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Posttraumatic Stress Disorder in the Wake of Heart Disease: Prevalence, Risk Factors, and Future Research Directions

HELLE SPINDLER, MSc, AND SUSANNE S. PEDERSEN, PhD

Background: There is increasing recognition that patients after a cardiac event may be at risk of posttraumatic stress disorder (PTSD). The present article reviews studies looking at PTSD as a sequel of heart disease with a focus on prevalence, risk factors, and future research directions. **Methods:** We conducted a search on PsychInfo and MEDLINE from 1980 to the present. Studies were included in the review if they looked at PTSD after a cardiac event, reported on the number of cases with PTSD, and had been published in English. **Results:** We identified 25 studies that fulfilled the inclusion criteria, of which 7 reported on the follow-up of previously published studies. The prevalence of PTSD after heart disease varied from 0% to 38% across studies. PTSD has been most rigorously researched after myocardial infarction with the best-powered studies finding a prevalence rate of 15%. Studies including control groups showed that cardiac patients were at risk of developing PTSD. Risk factors included sociodemographic and psychological characteristics and aspects related to the cardiac event. **Conclusion:** Despite substantial heterogeneity in the methodology of studies and differences in prevalence across studies, this review indicates that subgroups of patients are at risk of PTSD after a cardiac event. Future studies investigating PTSD as a sequel of heart disease should be more systematic, use a prospective study design with multiple assessments, and include sufficiently large samples. PTSD should not be ignored as a sequel of heart disease, given preliminary evidence that PTSD may be associated with nonadherence with medication and an increased risk of clinical adverse events. **Key words:** coronary artery disease, posttraumatic stress disorder, prevalence, risk, review.

CAD = coronary artery disease; **HT** = heart transplantation; **PTSD** = posttraumatic stress disorder; **MI** = myocardial infarction; **SCA** = sudden cardiac arrest; **CHF** = congestive heart failure; **CS** = cardiac surgery; **PCI** = percutaneous coronary intervention; **CABG** = coronary artery bypass surgery; **DSM** = Diagnostic and Statistical Manual.

INTRODUCTION

Coronary artery disease (CAD) is the most prominent cause of death in the Western world, but CAD may also lead to significant morbidity in patients who survive an initial cardiac event. Due to improvement in treatment options, the number of patients who survive a myocardial infarction (MI) has increased substantially; paired with an aging population, the burden of CAD is expected to increase significantly in the future, posing a major challenge to secondary prevention (1). However, despite advances in diagnosis and treatment of CAD, subgroups of patients may not benefit optimally from treatment, placing them at a higher risk for mortality and impaired health status (2–5). The identification of factors that influence the pathogenesis of CAD is therefore important for secondary prevention.

Posttraumatic stress disorder (PTSD) is one factor that has been identified as influencing the pathogenesis and progression of CAD (6,7). PTSD also composes a possible consequence of CAD (8–11). However, there is some debate whether PTSD should be considered an illness in its own right or whether it is a "fashionable" disorder that has appeared "out of sociopolitical ideas" (12,13).

A diagnosis of PTSD was first introduced in the *Diagnostic and Statistical Manual* (*DSM*) in 1980. In the *DSM Third Edition*, the stressor criterion was defined as "a recognizable stressor that would evoke significant symptoms of distress in almost anyone" (14). In the *DSM Third Edition Revised*, it was changed to "an event that is outside the range of usual human experience and that would be markedly distressing to almost anyone" (15). In both cases, focus was on the nature of the event, and cardiac events did not qualify as potential stressors, as they were not "outside the range of usual human experience." In the *DSM Fourth Edition* (16), medical illness was added explicitly as a qualifying event for PTSD, and the focus was widened to include the subjective perception of the event. This change in the diagnostic criteria for PTSD has made cardiac events more likely to fulfill the stressor criterion, which in turn may lead to an increase in the number of PTSD cases identified in studies of cardiac patients. In an empirical investigation of changes to the stressor criterion in DSM-IV, Breslau and Kessler (17) showed that 38% of PTSD cases were due to the addition of new qualifying events. However, the change in the stressor criterion does not imply that medical illness did not previously lead to PTSD symptoms in medical patients. It rather shows that the diagnostic system had not recognized that medical illness, including CAD, may be a sufficient stressor leading to PTSD.

PTSD is also a common comorbid disorder with depression. The impact of depression on prognosis in patients with established CAD has been studied extensively with depression being associated with a 2-fold increased risk of mortality (18,19). However, does the comorbidity between the 2 disorders and the considerable amount of literature on depression make it superfluous to study PTSD in its own right in cardiac patients? Pathophysiological studies have associated both depression and PTSD with increased secretion of corticotropin releasing factor; however, contrary to the pathophysiology in depression, this increased secretion is associated with hypocortisolemia in PTSD, indicating that the pathophysiology of the 2 disorders may be distinct (20). Another part of the answer to this question may be found in the treatment literature, as treating depression does not necessarily lead to improvement in PTSD symptoms, because conventional treatment of depression is not aimed at the core symptoms of

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PTSD. Moreover, risk factors may often act in synergy, affecting cardiac prognosis adversely (21). Hence, ignoring PTSD and only treating depression may have severe consequences for cardiac patients (21). For example, a recent study did not show any adverse effects of depression on clinical outcome and adherence with medication, but this was the case for PTSD (22).

The Current Review

Several recent reviews have looked at the relationship between medical illness and subsequent PTSD (8–10,23). However, these reviews are either very broad in their scope, incorporating such diverse areas as cardiac and vascular diseases, obstetrics and gynecology, intensive care unit treatment, cancer, and HIV (10), or narrow by focusing on one specific cardiac event, such as MI (8). This review seeks to expand on existing reviews by providing an up-to-date overview of the literature of studies on PTSD after cardiovascular disease with a focus on prevalence rates, risk factors, and future research directions.

We decided not only to focus on prevalence rates but also on risk factors, given that knowledge of risk factors is important in order to identify patients who may be at risk of PTSD with a chronic course. In addition, we included not only acute but also chronic cardiac events, such as congestive heart failure (CHF). Acute events may be more likely to lead to PTSD, but investigation of whether chronic conditions also comprise a risk factor for PTSD is important for secondary prevention. The risk to CHF patients of developing PTSD seems particularly important because CHF is an "emerging epidemic" due to an ageing population and the increase in the number of patients who survive an initial infarction (1). Moreover, CHF is the end stage of most heart diseases, and if an acute event, such as MI, can lead to PTSD, it seems likely that CHF may also be a risk factor. In addition, PTSD has been associated with an increased risk of nonadherence with medication (22), and nonadherence in heart failure is a risk factor for clinical adverse events (24).

METHODS

Identification of Studies for the Review

A literature search was conducted in the PsychInfo and MEDLINE databases (1980 to present) using the search terms *posttraumatic stress disorder*, *cardiovascular disorders*, *cardiovascular diseases*, *myocardial infarction*, *AMI*, *CHD*, *CAD*, *CABG*, *bypass*, *PTCA*, *percutaneous transluminal coronary angioplasty*, *angina pectoris*, *PCI*, *percutaneous coronary intervention*, *cardiac surgery*, *ICD*, *implantable cardioverter defibrillator*, *heart failure*, and *heart transplantation*. We also searched the reference lists of the identified studies by hand. However, this did not lead to the addition of further studies. No other hand searches were carried out. The first author carried out the computer search and the hand search. Criteria for inclusion in the review were as follows: (1) empirical study reporting on patients having had an MI, sudden cardiac arrest (SCA), cardiac surgery (CS), heart transplantation (HT), or CHF; (2) PTSD cases of the patients evaluated and reported as number of positive cases or as a prevalence rate; (3) study published in English. Due to time constraints, we did not contact authors, just as we did not use publications in languages other than English.

The search resulted in 109 hits in PsychInfo and 304 hits in MEDLINE. Examining all hits using the inclusion criteria, the first author reduced the number of studies to 25. Subsequently, both authors checked whether the 25 studies qualified for inclusion in the review. Seven of these 25 studies reported on the follow-up of previously published data, reducing the number of original studies to 18. An overview of the included studies is presented in Table 1. If the results of a study have been published in more than 1 paper, the papers are listed under the name of the first author of the first publication.

The identified studies were not suited for a meta-analysis, a more systematic review, or statistical weighting, given their heterogeneity in methodology, design, and the different time points used for assessing PTSD. Nevertheless, to the extent that it was possible, we attempted to adhere to the criteria used for the reporting of meta-analysis of observational studies in epidemiology (MOOSE) (25).

RESULTS

MI

Eleven studies were identified that looked at the prevalence of PTSD after MI. The prevalence rate in these studies varied from 0% (26) to 22% (27). Some studies incorporated only patients with a first MI, whereas other studies also included patients with multiple MIs. When looking at prevalence rates in patients with a first MI versus patients who had experienced several MIs, some differences emerge. Prevalence rates in the studies of first MI patients varied from 0% (26) to 22% (27), whereas in patients with multiple MIs, the prevalence rates varied from 8% (28) to 20% (22). One study presented data as to the temporal onset of PTSD and found that only 8% of their PTSD cases had delayed onset (29).

SCA

Four studies looking at the prevalence of PTSD in survivors of SCA were identified. The prevalence rate varied from 19% (30) to 38% (31); 19% was found in a study that assessed PTSD close to the index event (mean 9.6 months [range 3–18 months]) (30), whereas studies evaluating PTSD caseness >22 months found prevalence rates of 27% (32) and 38% (31). Although 3 studies found prevalence rates of a considerable magnitude, a case-control study looking at the risk of PTSD within various patient groups (extensive burns, spinal disorders, amputations, major chest trauma, heart failure, and cardiac arrest) did not identify SCA as a risk factor for PTSD (33).

CHF

Only 1 study has examined the risk of developing PTSD in CHF patients. CHF was associated with a 49% increase in the risk of PTSD in a case-control study of various patients groups (extensive burns, spinal disorders, amputations, major chest trauma, CHF, and cardiac arrest) (33). However, the study was conducted in a veteran population, which limits the ability to generalize the results.

CS

Four studies were identified that looked at PTSD following CS (ie, coronary artery bypass grafting, aortic valve replacement, and cardiac valve replacement). One study focused on children aged 5 to 12 scheduled for CS due to congenital heart disease (34). The prevalence rates of these studies varied from 8% (28) to 18% (35), with the congenital heart disease population showing a prevalence of 12% (34). Two of the studies

TABLE 1. Studies of the Prevalence of PTSD in Various Cardiac Populations

Study	Design	Population	Diagnostic Groups	Evaluation of PTSD Status	Prevalence	Risk Factors
Myocardial infarction						
Doerfler et al. (1994) 28	Cross-sectional Mean time since event 14 [6 to 18] mo	50 ♂ 27 MI 23 CABG	MI or CABG	RI score and an algorithm based on *DSM III-R* criteria using IES, IDD, and TAS	8% Had PTSD = 4 cases (18% = 9 pts >7 on RI)	—
Kutz et al. (1994) 29	Retrospective Mean time since event 6 to 18 mo	100 Post-MI pts 88 ♂; 12 ♀	MI	PTSD inventory adapted to MI and based on *DSM III* criteria	25% Had PTSD; 9 cases of acute PTSD had remitted at the time of evaluation; 16% had chronic PTSD	Ethnic origin; prior MI or cardiac hospitalization; prior PTSD; subjective expectation of incapacitation
Van Driel et al. (1995) 26	Prospective Mean time since event 22 to 26 mo	23 Pts 14 ♂; 9 ♀	First MI	Two evaluations of PTSD 1.1 to 2 weeks after admission SCID-R PTSD 2.22 to 26 mo SCID-R PTSD diagnosis according to *DSM III-R*	First year 4% = 1 case had probable partial PTSD Second year 0 cases; 8 reported distress during the first year; none by the second year	—
Bennett et al. (1999) 43	Cross-sectional Mean time since event 9.24 [6 to 12] mo	44 Pts 30 ♂; 14 ♀	MI	Mailed PDS questionnaires (part 3) adapted to MI	10.75% Had PTSD = 4 cases (PDS > 23)	Younger age; alexithymia; awareness of the event as MI
Bennett et al. (2001) 54	Longitudinal Mean time since event 3 mo	70 Pts 52 ♂; 18 ♀ 39 completed the study	First MI	PDS (part 3)	3% Had PTSD = 3 cases with PDS scores >23	Negative affect while in hospital; feeling terrified at the time of MI; dissociation at the time of event
Shemesh et al. (2001) 46	Prospective study Time since event 6 mo	102 Pts 81 ♂; 21 ♀	Recent MI	IES (adapted to MI)	9.8% Had PTSD = 10 cases; 40% had above threshold avoidance = 41 cases; 11.8% had above threshold intrusion = 12 cases	—
Bennett et al. (2002) 44	Prospective Mean time since event 3 mo	89 Pts 69 ♂; 20 ♀ 75 pts completed the study	MI	PDS (part 3, referring to most recent MI)	16% Had PDS-scores >23	Initial intrusion and avoidance symptoms; negative affect, lack of social support; dissociation at MI
Ginzburg et al. (2002, 2003, 2004) 42, 45, 47	Prospective Mean time since event: time 1: 3.45 days; time 2: 7 mo	116 Pts 94 ♂; 22 ♀ 72 healthy matched controls	MI	PTSD inventory combined with *DSM IV* criteria	Time 1, 18% had ASD = 21 cases; time 2, 16% had PTSD = 18 cases; 28% had subclinical PTSD = 33 cases	Subjective perception of threat predicted severity of ASD and PTSD symptoms; ASD; severity of ASD added to severity of PTSD; perceived severity of MI; non-repressive coping style

(*Continued*)

TABLE 1. Continued

Study	Design	Population	Diagnostic Groups	Evaluation of PTSD Status	Prevalence	Risk Factors
O'Reilly et al. (2004) 30	Case-control Mean time since event 9.6 [3 to 18] mo	27 SCA; 27 MI with no SCA	First SCA or MI without SCA with successful resuscitation in-hospital	SCID, PDS, and IES	According to SCID, 19% in the SCA group had PTSD = 5 cases; 7% in the MI-group had PTSD = 2 cases	—
Pedersen et al. (2003, 2004) 27, 48	Prospective Time since event: time 1: 4 to 6 weeks; time 2:9 mo	Time 1: 112 pts 79 ♂; 33 ♀ 115 healthy controls Time 2: 102 pts	First MI	PDS (adapted to MI)	Time 1: 24% (22%[a]) of patients had PTSD = 25 cases; 7% of controls had PTSD = 8 cases; time 2: 14% had PTSD	Lack of social support; depression; neuroticism
Shemesh et al. (2004) 22	Prospective Time since event 6 mo	65 Pts	MI 6 mo before enrolment	IES (adapted to MI)	20% Reported above threshold on the IES = 13 cases	—
Sudden cardiac arrest[b]						
Ladwig et al. (1999) 31	Prospective Mean time since event 39 mo [22 to 64]	21 Pts 17 ♂; 4 ♀ Comparison group of 35 pts with severe angina pectoris at rest	SCA with successful resuscitation	IES score >50% was considered positive PTSD status	38% Had PTSD = 8 cases	Lack of sedation during resuscitation increased the risk of PTSD
Gamper et al. (2004) 32	Prospective Mean time since event 45 mo [24 to 66]	143 Pts	SCA in or out of hospital and discharged with favorable function	Davidson Trauma Score	27% Had PTSD = 39 pts with scores >40	Younger age
Heart failure						
Martz et al., (2001) 33	Retrospective, case-control	2325 Veterans with PTSD Control group 42,995 veterans without PTSD	Amputation, heart failure/shock, major chest trauma, cardiac arrest, extensive burns, spinal disorders	Diagnosis of PTSD in hospital database	5.13% Of the total sample of veterans had a diagnosis of PTSD; heart failure patients had a 49% increase in risk of developing PTSD	Extensive burns, spinal disorders, amputations, major chest trauma, heart failure/shock
Cardiac surgery[c]						
Stoll et al. (2000) 63	Cross-sectional Median time since event 20 [18 to 26] weeks	80 Pts 51 CABG z 29 AVR Control groups I: pts after major maxillofacial surgery II: Healthy Ss	CABG or AVR	Mailed PTSS-10 questionnaires	15% Had PTSD = 12 pts with PTSS-10 scores >35	—
Connolly et al. (2003) 34	Prospective Measures taken 1 to 3 days before event and 4 to 8 weeks after discharge	43 Child pts 5 to 12 yr	Children scheduled to undergo cardiac surgery	DISC	Before surgery: no cases of ptsd; after surgery: 12% had PTSD = 5 cases	Spending more than 48 h in the ICU

(*Continued*)

TABLE 1. Continued

Study	Design	Population	Diagnostic Groups	Evaluation of PTSD Status	Prevalence	Risk Factors
Schelling et al. (2003) 35	Prospective Measures were taken the day prior to event, 1 week, and 6 mo after	148 Pts	CABG or CVR	PTSD status was evaluated using a previously validated questionnaire based on the criteria of *DSM IV*	Before surgery: 7 cases of PTSD; after surgery (6 mo) 18.2% had PTSD = 27 cases	—
Heart transplantation						
Dew et al. (1996, 1999, 2000, 2001) 36–39 and Stukas et al. (1999) 40	Prospective Mean time since event 12 and 36 mo	145 To 191 pts, 142 caregivers	HT patients that survived 6 weeks after surgery	SCID interview (*DSM-III-R*) on transplant-related PTSD	Cumulative risk of PTSD at 7 mo: 9.6%; 12 mo: 15.6%; 36 mo: 17%; caregivers: 12 mo: 7.7% definite PTSD, 12% probable PTSD	Personal positive psychiatric history, gender, length of hospitalization, social support, friend support, family cohesion, sense of mastery, self-esteem[d]

ASD = acute stress disorder; AVR = aortic valve replacement; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CVR = cardiac valve replacement; DISC = Diagnostic Interview Schedule for Children; DTS = Davidson Trauma Score (based on *DSM-IV* criteria); HF = heart failure; HT = heart transplant; IES = Impact of Event Scale; MI = myocardial infarction; PDS = Posttraumatic Diagnostic Scale (based on *DSM-IV* criteria); PTSD = posttraumatic stress disorder; PTSS-10 = Post-Traumatic Stress Syndrome 10-Questions Inventory (based on *DSM-III* criteria); RI = Reaction Index; SCA = sudden cardiac arrest; SCID = Structured Clinical Interview.

[a] Twenty-two percent of the original population of 112 patients had PTSD at time 1; however, when prevalence rates for time 1 and 2 were calculated at time 2, the population had decreased to 102 patients, and therefore the prevalence rate of PTSD at time 1 changed to 24%.

[b] O'Reilly et al. (2004) and Martz et al. (2001) are also relevant in relation to SCA.

[c] Doerfler et al. (1994) is also relevant for studies of CS.

[d] Some of these factors relate to psychiatric disorders in general and not specifically to PTSD. In addition, some results stem from a pooled population of patients and caregivers.

were cross-sectional with PTSD caseness being assessed relatively soon after CS (range, 4.5–12 months), and 2 were prospective, with PTSD caseness being assessed before and relatively soon after CS (range, 1–6 months); no information was available on the prevalence of PTSD beyond 12 months.

Heart Transplantation (HT)

We only found 1 study that looked at PTSD in relation to HT, but this study was prospective and evaluated the prevalence of PTSD at several time points (36–40). The prevalence rates varied from 10.8% (40) to 15.8% (37). The cumulative prevalence rates at 7, 12, and 36 months post-HT were 9.6%, 15.6%, and 17%, respectively (39). It is noteworthy that after 12 months, only 1 new case of PTSD was identified, suggesting that late onset is rare.

The Puzzle of Risk Factors

Kutz and colleagues (29) were the first to report on risk factors for the development of PTSD in the aftermath of MI. Subsequent studies have identified personality traits (27,41,42), sociodemographic factors (eg, age, female sex, and ethnic origin) (29,32,38,40,43), lack of social support (39,40,43,44), previous psychiatric history (39), prior traumatization (29), dissociative symptoms and acute stress disorder at the time of MI (42,44,45), and aspects related to the cardiac event (eg, the subjective perception of life threat and severity of MI, awareness of having a cardiac event, and anticipated incapacitation after MI) (22,29,45,43) as potential risk factors for the development of PTSD in cardiac patients (Figure 1).

DISCUSSION

The methodology of the presented studies varies considerably, making comparisons across studies difficult. Hence, the difference in the prevalence rates of PTSD, together with risk factors identified in the current review, is likely to be attributed to this heterogeneity. Nevertheless, the available studies suggest that it is relevant to study PTSD in relation to CAD, in particular given preliminary evidence that PTSD may lead to nonadherence with medication and adverse clinical outcome (22,46).

The most conclusive evidence comes from the study of MI patients. Of note, PTSD has also been most rigorously researched in MI patients. In general, the best-powered studies found a prevalence rate ranging from 10% (46) to 16% (42,45,47) 6 to 7 months after the index event and a prevalence of 24% and 14% in patients with a first MI at 4 to 6 weeks and 9 months, respectively (27,48). As late onset is rare (29), taken together these studies suggest a prevalence rate of around 15% in MI patients, allowing for a period of remission.

Results from studies of other cardiac conditions must be considered inconclusive, given the paucity of studies available. Similarly, our knowledge of risk factors for the development of PTSD in cardiac patients is sparse. Although several risk factors have been identified, these factors have been investigated in an unsystematic fashion.

In order to advance our knowledge of PTSD in relation to CAD, future studies need to be conducted in a more systematic and methodologically sound fashion. Particular methodological issues influencing the prevalence rate pertain to the time of assessment of PTSD, the choice of instrument (eg, diagnostic interview versus self-report), the nature of the cardiac event, which parameters (eg, demographic, social, clinical, or aspects related to the event) are assessed, and the power of the study.

Hence, future studies should be prospective and include multiple assessments of PTSD. This would provide us with more information about the natural course of PTSD in cardiac patients and which patients may be at risk of chronic PTSD. This is particularly important, given that PTSD symptoms may remit spontaneously, as demonstrated in a recent prospective study of first MI patients (48). Moreover, a study of patients undergoing percutaneous coronary intervention found that depression at 1 month was a better predictor of depressive symptoms at 6 months compared with depression assessed at the time of the index event (49).

Second, studies need to be sufficiently powered. With a small sample size, the risk of obtaining a selected group of patients is higher, in turn leading to a deflated or an inflated prevalence rate. In the studies identified in this review, the sample size varied from 23 (26) to 191 patients (38,39), with

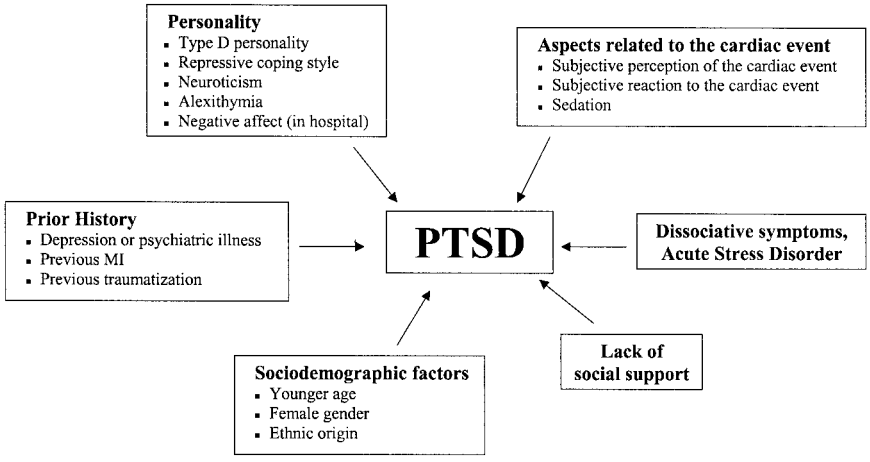

Figure 1. Risk factors for PTSD in cardiac patients

the study based on 23 patients identifying no cases of PTSD. In order to increase power, patients with different cardiac diagnoses have been pooled, but this may obscure the fact that the type of cardiac event may influence the prevalence of PTSD. O'Reilly and colleagues (30) compared the prevalence rate between 2 diagnostic groups (27 SCA and 27 MI patients) and found the prevalence to differ by 12%. Although this difference was not statistically significant, this may be due to reduced power. Therefore, pooling of small groups of patients with different cardiac diagnoses is questionable unless a post hoc power analysis is performed. To date, there is no conclusive evidence that the prevalence rate in cardiac populations is the same regardless of diagnostic group. In fact, it would seem plausible that an acute event, such as MI, may lead to a higher prevalence rate than, eg, valve replacement.

Third, the choice of instrument should be weighed carefully as this may also influence the prevalence rate. O'Reilly and colleagues (30) compared the Posttraumatic Diagnostic Scale (50) with the structured clinical interview and found a correspondence of 0.39, as measured by Cohen's κ. Foa and colleagues (50) found a better correspondence ($\kappa = 0.65$), but their study was not conducted in cardiac patients. By nature, cardiac events are different from other kinds of trauma, with cardiac events being oriented toward the future, contrary to general traumatic events that are oriented toward the past. Hence, it has been suggested that measures used for diagnosing PTSD in general trauma populations may not be appropriate in cardiac populations (23). Although self-report measures are often favored in empirical research as they are less time consuming, future research should consider the implications of choosing a self-report measure over a diagnostic interview—the gold standard—and whether this self-report measure has been validated in cardiac patients.

Fourth, it is important to note that the prevalence rate of PTSD in cardiac patients cannot be considered in isolation but needs to be weighed against the prevalence rate in the general population. Given that it is costly to conduct epidemiological studies, this information may not always be available. Epidemiological studies have mainly been carried out in the United States, finding a prevalence rate of 7.8% (51). Although informative, this prevalence rate may not generalizable to European populations. An alternative is to compare the prevalence rate in cardiac patients with that of a healthy matched control group. In a study by Pedersen and colleagues (27), first MI patients were above a 3-fold increased risk of developing PTSD compared with healthy controls. This confirms that cardiac patients are at increased risk of PTSD compared with the general population.

Fifth, when studying risk factors for the development of PTSD, current evidence suggests that several factors, including sociodemographic factors (29,32,38,40), social support (39,40,43,44), prior traumatization (29), previous psychiatric history (39), aspects related to the cardiac event (26,29,45,41), and personality may lead to the development of PTSD. Personality may be a particularly important explanatory factor of individual differences in risk, as the *distressed* (Type D) personality has been associated with a 4-fold increased risk of PTSD in first MI patients and controls (41). Type D is defined as the tendency to experience increased negative emotions paired with the nonexpression of these emotions in social interactions. Type D is an emerging prognostic risk factor in CAD that has been associated with adverse prognosis independent of established biomedical risk factors (52,53). We would suggest that future studies attempt to include the majority of these potential risk factors using the same definitions, as this would lead to a systematic investigation of the role of these factors in the development of PTSD. Although potentially informative, the use of ad hoc measures that appear similar but may not be, eg, awareness of having an MI (54) and subjective perception of life threat (42), restricts comparison across studies. Furthermore, it will also be informative to investigate whether risk factors have an additive or a synergistic effect (21).

Sixth, future studies should take into account clinical risk factors, including disease severity and previous (multiple) cardiac events, as they may serve as confounders for PTSD. Although perceived severity rather than severity of the MI as determined by objective clinical criteria has been found to be predictive of subsequent PTSD (45), this needs to be replicated in other studies.

Finally, focusing on PTSD symptomatology may be of equal importance to focusing on caseness, given that partial PTSD also result in significant distress. For example, Dew and colleagues (36) found that 73% of HT patients not diagnosed with PTSD reported multiple PTSD-like symptoms, such as intrusive thoughts. In turn, distress has been associated with adverse health status and prognosis in cardiac patients (2,52,55).

Consequences and Potential Mechanisms

There is increasing evidence that PTSD may have detrimental consequences for the health of cardiac patients. PTSD has been shown to lead to impairments in social functioning, vitality, physical health, and health status (45), increased psychological distress (56), and adverse prognosis (22,37,46). This suggests that PTSD may be a risk factor on par with depression, and given their comorbidity, this would seem plausible. The impact of depression on prognosis has been researched extensively in cardiac patients, and depression has been shown to be a sequel of CAD but also to confer an increased risk of mortality and nonfatal MI (2,18,19,47). Depression has gained status as a risk factor alongside biomedical risk factors (57), and hence it is not surprising that the search for mechanisms explaining the link between depression and cardiovascular prognosis is much further than that for PTSD and CAD.

To our knowledge, only 2 studies in patients with established CAD have investigated which mechanisms may explain the link between PTSD and adverse cardiac prognosis. Shemesh and colleagues (22,46) found that PTSD was associated with nonadherence with medication, in turn rendering patients at risk of adverse clinical events. Ingestion of medi-

cation may serve as a reminder of the trauma, ie, the cardiac event. Kario and colleagues (58) identified cardiovascular reactivity to stress and hemostatic factors as other potential pathways. Although they investigated changes in cardiovascular risk factors in outpatients with hypertension after an acute traumatic event rather than in patients with established CAD, hypertension is a risk factor for incident CAD. A recent review on cardiovascular effects of acute mental stress also suggests that increases in heart rate, blood pressure and arrhythmias, coagulation abnormalities, endothelial dysfunction, and platelet activation may comprise potential pathways (59). Some of these pathways have also been confirmed in the general PTSD literature (60,61) and are incorporated in the "allostatic load model." This model posits that PTSD presents an imbalance in the allostatic systems that usually help the body adapt to a variety of challenges (62). Chronic PTSD carries with it psychobiological demands, such that the body must find new steady states in which to maintain its vital functions. These new states represent an accommodation to stress, but they also result in sustained activity that places an excessive load on the allostatic systems due to chronic over- or underactivity. In turn, this may result in pathophysiological changes and eventually an increased risk of medical illness (62).

Besides the consequences to the individual patient, PTSD in relation to cardiac disease may also have consequences for society in general in terms of increased health-care consumption (7). However, recently it has been shown that although PTSD alone and in combination with depression led to increased use of health services, this use was not of an inappropriate nature (6).

CONCLUSIONS

Patients with CAD are at increased risk of PTSD, with a prevalence rate of around 15% in MI patients. Despite a surge in research investigating the link between PTSD and medical illness in general, and heart disease in particular, there is an urgent need for sufficiently powered and systematically conducted prospective studies that look at the clinical course of PTSD and its prognostic consequences for patients with established CHD. A clarification of which risk factors lead to the development of PTSD, which risk factors sustain this condition, and their relative impact would also provide us with a better understanding of the pathogenic pathways of PTSD. In turn, this would lead to better risk stratification in research and clinical practice. Nevertheless, until such information is available, PTSD as a sequel of CAD should not be ignored in clinical practice, given its impact on psychological distress, health status, and preliminary evidence, suggesting that PTSD leads to adverse prognosis and nonadherence with medication.

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