International Journal of Nursing Studies 47 (2010) 229–238

Contents lists available at ScienceDirect

International Journal of Nursing Studies

journal homepage: www.elsevier.com/ijns

Review

Cardiovascular risk in early bereavement: A literature review and proposed mechanisms

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ARTICLE INFO

Article history:
Received 1 April 2009
Received in revised form 5 June 2009
Accepted 28 June 2009

Keywords:
Bereavement
Cardiovascular
Mechanism

ABSTRACT

Objectives: The purpose of this review was to examine the evidence of cardiovascular risk in early bereavement to identify potential risk factors and possible mechanisms for risk that may inform future research directions.
Design: A comprehensive search of electronic databases PubMed Medline, CINAHL and PsycINFO, bereavement related textbooks and reviewed reference lists was undertaken on literature related to evidence of increased risk in bereavement. No limits were set on the searches in terms of date or publication type, but only English language articles were selected.
Findings: Bereavement represents a time of heightened cardiovascular risk for the surviving spouse. The immediate weeks following bereavement represent the highest risk period with both men and women across all ages. Risk is evident irrespective of the nature of death, expected or unexpected, although higher level of social support at the time of death may be protective. Evidence would suggest that for many, bereavement results in a time of increased psychological stress and potential for altered behavioural health risk factors that in the presence of altered physiological state, may serve as a potential trigger of cardiovascular events, especially in those most at risk.
Conclusion: The findings from this review provide insight into the impact of early bereavement on health and the recognition that bereavement is associated with increased cardiac risk. This recognition should provide an impetus for individuals to act on cardiac symptoms by seeking medical advice and for health care providers to monitor such individuals more closely.

What is already known about the topic?

- The death of a loved one is recognised as one of life's greatest stressors requiring significant psychological adjustment.
- Bereavement is associated with increased cardiovascular risk although sometimes it is considered to be incidental rather than bereavement related.

What this paper adds

- Bereavement results in a time of increased psychological stress and potential for altered behavioural health risk factors that in the presence of an altered physiological state, may serve as a potential trigger of cardiovascular events, especially in those most at risk.
- The immediate bereavement weeks present the highest risk period with both men and women across all ages.
- Risk is evident irrespective of the nature of death, expected or unexpected, although higher level of social support at the time of death may be protective.

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doi:10.1016/j.ijnurstu.2009.06.010

1. Introduction

The death of a loved one is recognised as one of life's greatest stresses requiring significant psychological adjustment (Maciejewski et al., 2007; Stroebe et al., 2007; Stroebe, 2001). The response to bereavement, commonly referred to as grief, is a unique psychological stress that may last for several weeks or months and for some may lead to chronic psychological stress. Bereavement can be particularly devastating for the surviving spouse, who is often required to deal with simultaneous disruption to living arrangements, financial security and social status (Stroebe, 2001). For some, spousal bereavement has the potential to result in social isolation that may have an impact on cardiovascular health in the longer term (Bunker et al., 2003). The death of a child has been associated with even greater significant symptoms of depression, anxiety and stress (Goodenough et al., 2004; Miyabayashi and Yasuda, 2007).

A growing body of evidence suggests that emotional stress is strongly associated with CHD and acute events (Angerer et al., 2000; Bunker et al., 2003; Muller et al., 1994). An Expert Group of the National Heart Foundation of Australia published an account of systematic reviews of the evidence relating to psychosocial risk factors and their relation to development or progression of CHD, concluding that increased risk contributed by psychosocial factors (depression, social isolation and lack of quality of social support) is of similar order to conventional risk factors such as smoking, dyslipidaemia and hypertension (Bunker et al., 2003).

Frequently referred to as "death from a broken heart", bereavement has long been associated with increased mortality risk for the surviving spouse, although sometimes considered to be incidental rather than bereavement related. The need to design preventative regimens to provide maximum protection during times of peak risk of myocardial infarction has been suggested (Tofler and Muller, 2006). However, the absence of insight into the impact of bereavement on risk factors in early bereavement results in uncertainty regarding appropriate strategies during this known risk period.

The purpose of this paper is to report in a narrative review the evidence of cardiovascular risk during the early bereavement period in order to identify potential risk factors that may provide evidence as to those who are most at risk. Additionally, we review potential mechanisms of risk and discuss a representation by which bereavement may trigger acute cardiovascular events as background to inform future research directions.

2. Search method

The electronic databases PubMed Medline, CINAHL and PsycINFO were searched using the key words bereavement, mortality, morbidity, spouses and parents, using various combinations. No limits were set on the searches in terms of date or publication type but only English language articles and studies involving humans were selected. Literature gathered in the search process were included for review if they were primary research articles reporting mortality or morbidity risk during bereavement. In all, 16 research studies reported evidence of a relationship between bereavement and increased health risk were found. Fourteen of these studies were included in this review and two papers excluded that were case study reports. Given that limited research has been conducted on bereavement outcomes, exclusion of earlier studies might discard meaningful information on risk factors in bereavement. Therefore subsequent studies published since the first large population study examining health risk during bereavement (Young et al., 1963) were reviewed. Additionally the electronic databases were searched for primary research papers reporting physiological assessments during the time of psychological stress. This search was conducted in various combinations of the following search terms: bereavement, work stress, depression, anxiety, anger, behavioural, sleep, alcohol, eating, appetite, prothrombotic factors, heart rate, immune changes, inflammation, cholesterol, cortisol, heart rate variability and blood pressure. Bereavement related textbooks were also searched and reference lists were reviewed from retrieved publications for related publications. Original research articles and systematic reviews demonstrating relationships between psychosocial stress and cardiovascular risk factors were included to explore potential mechanisms for cardiovascular risk during bereavement.

3. Findings

3.1. Bereavement and risk of mortality for the surviving spouse

Studies reporting excess mortality in early bereavement have predominantly reported on samples of bereaved spouses, possibly due to the ability to monitor spousal survival records from public records. In 1963, a landmark study reported a follow-up of 4486 widowers of 55 years or older comparing widowed mortality to that of married men (Young et al., 1963). The authors reported 66 excessive deaths in the bereaved group in the first six months following spousal death representing an odds ratio of 1.39 with little differential thereafter. While these findings were from secondary evidence, it was one of the first large epidemiological studies to demonstrate a relationship between spousal bereavement and increased mortality risk for the surviving spouse.

Since 1969, nine large retrospective cohort studies and two retrospective case matched studies that confirmed the earlier findings from Young et al. (1963) demonstrating increased mortality risk in the early acute bereavement period (Table 1).

While the increased risk of mortality in bereavement is well documented, the mechanism remains largely unexplained, possibly due to the perceived difficulties in conducting such research at a time great distress. Parkes et al. (1969) in a follow-up of almost 4500 bereaved spouses reported that 22.5% of deaths were from the same diagnostic group as the spouses' death, considered unlikely to be by chance. One explanation proposed is the tendency of unfit to marry unfit and the possibility that the bereaved and their spouses may have shared the same pathogenic

Table 1
Summary of studies discussed demonstrating mortality risk during bereavement.

Authors	Methods and sample	Key results
Young et al. (1963)	Review of General Register Office register of 4486 widowers older than 55 years.	Excessive deaths among widowers (40% increased risk) within the first six months following the death of their spouse.
Parkes et al. (1969)	National Health Service central register follow-up of the same 4486 widowers from Young et al.'s (1963) study.	CHD responsible for 53% of increased mortality. 22.5% of widowed deaths were from the same diagnostic group as the deceased spouse.
Ward (1976)	Prospective follow-up of 366 bereaved spouses for two years (87 men and 279 women).	Equal number of deaths among men as women. First six months was the highest mortality risk period for widowers. Deaths among widowers were spread across two-year period. Cardiovascular disease accounted for 20% of excess deaths. No difference between expected deaths and unexpected deaths for surviving spouse mortality risk. In-hospital death a possible risk factor for surviving spouse.
Cottington et al. (1980)	Retrospective case matched comparison of 81 Caucasian female sudden deaths from arteriosclerotic heart disease.	The odds ratio when death of a significant other was present in the six months prior to death was reported to be 6.5 (compared to neighbourhood controls).
Mor et al. (1986)	Analysis from quasi-experimental study exploring the impact of hospice care on quality of life. Included 1447 primary care givers. One-third of sample was female.	The odds ratio of hospitalisation was 2.1 times greater among bereaved with health limitations, and if that person was a spouse of the deceased, they had a 1.6 increased risk of hospitalisation compared to other relatives. Alcohol use increase reported following bereavement, more so in men and the potential protective role of social support highlighted. 21% of bereaved were hospitalised in the first four months of bereavement.
Jones (1987)	Ten-year analysis from population census in United Kingdom identifying mortality among surviving spouses.	Deaths from IHD were higher among all surviving bereaved spouses. Highest risk of IHD among widows <65 years and widowers >75 years. Unusually high number of same day deaths from IHD in widows. Highest risk period for widows was in the first six months, less sharp and more extended in widowers. Spousal mortality risk higher after unexpected death of spouse.
Kaprio et al. (1987)	Prospective study of 95,647 Finnish widows.	Cohort mortality was 6.5% higher among bereaved. Standardised mortality ratios were 2-fold higher in the first week for both men and women and decreased after one month in women and after six months in men. There was a 2.3-fold increased risk from IHD in women and 3.5-fold increase in men compared to population levels.
Jagger and Sutton (1991)	Prospective National database study of 344 elderly couples over a seven-year time period.	Reported a 3.8-fold increased risk of spousal mortality in women that returned to normal levels after six months. No significant risk reported among men.
Schaefer et al. (1995)	Retrospective cohort study of 12,522 middle income married couples.	The relative risk of mortality was higher for both men and women in first year after spousal death; higher for men in first six months and highest for women in second six months that lowered after 12 months. No evidence that shared environment influenced surviving spouse mortality risk.
Martikainen and Valkonen (1996)	Prospective study of 1.58 million Finnish residents for five years.	Highest risk period for men and women was in the first week that reduced to 20% at six months for men and 9% for women. Increased mortality was still evident after controlling for economic environment and common lifestyles of couples.
Lichtenstein et al. (1998)	Prospective national database study of 1993 pairs of twins discordant for marital status and 35,860 married individuals from the Swedish Twin Registry.	Spousal bereavement was a risk factor for mortality for both men and women using the still married co-twin as a control, after controlling for earlier health status and risk factors. The mortality risk was higher for under 70-year-old females in early bereavement.
Nicholas et al. (2003)	Matched retrospective cohort study of 30,838 couples where the deceased used hospice care compared to an equal number of couples where the deceased did not.	Bereaved spouses, whose deceased partner used hospice services, compared to bereaved that did not use hospice service, were less likely to die themselves in the first 18 months of bereavement with an adjusted odds ratio of 0.92 for widows and 0.95 for widowers.
Manor and Eisenbach (2003)	Longitudinal mortality study conducted in Israel. Included 20% sample of the country's population (90,830 people)	Across all age groups the relative risk of mortality among widowers was reported to be 1.38-fold and for widows 1.48 in the first six months when compared to married subjects. Women with one to three children had the lowest risk among the sample studied. Adjustment for ethnicity and education resulted in minimal changes to the relative risk among all bereaved.
Hart et al. (2007)	Prospective cohort study in Renfrew and Paisley in Scotland of 4395 married couples from 1972 to 2004.	All cause mortality was highest in the first six months (RR 1.31) and reduced in the next six months (RR 1.09). Risk of death from CVD or CHD was highest in the initial six months following bereavement (RR 1.21 or 1.31 respectively), even after adjustment for known individual cardiac risk factors.

environment, dietary and social factors (Genevro et al., 2004; Martikainen and Valkonen, 1996; Stroebe, 2001). There are minimal changes to the relative risk among all bereaved after adjustment for spouses' covariates (Schaefer et al., 1995), bias from common socioeconomic environmental and common lifestyles, accidents common to spouses (Martikainen and Valkonen, 1996), age, ethnicity and education (Manor and Eisenbach, 2003).

3.2. Risk factors during bereavement

3.2.1. Time of greatest risk

The risk of mortality for the surviving spouse appears to be greatest in the immediate weeks following bereavement and to remain significantly elevated during the first six months (Christakis and Iwashyna, 2003; Cottington et al., 1980; Hart et al., 2007). Bereaved women under 70 years, who were found in one study to have a pattern of increased mortality risk during the early bereavement period, had markedly decreased risk if they survived four years after bereavement with a hazard ratio 0.64 after four years (Lichtenstein et al., 1998).

3.2.2. Age and sex

Spousal bereavement is mainly a female phenomenon, in keeping with the fact that women live longer (Charlton et al., 2001). However, several studies that included both sexes in the analysis suggest that men may be more at risk following spousal death, especially in the initial six-month period (Manor and Eisenbach, 2003; Martikainen and Valkonen, 1996; Schaefer et al., 1995). Increased risk appears to be across all age groups, although younger men (less than 54 years) and older men (over 75 years) have been identified as possibly most at risk (Jones, 1987; Manor and Eisenbach, 2003). Mortality risk appears to be distributed across all female age groups (Manor and Eisenbach, 2003), although two studies suggest that women under 75 years may be most at risk of death from CHD related events following the death of a spouse (Jones, 1987; Lichtenstein et al., 1998).

3.2.3. Expected versus unexpected death

Intuitively, one would expect being unprepared for the death of a loved one would result in greater risk for the surviving spouse, as being unprepared may lead to difficulties in acknowledging and accepting the loss and be associated with increased psychological stress following loss (Barry et al., 2002). However, this has not been reported in studies that have explored differences between expected and unexpected deaths (Christakis and Iwashyna, 2003; Ward, 1976). One reason for the lack of data on this question may be the limitation of data collected in population studies that frequently do not identify the nature of the spouse's death. However, this remains an important question in determining those most at risk during bereavement.

3.2.4. The role of social support

For some, spousal bereavement has the potential to result in social isolation and therefore social support is an important factor to consider in light of evidence of the relationship between decreased social support and increased risk of CHD (Bunker et al., 2003).

Spousal mortality among couples where the deceased used hospice care, compared to "control bereaved" who did not, was significantly lower in the first 18 months of bereavement in one study (adjusted odds ratio of 0.92 for widows and 0.95 for widowers) (Christakis and Iwashyna, 2003). Women with one to three children had the lowest risk among a sample of Israeli adults, suggesting that having no children results in less support and having more than three children may add to strain and mortality risk (Manor and Eisenbach, 2003). Although not conclusive, these studies suggest that higher levels of social support at the time of the partner's death may reduce mortality risk in the early bereavement period.

3.3. Cardiovascular risk in early bereavement

Coronary heart events appear to account for a substantial amount of the increased deaths observed during spousal bereavement. Deaths with a diagnosis of "coronary thrombosis and other arteriosclerotic and degenerative heart disease" accounted for 53% of reported increased mortality in one nine-year follow-up of 4486 male bereaved subjects (Parkes et al., 1969). Similarly Ward (1976) reported that cardiovascular disease was a contributing factor in 20% of the excess deaths seen in early bereavement. Cottington et al. (1980) reported that women who died suddenly from arteriosclerotic heart disease, with no prior history of coronary heart disease (CHD), were more likely to have experienced death of a significant other, but no changes in living or work conditions with an odds ratio of 6.5 and estimated standard error of $\pm$4.9. In this sample of 81 Caucasian women, in which comparison was relative to matched controls, death of a significant other occurred in the six months preceding their own death.

Mortality secondary to ischaemic heart disease (IHD) in the first week of bereavement has been reported to be almost twice the risk of death from cerebrovascular disease (Kaprio et al., 1987). Additionally, in a study from the UK where recorded death from ischaemic heart disease (IHD) was compared to expected deaths, separate analysis of the deaths of ten women that occurred on the same day as their husbands' deaths revealed that six of the deaths were from circulatory diseases and four of these from IHD. While small in number, this was significantly higher than expected from all widows, among whom the expected number was two (Jones, 1987). More recently in the Renfern and Paisely Study, conducted in Scotland, where bereaved spouses had a relative risk of 1.27 compared to married individuals, risk of death from coronary vascular disease (CVD) or coronary heart disease (CHD) was highest in the initial six months following bereavement (RR 1.21 or 1.31 respectively), even after adjustment for known individual cardiac risk factors. This finding confirmed earlier findings of increased risk of mortality in early bereavement, with the risk of cardiovascular-related events highest in the first six months (Hart et al., 2007).

3.4. Psychological risk factors during bereavement

For most, early bereavement is associated with psychological stress, with symptoms of depression, anxiety or anger frequently reported (Gerra et al., 2003; Maciejewski et al., 2007; Prigerson et al., 1997). A growing body of evidence suggests that emotional stress is strongly associated with CHD and acute events (Angerer et al., 2000; Bunker et al., 2003; Steptoe and Whitehead, 2005). Commonly regarded components of stress, depression, social isolation and lack of quality of social support, are strongly and consistently associated with cause and progress of CHD, with increased risk contributed by these psychosocial factors of similar order to conventional risk factors such as smoking, dyslipidaemia and hypertension (Bunker et al., 2003).

3.4.1. Symptoms of depression

For most, symptoms of depression usually decline after the first few months of bereavement but some may remain unresolved at six months (Gerra et al., 2003; Maciejewski et al., 2007; Prigerson et al., 1997). Depression has long been associated with increased incidence of cardiac events, although the exact mechanism remains unclear (Kuper et al., 2002; Rozanski et al., 1999). Major depression is characterised by the presence of depressed mood and decreased interest in all activities persisting for at least two weeks and accompanied by at least four of the following symptoms: changes in appetite, sleep disturbance, fatigue, psychomotor retardation or agitation, feelings of guilt or worthlessness, problems concentrating, and suicidal thoughts. Major depression and the presence of depressive symptoms in the absence of major depression are both associated with increased cardiac risk (Kuper et al., 2002; Rozanski et al., 1999).

The prevalence of discrete time-limited episodes of moderately and severely depressed mood were reported to be 18.2% and 8.3% respectively in nearly 300 patients admitted to hospital with acute coronary syndrome (ACS) (Steptoe et al., 2006). Using a case-crossover methodology, where the critical time period of 2 h prior to symptom onset was compared with the same 2-h period 24 h earlier on a within-subject basis, the odds ratio of ACS following depressed mood was 2.5 (95% confidence intervals 1.05–6.56). Compared to usual levels of depressed mood, the relative risk of ACS onset following depressed mood was 4.33 (confidence intervals 3.39–6.11). Mechanisms proposed for increased cardiac risk during acute episodes of depression include both increased behavioural risk factors and direct biological processes, such as hypercortisolemia, procoagulant state, inflammatory processes and reduced heart rate variability enhancing arrhythmogenic potential (Carney et al., 2001; Rozanski et al., 1999; Steptoe et al., 2006).

3.4.2. Symptoms of anxiety

As with symptoms of depression, anxiety symptoms usually decline after the first few months of bereavement (Gerra et al., 2003; Maciejewski et al., 2007; Prigerson et al., 1997). A potential dose effect with anxiety and increased risk of sudden cardiac death was suggested by Rozanski et al. (1999) following a review of related literature. In one study of over 1600 patients interviewed after AMI, in the 2-h period prior to symptom onset, 5% of patients reported anxiety symptoms above the 75th percentile on an anxiety scale (Mittleman et al., 1995). Using the case-crossover methodology, when this time period was compared to a control period 24–26 h earlier, the relative risk was 1.6 (95% confidence intervals 1.1–2.2). In addition to this association between anxiety state and cardiac risk, considerable evidence exists that higher symptoms of anxiety are associated with poorer outcome in patients with prior cardiac disease (Benninghoven et al., 2006; Moser et al., 2007).

Increased sympathetic activation and subsequent occurrence of life threatening arrhythmias have been proposed as the likely mechanisms of increased cardiac risk during states of increased anxiety, in addition to possible increased behavioural risk factors (Rogowski et al., 2007).

3.4.3. Anger

Anger symptoms are not uncommon during bereavement with one study suggesting a peak in anger at five months after loss (Maciejewski et al., 2007). Reports of heightened anger state as a trigger of acute cardiac events are fewer than episodes of depression and anxiety. A study of over 1600 patients who experienced an AMI revealed that 39 (2.4%) patients reported anger $\geq$5 on a seven-point scale, that was associated with a relative risk of 2.3 (95% confidence intervals 1.7–3.2) when compared to a control period of usual annual frequency. The relative risk was 4.0 (95% confidence intervals 1.9–9.4) when the control period was the same 2-h period the day before the AMI (Mittleman et al., 1995). This association between anger and AMI risk was also reported in an analysis of 700 patients admitted to coronary care (Moller et al., 1999) with relative risk of 9.0 (95% confidence intervals 4.4–18.2) during and 60 min after an episode of anger. In this study, the effect of anger was less pronounced in patients who were more accustomed to outbursts.

Sympathetic activation resulting in elevated cortisol, increased heart rate and blood pressure and prolonged vasoconstriction aggravating endothelial dysfunction have been proposed as potential mechanisms of cardiac events triggered by increased anger (al'Absi and Bongard, 2006; Muller et al., 1994).

3.5. Behavioural changes in bereavement

Eating may be determined to a large extent by cultural, social and psychological pressures (Elsner, 2002) and loss of appetite has been previously reported during bereavement in elderly populations (Shahar et al., 2001). Parkes et al. (1969) suggested that the increased mortality reported in early bereavement may have resulted from the possibility that bereaved men alter their nutritional or health practices in the absence of their wives, making them more susceptible to cardiac disease. Similar to a study where work stress in nurses, accompanied by depression symptoms, was associated with lower cholesterol (Fraser et al., 1999), we recently reported lower cholesterol levels

in the first weeks of bereavement in the presence of reduced appetite, in a sample of bereaved spouses and parents. This suggests that increased food intake is not a contributor to increased cardiac risk in the acute early period of bereavement (Buckley et al., 2009).

Increased alcohol consumption has been previously reported in bereavement and proposed to be a potential mediator of increased cardiac risk, particularly in men (Stroebe et al., 2007). Mor et al. (1986) reported in a sample of mainly bereaved spouses that 6% of the sample reported increased use of alcohol and 18% reported use of antianxiety medications. Similarly, we recently reported, in a prospective evaluation of behavioural changes in early bereavement, that 19% of bereaved participants increased their alcohol consumption in the first two weeks of bereavement with men more likely to increase their consumption than women (Buckley et al., 2009). However, further investigation into the effects of alcohol consumption in bereavement is warranted in light of the complex relationship between alcohol consumption and cardiovascular risk (Baer et al., 2002).

Altered sleep patterns have been reported in early bereavement and while sleep disturbance in bereavement can become persistent and debilitating for some individuals, for most in uncomplicated bereavement it returns to pre-bereavement levels (Clayton, 1980; Richardson et al., 2003). Disturbed sleep patterns are a prominent feature of depressive symptomatology, affecting more than 80% of people experiencing depression (Armitage and Hoffmann, 2001; Reynolds and Kupfer, 1987). In bereavement, preservation of normal sleep has been previously associated with less depression (Armitage and Hoffmann, 2001). Reduced sleep time as a result of an increased hypothalamic–pituitary–adrenal axis stress reaction may exacerbate depressive symptoms since a strong bidirectional relationship between sleep and depression has been previously suggested (Riemann et al., 2001). In view of reports of an association between sleep loss and inflammatory activation (Irwin et al., 2006) and increased cardiac risk (Partinen et al., 1982; Gangwisch et al., 2006; Taylor et al., 2003), future research is needed to determine if reduced sleep early in bereavement contributes to increased cardiac risk.

3.6. Biological changes in bereavement

Despite numerous studies reporting increased cardiovascular risk in the first six months of bereavement, few prospective evaluations of biological changes have been reported.

The following is a review of published evaluations to date that have reported biological assessments of cortisol, immune response and cardiovascular alterations in early bereavement.

3.6.1. Cortisol

Elevated cortisol levels have been associated with bereavement (Irwin et al., 1988; Nicolson, 2004). Breier (1989) reported increased afternoon blood cortisol in adults who experienced early parental loss, with higher levels inversely associated with quality of life. We recently reported elevated cortisol in a sample of bereaved spouses in the first six months of bereavement, which was higher in men and associated with elevated alcohol intake (Buckley et al., 2009). In view of the reported association of cortisol with increased cardiac risk (Fraser et al., 1999; Koertge et al., 2002) and reduced quality of life (Breier, 1989), future research is needed to establish if cortisol mediates or modulates health risk in early bereavement.

3.6.2. Immune/inflammatory changes

Immune imbalance has been associated with bereavement with the first study to report immune changes in bereavement reporting reduced lymphocyte responses to mitogenic stimulation at two and eight weeks of bereavement (Bartrop et al., 1977). Since then, altered T-cell subpopulations and natural killer (NK) cell activity have been consistently reported during bereavement (Goodkin et al., 1996; Irwin et al., 1988; Linn et al., 1984), although it remains unclear what role, if any, these changes contribute towards cardiac risk.

3.6.3. Heart rate

Surprisingly, to date only one study has reported heart rate during bereavement. Ten bereaved individuals were assessed between 2 and 24 months following loss with bereaved having higher resting heart rate, measured over a 5-min interval, compared to both a depressed group and a non-depressed control group (O'Connor et al., 2002). Increased heart rate has been reported to be associated with psychological stress in other life circumstances, with symptoms of anxiety associated with raised heart rate during laboratory induced stress (Cumming et al., 2007) and during times of mental stress in Air Force cadets (Falaschi et al., 2003). Likewise, symptoms of anger, which characteristically arise from a perceived demeaning offence or personal injustice (Lazarus, 1991), have been consistently associated with increases in heart rate (Fredrickson et al., 2000; Siegman, 1993; Sinha et al., 1992).

Higher heart rates have been linked to greater cardiovascular risk and mortality (Kizilbash et al., 2008; Koh et al., 1999; Palatini and Julius, 2004) and reported to independently predict coronary artery plaque rupture (Heidland and Strauer, 2001). The elevated heart rate which may occur in bereavement is possibly due to sympathetic overactivity and may be an important contributor to cardiovascular risk in early bereavement.

3.6.4. Heart rate variability

To date, autonomic function in bereavement has also been reported only in the small study of O'Connor et al. (2002). The study reported no difference in heart rate variability between bereaved, depressed and non-depressed groups assessed between 2 and 24 months following bereavement (O'Connor et al., 2002). However in light of the known association between psychological stress and reduced heart rate variability (Virtanen et al., 2003; Horsten et al., 1999), and the association between lower HRV and increased cardiovascular risk (Bigger et al., 1996) further prospective evaluations of HRV during bereavement are warranted before excluding reduced

HRV as a contributor to the incidence of sudden death reported in early bereavement.

3.6.5. Blood pressure

Elevated blood pressure has been associated with bereavement (Prigerson et al., 1997; Grant et al., 2002; Santic et al., 2006). Traumatic grief symptoms approximately six months after the death of the spouse predicted self-reported high blood pressure at 13- or 25-month follow-up in a prospective survey of 150 future widows and widowers interviewed at the time of their spouse's hospital admission and at 6-, 13-, and 25-month follow-up (Prigerson et al., 1997). Higher clinic systolic BP was reported in a sample of bereaved individuals, compared to a control group, in a longitudinal study of surviving spouses from deceased Alzheimer patients, studied at six-month intervals for 18 months (Grant et al., 2002). In Grant's study, despite improvement seen in mood, raised systolic blood pressure persisted at the final assessment (on average 12 months after bereavement).

More recently, increased prevalence of hypertension was reported in family members of deceased soldiers (Santic et al., 2006). Comparing family members of killed soldiers to neighbouring families who did not experience bereavement, only the stress of mourning was associated with higher prevalence of hypertension after controlling for other cardiac risk factors. Over time, on average four years, the proportion of hypertensive participants decreased in the group with a killed family member, further suggesting that at least a part of their hypertension might have been of psychological origin, and that blood pressure takes considerable time to resolve after bereavement (Santic et al., 2006).

A lack of prospective studies in the early bereavement period makes it difficult to be confident that elevated blood pressure contributes to increased cardiac risk in the early months after the death of a loved one. However, elevated blood pressure has been reported in response to emotions, with several studies reporting increased vascular resistance and subsequent raised blood pressure in response to anger and fear (Roberts and Weerts, 1982; Schwartz et al., 1981; Sinha et al., 1992), making it likely that bereavement results in elevated blood pressure for some.

4. Discussion

Bereavement, a unique psychological stress where acute symptoms of depression, anxiety and anger may last for several weeks and months, has been associated with increased morbidity and mortality, most notably in surviving spouses. Coronary heart events appear to account for a substantial proportion of increased deaths during early bereavement, although the exact physiological changes contributing to increased risk remain relatively unexplored during this vulnerable time. Risk appears higher in the first six months among all ages and both sexes. Risk is elevated irrespective of whether the death is expected or not, although social support at the time of death appears to have a protective effect for the surviving spouse.

Recent advances have lead to greater understanding of the physiological mechanism of acute coronary events and activities that promote acute changes and provide direction for future physiological evaluations during bereavement. Most, but not all, acute coronary occlusions occur as the result of rupture of an unstable atherosclerotic plaque and superimposed thrombus formation (Davies and Thomas, 1984; Libby, 1995; Servoss et al., 2002). Additionally, myocardial necrosis may occur secondary to coronary vasospasm, with or without thrombus formation (Kloner, 2006).

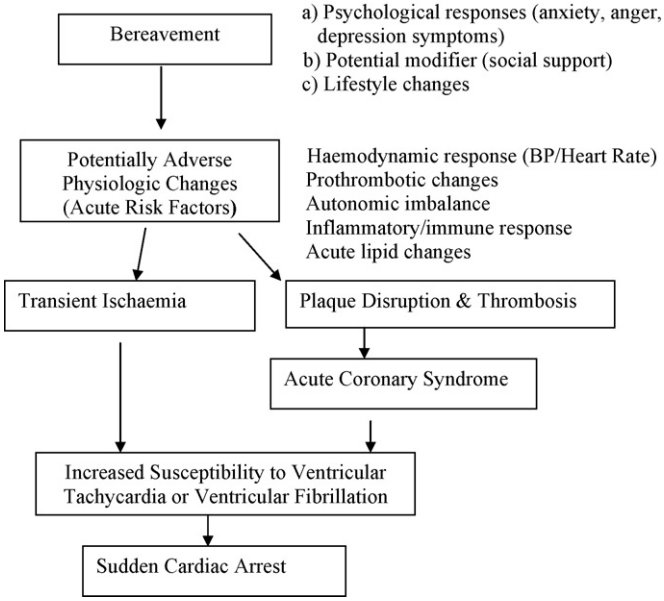

Fig. 1. Representation of the manner in which bereavement may trigger acute myocardial infarction and sudden cardiac death. Adapted from: Tofler, G., Buckley, T., 2007. Psychological triggers for plaque rupture. In: Walksman, R., Seruys, P.W., Schaar, J. (Eds.), The Vulnerable Plaque, 2nd ed. Informer Health Care, Oxon, UK, pp. 87–102.

Based on the literature reviewed, we propose a representation of the manner in which bereavement may trigger acute myocardial infarction and sudden cardiac death (Fig. 1). Evidence to date suggests that heart rate and blood pressure changes may contribute to the increased cardiac risk in bereavement, but there is a need for prospective longitudinal evaluations to determine if in fact these changes are bereavement related and if so, to determine the hazard period. While immune imbalance has been widely reported during bereavement, future work is needed to establish if these immune changes are associated with acute cardiovascular events. To date there have been no evaluations of prothrombotic factors during bereavement despite evidence that mental stress may be associated with increased prothrombotic factors. For example higher circulating von Willebrand factor antigen (vWF-ag) levels have been associated with post-traumatic stress symptoms (von Kanel et al., 2008) and work stress has been associated with higher fibrinogen in several studies (Brunner et al., 1996; Fenga et al., 2004; Theorell, 2002). Additionally, while evidence to date suggests increased cardiovascular risk may not be the result in raised lipid levels in early bereavement, further work is required to determine if lipid catabolism has any detrimental health effects.

5. Future research directions

While the data are compelling for a link between bereavement and cardiovascular risk, there is a need for further work to better understand the mechanism by which risk occurs. Two major reviews of bereavement research in recent times recommend that research priorities focus on the physiological, behavioural and support mechanisms that place bereaved persons at increased risk (Genevro et al., 2004; Stroebe, 2001).

Identification of biological changes in bereavement is an important step towards identification of those most at risk and would provide clinicians impetus to monitor such individuals more closely, particularly in the early bereavement period. Additionally, as loss of a loved one is a universal experience, consideration should be given to potential interventions to reduce cardiac risk, although large samples may be required to evaluate their effectiveness. While the authors do not suggest interventions to modify the natural grief response, the early bereavement period may be susceptible to increased cardiac protection, particularly if risk factors such as elevated heart rate and blood pressure, or increased procoagulant factors, are found to be elevated in prospective evaluations.

6. Limitations

The results of increased mortality and morbidity in bereavement presented in this review relate findings in bereaved spouses or parents and therefore may not be relevant to all bereaved individuals. The grief response in bereavement is a highly individualised experience and it is possible that risk is not confined to spouses or parents. In this review there is a possibility of publication bias because studies that found no changes in psychological and biological factors in the bereaved may not have been published. Additionally, this review was limited to English language literature and therefore may not be representative of non-English published studies.

7. Conclusion

While the focus at the time of bereavement is naturally directed on the deceased person, the health and welfare of bereaved survivors should be of great concern to medical, nursing and social work professionals, as well as family and friends. The insights from this review into the impact of early bereavement on health, and the recognition that bereavement is associated with increased cardiac risk, should provide an impetus for individuals to act on cardiac symptoms by seeking medical advice and for health care providers to monitor such individuals more closely. The results also provide a framework for future research directed at identification of the mechanisms of increased risk and potential future preventative strategies.

Acknowledgements

This work was supported by grants from the North Shore Heart Research Foundation and the Heart Foundation, Australia.

Conflict of interest: None declared.

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