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### Interview-Based Ratings of Somatic and Cognitive Symptoms of Depression and Their Impact on Cardiovascular Prognosis

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Evidence indicates that self-reported somatic/affective but not cognitive/affective symptoms of depression are highly prevalent in cardiac patients [1], and are predictive of cardiovascular mortality and cardiac events, even after somatic health status has been controlled for [2, 3]. Recently, these findings were replicated in 2 independent samples of post-MI (myocardial infarction) patients [4, 5] and in patients with chronic heart failure [6]. These findings may help to develop symptom-targeted interventions to reduce both depression and cardiac disease progression. However, one major disadvantage of the analyses conducted so far is that they relied on self-report instruments, such as the Beck Depression Inventory. A drawback of self-reported depressive symptoms is that no weighing of symptoms is performed, as is carried out when establishing a psychiatric diagnosis with a structured interview. In the latter, symptoms only count when they are present most of the time, for at least 2 weeks, affect daily functioning and are not a consequence of a physical condition. As a result, it remains unclear to what extent findings using self-reported symptoms reflect clinically meaningful information.

We therefore evaluated the independent association between cardiovascular prognosis and ratings of the individual depressive symptoms based on a structured diagnostic interview. We used data from the Depression after Myocardial Infarction study (DepreMI), a naturalistic follow-up study which took place in 4 hospitals in the northern part of the Netherlands [7]. The study included 468 MI patients, of whom 118 met DSM-IV criteria for post-MI depressive disorder, and 115 had a cardiac event during a mean follow-up of  $2.5 \pm 0.8$  years. We used an adapted version of the Composite International Diagnostic Interview (CIDI) version 1.1, a fully standardized psychiatric diagnostic interview that can be used to assess mental disorders according to the definitions and criteria of DSM-IV [8]. The CIDI is recommended for epidemiologic research that requires diagnostic measures of depression and for which the time and resources to diagnose depression are available [9]. A specific advantage of the version used in the DepreMI study is that each individual symptom of depression was assessed in all participants, in contrast with most psychiatric interviews, which terminate the depression section when no core symptoms of depression are present.

Based on our previous work, we computed sum scores for the presence of cognitive symptoms (lack of interest, depressed mood, worthlessness, concentration problems, suicidal ideation; score range 0–5) and somatic symptoms (sleeping difficulties, fatigue, appetite problems, psychomotor changes; score range 0–4). Cox regression analyses were conducted to evaluate the associations of the somatic and cognitive sum scores with the risk of subsequent cardiovascular events. To further pinpoint the potential effects, the association of each individual depressive symptom with prognosis was evaluated on an explorative basis. In univariate analyses, interview ratings of somatic symptoms were found to be associated with poor cardiovascular prognosis (HR = 1.28;  $p = 0.002$ ), while ratings of cognitive symptoms were not (HR = 1.11;  $p = 0.102$ ). After adjustment for confounders (age, gender, left ventricular ejection fraction, history of MI, Killip class, history of diabetes, anterior site of MI, smoking, hypertension, dyslipidemia and BMI), both somatic and cognitive symptom ratings were found to be associated with adverse cardiac outcome (HR = 1.38,  $p < 0.001$  and HR = 1.19,  $p = 0.014$ , respectively; table 1). Multivariate analyses revealed the following somatic depressive symptoms to be significantly associated with cardiovascular events (ranked by HR): psychomotor agitation/retardation, fatigue and appetite problems. Importantly, 2 cognitive depressive symptoms were also significantly associated with cardiovascular events: lack of interest and suicidal ideation (table 1).

Thus, using symptom-specific data from a structured diagnostic interview, the following findings were obtained. First, we confirmed that, after adjusting for potential confounders, the presence of somatic symptoms of depression was associated with an increased risk of cardiovascular events. Second, in contrast with previous studies using self-report data, interview ratings of cognitive symptoms of depression were also associated with a significantly increased risk in multivariate analysis, although less strongly than somatic symptoms (HR = 1.20 and 1.39, respectively). Third, contrary to previous studies, adjustment for potential confounders resulted in higher effect estimates, while generally in studies using self-report data adjustment leads to lower estimates.

These discrepancies may be explained by the fact that interview-based symptoms are based on strict criteria derived from the DSM, based on their presence, severity, consequences and etiology. This may result in less attenuation of the estimates by potential confounders compared to self-report data. The use of interview-based measurement may be more sensitive in detecting clinically relevant cognitive symptoms, and it is possible that these clinically relevant cognitive symptoms result in a higher level of cardiotoxicity.

The recent distinction between somatic and cognitive symptoms supports the conceptualization of depression as a heterogeneous syndrome, in which some symptoms are more related to cardiovascular prognosis than others. It is possible that, in order to improve cardiovascular outcome, interventions for depression should be directed at specific depressive symptoms. Cognitive symptoms have been specific targets for intervention in psychotherapy, while exercise interventions (for example) may improve

**Table 1.** Association of specific depressive symptoms with cardiac death or events

	Univariate model 1		Multivariate model 2 <sup>1</sup>	
	HR and 95% CI	p	HR and 95% CI	p
<i>Somatic symptoms</i>				
Psychomotor agitation/retardation	1.91 (1.29–2.83)	0.001	2.14 (1.44–3.20)	<0.001
Fatigue	1.47 (1.00–2.16)	0.049	1.89 (1.26–2.83)	0.002
Appetite problems	1.51 (1.04–2.19)	0.031	1.49 (1.01–2.21)	0.047
Sleeping difficulties	1.12 (0.77–1.64)	0.560	1.21 (0.81–1.80)	0.356
Sum score	1.28 (1.10–1.50)	0.002	1.38 (1.18–1.62)	<0.001
<i>Cognitive symptoms</i>				
Lack of interest	1.63 (1.11–2.39)	0.014	1.66 (1.11–2.48)	0.015
Suicidal ideation	1.35 (0.91–2.01)	0.135	1.54 (1.00–2.37)	0.048
Worthlessness	1.36 (0.90–2.07)	0.159	1.33 (0.86–2.07)	0.198
Concentration problems	1.13 (0.77–1.65)	0.539	1.36 (0.89–2.08)	0.158
Depressed mood	0.94 (0.64–1.39)	0.769	1.06 (0.69–1.63)	0.778
Sum score	1.11 (0.98–1.25)	0.102	1.19 (1.04–1.36)	0.014

<sup>1</sup>Included confounders age, gender, left ventricular ejection fraction, history of MI, Killip class, history of diabetes, anterior site of MI, smoking, hypertension, dyslipidemia, and BMI as covariates.

somatic symptoms in particular. However, cognitive-behavioral therapy potentially affects both cognitive and somatic symptoms, with some variation due to different foci of attention (e.g. behavioral activation vs. cognitive therapy). The specificity with which specific depressive symptoms could be targeted with standard interventions is unclear, but might have important implications for improving cardiovascular prognosis.

In conclusion, when using a structured diagnostic interview, both somatic and cognitive symptoms of depression were associated with adverse cardiac outcome after adjusting for potential confounders. In contrast to previous studies, the findings were actually strengthened in the multivariate model. As yet, cognitive symptoms of depression cannot be simply discarded as risk factors for heart disease progression. Rather, we argue that for a better understanding of the association between depression and cardiovascular disease progression, a more thorough assessment of depressive symptoms is needed by using interview-based ratings in addition to self-report data.

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