

## Myocardial Infarction and Risk of Suicide A Population-Based Case-Control Study

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**Background**—Myocardial infarction (MI) is associated with an increased risk of anxiety, depression, low quality of life, and all-cause mortality. Whether MI is associated with an increased risk of suicide is unknown. We examined the association between MI and suicide.

**Methods and Results**—We conducted a population-based case-control study by retrieving data from 5 nationwide longitudinal registers in Denmark. As cases, we selected all persons aged 40 to 89 years who died by suicide from 1981 to 2006. As controls, we randomly selected up to 10 persons per case matched by sex, day of birth, and calendar time. We identified 19 857 persons who committed suicide and 190 058 controls. MI was associated with a marked increased risk of suicide. The risk of suicide was highest during the first month after discharge for MI for patients with no history of psychiatric illness (adjusted rate ratio, 3.25; 95% confidence interval, 1.61 to 6.56) and for patients with a history of psychiatric illness (adjusted rate ratio, 64.05; 95% confidence interval, 13.36 to 307.06) compared with those with no history of MI or psychiatric illness. However, the risk remained high for at least 5 years after MI.

**Conclusions**—MI is followed by an increased risk of suicide for persons with and without psychiatric illness. Our results suggest the importance of screening patients with MI for depression and suicidal ideation. (*Circulation*. 2010;122:2388-2393.)

**Key Words:** acute myocardial infarction ■ depression ■ epidemiology ■ mortality ■ suicide

Acute myocardial infarction (MI) is a severe life event followed by an increased risk of anxiety,<sup>1</sup> depression,<sup>2–5</sup> low quality of life,<sup>1,6</sup> and all-cause mortality.<sup>7</sup> A small study has indicated that some patients with acute life-threatening physical illnesses such as MI and stroke even have suicidal plans.<sup>8</sup> Although it has been shown that patients with stroke,<sup>9</sup> epilepsy,<sup>10</sup> and diabetes mellitus<sup>11</sup> have an increased risk of suicide, no studies have evaluated whether this risk also applies to patients with MI. However, a recent study found a positive correlation between the incidence of deaths from suicide and deaths from ischemic heart disease from 1979 to 2005,<sup>12</sup> and more studies on the association between MI and suicide have been deemed necessary.<sup>12</sup>

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Depression, other psychiatric illnesses, and low socioeconomic status tend to increase the risk of MI<sup>13–15</sup> and suicide<sup>16,17</sup> and may confound the association between MI and suicide. Over the last decades, the treatment of MI has improved markedly by thrombolysis, percutaneous coronary intervention, and intensive drug therapy,<sup>7,18</sup> which may have

reduced the emotional strain. The aim of this study was to evaluate the association between MI and suicide, taking diabetes mellitus, stroke, psychiatric illnesses, socioeconomic factors, and calendar time into account.

## Methods

### Study Design and Data Sources

We conducted a population-based case-control study by linking data on an individual level from 5 nationwide longitudinal registers in Denmark. The Cause of Death Register<sup>19</sup> provided information on suicide from 1981 to 2006. Individuals were diagnosed according to the Danish version of the *International Classification of Diseases (ICD)*. From 1981 to 1993 the cases were identified by *International Classification of Diseases, Eighth Revision (ICD-8)* (E950 to E959) and from 1994 to 2006 by *International Statistical Classification of Diseases, 10th Revision (ICD-10)* (X60 to X84).<sup>19</sup> The Danish Civil Registration System<sup>20</sup> was established in 1968, registering all persons alive and living in Denmark with a unique personal identification number. All newborns have subsequently been provided with the number that follows people from cradle to grave. The personal identification number was used to link individual information from different registers. The Civil Registration System holds information on age, sex, day of birth, residence, and vital status of all residents in Denmark.

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The Danish National Patient Register<sup>21</sup> contains information on all patients admitted to any Danish somatic hospital since 1977 and emergency departments and outpatient clinics since 1995. Data on MI (*ICD-8*: 410; *ICD-10*: I21), stroke (*ICD-8*: 431, 433; *ICD-10*: I61, I63 to I64), and diabetes mellitus (*ICD-8*: 249 to 250; *ICD-10*: E10 to E14) were collected. The Danish Society of Cardiology adheres to the European Society of Cardiology criteria for MI,<sup>22</sup> which currently is based on myocardial necrosis detected by cardiac biomarkers and symptoms, ECG changes, or imaging evidence.<sup>23</sup> Only incident cases of MI were included, and we extracted data on MI, stroke, and diabetes mellitus for both cases and controls until the day when the case committed suicide (index day).

The Danish Psychiatric Central Register<sup>24</sup> stores information on all patients admitted to any psychiatric hospital and psychiatric ward in hospitals in Denmark. The register includes inpatient data since 1969 and outpatient data from 1995. The register provided information on schizophrenia (codes 295, 296.89, 297, 298.39, 301.83 [*ICD-8*], and F20 [*ICD-10*]), affective illnesses (codes 296.09 to 296.99, 298.19, 300.19, 300.49 [*ICD-8*], and F30–F39 [*ICD-10*]), and other psychiatric illnesses not included in the former categories (codes 290 to 315 [*ICD-8*] and F00–F99 [*ICD-10*]). We extracted data on history of psychiatric illnesses updated to the index day. We used the initial diagnosis for patients with >1 contact to a psychiatric hospital or ward.

The Danish Integrated Database for Labor Market Research<sup>25</sup> holds information on labor market conditions and socioeconomic data for the entire population from 1980 onward. We retrieved these data from the database for the calendar year before the index day. In a subanalysis, we also used data on socioeconomic 5 years previous to the index day.

## Study Participants

As cases, we selected persons aged 40 to 89 years and recorded with suicide in the Cause of Death Register from January 1, 1981, to December 31, 2006. As controls, we randomly selected 25% of the persons who had the same sex, were born on the same day as the case, and were alive on the day the case committed suicide (incidence density sampling). For cases born before January 1, 1900, the numbers of eligible controls were few, and we had to use a sampling fraction >25%. We selected no more than 10 controls per case. For 22 cases, it was not possible to find controls born on the same day, but we found 99 controls born the day before or after the case. Cases and controls were included only if they were resident in Denmark throughout the preceding year.

## Statistical Analysis

With incidence density sampling (cases were sampled at the time of suicide, and a subset of controls from all individuals at risk were sampled at the time of each suicide), the odds ratios estimated by conditional logistic regression provide unbiased estimates of the incidence rate ratio (RR) with 95% confidence intervals (CIs).<sup>26</sup> Thus, the RR of suicide among patients discharged from hospital with a diagnosis of MI was estimated by use of conditional logistic regression (STATA, version 10; StataCorp LP, College Station, Tex). RRs were adjusted for day of birth, sex, and date of suicide by stratification. RRs were adjusted for marital status (single versus married or cohabiting), labor market status (unemployed or pension versus employed or student), annual income (quartiles), and history of psychiatric illness (yes, no), stroke (yes, no), or diabetes mellitus (yes, no) by regression analysis. In subanalyses, we also adjusted for education (secondary school versus more than secondary school). Interaction between the variables was assessed by likelihood ratio test. Owing to the nationwide nature of the registers, we had complete registration of the main variables (MI and suicide), the matching variables (sex, age, index day), marital status, annual income, labor market status, psychiatric illness, stroke, and diabetes mellitus. Information on education was missing for 24% of the study population primarily because of lack of information on people older than 60 years. Therefore, we adjusted for education in subanalyses only and used sensitivity analyses in which people with missing

**Table 1. Characteristics of Cases and Controls**

	Controls, n (%)	Cases, n (%)
All	190 058 (90.5)	19 857 (9.5)
Sex		
Male	118 283 (62.2)	12 555 (63.2)
Female	71 775 (37.8)	7302 (36.8)
Age, y		
40–49	53 119 (28.0)	5324 (26.8)
50–59	51 094 (26.9)	5118 (25.8)
60–69	41 576 (21.9)	4166 (21.0)
70–79	32 347 (17.0)	3406 (17.2)
80–89	11 922 (6.3)	1843 (9.3)
Calendar year of suicide/matching		
1981–1985	50 481 (26.6)	5181 (26.1)
1986–1990	47 760 (25.1)	4967 (25.0)
1991–1995	38 057 (20.0)	3991 (20.1)
1996–2000	26 683 (14.0)	2839 (14.3)
2001–2006	27 077 (14.3)	2879 (14.5)

Because of fewer eligible controls for the oldest cases, the distribution between cases and controls deviates slightly from uniformity.

information were categorized in the lowest and the highest educational group, respectively.

## Results

We identified 19 857 persons who committed suicide during the study period and 190 058 controls. The characteristics of the matching criteria are shown in Table 1. Because of fewer eligible controls for the oldest cases, the distribution between cases and controls deviates slightly from uniformity. Among the individuals who committed suicide, 851 (4.3%) had a history of MI compared with 5537 controls (2.9%). Overall, the adjusted RR of suicide for persons with MI compared with persons without MI was 1.24 (95% CI, 1.14 to 1.35). The RR of suicide was the same for men (RR, 1.24; 95% CI, 1.13 to 1.36) and women (RR, 1.32; 95% CI, 1.09 to 1.60) ( $P=0.64$  for interaction with sex). The RR remained virtually the same throughout the study period ( $P=0.79$  for interaction with calendar year) (Table 2).

The risk of suicide was highest within the first month after discharge for MI for persons with (RR, 64.05; 95% CI, 13.36 to 307.06) and without (RR, 3.25; 95% CI, 1.61 to 6.56) a psychiatric illness but remained high for the entire study period (Table 3). The association between MI and suicide was strongest for the youngest persons between the ages of 40 to 59 with a psychiatric illness (RR, 13.85; 95% CI, 10.68 to 17.98) or without a psychiatric illness (RR, 1.51; 95% CI, 1.22 to 1.87), and the RR tended to decrease with age ( $P=0.119$  for trend) (Tables 2 and 4).

As expected, psychiatric illness was strongly associated with suicide (Tables 3 through 5). The association between MI and suicide was modified by type of psychiatric illness ( $P<0.001$  for interaction), with the highest risk for persons with an affective disorder. The RR of suicide was high the first year after discharge for MI for persons with an affective disorder, whereas it remained high until 5 years after dis-

**Table 2. Association of MI and Suicide According to Selected Characteristics**

	RR* (95% CI)	Adjusted† RR (95% CI)	P for Interaction
All	1.41 (1.31–1.53)	1.24 (1.14–1.35)	
Sex			0.64
Male	1.42 (1.30–1.54)	1.24 (1.13–1.36)	
Female	1.41 (1.19–1.66)	1.32 (1.09–1.60)	
Age, y			0.16
40–49	2.40 (1.85–3.11)	1.77 (1.29–2.44)	
50–59	1.66 (1.39–1.97)	1.15 (0.94–1.41)	
60–69	1.41 (1.22–1.63)	1.26 (1.07–1.49)	
70–79	1.24 (1.08–1.42)	1.19 (1.02–1.38)	
80–89	1.24 (1.03–1.49)	1.23 (1.02–1.49)	
Calendar year of suicide/matching			0.79
1981–1985	1.51 (1.27–1.79)	1.40 (1.15–1.70)	
1986–1990	1.41 (1.21–1.64)	1.18 (1.00–1.40)	
1991–1995	1.41 (1.20–1.65)	1.21 (1.01–1.44)	
1996–2000	1.35 (1.11–1.64)	1.18 (0.95–1.46)	
2001–2006	1.39 (1.15–1.67)	1.27 (1.04–1.56)	

\*Adjusted for sex, day of birth, and calendar time by stratification.

†Adjusted for sex, day of birth, and calendar time by stratification and further adjusted for marital status, labor market status, annual income, psychiatric illness, stroke, and diabetes mellitus by regression analysis.

charge for MI for persons with schizophrenia and other psychiatric illnesses. Overall, the risk of suicide after MI remained high (RR, 1.39; 95% CI, 1.26 to 1.53) even among those without psychiatric illness and after adjustment for diabetes mellitus, stroke, marital status, labor market status, and annual income (Table 5).

## Discussion

In this population-based case-control study, we found that MI was strongly associated with an increased risk of suicide. The RR was highest for the patients with MI shortly after

discharge, tended to decrease with age, and was particularly high among persons with a history of psychiatric illness. No other studies have examined the association between MI and suicide. However, previous studies found a positive correlation between the incidence of deaths from suicide and deaths from ischemic heart disease from 1979 to 2005 in Brazil<sup>12</sup> and found a positive association between the lifetime prevalence of coronary artery disease and suicide attempts in an elderly population in the South of France.<sup>27</sup> Furthermore, a small study from Baltimore, Md, found that 7.3% of patients had suicidal plans after acute life-threatening physical illnesses such as MI and stroke.<sup>8</sup> Two studies<sup>28,29</sup> have examined the association between several physical illnesses and the risk of suicide in elderly people and found no association between cardiovascular disease and suicide. The difference between their results and ours may be due to their smaller sample size, their broader diagnostic categories, and the fact that they did not take time since diagnosis into account.

The major strengths of this study are the sample size, the population-based nature, and the opportunity to adjust for important confounders such as stroke, diabetes mellitus, psychiatric illnesses, and socioeconomic factors. Our information on MI was registered prospectively and did not rely on the memory of participants or relatives. The MI diagnosis in the National Patient Register was based on current European Society of Cardiology criteria for MI, coded by the physician in charge of the discharge, and is known to have a high sensitivity (90%) and specificity (92%), which is unrelated to age.<sup>21</sup> We therefore identified nearly all patients with MI, and only a few patients were misclassified, reducing the risk of information bias. The overall necropsy rate declined from 44% in 1971 to 9% in 2001,<sup>30</sup> but medicolegal inquest is statutory when suicide is suspected. In the present study, we included only suicide cases for which the coroner's verdict was "suicide." This ensures a high specificity of the suicide diagnoses, which is important in case-control studies. The quality of a suicide diagnosis is likely to be the same for those with and without a previous MI diagnosis, although we cannot exclude that some suicides may have been misclassified.

**Table 3. Association Between MI and Suicide According to Psychiatric Illness and Time Since MI**

	Cases, n	Controls, n	RR* (95% CI)	P	Adjusted† RR (95% CI)	P
No psychiatric illness						
No MI	10 617	174 155	1.00 (reference)		1.00 (reference)	
MI, <1 mo	11	43	3.21 (1.61–6.42)	0.001	3.25 (1.61–6.56)	0.001
MI, 1 mo to 1 y	70	540	1.89 (1.46–2.43)	<0.001	1.80 (1.39–2.32)	<0.001
MI, 1–5 y	206	1992	1.50 (1.30–1.74)	<0.001	1.44 (1.24–1.68)	<0.001
MI, >5 y	239	2571	1.29 (1.12–1.48)	<0.001	1.23 (1.07–1.41)	0.003
Psychiatric illness						
No MI	8389	10 366	14.23 (13.71–14.78)	<0.001	11.74 (11.29–12.22)	<0.001
MI, <1 mo	9	2	64.11 (13.51–304.23)	<0.001	64.05 (13.36–307.06)	<0.001
MI, 1 mo to 1 y	43	34	20.49 (12.80–32.79)	<0.001	18.29 (11.37–29.43)	<0.001
MI, 1–5 y	131	138	15.56 (12.13–19.95)	<0.001	12.53 (9.74–16.12)	<0.001
MI, >5 y	142	217	10.23 (8.20–12.76)	<0.001	8.21 (6.57–10.26)	<0.001

\*Adjusted for sex, day of birth, and calendar day by stratification.

†Adjusted for sex, day of birth, and calendar day by stratification and further adjusted for marital status, labor market status, annual income, stroke, and diabetes mellitus by regression analysis.

**Table 4. Association Between MI and Suicide According to Age on Index Day and Psychiatric Illness**

	Cases, n	Controls, n	RR* (95% CI)	P	Adjusted† RR (95% CI)	P
No psychiatric illness						
No MI	10 617	174 155	1.00 (reference)		1.00 (reference)	
MI, 40–59 y	97	1112	1.65 (1.33–2.04)	<0.001	1.51 (1.22–1.87)	<0.001
MI, 60–79 y	297	3276	1.37 (1.21–1.55)	<0.001	1.34 (1.18–1.52)	<0.001
MI, 80–89 y	132	758	1.26 (1.03–1.54)	0.022	1.28 (1.04–1.56)	0.018
Psychiatric illness						
No MI	8389	10 366	14.23 (13.70–14.78)	<0.001	11.75 (11.29–12.22)	<0.001
MI, 40–59 y	128	130	18.53 (14.34–23.94)	<0.001	13.85 (10.68–17.98)	<0.001
MI, 60–79 y	169	215	12.43 (10.07–15.33)	<0.001	10.55 (8.52–13.07)	<0.001
MI, 80–89 y	28	46	4.67 (2.85–7.64)	<0.001	4.70 (2.87–7.71)	<0.001

\*Adjusted for sex, day of birth, and calendar time by stratification.

†Adjusted for sex, day of birth, and calendar time by stratification and further adjusted for marital status, labor market status, annual income, stroke, and diabetes mellitus by regression analysis.

fied as sudden cardiac death if they occur shortly after the MI. If so, we might have underestimated the true association between MI and suicide. We included all suicides in Denmark during the study period and had valid information on all participants with MI; selection bias is therefore an unlikely explanation for our findings.

A potential limitation of this study is residual confounding by unrecorded psychiatric illness. Psychiatric outpatients were not included before 1995, and patients with milder psychiatric illnesses, such as mild depression, may not be in the register. However, the risk of suicide after MI was the same during the study period 1981–1995 as during 1996–2006, indicating that the RR was not affected by including less severe cases. Furthermore, the RR decreased only

slightly when adjusted for psychiatric illness as registered in the Psychiatric Central Register. In this study, 467 (65%) of the patients with a psychiatric illness were registered with the psychiatric illness before they had their MI. In a subanalysis, we found virtually the same results when we restricted the analyses to these patients (results not shown). However, if MI leads to psychiatric illness, which leads to suicide, psychiatric illness is a step on the causal pathway between MI and suicide and should not require adjustment.

Men tend to have the highest risk of completed suicide in the general population,<sup>31</sup> but sex did not modify the RR of suicide in our study. The risk of suicide increases with age, probably because burdensome life events, such as bereavement, decreased physical functioning, poor economy, and

**Table 5. Association Between MI and Suicide According to Type of Psychiatric Illness and Time Since MI**

	Cases, n	Controls, n	RR* (95% CI)	P	Adjusted† RR (95% CI)	P
No psychiatric illness						
No MI	10 617	174 155	1.00 (reference)		1.00 (reference)	
MI	526	5146	1.45 (1.32–1.59)	<0.001	1.39 (1.26–1.53)	<0.001
Affective disorder						
No MI	2072	1765	21.71 (20.21–23.32)	<0.001	18.97 (17.64–20.40)	<0.001
MI, <1 y	10	5	32.13 (10.20–101.23)	<0.001	31.93 (9.93–102.66)	<0.001
MI, 1–5 y	28	31	15.99 (9.36–27.31)	<0.001	13.62 (7.93–23.41)	<0.001
MI, >5 y	37	42	14.56 (9.12–23.25)	<0.001	12.22 (7.67–19.47)	<0.001
Schizophrenia						
No MI	1483	1582	16.91 (15.65–18.28)	<0.001	12.15 (11.20–13.18)	<0.001
MI, <1 y	6	4	21.12 (5.80–76.93)	<0.001	16.30 (4.42–60.04)	<0.001
MI, 1–5 y	14	13	19.91 (9.05–43.81)	<0.001	14.46 (6.49–32.24)	<0.001
MI, >5 y	18	18	15.76 (8.03–30.93)	<0.001	11.72 (5.97–23.01)	<0.001
Other psychiatric illnesses						
No MI	4834	7019	11.95 (11.44–12.49)	<0.001	9.99 (9.54–10.46)	<0.001
MI, <1 y	36	27	21.82 (12.97–36.71)	<0.001	20.00 (11.84–33.75)	<0.001
MI, 1–5 y	89	94	15.06 (11.15–20.34)	<0.001	12.11 (8.93–16.41)	<0.001
MI, >5 y	87	157	8.58 (6.53–11.27)	<0.001	6.83 (5.18–9.01)	<0.001

\*Adjusted for sex, day of birth, and calendar day by stratification.

†Further adjusted for sex, day of birth, and calendar day by stratification and marital status, labor market status, annual income, stroke, and diabetes mellitus by regression analysis.



loss of social support, are more common.<sup>32</sup> Because risk factors for suicide are so common in the elderly, the relative risk of a single risk factor tends to be low.<sup>32</sup> In our study, the RR of suicide after MI was highest for the youngest age group and decreased with age. The association between MI and suicide remained stable throughout the study period, although many other factors changed. The overall suicide rate declined markedly in the Danish population for men (from 42/100 000 in 1980 to 18/100 000 in 2001) and women (from 22/100 000 in 1980 to 7/100 000 in 2001).<sup>30</sup> During the study period, the acute treatment of MI was improved by thrombolysis and percutaneous coronary angioplasty,<sup>7,18</sup> and the subsequent treatment was improved by drugs and comprehensive rehabilitation.<sup>33,34</sup> Furthermore, the number of days spent at the hospital after MI decreased significantly. These factors might have affected the mental condition of persons with MI in different ways, but the association between MI and suicide remained virtually unchanged.

We found that the risk of suicide after MI decreased slightly when we adjusted for previous admission due to stroke or diabetes mellitus, annual income, and labor market status and increased slightly when we adjusted for marital status. We found virtually no change in estimates when we adjusted for education in subanalyses using sensitivity analyses. Furthermore, in subanalyses we used information on socioeconomic factors that were collected 5 years before the index day to evaluate whether socioeconomic factors were only intermediate variables (that is, MI causing a decline in socioeconomic status causing suicide). However, the results did not change significantly (results not shown). Thus, our results imply that MI per se is a risk factor for suicide even after adjustments for stroke, diabetes mellitus, and various socioeconomic factors known to pose a risk for suicide in the general population.<sup>9,11,17</sup>

As expected, psychiatric illness was strongly associated with suicide, and persons with a history of psychiatric illness had a very high risk of suicide shortly after discharge. The statistical power is limited in these analyses because of low numbers, and the results must be interpreted with caution. This group needs special attention, intensive clinical care, and ongoing care beyond the point of clinical recovery to reduce the risk of suicide.<sup>35</sup>

Several risk factors contribute to suicide. The stress-diathesis model<sup>36</sup> suggests that a stressful life event combined with a genetic predisposition may lead to a suicidal act. MI is known to be significantly associated with psychological distress,<sup>37</sup> and many patients are affected by depression after MI.<sup>2–4,38</sup> Components of the diathesis include hopelessness, aggression, and impulsivity due to low hormonal activity (serotonin, noradrenaline).<sup>36</sup> Other factors associated with MI that have been linked to suicide are low cholesterol and physical disability, but the underlying evidence is vague.<sup>36,39</sup>

## Conclusion

In this large population-based study, we found a higher risk of suicide in patients with MI that was not explained by stroke, diabetes mellitus, psychiatric illness, or socioeconomic factors. The RR of suicide was particularly high shortly after discharge, tended to decrease with age, and tended to be

particularly high among persons with a known psychiatric illness. Our results support the recommendations for screening patients with MI for depression and suicidal ideation.<sup>38</sup>

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## Disclosures

None.

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### CLINICAL PERSPECTIVE

Myocardial infarction (MI) is associated with an increased risk of anxiety, depression, low quality of life, and all-cause mortality. Whether MI is associated with an increased risk of suicide is unknown. We conducted a population-based case-control study by retrieving data from 5 nationwide longitudinal registers in Denmark. As cases, we selected all persons aged 40 to 89 years who died by suicide from 1981 to 2006. As controls, we randomly selected up to 10 persons per case matched by sex, day of birth, and calendar time. We identified 19 857 persons who committed suicide and 190 058 controls. We found that MI was associated with a marked increased risk of suicide. The risk of suicide was highest within the first month after discharge for MI for patients with no history of psychiatric illness (adjusted rate ratio, 3.25; 95% confidence interval, 1.61 to 6.56) and for patients with a history of psychiatric illness (adjusted rate ratio, 64.05; 95% confidence interval, 13.36 to 307.06) compared with those with no history of MI or psychiatric illness. However, the risk remained high for at least 5 years after MI and when adjusted for stroke, diabetes mellitus, and socioeconomic factors. Our results suggest the importance of screening patients with MI for depression and suicidal ideation.