Does the association between broken partnership and first time myocardial infarction vary with time after break-up?

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Background Marriage is associated with lower risk of coronary heart disease, but it is unknown if the association depends on time since break-up with a partner. In this study we included both married and unmarried couples to study if the association between broken partnership (BP) and first time incident myocardial infarction (MI) changes with time since BP.

Methods Register study of the entire Danish population: the population was restricted to those aged 30 to 65 years with follow-up for incident MI between 1985 and 2006 with an annual record on each individual; in total 43 million records. The register data were used to identify MI events. Poisson regression was used to study associations between time since BP and MI adjusted for socio-demographic confounders and hospital admissions. Analyses were stratified by sex.

Results Compared with unexposed (no BP), the incidence rate ratio (IRR) of MI in men with BP in the same year was 0.97 [95% confidence interval (CI) 0.90–1.05], year before BP was 1.25 (95% CI 1.17–1.34), 2–3 years after BP was 1.12 (95% CI 1.06–1.18), 4–8 years after BP was 1.09 (95% CI 1.05–1.14) and 9+ years since BP was 1.09 (95% CI 1.05–1.12). In women, the IRR same year as BP was 1.45 (95% CI 1.26–1.66), the year after BP was 1.30 (95% CI 1.14–1.50), 2–3 years after BP was 1.26 (95% CI 1.13–1.39), 4–8 years after BP was 1.17 (95% CI 1.08–1.26) and 9+ years since BP was 1.24 (95% CI 1.17–1.32).

Conclusions We found both a short-term elevated risk of first time MI following BP and a weaker long-term elevated risk, in both men and women.

Keywords Myocardial infarction, Life events, cohabitation

Introduction

During the past few decades changes in family life have lead to an increase in divorce and to more people living alone or in unmarried unions. However, although divorce has become more common and arguably more socially accepted, the difference in health between the married and the unmarried seem to have grown. Breaking up with a partner is a common experience in adult life and it is important to investigate its immediate and long-term health consequences.
Several studies have demonstrated that marriage is protective against coronary heart disease (CHD) mortality and the results almost consistently show a higher mortality among divorced and widowed people. The association between marital status and cardiovascular mortality may be due to a lower incidence among married individuals or due to better survival among the married with cardiovascular disease. Fewer studies have investigated the association between marital status and incident CHD. In a study of Finnish middle-aged men, Koskenvuo et al. found a higher incidence of CHD in the divorced and widowed compared with the married but a lower incidence in singles. In a population of Australian men, Malcolm and Dobson found that the widowed and divorced but not the never married had an increased risk of acute myocardial infarction (MI) or of sudden coronary death compared with the married. Two studies on Swedish men found excess risk of fatal and non-fatal MI in non-cohabiting men and association between being never married or divorced and non-fatal MI. However, Mendes de Leon et al. found no significant association between marital status and fatal and non-fatal MI among middle-aged men. Only one previous study on the association between marital status and incident MI included women and this study found stronger association between marital status and MI in women compared with men, which suggests that the association between divorce and MI may differ between men and women. These studies have all studied marital status as a stage which suggests that resources in marriage promote good health. An alternative approach is the stress model which would suggest that it is the change in marital status that has consequences for health. A break-up of a romantic relationship has been rated as one of the most stressful life events. Other studies have linked stressful life events to CHD and MI. Death of a spouse has been related to CHD mortality and death of a child has been related to incidence MI several years after the exposure. Death of a sibling was related to MI a few years after the exposure. Broken partnership is common in adult life but it is unknown how this is related to incident MI and how this association may vary with time since broken partnership. In this paper, we set out to study the stress model and hence focus on consequences of breaking up a romantic relationship.

Most previous studies used official marital status. Therefore, in populations (such as the Danish) where unmarried cohabitation is common, relying on official marital status would imply that many unmarried individuals who are cohabitating are misclassified as ‘single’. Further, when the focus is on change in intimate relationships with a partner, it is an advantage to use change in cohabitation status, because moving apart most commonly precedes divorce. Throughout this paper we use the terms marriage, marital status and divorce when we refer to studies which used official marital status. The term broken partnership refers to breaking an intimate relationship regardless of marital status, which is the focus of the present study.

The aim of this study was to investigate if the association between broken partnership and first time incident fatal and non-fatal MI depends on time since broken partnership in a population of men and women who were initially cohabiting with a partner and free of earlier MI at baseline, and if any associations differ between men and women and in different age groups.

Methods

Population

This study was based on register data from Statistics Denmark, and the study population was all adults living in Denmark. In older adults, end of cohabitation is more likely to be due to a partner’s death or one partner moving into residential care. In this study, the focus is on end of cohabitation due to the end of a romantic relationship. Hence, we limited the study population to those living in Denmark on 1 January 1985, aged 30 to 65 years, who were cohabiting or previously cohabiting. In addition, individuals were included in the cohort from 1986 to 2006 if they turned 30 years of age, started cohabitation later than at age 30 or immigrated and fulfilled inclusion criteria.

Analyses were carried out on a dataset with complete information on all covariates. We excluded those who were born before 1920 because information on educational attainment was unavailable for those born earlier than 1920. Those who emigrated or disappeared were followed to the time of emigration of disappearance, and individuals whose partner died were followed until the date of their partner’s death. There was complete information on gender, age at cohabitation, ethnicity and children in the household. Those with missing information on income or education were deleted. The number with missing information on income was 2065 (0.08), and 84 381 (3.21%) had missing information on education. More immigrants (25.5%) and descendants of immigrants (9.3%) than people of Danish origin (1.0%) were excluded due to missing information on education, and slightly more young individuals compared with older individuals had missing information on education. Patterns were similar for men and women. We excluded all individuals with one or more admission with MI between 1 January 1980 and 31 December 1984 (N = 3632).

Follow-up was carried out on 2 466 684 unique individuals (1 244 225 (50.44%) men and 1 222 459 (49.56%) women).

Measurement of MI

First time MI diagnoses were classified according to the 8th Revision of the International Classification of
Diseases (ICD-8) for the years from 1980 to 1993, and the 10th Revision (ICD-10) from 1994. A study of the validity of diagnosis in the Danish National Hospital Register found high validity for the MI diagnosis. MI was defined as fatal or non-fatal cases with a main or contributory diagnosis of 410 (ICD-8) and 121-22 (ICD-10). Information on causes of death and diagnoses and time of admission to hospital wards from 1980 to 2006 was retrieved from the National Patient Registry and Cause of Death Registry from 1980 to 2006.

Measurement of broken partnerships
Statistics Denmark provides information on cohabiting couples on an annual basis. In addition to married couples, two individuals living at the same address were classified as a cohabiting if they had common children or were of opposite sex, both were at least 16 years old, the age difference was less than 15 years, they were not related and there were no other adults in the household. These criteria capture couples who most likely live in a romantic relationship similar to marriage, and exclude for instance siblings with shared address. Broken partnership was defined as end of cohabitation and comprised individuals who were cohabiting in year x-1 but during year x were living without a partner or with a new partner. Individuals who returned to the same partner within 1 year were not counted as having a broken partnership. Those with broken partnerships were classified according to the time since broken partnership. In the case of multiple broken partnerships, time since broken partnership was calculated from the most recent broken partnership. If a partner died, follow-up ended at date of death of their spouse. The exposure variable was grouped as: no broken partnerships (reference group), year of broken partnership, 1 year after broken partnership, 2–3 years after broken partnership, 4–8 years after broken partnership and 9 or more years since broken partnership.

Covariates
The covariates included in this study were age, gender, calendar year, ethnicity, educational attainment, income, children in the household, current cohabitation status and hospitalizations. All covariates came from Statistics Denmark or the National Patient Registry and were recorded annually from 1980 to 2006. Educational attainment was available for those born in 1920 or later and was grouped in those with primary school or less (low) and any education beyond primary school (high). Low income was the lowest quartile of equivalent income calculated as the sum of disposable household income in the previous year divided by a factor for household composition (number of adults + number of children)\(^{10,6}\). The calculation of the factor for household composition followed the calculation used by the Danish Ministry of Finance. Children in the household were children aged 17 years or younger living in the household on 1 January of the year examined. This was coded as 0 vs 1 or more. Current cohabitation status on 1 January of the year was used as a confounder to distinguish the effect of experience of broken partnership from the effect of living without a partner. Ethnicity was coded as Danish origin or immigrant origin or descendant of immigrant. Hospital admissions during the preceding 2 years was treated as a potential confounder of the association between broken partnership and MI. Hospitalizations were coded following the Charlson Comorbidity Index (CCI). We used ICD-8 and ICD-10 codes from the National Patient Registry, which has been shown to be a valid measurement of CCI. Diagnoses and coding of the CCI has been described in detail by Christensen et al.\(^{19}\). We coded CCI as no hospitalization, CCI score 1–2 and CCI score 3 or higher.

Statistical methods
Age-adjusted rates of MI were calculated by direct standardization using the age distribution in the study population as the standard population. Adjusted incidence rate ratios (IRR) and 95% confidence intervals were analysed by a Poisson regression model with log person-years as offset.\(^{20}\) Follow-up was from 1 January of each calendar year until MI event or censoring by date of death, partner’s death, age 65 years or 31 December of the same calendar year. The Poisson model included age, calendar year, ethnicity, educational attainment, income, children in the household, current cohabitation status and CCI. Analyses were performed using PROC GENMOD in SAS version 9.2. Follow-up for MI was from 1 January 1985 to 31 December 2006. Analysis of interaction between sex and time since broken partnership was tested by including an interaction term in the models. The result of the test indicated that the IRR differed between men and women, and further analyses were stratified by sex. The CONTRAST statement was used to test differences between immediate and long term effects of broken partnership.

Results
In men, a total of 22406337 person-years were observed, during which 56216 incident cases of fatal or non-fatal MI occurred. In women, a total of 22733638 person-years were observed, during which 16497 incident cases of fatal or non-fatal MI occurred. Table 1 shows the number of MI cases and age-adjusted incidence rates according to time since broken partnership and socio-demographic variables for men and women. The age-adjusted incidence rates indicate that broken partnership and all covariates were associated with MI.

The result of the test for interaction between sex and time since broken partnership was \(P < 0.0001\), which
indicated that the associations between time since broken partnership differ between men and women. Table 2 shows the IRR of MI, 95% CI and P-values in men and women adjusted for age and calendar year (model 1) and for all covariates (model 2). In the fully adjusted model compared with the reference group, the rate of MI in men with broken partnership in the same year was not increased when comparing with the consistently cohabiting IRR 0.97 (95% CI 0.90–1.05). In the year after broken partnership, men had an increased rate of MI with IRR 1.25 (95% CI 1.17–1.34). The higher rate of MI declined to a lower level during the following years but remained different from the continuously cohabiting [2–3 years after broken partnership, IRR was 1.12 (95% CI 1.06–1.18), 4–8 years IRR was 1.09 (95% CI 1.05–1.14) and 9 years or longer since broken partnership IRR was 1.09 (95% CI 1.05–1.12)]. In men, the CONTRAST test for the difference between same year as broken partnership and all following years was p = 0.0001. Further, we tested if the excess risk found 1 year after broken partnership differed from 2 or more years after broken partnership. The result of this test was p = 0.0009. In women, those who experienced broken partnership in the same calendar year had an increased rate of MI compared with those who consistently cohabited, with IRR 1.45 (95% CI 1.26–1.66). The following years, until 4–8 years, the higher rate of MI declined [1 year after broken partnership IRR 1.30 (95% CI 1.14–1.50), 2–3 years after broken partnership 1.26 (95% CI 1.13–1.39) and 4–8 years after broken partnership 1.17 (95% CI 1.08–1.26)]. After 9 years or longer since broken partnership, the IRR increased to 1.24 (95% CI 1.17–1.32). In women, the CONTRAST test for the difference between same year as broken partnership and all following years was p = 0.0229.
Table 3 shows IRR of MI and 95% CI in men and women stratified by age (30–49 years and 50–65 years). In the fully adjusted models, the pattern between broken partnerships and MI was similar in men regardless of age. In women, the pattern differed with age group. In women aged 49 years or younger, the largest IRR was found in the 1st year after BP (similar to men), whereas in women aged 50 years or older, the IRR was highest the same year as BP.

### Discussion

In both men and women, we found an association between broken partnerships and MI and we found that the strength of the association varied according to time since broken partnership. In men, there was no association with MI the same year as broken partnership, but an excess risk of MI in the year following broken partnership and the IRR declined to a low level 2–3 years after broken partnership. In women, the IRR was largest in the same year as the broken partnership and then declined until 4–8 years after the event. Although stroke is a different outcome, the risk factors are similar to those of MI. Broken partnerships may differ between death of a spouse and death of a significant other, in time frame of the stressor. Death of a spouse may be preceded by strain from a period of worries and anxiety due illness of the spouse and broken partnership is most often preceded by strain from conflicts between partners and unsupportive relationship. We found that the short-term effect of MI was most pronounced in women aged 50–65 years; this may suggest that women in this age group are more vulnerable to the acute stresses of a broken partnership. These differences may be due to different experience of the same stressful life event in different age groups or to variation in the physiological response to a stressful life event according to age.

We found that the association between time since broken partnership and MI differed between men and women. Most previous studies investigating the association between marital status and MI or coronary heart disease included only men and most, but not all, studies found an increased risk in among unmarried
Table 3  Incidence rate ratios (IRR) and 95% confidence intervals of myocardial infarction for the adjusted association with time since broken partnership in relation to gender and stratified by age

<table>
<thead>
<tr>
<th></th>
<th>Age 30 to 49</th>
<th></th>
<th>Age 50 to 65</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Model 1 IRR</td>
<td>P-value</td>
<td>Model 2 IRR</td>
<td>P-value</td>
</tr>
<tr>
<td></td>
<td>(95% CI)</td>
<td></td>
<td>(95% CI)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 (ref.)</td>
<td>0.0022</td>
<td>0.95 (0.84–1.07)</td>
<td>0.3856</td>
</tr>
<tr>
<td></td>
<td>1 (ref.)</td>
<td></td>
<td>0.96 (0.92–1.01)</td>
<td>0.1203</td>
</tr>
<tr>
<td>No broken partnership</td>
<td>1.09 (1.03–1.15)</td>
<td>0.0001</td>
<td>1.24 (1.11–1.39)</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>1.23 (1.18–1.28)</td>
<td>&lt;0.0001</td>
<td>1.14 (1.10–1.17)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Years after broken partnership</td>
<td>1.21 (1.16–1.25)</td>
<td>&lt;0.0001</td>
<td>1.06 (0.97–1.16)</td>
<td>0.1682</td>
</tr>
<tr>
<td></td>
<td>1.14 (1.10–1.17)</td>
<td>&lt;0.0001</td>
<td>1.08 (1.06–1.10)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>1.15 (1.12–1.18)</td>
<td>&lt;0.0001</td>
<td>1.11 (1.04–1.17)</td>
<td>0.0012</td>
</tr>
<tr>
<td></td>
<td>1.08 (1.06–1.10)</td>
<td>&lt;0.0001</td>
<td>1.07 (1.03–1.11)</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

Model 1: adjusted for age and calendar year 95% CI.
Model 2: adjusted for age, calendar year, ethnicity, education, income, cohabitation with partner and children and hospitalization past 2 years.
men compared with married men. A recent case-control study by Hu et al. found that unmarried women were more susceptible to MI development than men. This result is similar to the finding of the present study, although Hu et al. studied marital status as a state rather than the change. The stronger relative association between broken partnerships and MI among women compared with men is in contrast to the findings of a meta-analysis which concluded that association between marital dissolution and mortality is stronger in men.

The pathways which link broken partnership and MI include behavioural, psychological and physiological pathways. We did not have access to information on these pathways in the register data used for this study, but previous studies support a causal association between broken partnership and MI. Further, these studies may contribute to an understanding of the observed patterns in relation to time and gender.

Psychological reactions to broken partnership and their physiological counterparts may explain the increased risk shortly after broken partnership. Anger, anxiety and depression have been identified as triggers of MI. These reactions are common following divorce or break-up with a partner, and these negative emotions are most intense during and shortly after divorce and decline after 6–12 months after divorce. Willits et al. found that women’s mental health was more adversely affected than men’s and that the negative effects lasted longer in women. This suggests that the observed differences between men and women may be related to differences in psychological reactions to broken partnership. Some studies have found that depression is associated with increased risk of MI, but other studies did not find an association or pointed to the fact that the association may be bidirectional. A few studies have investigated the association between divorce and MI risk factors. Sbarra et al. found that marital dissolution was associated with elevated blood pressure and Kiecolt-Glaser found that marital disruption was related to immune function in women. Powell et al. studied women undergoing divorce or separation and found elevated evening cortisol and lower morning testosterone levels.

Changed health behaviour is another possible pathway between broken partnerships and MI. Changes in health behaviour such as increased smoking lead to physiological changes which could lead to MI. However, it is likely that there is some induction time before health behaviour results in MI. Hence, changes in health behaviours may explain why the risk of MI continues to be increased several years after broken partnership. Most studies have found that smoking behaviour has been related to marital status and change in cohabitation status, showing that the divorced are less likely to quit smoking and more likely to be current smokers. However, a longitudinal study found that getting divorced or widowed was not associated with smaller chances of smoking cessation. Physical activity, diet and body mass index (BMI) may change following break-up with a partner; however, the evidence in this area is inconsistent. Molloy et al. made an effort to quantify the behavioural, psychological and physiological mechanisms between marital status and cardiovascular mortality and found that behavioural mechanisms explained most of the excess risk of cardiovascular mortality among the separated or divorced.

The study population for the current study is the entire Danish population, which means that there is no selection bias. Because of the large size of the study population it was possible to study events in rather short time intervals in order to answer the study question. Further, the study used register-based exposure, and outcome and confounders with minimal or no missing information or loss to follow-up. It is an advantage of the Danish register data that it is possible to study break-up of both married and unmarried relationships. The Danish National Hospital Register provides valid information on MI in patients; however, some cases of MI are silent and do not lead to hospitalization. The design and available data were limited on some points. Information of broken partnerships was available on a yearly basis only. This time interval might be too large to capture the variation of effects following break-up with a partner. Further, because it was only possible to study broken partnership on an annual basis, we do not know if the break-up of partnership was before MI in the year of broken partnership. Some studies have reported that poor health may lead to an increased risk of divorce (i.e. reverse causation), however, it has not been studied whether MI as a specific health outcome is associated with increased divorce risk. MI may lead to depression and poorer economy, which are known risk factors for divorce, but on the other hand it may be socially unacceptable to leave a partner who recently experienced MI. We started follow-up for MI from 1 January 1985, but observed cohabitation status since 1980 to minimize the possibility of misclassification of cohabitation status; however, there may still be some misclassification in the case of those who experienced broken partnership before 1980. Register data do not provide information on important MI risk factors such as smoking status or blood pressure. These factors are, according to the literature reviewed above, likely to mediate the association between broken partnership and MI and should not be controlled for. Drug and alcohol abuse could be potential confounding factors which are related to broken partnership and to cardiovascular mortality.

In conclusion, we found that the risk of MI was increased following broken partnership, with the strongest association the same year as broken partnership for women and the year after broken partnership for men. This means that the period around and just after broken partnership may be a period of susceptibility to MI.
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CONFLICT OF INTEREST: None declared.

KEY MESSAGES
- Broken partnership is associated with first MI in both men and women.
- The association between time since broken partnership and first MI is different in men and women.
- In women, the highest excess risk occurs the same year as broken partnership.
- In men, the highest excess risk occurs the year after broken partnership.

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