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The symptom profile of vascular depression

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SUMMARY

Objectives Vascular depression is regarded as a subtype of depression, especially in—but not limited strictly to—older persons, and characterized by a specific clinical presentation and an association with (cerebro)vascular risk and disease. It is also known that depression is a risk factor in the development of myocardial infarction. The possibility of identifying depressed subjects at risk of a first cardiac event by their clinical presentation in general practice would have significant implications.

Methods We studied the baseline depression symptom profiles of subjects in the Longitudinal Aging Study Amsterdam and compared the profile of depressed subjects who had and had not suffered a first cardiac event at a follow-up after eight years.

Results We could not confirm the specific symptom profile in depressed subjects who suffered from a first cardiac event at follow-up. Most notably, the presumed specific symptoms of vascular depression, psychomotor retardation, and anhedonia were not significantly associated with the occurrence of a first cardiac event at follow-up.

Conclusions In this large community study we failed to identify a difference in the depression symptom profile between incident cardiac and non-cardiac cases.

KEY WORDS — depression; myocardial infarction; vascular risk; symptom profile; 'vascular depression'

INTRODUCTION

Depression is a risk factor for cardiac disease and cardiac mortality in the elderly (Carney *et al*., 1988; Frasure-Smith *et al*., 1993). The precise nature of this relationship is still unclear. Some have postulated that the depression is a first sign of diminished vitality and thus of cardiac failure. These depressions thus would be among the first signs of vascular disease or impending myocardial dysfunction and therefore could be entitled 'vascular depressions'. Krishnan and Alexopoulos revitalized the concept of vascular depression in the 1990s (Alexopoulos *et al*., 1997a, 1997b; Krishnan *et al*., 1997). According to them, clinical characteristics of this depression include more pronounced psychomotor retardation, anhedonia, greater overall cognitive impairment and physical disability, fewer feelings of guilt, and greater lack of insight. Furthermore, non-psychotic symptoms prevailed whereas a family history of mental illness and especially affective disorder was less common. Both Alexopoulos and Krishnan conducted their studies in hospital-based settings that limit generalization to the general population. We have analyzed two large community samples and found no specific association of cerebrovascular risk factors (CVRFs) and depression subtypes in the general population (Naarding *et al*., 2007). The clinical importance of recognizing vascular depression when it precedes cardiac events is obvious. If a simple test or risk-profile, for example, a specific set of symptoms, could identify depressed subjects at increased risk for cardiac events, this would be of major importance in predicting the course of illness and the effect of medication and other

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therapeutic interventions. In this study, our aim was to assess these phenomenological characteristics of depressed subjects in the general population and compare those who had and had not suffered a first cardiac event at an 8-year follow-up. We assumed subjects to have suffered from arteriosclerosis in the years preceding myocardial infarction and that they thus could suffer from a 'pre-myocardial' depression as a variant of vascular depression. We tested the hypothesis that subjects who had suffered a first cardiac event during follow-up would show more anhedonia and psychomotor retardation, and less feelings of guilt as part of their depression at baseline.

METHOD

Subjects and procedures (Figure 1)

Data from the Longitudinal Aging Study Amsterdam (LASA) was used in our study. The sampling and data collection procedures have been described elsewhere (Beekman *et al*., 2002; Deeg *et al*., 2002). In short, the population base for LASA included individuals in the 55–84 age brackets drawn from the census records of 11 municipalities in The Netherlands. The study sample was stratified by age and sex and corresponded to the population in terms of geographic dispersion. The LASA study makes use of a sample first approached for the NESTOR-LSN study (response rate 62.3%). From the 3,677 eligible participants 3,107 (response rate 81.7%) took part in the LASA study and were interviewed every 3 years during home visits by lay interviewers who received a training program and were regularly supervised. Information on psychiatric symptoms, demographic and medical status, previous history and family history was gathered.

The local Medical Ethics Committee approved the study and informed consent was obtained from all participants according to prevailing Dutch law.

For this analysis, only subjects with no cardiac condition at baseline were included ($n = 2{,}433$). Baseline depression data was missing in 30 of these, and from the remaining 2,403 subjects 323 were screened positive for depression. These subjects were followed to assess first cardiac events in the following 8 years.

Psychiatric evaluation

In the LASA study, depression diagnosis was assessed in a two-step procedure. First, a screening was performed with help of the Dutch version of the Center for Epidemiological Studies Depression Scale (CES-D, Radloff, 1997). We used a score of 16 as a cutoff to indicate relevant depressive symptoms, and in our further analysis we used this group as 'depressive cases'. This cutoff had a very high sensitivity for major depression in the elderly (Beekman *et al*., 1997). CES-D items can be summarized into four different subscales: 'positive affect', 'depressed affect', 'somatic-retarded activity' and 'interpersonal affect'. On each of these subscales a total score can be achieved. CES-D positive subjects

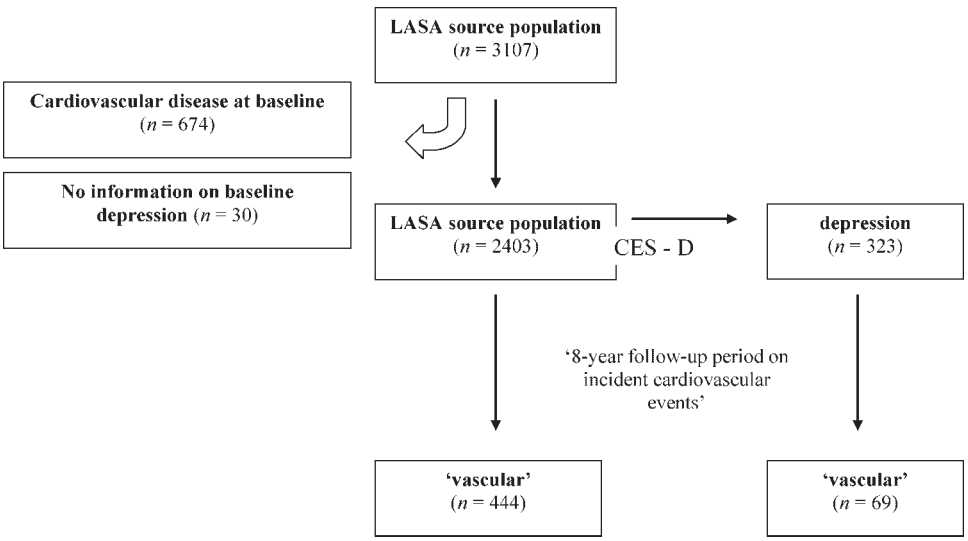

Figure 1. Flow-chart study symptom profiles vascular depression.

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were approached for a diagnostic interview, based on the National Institute of Mental Health Diagnostic Interview Schedule (DIS), to obtain a DSM-III-R diagnosis of major depression (APA, 1987). In our 2,403 subjects, 323 (13.4%) were screened positive as measured by the CES-D. Forty-one of them were diagnosed as suffering from a major depression with help of the DIS, the other 282 were diagnosed as 'sub-threshold depression'. In our further analysis on symptom profiles, scores on the CES-D were used.

Vascular disease

All first cardiac events were considered in this analysis, either fatal or non-fatal. Ischemic cardiac events were defined as fatal or non-fatal myocardial infarction or angina pectoris. Onset of cardiac disease was established during 6 years at 3 yearly intervals by interviews, enhanced by information obtained from the records of the subjects' general practitioners (GPs) and data on the use of cardiac medication.

Using death certificates from the Netherlands Central Bureau of Statistics, all cardiac deaths that occurred between the baseline interview and 1 January 2000, were recorded. Details on the procedure on establishing death cause and cardiac disease are described elsewhere (Bremmer, 2006). For our analysis we identified those subjects that were suffering from depression at baseline and had developed cardiac disease or died of cardiac failure by the time of the follow-up. Those subjects suffering from depression at baseline but with no cardiac disease or who died of non-cardiac-related disease were considered to be the control-group.

Other variables

Sociodemographic factors (age, sex, educational level and marital status), cognitive functioning [score on the MiniMentalStateExamination (Folstein *et al*., 1975)] and the use of antidepressant medication or benzodiazepines were included as potential confounding variables. Disability was assessed by asking respondents whether they experienced difficulties with daily activities, using a set of nine items from the OECD scale (van Sonsbeek, 1988; Verbrugge *et al*., 1999). We combined these items into a single item: 'disability'. Subjects suffering no difficulties at all or who could perform more than two ADL activities scored 0, and subjects only able to perform one item or who experienced difficulties with all categories, scored 1. This was called the disabled group.

Statistical analysis

For statistical analysis we used the Statistical Package for the Social Sciences (SPSS) for Windows version 12.0. Chi-square analysis was used to compare categorical variables and the independent samples *t*-test to compare continuous variables. Prevalence of major and sub-threshold depression was established for the vascular and the non-vascular group and also the mean total score on the CES-D. Prevalence of all individual depressive symptoms was calculated for both the vascular and non-vascular groups.

RESULTS

General characteristics of the study groups

In the study sample of 323 subjects who were diagnosed as being depressed at baseline, at follow-up after 8 years, new cardiac events were reported in 69. These were the cases in our study; the control-group thus consisted of the remaining 254 subjects who were depressed at baseline but who did not suffer from any cardiac event in the subsequent 8 years (control group). Baseline data are given in Table 1.

Clinical profile of pre-myocardial infarction depression

The prevalence of CES-D depressive symptoms in both the cardiac event and the control group is shown in Table 2. Only one symptom, concentration disturbances (item 5, 'mind'), was more frequent in the vascular than in the control group. The aspects suggested to be specific for vascular depression—increased anhedonia and psychomotor retardation—were not more prevalent in the vascular, 'pre

Table 1. Baseline characteristics of vascular and non-vascular depression

	Vascular Depression (n = 69)	Non-vascular Depression (n = 254)	P
Mean age	73.2 (8.2)	70.6 (8.9)	0.028
% Female	66.7	66.9	0.537
Mean educational years	2.9 (2.0)	3.2 (1.9)	0.266
Antidepressant use (%)	11.7	6.1	0.152
Diagnosis MDD (%)	17.4	11.4	0.220
Disability (%)	50.7	39.8	0.130
Mean MMSE score	25.1 (4.9)	25.8 (4.7)	0.265
Mean CES-D score	23.1 (7.2)	22.5 (7.5)	0.498

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Table 2. Depressive symptoms in vascular and non-vascular depression

	Vascular Depression (n = 69)	Non-vascular Depression (n = 254)	*P*
CES-D item:			
1 (bothered)	42.0	42.1	0.988
2 (appetite)	13.0	16.5	0.481
3 (blues)	39.1	37.4	0.793
4 (good/positive)	52.2	51.6	0.930
5 (mind)	**37.7**	**24.8**	**0.034**
6 (depressed)	34.8	32.3	0.695
7 (effort)	44.9	44.5	0.948
8 (hopeful/positive)	14.5	13.4	0.812
9 (failure)	15.9	10.2	0.187
10 (fearful)	11.6	15.0	0.478
11 (sleep)	53.6	48.0	0.410
12 (happy/positive)	20.3	20.1	0.969
13 (talk)	27.5	18.9	0.117
14 (lonely)	31.9	31.5	0.951
15 (unfriendly)	4.3	4.3	0.995
16 (enjoy/positive)	20.3	16.9	0.516
17 (cry)	14.5	20.5	0.263
18 (sad)	30.4	31.9	0.818
19 (dislike)	11.6	6.7	0.177
20 (get going)	44.9	40.6	0.513

The bold entry accentuates the only factor in the table with a *p*-value < 0.05.

myocardial infarction' group and the guilt aspect, hypothesized to be less prevalent in vascular depression, also showed no differences across groups. The scoring on the four subscales of the CES-D also revealed no differences between the vascular and non-vascular depressed subjects (Table 3). A further discriminant analysis with the vascular subgroup as the grouping variable and sociodemographic and depression variables as the independent predictors, revealed age and item 5 (difficulties concentrating) of the CES-D as the remaining predictors. (Data not shown)

Table 3. CES-D symptom cluster-score in vascular and non-vascular depression

	Vascular Depression (n = 69)	Non-vascular Depression (n = 254)	P
Somatic-Retarded Activity	8.8 (3.7)	8.2 (3.7)	0.263
Depressed Affect	4.9 (3.0)	4.9 (2.9)	0.993
Positive Affect	4.4 (2.4)	4.3 (2.6)	0.724
Interpersonal Affect	0.7 (1.1)	0.6 (1.1)	0.471

'Somatic Retarded Activity' (Item 1, 2, 3, 5, 7, 11, 20. Range: 0–21); 'Depressed Affect' (Item 6, 10, 14, 17, 18. Range: 0–15); 'Positive Affect' (Items 4, 8, 12, 16. Range: 0–12); 'Interpersonal Affect' (Items 15, 19. Range: 0–6).

DISCUSSION

In this study, we tried to uncover further evidence to support the vascular depression hypothesis in which specific symptomatology is presented as one of the key-features. By analyzing data of subjects who presented symptoms of depression at baseline and subsequently developed a first cardiac event, we attempted to define a group of depressed subjects who would fit in the 'vascular depression' definition. If a specific symptom profile would help to identify those depressed individuals at risk to later develop cardiovascular disease, that would be of great clinical interest. The main finding of this paper was, however, that no specific clinical presentation in these 'vascular' subjects was found. They did not show more prominent anhedonia or psychomotor retardation or fewer feelings of guilt. Although disability was one of the key features in the original descriptions of Alexopoulos and Krishnan, we also did not find an association between disability and our vascular subgroup. The only difference we did find in this 'vascular' group was that the subjects had more trouble with concentration and thinking. We were therefore unsuccessful at identifying subjects who are at risk of developing a first cardiac event based on the depression symptom profile.

For more than 15 years, it has been known that depression and myocardial infarction are interrelated and that depression increases the risk of subsequent MI and also increases the risk of mortality after MI (Carney *et al*., 1988; Frasure-Smith *et al*., 1993; Penninx *et al*., 2001). In recent studies interventions that were aimed at depression showed only a modest effect on depression and improved survival rates only in part (Berkman *et al*., 2003; de Jonge *et al*., 2007). Of course, the failure to find a specific 'vascular' profile for depressed subjects who eventually develop vascular disease may lie in how the groups were defined, or the accuracy of the definition of depression or vascular disease. However, at this point we have done various analyses on the same subject in several different (community based) study-groups, and have not confirmed the clinically defined vascular depression profile proposed by Alexopoulos and Krishnan (Naarding *et al*., 2007). Licht-Strunk *et al*. (2004) performed a similar analysis in the open population and only found an association of vascular burden and more disability, but not with a specific depression symptom profile. Holzapfel *et al*. (2008) did find differences in the depression profile of patients with and without chronic heart failure (CHF) studying subjects from a CHF and psychosomatic outpatient

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clinic. In this study the most prominent finding was that the difference between depressed patients with and without CHF are found in the cognitive and emotional symptoms (CHF patients were less depressed and exhibited less feelings of guilt) and not in the psychomotor or somatic symptoms. Most probably, the fact that we used population based rather than clinical study-groups explains the differences with findings from these other studies. Thus, we must conclude that in the general population the depressive symptom profile is not a reliable marker for vascular depression. Others have provided several explanations for this finding (McDougall and Brayne, 2007). One of these is the possibility that depression is not a prodromal sign of cardiac events, but rather that depression and cardiac disease are both concomitant disorders that result from the same underlying risk factor. This risk factor could be inflammatory, genetic, or environmental in nature (Naarding *et al*., 2005). In this case, some subjects would suffer only from depression, some only from vascular disease, and there could be a group of subjects that would suffer from both, depending on this risk factor and probably the interaction of this risk factor with other risk factors. Consequently, analysis of just one of these factors will not lead to a specific profile. New studies will have to search for combinations of risk factors to arrive at more stable groups and thus more stable patterns of symptoms and symptom clusters.

CONFLICT OF INTEREST

None known.

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