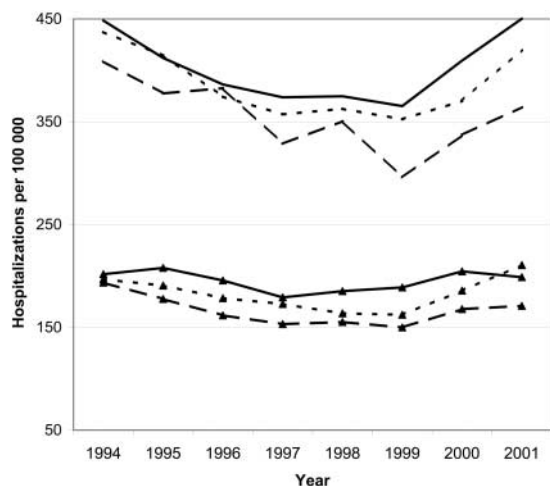


Figure 2 Age-adjusted hospitalization rates for first AMI per 100 000 population in Denmark according to gender, use of troponin, and calendar year in the population 30 years or older, 1994–2001. Lines without triangles: men; lines with triangle: women; plain lines: troponin introduced before 1999; dotted lines: troponin introduced 1999–2001; dashed lines: troponin not used.

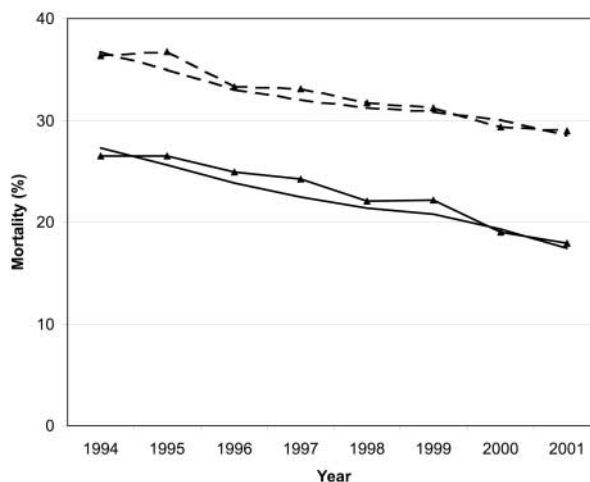


Figure 3 Age-adjusted 28 day and 1 year mortality (%) after first AMI in Denmark according to gender and calendar year, 1994–2001. Lines without triangles: men; lines with triangles: women. Plain line: 28 day mortality; dashed line: 1 year mortality.

Table 3 Rate ratios for AMI hospitalization rates in Denmark in 1994–98 and 1999–2001 associated with the use of troponin as a diagnostic marker adjusted for gender in two age groups

Period	Age (years)	Rate ratio	95% CI	P
1994–98	30–69	1.06	0.99–1.12	0.09
	70+	1.09	1.02–1.15	<0.01
1999–2001	30–69	1.09	1.05–1.14	<0.0001
	70+	1.19	1.14–1.23	<0.0001

Discussion

This study demonstrated for the first time on a nationwide basis that introducing troponin in diagnosing AMI was associated with an increased hospitalization rate for AMI. Mortality after AMI declined steadily during the study period, independent of the changing hospitalization rate.

Further, the hospitalization rate for AMI increased after the new diagnostic criteria for AMI were implemented in 2000, even in hospitals that did not introduce troponin for diagnosing AMI. This increase was probably caused by the change in the interpretation of slight elevations in the enzymatic markers used, which in Denmark was primarily creatinine kinase MB isoenzyme. Before the diagnostic criteria changed, elevated cardiac enzymes together with dyspnoea could be diagnosed as congestive heart failure. The new criteria make a diagnosis of AMI more likely. This also partly explains why the increased hospitalization rate was most pronounced among older patients. The decline in the hospitalization rates for congestive heart failure and unstable angina from 2000 to 2001 also indicates this shift in diagnosis to AMI.

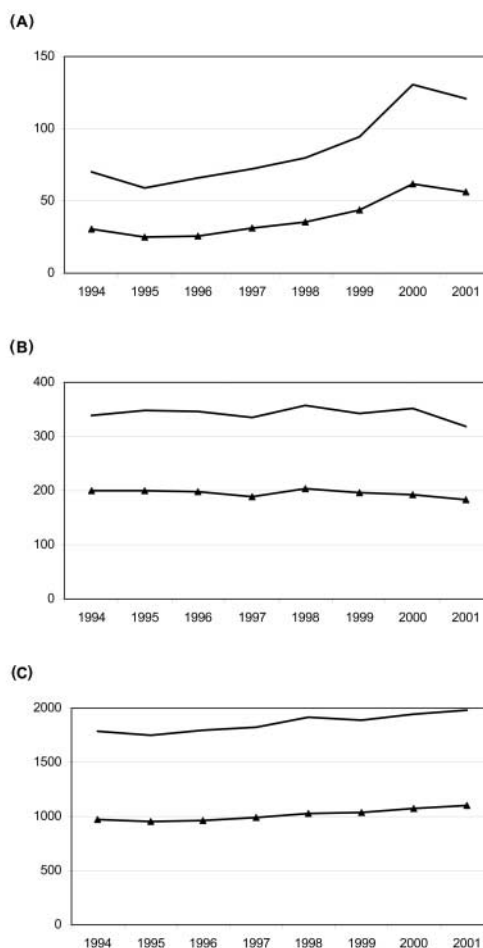


Figure 4 Age-adjusted hospitalization rates per 100 000 population according to gender and calendar year in the population 30 years or older in Denmark, 1994–2001. Lines without triangles: men; lines with triangles: women. (A) Unstable angina. (B) Congestive heart failure. (C) All heart diseases. The scales on the y-axes differ.

Many possible factors may have contributed to our findings. Our data represent only the reported hospitalized cases and do not represent the true incidence of AMI. We cannot determine to what extent the observed increase in hospitalization rate is due to a possible increase in the true incidence of AMI. The increasing rate of overweight and non-insulin-dependent diabetes mellitus could well outweigh the reduced rate of smoking, the reduced levels of serum cholesterol, and the improved treatment of ischaemic heart disease. The introduction of hospital financing according to diagnosis-related groups may also have tended to increase the number of AMIs reported. Hospitals may have facilitated the adoption of troponin as a diagnostic marker and the new diagnostic criteria to boost the number of patients with AMI. However, the clear definition of an AMI and the implications for the patient being given this diagnosis do not allow this diagnosis to be abused on any great scale. Another possible bias would be if troponin had been adopted predominantly at hospitals that already had very high or very low hospitalization rates or mortality. To account for this, the analyses were carried out using the stratification presented in *Figure 2*, and the hospitalization rates before troponin measurement was introduced did not differ significantly. All three categories of hospital had similar mortality (data not shown).

We found that troponin measurement was associated with an increase in the reported hospitalization rate of 14%. The effect among patients older than 70 years was slightly higher (19%). This effect is lower than found by others.^{7,8} The difference may indicate that even if troponin measurement was introduced at the hospital it was not applied to all patients with chest pain. Another possible explanation is that an increase in cardiac troponin was not readily classified as an AMI.

Divergent results have been reported on how using troponin as a marker affects mortality. Mortality was expected to decline among the additional patients identified, since troponin is a more sensitive marker than the others used and identifies patients with less severe myocardial damage.⁵ However, most published studies have found even higher mortality among the additional patients identified.^{7,8} Higher 28 day mortality tended to be associated with the use of troponin. This may result from the characteristics of the additional patients identified by troponin. Troponin use increased the hospitalization rate the most among patients 70 years or older. However, the additional patients may also differ in other ways for which we cannot adjust. For example, older patients are more likely to have congestive heart failure, and patients admitted with heart failure are more likely to be diagnosed with AMI under the new diagnostic criteria and even more when the more sensitive markers of myocardial damage are used. This makes determining the effect of troponin for each patient difficult. Nevertheless, given how hospitals in Denmark have implemented troponin measurement, using these sensitive markers would not be likely to change the prognosis for the patient population in Denmark substantially. Several studies have evaluated the prognosis of patients

with chest pain who did not have a classical AMI, and all have found a poor prognosis among these non-AMI patients, quite similar to that of the AMI patients.^{10,11}

The mortality in our study is higher compared with registries describing prognoses for patients admitted to coronary care units or invasive centres.¹² The main explanation for this difference is that all patients at all wards are included and not only the patients selected for the coronary care unit or invasive therapy. Also, patients undergoing surgery will appear in our data if the patient experiences an AMI. These patients tend to have a poorer prognosis leading to the higher overall mortality.

Debate about the new diagnostic criteria for AMI has been intense.¹³⁻¹⁵ There has been little doubt that the new and sensitive markers should be incorporated in some way. However, the weight these measurements should be given is not agreed. Some argue that the diagnosis should reflect the pathophysiology and others that the prognosis is more important. In any case, the surveillance of AMI incidence has become more complex because new diagnostic criteria and the use of troponin as a diagnostic marker have been introduced. Failing to control for these changes may produce a spurious positive correlation between any risk factor increasing in the population and the hospitalization rate for AMI. However, if the introduction of new diagnostic criteria is the main reason that the incidence increased after 1999, we expect the hospitalization rate for AMI to start decreasing again when the diagnostic criteria are fully implemented. Further, the new criteria may result in a more uniform definition of AMI, making comparisons within and between countries easier to interpret.

Decision-makers may also have to relate to the increase in the reported hospitalization rate for AMI caused by the change in diagnostic criteria; given the dismal prognosis, this trend may influence the distribution of health care resources.

Study limitations

Information about the kit used and the threshold for troponin leading to a diagnosis of AMI at the various hospitals was not obtained. Different kits and thresholds may lead to differences in the observed effect of troponin measurement on the hospitalization rate, but we could not account for this here.

Mortality status could not be obtained for the patients who emigrated within the first year after AMI. However, this is expected to be a small number with no influence on the results reported.

Conclusion

The reported hospitalization rate for AMI in Denmark increased significantly after new diagnostic criteria for AMI were introduced in 2000. The increasing use of cardiac troponin as a diagnostic marker further increased the reported hospitalization rate. The mortality among hospitalized patients with AMI declined steadily and was not affected by the use of troponin in diagnosis. Future surveillance of cardiovascular disease might

benefit from shifting the focus to hospitalization for heart disease or for ischaemic heart disease instead of AMI.

Acknowledgements

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