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Effects of Multimodal Interventions for Primary Prevention of CVD on Depression, Anxiety, and the Type D Personality

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Abstract

Psychosocial risk factors like depression, anxiety, and the type D ("distressed") personality are associated with an earlier development and faster progression of cardiovascular disease (CVD). Thus, they may be targets to primary prevention interventions, but evidence is sparse. In a line with comparable clinical trials, the German PreFord study, a randomized-controlled trial (RCT) to evaluate guideline based primary prevention of CVD, did not provide evidence that these psychosocial risk factors can be effectively treated by multimodal behavioral interventions. These null results in primary prevention contrast with findings obtained in secondary prevention. Up to now, it is not possible to assess whether the lack of effect of previous trials on psychosocial risk factors is primarily attributable to the structure and/or the content of the interventions or whether other effects may be responsible. However, recent evidence supports the necessity for more targeted approaches.

Keywords: Primary prevention; Cardiovascular disease; Depression; Anxiety; Type D personality

Abbreviations

CVD: Cardiovascular Disease; ESC: European Society of Cardiology; INT: Intervention; CO: Control; CBT: Cognitive Behavioral Therapy; HADS: Hospital Anxiety and Depression Scale; DS-14: Type D Scale

Introduction

Despite of recent advances, control of "classical" risk factors in both primary and secondary prevention of cardiovascular disease (CVD) is still inadequate [1,2]. At the same time, it is beyond dispute that not only guideline-based pharmacotherapy, but also behavioral interventions (e.g. nutritional counseling, sports and exercise therapy and smoking cessation) should be deployed [3-5]. In addition to "classical" risk factors, a number of psychosocial factors can also have a negative impact on the development and course of CVD [6-8]. Low socio-economic status, lack of social support, stress at work and in family life, hostility and mental disorders contribute to the risk of developing CVD and a worse prognosis of CVD, while the absence of these items is associated with a lower risk of developing CVD and a better prognosis of CVD [9-15]. In particular, there is increasing recognition of the contributory role played by depression, anxiety disorders and so-called type D personality (combination of overall "negative affectivity" and "social inhibition" [16]). Not only are these variables associated with negative health behaviors (e.g. smoking, poor diet, lack of exercise and non-adherence to medication), but various psychobiological mechanisms (e.g. activated inflammation and coagulation, autonomic imbalance etc.) have also been demonstrated to exert a direct effect on the pathogenesis of CVD [17-20].

In secondary prevention, multimodal and psychosocial interventions can counteract psychosocial stress, depression and anxiety, thus facilitating behavior change and improving quality of life and prognosis [21-26]. To date, however, there have been very few multimodal intervention studies that have also explicitly evaluated depression or anxiety in the primary prevention of CVD, and those who did have shown no significant effect [3]. In addition, to our knowledge, no study addressed type D personality. Aim of the PreFord study, a randomized controlled trial (RCT) on the primary prevention of CVD was to achieve a longer-term improvement in the biological and psychosocial risk profile by means of a novel, multimodal group intervention in conjunction with guideline-based medication [27,28]. In this publication the effects of the PreFord RCT on depression, anxiety and type D personality are presented and compared with the present literature.

Methods

In the PreFord RCT (SRCTN: 23536103) the identification of eligible subjects took place in the framework of an epidemiological study on the distribution of ESC risk scores in current and former employees of Ford Motor Company in Cologne, Germany [28]. An ESC score of more than 5% was found in 654 women and men. After

the exclusion of unsuitable patients (e.g. detection of a hitherto unknown CVD, no consent to take part in the study), 447 men and women were randomized either to multimodal intervention (INT) or to routine care (CO). INT consisted of health education, exercise based therapy, smoking cessation training, where applicable, and a 12-hour CBT-based stress management program (LifeSkills® [29]). The outpatient group intervention was offered on 2 days of the week over a course of 30 appointments of 2.5 h each (in total 75 h over 15 weeks). The intervention was accompanied by guideline-based pharmacotherapy. Somatic and psychosocial variables (Hospital Anxiety and Depression Scale, HADS-D; Type D Scale, DS-14) were measured and evaluated before and after INT and also annually until the follow-up history was taken at two years [16,30]. The current presentation is restricted to the psychosocial variables. The effects of intervention on depression and anxiety were calculated both for the overall population and also for those suffering from HADS depression or anxiety score >7. The effects on the type D personality were recorded using both a dimensional model (negative affectivity (NA) *vs.* social inhibition (SI)) and a categorical model (NA & SI ≥ 10). Analysis was based on the intention-to-treat approach ("last observation carried forward") using t-tests, baseline-adjusted ANCOVA or logistic regression analysis, depending on the variable. The trial was conducted in accordance with Good Clinical Practice and the Helsinki Declaration. The trial protocol was approved by the local ethics committee and all patients gave written informed consent before inclusion. Further detailed information about the study is published elsewhere [28].

Results

The sociodemographic and clinical features were equally distributed between the groups except for systolic blood pressure (INT>CO, p=0.042) and the use of antihypertensive medication (INT>CO, p=.010). In INT the mean age was 60.6 years; 91.0% were men, and 68.2% were retired. A BMI of more than 25 showed 81.6%; a high proportion were found to have cholesterol and blood pressure values in need of treatment (96.0% total-cholesterol>175 mg/dl resp. 72.1% systolic blood pressure>130 mmHg). The use of statins and acetylsalicylic acid was reported to be rare (17.0% resp. 12.1%) and antihypertensive agents comparatively common (43.9% *vs.* 32.1% in CO). 17.0% of subjects smoked; 47.5% reported having already stopped smoking. A depression>7 was seen in 12.4% and an anxiety score>7 in 27.2% of subjects. A type D personality was found in 23.7% of subjects.

After randomization, n=68 (30.5%) subjects did not take up the intervention, either because they lived too far from the study center or because they could not fit participation in the program into their schedule. In the control group, n=52 (23.5%) subjects did not attend the two-year follow-up assessment. In 5 patients in each group, a clinically significant CV event (acute coronary syndrome, myocardial infarction, arterial occlusion, stroke or cardiac death) was recorded within two years.

The results for depression, anxiety and type D personality are presented in Table 1. A significant effect of the intervention on depression or anxiety was not demonstrated in the overall population. However at 12 months, a trend towards reduced depressiveness was seen in subjects with initial psychological distress (b: 0.937; 95% CI: -0.043–1.1916; p=0.060). With regard to type D personality, there was no significant influence either on the dimensions "negative affectivity" and "social inhibition" or on overall type D personality.

Parameter	Time	n	b	95% CI	p
Depression	1 year	447	0.177	-0.183–0.536	0.334
Anxiety			-0.043	-0.384–0.298	0.806
Negative affectivity			-0.312	-0.869–0.245	0.271
Social inhibition			-0.220	-0.751–0.311	0.416
Depression	2 years	447	-0.053	-0.386–0.279	0.752
Anxiety			0.086	-0.241–0.412	0.606
Negative affectivity			-0.028	-0.530–0.585	0.992
Social inhibition			0.17	-0.408–0.764	0.551
b=baseline-adjusted effects; 95%CI=confidence interval of b					

Table 1: Baseline-adjusted effects of the PreFord trial on depression, anxiety, and the type D personality.

Discussion

In the PreFord RCT, a multimodal intervention on primary prevention of CVD, no significant effect, neither on depression and anxiety, nor on type D behavior was shown in the full sample. However, in subjects with initial psychological distress, there was a trend in the direction of reduced depressiveness after one year, but this effect was not maintained. These results are in line with comparable clinical trials on primary prevention of CVD, which also yielded null results with respect to depression and/or anxiety [3]. Thus, until now it is not possible to assess whether the lack of effect on psychosocial risk factors is primarily attributable to the structure and/or the content of the interventions or whether possibly other effects may be responsible, such as the selection of a population showing relatively minor psychological distress. These null results in primary prevention contrast with findings obtained in secondary prevention, where a slight to moderate effect on depression and anxiety was demonstrated using multimodal or psychological interventions [26]. A recent study on a stepwise psychotherapy intervention for depressive symptoms in CVD patients has shown a response on depression especially in patients with type D personality [31], indicating that more targeted psychological interventions may be necessary. With respect to primary prevention, a recent study on collaborative care for depression could significantly reduce the excess risk of a first CVD event among older, depressed patients [32]. This first positive study aiming at primary prevention of CVD *via* modifying psychosocial risk factors also underlines the usefulness of a more targeted approach and should stimulate further research.

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Conflict of Interest

There is no conflict of interest.

Lecturing for the sponsors Bayer Pharma AG and Bristol-Myers Squibb took place in the context of disease management program training for family doctors. These were unrelated to the PreFord study.

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