Study Protocol and results

Internet based cognitive behavioural therapy for depression in patients with Cardiovascular disease - The DOHART Study

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Purpose and aims

Tailored internet-based cognitive behavioural therapy (I-CBT) is a new innovative and person-centred method that is promising that may be used to decrease depression in CVD patients. In patients with cardiovascular disease (CVD), depressive symptoms is a common co-morbidity leading to decreased wellbeing, and increased morbidity and mortality. Depressive symptoms are both underdiagnosed and undertreated in CVD patients. Earlier studies have demonstrated the efficiency of cognitive behavioural therapy (CBT) for many psychiatric conditions, but few studies have evaluated CBT in patients with CVD.

The purpose of this study is to evaluate the effects of the tailored I-CBT program on reducing depressive symptoms and other patient reported outcomes in patients with cardiovascular disease (CVD) and to explore factors related to implementation of the I-CBT program in clinical cardiac care.

Aims of the study

- To evaluate the effects of the tailored I-CBT depression program on depressive symptoms and quality of life.

Survey of the field

Background: The World Health Organisation (WHO) has estimated that CVD and depressive symptoms will in the near future become the two most common causes of disability.[1] Depressive symptoms, according to the WHO, produces greater decrements in health than other chronic physical diseases and a comorbid depression significantly worsens the health of patients with such diseases.[2]

In Europe, CVD is the major cause of hospital discharges and accounts for 43% of all deaths at all ages (i.e., > 4 million deaths annually).[3] Depressive symptoms is highly prevalent in patients with CVD (20%–40%)[4] and it significantly worsens the health of CVD patients. Depressed CVD patients experience poorer quality of life,[5] more frequent rehospitalisation,[6] higher healthcare costs and a shorter life expectancy than CVD patients without depression.[6] Both biological and behavioural mechanisms can explain the negative effects of depressive symptoms in CVD. With regard to the biological mechanisms, our own and other studies have shown that depressive symptoms increases plasma levels of stress hormones and inflammatory activity, which may speed up the progression of atherosclerosis and impairment of cardiac function.[4,7] Regarding behaviour, depressive symptoms can influence non-adherence to medication, development of a sedentary lifestyle and poorer self-care performance.[4,8]

The WHO states that our 'traditional care approaches' such as primary care centres or outpatient clinics do not offer enough support or treatment to patients with a chronic disease and depressive symptoms, such as those with CVD.[2] The WHO emphasises that the implementation of interventions targeting depression in healthcare should thus be prioritised.[2] In line with this recommendation, our proposed study will contribute to the development, feasibility testing, and evaluation of the effectiveness of an internet-based cognitive behavioural therapy treatment program (I-CBT) aimed at treating depressive symptoms in CVD patients.

Rationale for the intervention: Why should CBT be chosen for this purpose? Antidepressant medication seem to have limited effect on depressive symptoms in CVD patients.[4] Furthermore, adding anti-depressant to the existing complex medical treatment for CVD may be perceived as burdensome and also increase the risk of developing side effects. CVD

patients with depression prefer 'talking' therapies.[9] There are other psychotherapies, but rarely, if ever, do they result in better outcomes than CBT.[10] However, earlier studies of CBT in CVD patients' only reports small effects on depressive symptoms. One probable reason is that most studies only used a single CBT component, such as psychoeducation alone, problem-solving therapy alone, relaxation alone or behavioural activation alone.[11] A program that combines different CBT components has been suggested to improve treatment efficacy.[12] Moreover, generic CBT programs may not be optimal for targeting depression in patients with chronic diseases since these programs are not adapted to the context of the disease,[13] for example, by acknowledging the association between CVD and depression. We therefore believe that a CBT program that (I) includes different CBT components and (II) tailored to fit the context of CVD has the potential to improve the effect of CBT on depressive symptoms. This might also prevent the progression of CVD as well as improve quality of life and survival.

Project description

The study has the following research questions:

- What are the short- (nine weeks) effects of a nine-week I-CBT program on depressive symptoms and quality of life in patients with CVD and depressive symptoms.

Methods

Design of the study

The effects of the I-CBT program will be evaluated in a randomised controlled study (RCT).

Enrolment of study participants in the RCT

For the RCT study, 144 patients were recruited (Figure 1).

Power calculation: A recent published meta-analysis[14] of studies evaluating the effect of internet based CBT on depression, that will be the primary outcome in the study, reported the effect size in studies including patients with depression to vary between 0.56-1.26 (mean 0.89), the mean number of patients in these studies was 107. Own power calculation: Effect size=0.5, alpha=0.05 (Z=1.96), Power 0.80 (Z -0.84) = 122 participants. Due to drop-outs or deaths the size of the study population for the RCT study was decided to n=140.

Step 1. Screening for participants. All CVD patients who received care at the department of cardiology the last 12 months in four hospitals in southeast of Sweden was contacted by a letter with information (n=11,992) about the study.

Step 2. Patients interested (n=272) in participating registered as interested on our website (www.dohart.se) for more information, registration and the provision of informed consent. After registration, the participants will respond to questions on the website (see figure 1). Inclusion or exclusion will be assessed by a board consisting of a cardiologist, a psychologist, a cardiology nurse specialists and a psychiatric nurse specialist.

Inclusion

- age > 18 years
- treatment for CVD according to European Society of Cardiology guidelines
- stable CVD (NYHA class I–III) and not having been hospitalised for CVD in in the last four weeks.
- depressive symptoms (Patient Health Questionnaire-9 [15] (PHQ-9) > 5 points)

Exclusion

- severe CVD (NYHA IV) or another severe chronic life-threatening disease
- severe depression assessed as requiring acute treatment
- not being able to dedicate 3-4 hours to participate in the program
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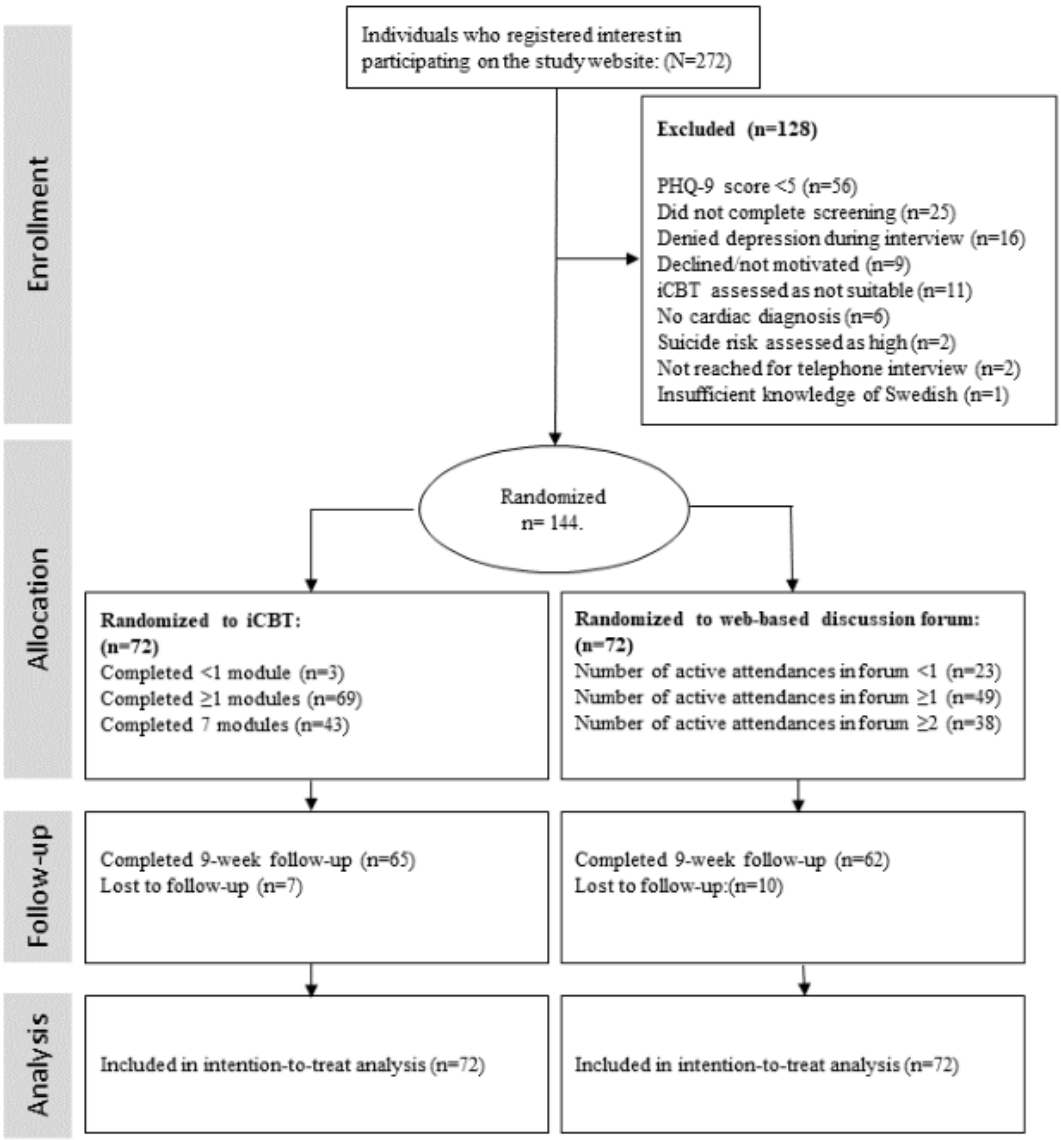
Figure 1. *Description of the enrolment and randomisation of study participants*



Step 3. Before final inclusion and randomisation, eligible participants was contacted for a telephone interview held by the psychiatric nurse specialist. Mini International Neuropsychiatric Interview (MINI) will be used to assess depression at this stage.

Step 4 The included (n=144) patients completed the baseline study questionnaires on our website and was then be randomised to nine weeks of internet-based CBT (n=72) or nine weeks in an web based discussion forum (n=72). As suggested by the ethical committee, those in the web-based discussion forum was offered I-CBT treatment after the termination of the study.

Theoretical underpinning for the CBT intervention

According to CBT theory[16], depression arises from negative thoughts, emotions and behaviours that can be activated as a response to stressful life events, such as the development of CVD. Figure 2 shows a CBT model, inspired by Moorey[17] of how CVD can cause depression. The inner circle of the model describes perceived losses, threats and stressful symptoms caused be CVD. This activate negative thoughts, emotions and behaviours, thus a process leading to development of depression (the outer circle). In the model, a vicious circle can be seen since the negative thoughts, emotions and behaviours in turn can worsen patients' perceived stress of CVD and thus both worsen depressive symptoms and CVD.

Intervention: With CBT the patients become active participants and perform exercises that enable them to become aware of, modify, as well as learn skills to cope with negative thoughts and unhelpful behaviours, which contributes to decrease negative emotions.[16] CBT can help CVD patients to break the vicious circle. The nine-week tailored I-CBT program consists of the components of psychoeducation, relaxation, problem-solving and behavioural activation. Table 1 describes the I-CBT program and Figure 2 describes how the four components in the I-CBT will work to decrease depression. CBT usually includes some form of homework. Specifically, just seeing a therapist is insufficient, and change must be implemented in real life, which is achieved by collaborating with the patient and prescribing homework. The present I-CBT program thus also has homework assignments (Table 1) and the patients are provided with weekly feedback on them by a nurse specialising in mental health care who is supported by a psychologist and can consult with a cardiologist as well as a specialist cardiac nurse. Feedback is delivered in writing and focuses on positive aspects of the patient's progress; support is also provided to help the patients proceed with the program.

Figure 2. *A CBT model describing how CVD can cause depression. The figure also describes how the 4 components in the I-CBT program (1) psychoeducation, (2) problem solving, (3) behavioural activation and (4) relaxation can help to decrease depression by modification of negative thoughts, behaviours and emotions.*

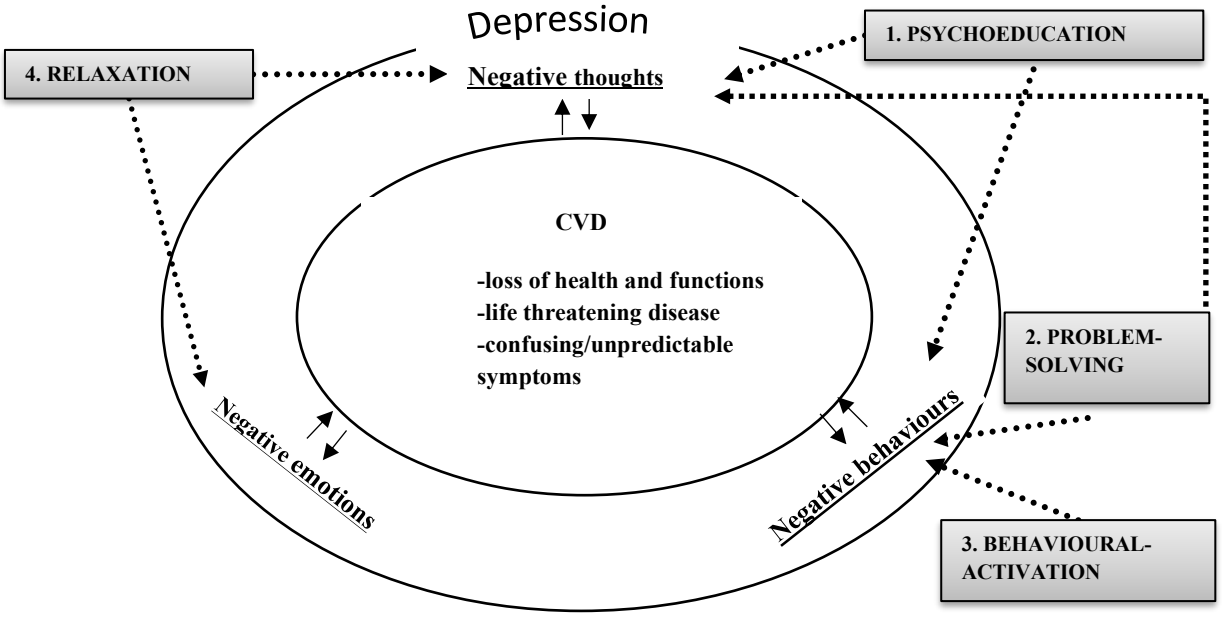


Table 1. A brief overview of the I-CBT program

CBT component/Content	Aim	Homework
Week 1: Psychoeducation Introduction	Inform and engage the participant. Goal setting.	Identify values and set up goals for the participation in the program
Week 2: Psychoeducation Living with CVD	To understand what CVD is and its impact on life.	Self-assessment of CVD symptoms. Identification of situations when symptoms occurs. Propose coping strategies.
Week 3 Psychoeducation Depression and CVD	To understand what depression is and its link to CVD.	Identify symptoms of depression, fear and worries Identify situations when symptoms affects the participant.
Week 3: Relaxation	To learn relaxation	Practice relaxation continuously during the CBT program.
Week 4 and 5: Behavioural activation	To identify behaviours that have negative and positive impacts on wellbeing.	Mapping activities in a week schedule. Making a list of desirable activities. Planning and implementing new activities
Week 6 and 7: Behavioural activation	To reduce negative behaviours and increase positive ones.	Eliminate or reduce negative activities. Increase number of positive activities.
Week 8: Problem-solving	To identify perceived problems. To solve or cope with a problem.	Practicing problem solving in accordance to the problem solving tool
Week 9: Final module	Learn strategies to maintain the changes achieved.	Set up a personal strategy that can be used if depressive symptoms re-occur.

The control group participated in a web-based moderated discussion forum (i.e. ODF group) where new discussion topics were presented each week over a nine-week period. During participation in the ODF, no individual feedback was provided. However, participants could contact the moderator for support regarding how to use the ODF and for technical support. The topic was introduced without any extended background in a presentation consisting of statements and questions such as: What are the symptoms of CVD? Do you have any tips you would like to share on how you can handle the symptoms of CVD? How do you think that depressive symptoms and CVD affect the relationship between you and your significant others? Do you have any suggestions about how to handle problems related to feeling depressed or downhearted? The discussion took place in writing.

Measurements to evaluate the RCT

The PHQ-9[15] will be used to measure the primary outcome (i.e. depressive symptoms). The PHQ-9 is a valid and frequently used depression questionnaire. To detect depression a sensitivity of 88% and a specificity of 88% has been reported in primary care patients[18] whereas a sensitivity and specificity of 70 %r respectively 92% has been reported in patients with CVD.[19] Table 2 gives an overview of the primary and secondary outcomes and the timing for measurements in the RCT.

Statistical analysis plan

Primary and secondary outcome data were checked for normal distribution by visual inspection or Q-Q plots. The primary analysis for comparison between groups (i.e. iCBT vs. ODF) was made on an intention-to-treat basis. Analysis of covariance (ANCOVA), which allows adjusting for baseline scores and regression to the mean was used for the comparison between groups. Missing data in the ANCOVA was imputed using last observation carried forward.

Table 2. *The different measurements and the timing for measurements in the study***.**

	Questionnaires	**Baseline**	**Post-CBT 9 weeks,**
Primary outcome **Depressive symptoms**	Patient Health Questionnaire-9[15]	**X**	**X**
Secondary outcomes Depressive symptoms	Montgomery-Asberg Depression Scale	**X**	**X**
		X	**X**
Quality of life	Short Form-12[20] Euro-QoL-5D[21]	**X** **X**	**X** **X**

Results of the I-CBT program

Main results (Table 3) Compared to web-based discussion forum (ODF), iCBT had a significant and moderate treatment effect on the primary outcome depression (i.e. PHQ-9) (mean group difference -2.34 [95 % CI -3.58 to -1.10], *P* <0.001, Cohen's *d*=0.62). In the secondary outcomes, compared to ODF, iCBT had a significant and large effect on depression (i.e. MADRS-S) (*P*<.001, Cohen's *d*=0.86) and a significant and moderate effect on the mental component scale of the SF-12 (*P*<.001, Cohen's *d*=0.66) and the EQ-VAS (*P*<.001, Cohen's *d*=0.62). A total of 60% (n=43) of the iCBT group completed all seven modules, whereas 82% (n=59) completed at least half of the modules. No patients were discontinued from the study due to high risk of suicide or deterioration in depression.

Table 2: Treatment effects for the primary and secondary outcomes. Data are mean (SD) unless otherwise stated.

	Internet-cognitive behavioural therapy (n=72)		**Online discussion forum (n=72)**		**Mean between-group treatment difference, 95 % CI**		***P***	**Effect-size (d)**
	Baseline	9 weeks	Baseline	9 weeks				
PHQ-9	10.71 (4.47)	6.63 (4.76)	10.22 (5.10)	8.68 (4.60)	-2.34	-3.58 to -1.10	<.001	0.62
MADRS-S	18.27 (6.98)	10.90 (7.45)	17.67 (6.19)	16.10 (7.93)	-5.58	-7.72 to -3.44	<.001	0.86
EQ-VAS	53.31 (20.03)	65.11 (21.81)	57.15 (18.10)	56.99 (22.08)	10.83	5.02 to 16.64	<.001	0.62
PCS12	39.70 (10.07)	41.84 (10.56)	37.63 (10.98)	37.80 (11.61)	2.46	-0.11 to 5.03	.06	0.32
MCS12	35.88 (9.22)	43.41 (11.04)	36.38 (10.02)	38.03 (10.52)	5.71	2.83 to 8.60	<.001	0.66

Abbreviations: PHQ-9 = Patient Health Questionnaire 9. MADRS-S = Montgomery Åsberg Depression Rating Scale (self-rating version). EQ-VAS = EuroQol Visual Analogue Scale. PCS12 = Physical Component Score of the Short Form 12. MCS12 = Mental Component Score of the Short Form 12.

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