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Published in:
Journal of Human Hypertension

DOI:
10.1038/jhh.2015.123

2016

Document Version:
Peer reviewed version (aka post-print)

IMPACT OF A SHORT HOME-BASED YOGA-PROGRAM ON BLOOD PRESSURE IN PATIENTS WITH HYPERTENSION – A RANDOMIZED CONTROLLED TRIAL IN PRIMARY CARE

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Short title: **Neutral results for yoga on hypertension**

Funding

This study was funded by the Faculty of Medicine at Lund University, the Ekhaga Foundation, the Swedish Heart-Lung Foundation and the Swedish Southern Health Care Region, Agreement for Medical Education and Research (ALF) funding from Region Skåne and a Swedish Research Council grant awarded to Kristina Sundquist.

Word count: 4233, **Number of tables**: 4, **Number of figures**: 1, **Number of supplementary files**: 4

Abstract

The present study was designed to evaluate yoga's impact on blood pressure and quality of life and on stress, depression and anxiety in patients with hypertension in a primary care setting.

We conducted a multi-center randomized controlled trial with follow up after 12-week intervention completion. Adult primary care patients diagnosed with hypertension were randomly allocated to yoga or usual care. The intervention group performed a short home-based Kundalini yoga program 15 minutes twice daily during the 12 week intervention period. At baseline and follow up the participants underwent standardized blood pressure measurements and completed questionnaires on quality of life, stress, anxiety and depression.

Data obtained from 191 patients (mean age 64.7 years, SD 8.4) allocated to yoga intervention (n=96) and control group (n=95), with a total proportion of 52% women, showed significant reduction for systolic and diastolic blood pressure for both groups (-3.8/-1.7 mmHg for yoga and -4.5/-3.0 mmHg for control groups respectively). However, the blood pressure reduction for the yoga group was not significantly different to control. There were small but significant improvements for the yoga group in some of the quality of life and depression measures ($p<0.05$, Hospital anxiety and depression scale, HADS-D) compared to control.

The findings of our study, which is the largest study from an OECD-country (Organization for Economic Co-operation and Development) to date, do not support the suggestion from previous smaller studies that yoga lowers blood pressure. Further clinical trials are needed to confirm these findings. However, the yoga patients had other health benefits.

Introduction

A recent multinational study suggests that the prevalence of hypertension in adults is around 40% [1]. Hypertension is important not only because of its high frequency but also because it is a major modifiable risk factor for heart disease, stroke and kidney disease, which are among the most common causes of death worldwide [2, 3]. For primary care physicians, hypertension is the number one diagnosis for office visits and for our communities, the treatment of high blood pressure (BP) and its consequences constitutes a substantial economic burden [4, 5]. The primary care physician faces a considerable challenge in trying to convince hypertensive patients to implement and maintain life style changes, including dietary changes and increased physical activity.

Yoga is a mind-body practice in complementary and alternative medicine with origins in ancient Indian philosophy [6]. Yoga is gaining popularity as a therapeutic measure in the western world and a majority of yoga practitioners in America have reported that they utilize yoga to improve their health status [7]. In several studies yoga has been shown to reduce BP [8-10]. However, many of these studies have been small and of questionable power to determine clinically relevant (i.e, 4-5 mm Hg) changes in BP [9, 10], and the need for larger randomized trials has been highlighted [11]. Furthermore, it is important to study the effects of yoga on BP in a primary health care setting, where most patients with hypertension are evaluated and managed.

There are several theories about the pathogenesis of hypertension and about how BP is affected by yoga. According to a previous study, slow breathing increases baroreceptor sensitivity and reduces sympathetic activity and chemoreflex activation [12]. Yoga exercise can increase heart rate variability, indicating an increase in parasympathetic activity [13]. It has also been shown in a previous study that yoga can reduce levels of cortisol in saliva [14]. The mechanisms by which cortisol raises BP remain unknown, but it is suggested that it might

be through inhibition of the vasodilator nitric oxide system and through increased vasoconstrictor erythropoietin concentration [15].

Our research group conducted a small pilot study in 2011, which evaluated yoga as a treatment for primary care patients with hypertension [16]. The results suggested that a short home-based program of yoga had a BP-lowering effect and a positive effect on self-rated quality of life (QOL) [16]. In view of this, we decided to conduct a new and larger randomized trial to further evaluate the effect of the home-based yoga program on BP. We also chose to examine whether the slight improvement observed in QOL was related to stress, depression and/or anxiety. According to the advice from the founder of the yoga intervention, Göran Boll, we increased the intervention in the present study from 15 minutes daily to 15 minutes twice daily [17]. Other studies have shown positive effects of yoga on health-related QOL [18], stress [8], anxiety [8, 19] and depression [20]. However, systematic reviews have pointed out the need for larger randomized trials in these areas as well [18, 20].

The present study was designed to evaluate yoga's impact on blood pressure and quality of life and on stress, depression and anxiety in patients with hypertension presenting to primary care physicians.

Materials and Methods

Trial design

We conducted a multi-center parallel group randomized controlled trial with follow up after 12-week intervention completion. An a priori sample size calculation determined that 200 patients were required (100 per group) to allow 80 % power to detect as significant at the 5% level, a 5 mmHg between-group difference in systolic BP, allowing for 15% dropouts (two-sided test). The primary outcome was change in BP. The key secondary outcome was self-rated QOL (World Health Organization Quality of Life Assessment, WHOQOL-BREF) [21].

Other secondary outcomes included stress (Perceived Stress Scale, PSS) [22], depression and anxiety (Hospital Anxiety and Depression Scale, HADS) [23]. To ensure allocation concealment, randomization to groups was undertaken by a research assistant not involved in recruitment using a computer-generated random number schedule with block size of four. Randomization to study groups occurred after completion of baseline assessments and questionnaires. We used the CONSORT 2010 guidelines from the website http://www.consort-statement.org [24].

The study design and procedures were approved by the Regional Ethical Review Board in Lund, Sweden (2013/262). The study was registered at ClinicalTrials.gov (NCT01984593).

Participants and recruitment

In September 2013, patients aged 30-80 years old with diagnosed hypertension were identified by electronic charts search at three health care centers in southern Sweden. The health care centers were chosen on the basis that they had general practitioners (GPs) willing to commit time for research on yoga and hypertension. Participants were invited to participate if their BP when most recently measured at the health care center was between 130 and 160 mmHg (systolic) and 85 and 100 mmHg (diastolic), and thus fell within the range of high normal or grade 1 hypertension [25]. However, at the baseline assessment they were included if they satisfied either of these criteria (130-160 mmHg systolic and/or 85-100 mmHg diastolic). Exclusion criteria included BP measurements at baseline control outside the range 120-180 (systolic) or 80-110 mmHg (diastolic), that is below the definitions for optimal or above those for grade 3 hypertension respectively. Patients requiring ongoing adjustment of BP medication during the 4 weeks prior to baseline were also excluded. Patients with expected inability to understand instructions about the yoga exercises, physical or mental incapacity to carry out yoga exercises, or language problems/interpreter needs were also excluded. Aside from the above there were no medical exclusion criteria. The inclusion and

exclusion criteria were established before study start.

A random sample of 2144 patients (computer-generated randomization list) was screened for eligibility by the lead investigator (M.W.). About half of the patients (1020) met the inclusion criteria and were invited by mail to participate in the study. After two weeks they were contacted by telephone by a research assistant to provide further information about the study. Those who agreed to participate were invited for baseline assessment at their regular health care center. Baseline assessments and study questionnaires (WHOQOL-BREF, PSS-14, HADS and a health status and lifestyle survey) were completed after written informed consent was obtained from the participants. The physical assessments at baseline and follow-up were conducted by trained nurses and care assistants who remained blinded to group allocation throughout the study. After 12 weeks of intervention, all participants were reassessed for BP and questionnaires.

All patients (intervention and control group) were asked not to change their medication during the study, and any change in medication was registered at follow-up.

Intervention

The yoga performed in the study is a form of Kundalini yoga (Mediyoga) developed at the Institute for Medical Yoga (IMY) [17]. The yoga program used in the study takes about 15 minutes to perform and incorporates the following two exercises: 1) "Left nostril breathing" – deep breaths in and out through the left nostril while sitting or lying down, with the right nostril closed off by the right thumb or a nose plug (duration about 11 minutes); and 2) "spinal flex" – a movement that alternates between flexing the spine forwards (arching) and back in time with deep breaths while sitting on a chair or the edge of a bed (about 4 minutes). The same yoga program was used in the YHIP-study [16]. The yoga exercises are listed in the appendix.

Intervention group

The patients randomized to yoga (96 persons) received information and instructions concerning the two yoga-exercises (provided in supplementary appendix), during a single 30 minutes GP consultation. They were asked to perform these exercises for 15 minutes twice daily (just after getting out of bed in the morning and just before going to bed in the evening). Patients that did not manage to perform the exercises in the correct way were obliged to quit the study. However, mediyoga is permissive, which means that the instructors do not correct the patients doing the exercises if not necessary. During the consultation the patients also received a CD, a nose plug to use during the left nostril breathing exercise, a manual to facilitate their home exercises and a yoga diary in which to record details of when they had done yoga training. The participants were also able to listen to and download the audio guided yoga program to their smartphone or computer via a web-site specifically made for the study. The three doctors who conducted the study and were involved in the yoga teaching were employed at the respective health care center. Two of the doctors were trained mediyoga instructors and the third doctor was a study physician who was not a trained yoga instructor but was familiar with the yoga exercises. The doctors were given instructions by the Mediyoga founder (Göran Boll) during a two hour lecture. The patients, in turn, received information and instructions concerning the two yoga-exercises from the doctor during a single 30 minute GP consultation. If the patients did not manage to perform the exercises in the correct way they were obliged to quit the study. This did not happen to any of the participants. To make the doctor's consultations as similar as possible between the centers, a common template was drafted and the template was then used during the visits.

Control group

No changes were made for the control group (95 persons), which received "treatment as usual" (treatment with the medication they were already taking and annual medical examination by the general practitioner).

Study measures

Data were collected at baseline and after completion of the 12-week intervention. The research assistants who collected the data were blinded to the group assignment.

BP was measured following the guidelines of the European Society of Hypertension [26], in a sitting position after 5-10 minutes of rest with validated electronic blood pressure devices (Omron 705-IT) using an appropriate sized cuff. All patients had their arm size measured by a nurse using a tape measure to ensure that the right cuff size was used. The mean of two readings were calculated (mean of three readings when the first and second readings differed by >5 mmHg).

The WHOQOL-BREF is a validated QOL questionnaire containing 26 items which measure the following four domains: physical health, psychological health, social relationships and environment [21]. The first two items (WHO1 and WHO2) are so called global items that can be analyzed separately. They measure overall of quality of life and overall health satisfaction respectively. Each individual item of the WHOQOL-BREF is scored from 1 to 5. Higher scores indicate better quality of life.

The perceived stress scale, PSS-14, is a self-reported questionnaire that is designed to measure "the degree to which individuals appraise situations in their lives as stressful" [22]. The instrument is a 14-item scale with 7 positive items and 7 negative items rated on a 5-point Likert scale.

The Hospital Anxiety and Depression Scale (HADS) was originally developed to identify cases (possible and probable) of anxiety and depression among patients in non-psychiatric hospital clinics [23], but has since also been found to perform well in assessing outpatient populations [27]. The scale consists of fourteen items that can be divided into an Anxiety subscale (HADS-A) and a Depression subscale (HADS-D). Every single item is scored 0-3,

where 0 means a low and 3 a high level of anxiety or depression. Participants with a score on HADS-A or HADS-D of 8 or higher were classified as a case of anxiety or depression, respectively.

The health status and lifestyle survey was designed for this study and is not validated (provided in supplementary appendix). The survey contained questions regarding comorbidity for diabetes and cardiovascular disease, smoking and drinking habits and physical activity.

On their yoga calendars, the participants marked with a cross each time they completed the yoga training. The information in the calendars was not validated or questioned.

Statistics/Data analysis

Data were analyzed using IBM SPSS Statistics 22 (IBM Corp. Released 2013, IBM SPSS Statistics for Windows, Version 22.0, Armonk, NY: IBM Corp.) and SAS 9.4 (SAS Institute, Cary NC, USA). The analysis used an intention to treat approach. We also performed per protocol analyses. Differences in BP, QOL, stress and continuously measured HADS-A and HADS-D variables between baseline and follow-up were calculated by paired-samples Student's t-test in each group (normally distributed data). Differences in mean change between the yoga and control groups were calculated by ANCOVA [28], with baseline values as covariates. For change in mean SBP, we also used regression analysis with adjustment for age, sex and BMI. For differences in change from baseline to follow-up in dichotomized HADS-A and HADS-D scores, we used a marginal model (generalized estimating equation) with robust errors [29], with a binomial distribution and log link (log-binomial model) and included an interaction between time of measurement and group to test whether there was an important change from baseline.

Results

Figure 1 shows the flow of participants through the study. Of the 315 patients who attended the baseline assessment, 124 patients (39%) did not meet the inclusion criteria regarding blood pressure, mainly due to optimal DBP (<80 mmHg, n=83, 67%). The sample of 191 participants consisted of 92 men and 99 women aged 34-79 years (mean age 64.7, SD 8.4). The baseline characteristics are presented in table 1. A majority of the patients were overweight (BMI>25 kg/m^2) and the criterion for central obesity was fulfilled for 67.7% of the women (≥88 cm) and for 55.4% of the men (≥102 cm). Less than one third of the patients (29.4%) stated that they completed more than one hour of vigorous exercise a week. None of the participants in the yoga group were excluded because they were unable to perform the yoga exercises.

Effect of intervention on outcome measures

Table 2 shows the follow up measures and adjusted changes for SBP and DBP. There were no significant differences in mean change of either SBP or DBP between the control and yoga groups. These results were stable after adjustment for sex, age, BMI, waist circumference, number of performed yoga sessions, number of BP-lowering medicines and level of anxiety, stress and depression or other comorbidities at baseline**.** We also did logistic regression looking at probability of reaching a BP reduction of at least 5 mm Hg. There were no indications that a specific subgroup would benefit more from the intervention. However, using within-group comparisons, both yoga and control group data demonstrated significant decrease in SBP (-3.8±12.3 vs -4.5±12.1; P<0.05) and DBP (-1.7 ±7.1 vs -3.0±7.4; P<0.05).

Significant improvements were found in the yoga group for parts of the secondary outcome measure, namely regarding health satisfaction (WHO2, table 3) and for the domains physical health (p<0.007), psychological health (p<0.039) and environment (p<0.026) (data provided in supplementary appendix) compared to control. However, the global item for QOL (WHO1)

did not improve in any of the groups and there were no significant changes in the social relationships domain compared to control.

Data from the PSS and HADS assessments are shown in table 4. There were no significant change in the PSS and continuous HADS-A scores compared to control, but there was a significant difference in the HADS-D score from baseline to follow-up between the yoga group compared to control (-0.9 (95% CI, -1.5 to -0.4), p=0.001). In total, 44 patients (23.2 %) fulfilled the criteria for at least mild anxiety and 13 patients (6.8%) fulfilled the criteria for at least mild depression at baseline. However, despite a significant change in the continuous HADS-D score, when examined as defined cases there were no important differences between groups in change of the proportions fulfilling the criteria for depression (p=0.087).

The mean number of yoga sessions completions during the 12 weeks was 118.6 (i.e. 1.4 yoga sessions/day), ranging from 3 to 195. The most cited reasons for barriers to compliance were lack of time/holiday (27 persons) and physical barriers such as illness/cold/stuffed nose (20 persons). Four patients withdrew during the intervention and the reasons given for withdrawal were: illness (n=1); felt stressed by doing the yoga (n=2) and; no stated reason (n=1).

We also performed per protocol analyses through which patients who did not perform yoga for at least 9/12 weeks or who changed their medication were excluded, but there were no noticeable differences compared to the intention to treat analysis (data provided in supplementary appendix 4). According to the yoga calendars, 75 of 96 participants in the yoga group did yoga at least 9/12 weeks (78%), 15 participants did yoga less frequently and 6 participants did not return their yoga calendars. This criterion (yoga at least 9/12 weeks) was set up together with the IMY founder, and it was not known to the patients.

At the follow-up assessment, intervention participants rated their physical and mental experience of the yoga intervention. Almost three quarters (73.9%, n=65) of the participants

reported positive or very positive physical experience and 71.1% (n=62) reported positive or very positive mental experience of the yoga intervention. Forty-nine participants (56.3%) felt confident they would continue doing the yoga after study completion. The control participants were also able to rate their experience of taking part in the study, and 64 (74.4%) rated it as positive or very positive.

According to the lifestyle survey there were no significant changes in level of physical activity during the intervention period either within or between the groups.
There were no serious adverse events reported by the yoga group participants.

Discussion

We recorded no evidence that this yoga intervention (Mediyoga) decreased SBP or DBP in primary care patients with diagnosed hypertension more than usual care. However, both yoga and control groups had significant within group decrease of SBP and DBP. We found a small improvement in the HAD depression score (HADS-D) for the yoga group compared to control, although we could not demonstrate any significant reduction in the actual number of patients with depression. Significant improvements were also found for some of the quality of life measures (health satisfaction, physical health, psychological health and environment).

Yoga is gaining popularity in the western world and an increasing number of patients are practicing yoga for health reasons. Several yoga reviews have stated the need for well powered randomized studies to evaluate the effect of yoga on hypertension [12, 30, 31]. Accordingly, our research group conducted a pilot study using the same yoga intervention, in which we demonstrated a significant BP reduction and a positive effect on QOL [16]. In the present study we increased the intervention from 15 minutes daily to 15 minutes twice daily and we also increased the sample size from 83 to 191. Furthermore, the present study is a

290 fully randomized clinical trial, whereas the pilot study was a matched controlled study. This
291 study is also a three-center study with three different therapists, which diminishes the risk of
292 therapist's bias. Thus, our conclusion is that the findings of the present study are more
293 reliable, and that the results from the pilot study are more subject to confounding and bias.

294 There is indeed an increasing number of studies on the effects of yoga for numerous
295 conditions. BP measurement is relatively easy and cheap to perform, and there are probably
296 many studies with other main outcomes that include measurements of BP. However, if the
297 results of the BP change are not positive, they might well not be highlighted and difficult to
298 find [32].

299 However, a recent, large RCT from India on the effectiveness of yoga in hypertensive
300 patients, does report a very large reduction in blood pressure [8]. There are a number of
301 differences to our study which might contribute to the different result. The Indian study
302 practices another form of yoga, and the intervention period started with an instructor-led
303 intensive course for five days. The patients were younger (30-60 years) and were recruited by
304 means of announcements on radios and newspaper which could have led to a selection bias.
305 The participants of the Indian study also had a much stronger compliance than we found, with
306 all participants in the yoga group (n=118) reporting 100% commitment to the yoga program.
307 Another Indian study from 2009, comparing slow and fast breathing yoga exercises to control
308 in adults with grade 1 hypertension, showed significant reduction in SBP and DBP for both
309 breathing exercise groups [33]. The exact sizes of the BP-reduction for the two groups are not
310 presented in the paper. The breathing exercises were taught during daily lessons for 14
311 consecutive work days and the patients were then instructed to perform the program at home
312 15 minutes twice daily throughout the 3 month intervention period. A recent review on yoga
313 trials showed that RCT's on yoga conducted in India have about 25 times the odds of reaching
314 positive results [34]. There could be several reasons for this finding. Firstly, Indian yoga

interventions are often more intense [35] which means that the BP reduction could be due to vigorous physical activity rather than the consequence of a specific yoga effect. It is also likely that Indian patients, being familiar with the spiritual and philosophical tradition of yoga, find it easier to incorporate yoga into daily life. The understanding of the spiritual part of yoga may also influence the impact that yoga can cause. Indian yoga instructors may well be more skilled and/or dedicated than yoga instructors from other countries, resulting in better outcomes. These differences make it difficult to generalize the effectiveness of Indian yoga trials to hypertensive patients in other countries.

Two American RCTs have evaluated yoga for pre-hypertensive and hypertensive patients, compared to active control groups [9, 10]. In these studies, the change in BP was evaluated with 24 hour ambulatory BP after 12 weeks of intervention, which is the most accurate method to detect BP change. Unfortunately, both studies were underpowered, with group sizes of around 30 patients. One of the studies also suffered from large dropout-rates in the yoga group (20 of 46 randomized patients withdrew), causing a major selection bias [10]. The interventions consisted of instructor led yoga classes for at least 60 minutes weekly plus home practice. One study showed significant within group reductions for both SBP and DBP, but these were not significant compared to control [10]. The other study presented a significant within group reduction for DBP, that remained significant only for nighttime DBP in the between group comparisons (-5.17±15.70 vs. -0.85±15.80, $P<0.038$) [9].

One possible explanation for the lack of an additional BP reduction in the yoga group compared to control in our study could be that the participants in the yoga group considered doing yoga twice daily too time consuming and stressful, and that this might have counteracted the BP reduction of the yoga intervention. Adherence to the yoga intervention was 78% which indicates a fairly good compliance. However, since lack of time was the most cited barrier to adherence, yoga once daily might have led to better compliance and a better

effect. Compared to other yoga studies in OECD-countries (Organization for Economic Co-operation and Development), the adherence to intervention was good [9, 10]. It could also be that 12 weeks is too short a period to be able to detect the changes that the yoga intervention exerts. However, 12 weeks is a common duration for interventions in previous yoga studies [8-10, 33]. In comparison with other yoga studies, our study differs by not offering formal yoga classes led by an instructor. Instead, the yoga was taught on one single occasion by a GP (with varying yoga teaching experience). At baseline, 26% of the yoga patients were well controlled (≤140/90 mm Hg) compared to 17% in the control group. Since it is easier to lower a blood pressure that is high, this could have contributed to the lack of BP-reduction in the yoga group compared to control. On the other hand, mean BP values were equal between the groups at baseline and SBP and DBP were normally distributed within the groups.

The study has a number of strengths. Primarily, this is the largest randomized controlled trial in the western world to date on yoga's effect on blood pressure with blood pressure as the primary outcome. It also examined several other secondary outcomes. The study examined the effects of yoga in a primary health care setting, where most patients with hypertension are treated. It is a three-center trial which diminishes the risk of therapists' bias. On the other hand we acknowledge that the study has a number of limitations. Firstly, our study is limited to a single form of yoga. It may be that other schools of yoga or other yoga programs have a better impact on BP and on the other outcomes. The self-reported data (yoga calendar) is a source of uncertainty, which is a problem in all studies of this kind. We only measured BP on two occasions during the 12 week intervention. Given that BP varies considerably within individuals over time, a 24-hour ambulatory BP is the most accurate method to measure the patient's actual BP and to avoid impact of white coat hypertension on the results [36]. This is however time consuming and expensive and requires a much larger effort from the participants, possibly causing more dropouts.

The findings of our study, which is the largest study from an OECD-country to date, do not show that this yoga intervention (Mediyoga) lowers blood pressure compared to control. However, the patients in the yoga group had significant improvement regarding health satisfaction and depression measures. Further clinical trials are needed to confirm the effects of yoga on these outcomes.

Acknowledgements

We would like to thank the staff and management group at Löddeköpinge, Hjärup and Bara Primary Health Care Centers. A special thanks to general pracitioner Beata Borgström Bolmsjö and Camilla Richardson for their willingness to commit time and effort for the research on yoga and hypertension.

We are grateful to Göran Boll, the founder of the IMY, who has provided inspiration, knowledge and educational materials.

Conflict of interest: The authors declare no conflict of interest.

Summary table

What is known about topic	• Yoga is gaining popularity as a therapeutic measure in the western world • In several studies yoga has been shown to reduce BP • The need for larger randomized trials have been highlighted
What this study adds	• This is the largest study on yoga and hypertension from an OECD-country to date • The findings do not support the suggestion from previous studies that yoga lowers blood pressure • The patients in the yoga group had significant improvement regarding health satisfaction and depression measures

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Figure legends

Figure 1: Flow chart outlining patient recruitment and the allocation of patients to different groups

Table 1 Baseline characteristics

	Yoga group n=96	Control group n=95	P-value
Age (years)	64.7 (9.2)	64.8 (7.6)	0.95
Female gender, n (%)	52 (54.2)	47 (49.5)	0.52
BMI (kg/m²)	28.4 (3.8)	28.3 (4.2)	0.98
Waist circumference (cm)	98.1 (11.3)	99.1 (12.2)	0.53
SBP (mmHg)	148.8 (11.6)	150.0 (10.6)	0.47
DBP (mmHg)	88.3 (6.1)	88.1 (5.7)	0.83
Well controlled ≤140/90 mmHg, n (%)	26 (26.3)	16 (16.8)	0.11
On BP medication, n (%)	85 (89.5)	86 (90.4)	0.48
Number of antihypertensive drugs	1.5 (0.9)	1.5 (0.9)	0.72
Medical conditions			
Stroke/TIA, n (%)	12 (13.2)	5 (5.5)	0.08
Diabetes, n (%)	3 (3.3)	6 (6.5)	0.31
AMI or cardiac intervention, n (%)	3 (3.7)	7 (7.5)	0.19
WHO 1 (Quality of Life)§	4.1 (0.8)	4.1 (0.8)	0.99
WHO 2 (Health satisfaction)§§	3.5 (1.0)	3.5 (0.8)	0.66
Perceived stress scale score	21.6 (7.7)	20.2 (7.6)	0.24
HADS, total score	8.3 (6.5)	7.4 (6.3)	0.31
HADS-A, anxiety score	5.5 (4.1)	4.8 (3.9)	0.27
HADS-D, depression score	2.9 (3.0)	2.6 (2.8)	0.48

Notes: Means (SD) unless stated otherwise.

AMI; Acute Myocardial Infarction; BMI, Body Mass Index; DBP, Diastolic Blood pressure; HAD, Hospital Anxiety and Depression Scale; SBP, Systolic Blood Pressure; TIA, Transient Ischemic Attack

§WHO 1: How would you rate your quality of life? Very poor (1), poor (2), neither poor nor good (3), good (4), very good (5).

§§WHO 2: How satisfied are you with your health? Very dissatisfied (1), dissatisfied (2), neither satisfied nor dissatisfied (3), satisfied (4), very satisfied (5).

Table 2

Mean BP after intervention and adjusted mean change in BP

	Yoga group ITT, n=85	**Control group ITT, n=86**
SBP (mmHg), mean (SD)	145.4 (13.4)	145.2 (12.8)
Change from baseline	-3.8 (-6.5 to -1.2)	-4.5 (-7.0 to -1.9)
P-value	**0.006***	**0.001***
Difference vs. control[§]	0.5 (-3.0 to 3.9)	
P-value	0.783	
DBP (mmHg), mean (SD)	86.3 (7.7)	84.9 (7.7)
Change from baseline	-1.7 (-3.3 to -0.2)	-3.0 (-4.6 to -1.4)
P-value	**0.028***	**0.000***
Difference vs. control[§]	1.4 (-0.7 to 3.4)	
P-value	0.201	

Notes: Means (95% CI) unless stated otherwise.

* Significant change from baseline

[§] ANCOVA

ITT, intention to treat; SE, standard error of the mean; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 3

Self-rated quality of life and health satisfaction after intervention and adjusted mean change

	Yoga group ITT, n=91	**Control group ITT, n=90**
WHO1† score, mean (SD)	4.2 (0.6)	4.2 (0.8)
Change from baseline	0.1 (-0.0 to 0.2)	0.1 (-0.1 to 0.2)
P-value	0.225	0.401
Difference vs. control§	0.0 (-0.1 to 0.2)	
P-value	0.865	
WHO2‡ score, mean (SD)	3.8 (0.8)	3.6 (0.8)
Change from baseline	0.3 (0.1 to 0.4)	0.0 (-0.1 to 0.2)
P-value	**0.000***	0.453
Difference vs. control§	0.2 (0.1 to 0.4)	
P-value	**0.008***	

Notes: Means (95% CI) unless stated otherwise.

* Significant change from baseline

§ ANCOVA

ITT, intention to treat; SE, standard error of the mean; SBP, systolic blood pressure; DBP, diastolic blood pressure.

†**WHO 1**: How would you rate your quality of life? Very poor (1), poor (2), neither poor nor good (3), good (4), very good (5)

‡**WHO 2**: How satisfied are you with your health? Very dissatisfied (1), dissatisfied (2), neither satisfied nor dissatisfied (3), satisfied (4), very satisfied (5)

Table 4

Scores on stress (PSS), anxiety (HADS-A) and depression (HADS-D) after intervention and adjusted mean change

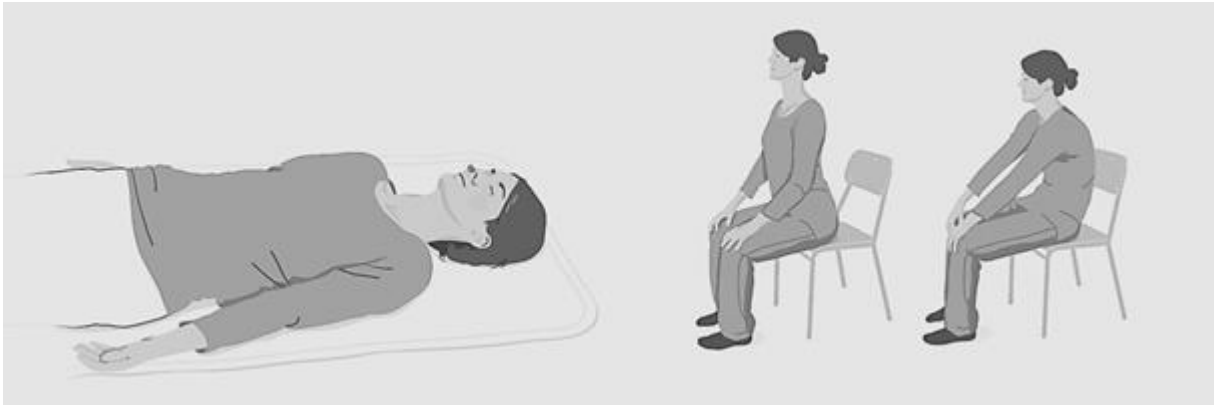
	Yoga group ITT, n=84	**Control group ITT, n=86**
PSS score		
Mean (SD)	19.7 (7.6)	18.6 (8.2)
Change from baseline	-1.8 (-3.1 to -0.7)	-1.3 (-2.7 to 0.1)
P-value	**0.002***	0.071
Difference vs. control[§]	-0.4 (-1.9 to 1.6)	
P-value	0.849	
HADS-A anxiety score		
Mean (SD)	4.4 (3.3)	4.1 (3.6)
Change from baseline	-0.9 (-1.5 to -0.3)	-0.5 (-1.0 to 0.1)
P-value	**0.006***	0.095
Difference vs. control[§]	-0.2 (-1.0 to 0.5)	
P-value	0.531	
% Anxiety case (≥8)		
Baseline	23%	23%
Follow up	17%	18%
P-value	0.99	
HADS-D depression score		
Mean (SD)	1.8 (2.2)	2.5 (3.0)
Change from baseline	-0.8 (-1.1 to -0.4)	0.2 (-0.2 to 0.6)
P-value	**0.000***	0.389
Difference vs. control[§]	-0.9 (-1.5 to -0.4)	
P-value	**0.001***	
% Depression Case (≥8)		
Baseline	6%	7%
Follow up	3%	10%
P-value	0.08	

Complete case analysis. Notes: Means (CI) unless stated otherwise.

* Significant change from baseline

[§] ANCOVA

ITT, Intention to treat; PSS, perceived stress scale; HAD, hospital anxiety and depression scale; SE, standard error of the mean; SBP, systolic blood pressure; DBP, diastolic blood pressure



1. Left nostril breathing (11 minutes)

2. Back flex (4 minutes)

Right nostril closed off by nose plug.

Supplementary figure: The yoga program (15 minutes twice daily)

Below are questions about your health and your lifestyle. Select the most suitable option.

Thank you!

		<2 years	2-5 years	5-10 years	10-20 years	>20 years
1	How many years ago did you get diagnosed with high blood pressure?					

		No	Yes
2	Do you have one or more biological relatives who have or have had high blood pressure?		

If yes, what kind of relationship? (eg, parent, sibling, uncle, cousin, etc.): _____

		No	No, but I have in the past	Yes
3	Do you smoke?			

		No	No, but I have in the past	Yes
4	Do you use snuff?			

		No, or <1 glass/w	Yes, 1-5 glasses/w	Yes, 5-9 glasses/w	Yes, 10-14 glasses/w	Yes, 15-19 glasses/w	Yes, >19 glasses/w
5	Do you drink alcohol? (wine, beer or spirits) See explanation below of the term "standard glass of alcohol"						

A standard glass of alcohol corresponds to a glass of table wine (12-15 cl), a bottle of beer (33 cl, 5 percent), a small glass of dessert wine (8 cl) or a measure (almost 4 cl of spirits).

		No time	0-30 min	30-60 min	60-120 min	>120 min
6	How much time do you spend during a typical week doing physical exercise, which will make you feel short of breath, such as running, fitness classes, ball sports?					

		No time	0-30 min	30-60 min	1-2 hours	2-3 hours	3-5 hours	>5 hours
7	How much time do you spend during a typical week doing everyday exercise, such as walking, cycling, gardening? Adding together all the time (at least 10 minutes at a time)							

	Do you have or have had any of the following conditions?	Yes	No	I don't know
8	Cerebral infarction/stroke?			
9	Cerebral haemorrhage?			
10	Transient symptoms of stroke, TIA-attack?			
11	Angina?			
12	Coronary heart attack?			
13	Diabetes?			

	Have you had any of the following surgeries?	Yes	No	I don't know
14	Insertion of so called stents in any of the coronary arteries?			
15	Balloon angioplasty in any of the coronary arteries?			
16	Bypass surgery of the heart?			

Do you have any comments on this questionnaire?

_____

_____

THANKS FOR YOUR COOPERATION!

Här följer frågor som handlar om din hälsa och dina levnadsvanor. Markera det mest passande alternativet.

Tack för hjälpen

		<2 år	2-5 år	5-10 år	10-20 år	>20 år
1	För hur många år sedan fick du diagnosen högt blodtryck?					

		Nej	Ja
2	Har du någon eller några biologiska släktingar som har eller har haft högt blodtryck?		

Om ja, vilken typ av släkskap? (t ex förälder, syskon, morbror, kusin etc):

_____

		Nej	Nej, men har rökt förr	Ja
3	Är du rökare?			

		Nej	Nej, men har snusat förr	Ja
4	Är du snusare?			

		Nej, eller <1 glas/v	Ja, 1-5 glas/v	Ja, 5-9 glas/v	Ja, 10-14 glas/v	Ja, 15-19 glas/v	Ja, >19 glas/v
5	Dricker du alkohol? (vin, öl eller sprit) Se nedan förklaring av begreppet ”standardglas”						

Ett standardglas alkohol motsvarar **ett glas bordsvin** (12-15 cl), **en flaska starköl** (33 cl, 5 procent), **ett litet glas dessertvin** (8 cl) eller **en grogg** (knappt 4 cl sprit).

		Ingen tid	0-30 min	30-60 min	60-120 min	>120 min
6	Hur mycket tid ägnar du en vanlig vecka åt fysisk träning, som får dig att bli andfådd, t ex löpning, motionsgymnastik, bollsport?					

		Ingen tid	0-30 min	30-60 min	1-2 tim	2-3 tim	3-5 tim	>5 tim
7	Hur mycket tid ägnar du en vanlig vecka åt vardagsmotion, t ex promenader, cykling, trädgårdsarbete? Räkna samman all tid (minst 10 min åt gången)							

	Har eller har du haft någon av följande sjukdomar?	Ja	Nej	Vet inte
8	Hjärninfarkt/stroke?			
9	Hjärnblödning?			
10	Övergående symtom på stroke, sk TIA-attack?			
11	Kärlkramp			
12	Hjärtinfarkt			
13	Diabetes			

	Har du genomgått någon av följande operationer?	Ja	Nej	Vet inte
14	Inläggning av nät (sk stent) i något av hjärtats kranskärl?			
15	Ballongvidgning av kranskärl i hjärtat?			

16	Bypassoperation i hjärtat?			

Har du några kommentarer till detta frågeformulär?

_____

_____

TACK FÖR DIN MEDVERKAN!

Quality of life measures (WHOQOL-BREF) after baseline and mean change

	Yoga group ITT, n=91	**Control group ITT, n=90**
WHO1† score, **overall quality of life**, mean (SD)	4.2 (0.6)	4.2 (0.8)
Change from baseline	0.1 (-0.0 to 0.2)	0.1 (-0.1 to 0.2)
P-value	0.225	0.401
Difference vs. control	0.0 (-0.1 to 0.2)	
P-value	0.865	
WHO2‡ score, **health satisfaction**, mean (SD)	3.8 (0.8)	3.6 (0.8)
Change from baseline	0.3 (0.1 to 0.4)	0.0 (-0.1 to 0.2)
P-value	**0.000***	0.453
Difference vs. control	0.2 (0.1 to 0.4)	
P-value	**0.008***	
WHOQOL-BREF, physical domain score, mean (SD)	73.5 (14.7)	69.8 (14.1)
Change from baseline	1.9 (0.1 to 3.7)	-2.0 (-4.1 to 0.0)
P-value	**0.035***	0.055
Difference vs. control	4.0 (1.2 to 6.7)	
P-value	**0.005***	
WHOQOL-BREF, psychological domain score, mean (SD)	71.7 (12.8)	70.7 (12.0)
Change from baseline	1.9 (0.3 to 3.5)	-1.0 (-2.7 to 0.7)
P-value	**0.023***	0.233
Difference vs. control	2.9 (0.6 to 5.2)	
P-value	**0.015***	
WHOQOL-BREF, social relations domain score, mean (SD)	73.4 (15.5)	71.1 (14.3)
Change from baseline	0.6 (-1.9 to 3.2)	-0.1 (-1.9 to 1.7)
P-value	0.613	0.918
Difference vs. control	0.7 (-2.3 to 3.8)	
P-value	0.638	
WHOQOL-BREF, environment domain score, mean (SD)	77.2 (8.9)	74.9 (10.2)
Change from baseline	1.3 (-0.1 to 2.7)	-0.7 (-2.2 to 0.7)
P-value	0.060	0.339
Difference vs. control	2.0 (0.3 to 4.0)	
P-value	**0.046***	

Notes: Means (95% CI) unless stated otherwise.

* Significant change from baseline

ITT, intention to treat; SE, standard error of the mean; SBP, systolic blood pressure; DBP, diastolic blood pressure.

†**WHO 1**: How would you rate your quality of life? Very poor (1), poor (2), neither poor nor good (3), good (4), very good (5)

‡**WHO 2**: How satisfied are you with your health? Very dissatisfied (1), dissatisfied (2), neither satisfied nor dissatisfied (3), satisfied (4), very satisfied (5)

Table 5

Mean BP after intervention and adjusted mean change in BP, including per protocol set analysis

	Yoga group		Control group	
	OC, n=85	**PPS, n=72**	**OC, n=86**	**PPS, n=81**
SBP (mmHg), mean (SD)	145.4 (13.4)	145.1 (13.7)	145.2 (12.8)	145.4 (13.0)
Change from baseline	-3.8 (-6.5 to -1.2)	-4.5 (-7.4 to -1.5)	-4.5 (-7.0 to -1.9)	-3.9 (-6.6 to -1.2)
P-value	**0.006***	**0.003***	**0.001***	**0.005***
Difference vs. control	0.5 (-3.0 to 3.9)	-0.5 (-4.2 to 3.2)		
P-value	0.783	0.805		
DBP (mmHg), mean (SD)	86.3 (7.7)	85.7 (7.6)	84.9 (7.7)	85.1 (7.8)
Change from baseline	-1.7 (-3.3 to -0.2)	-1.8 (-3.5 to -0.1)	-3.0 (-4.6 to -1.4)	-2.7 (-4.3 to -1.1)
P-value	**0.028***	**0.034***	**0.000***	**0.001***
Difference vs. control	1.4 (-0.7 to 3.4)	0.8 (-1.4 to 3.0)		
P-value	0.201	0.468		

Notes: Means (CI) unless stated otherwise.

* Significant change from baseline

OC, observed cases; PPS, per protocol set; SE, standard error of the mean; SBP, systolic blood pressure; DBP, diastolic blood pressure.

The PPS consists of all patients who (1) practiced yoga at least once a week for nine weeks or more and (2) had no change in medication during the study period

Table 6

Self-rated QOL and health satisfaction after intervention and adjusted mean change, including per protocol set analysis

	Yoga group		Control group	
	OC, n=90,91	**PPS, n=72**	**OC, n=90**	**PPS, n=81**
WHO1 score, mean (SD)	4.2 (0.6)	4.3 (0.6)	4.2 (0.8)	4.3 (0.7)
Change from baseline	0.1 (-0.0 to 0.2)	0.1 (-0.1 to 0.2)	0.1 (-0.1 to 0.2)	0.1 (-0.1 to 0.2)
P-value	0.225	0.357	0.401	0.292
Difference vs. control	0.0 (-0.1 to 0.2)	0.0 (-0.2 to 0.2)		
P-value	0.865	0.930		
WHO2 score, mean (SD)	3.8 (0.8)	3.9 (0.8)	3.6 (0.8)	3.6 (0.7)
Change from baseline	0.3 (0.1 to 0.4)	0.3 (0.1 to 0.4)	0.0 (-0.1 to 0.2)	0.0 (-0.1 to 0.2)
P-value	**0.000***	**0.003***	0.453	0.436
Difference vs. control	0.2 (0.1 to 0.4)	0.2 (0.1 to 0.4)		
P-value	**0.008***	**0.010***		

Notes: Means (95% CI) unless stated otherwise.

* Significant change from baseline

OC, observed cases; PPS, per protocol set; SE, standard error of the mean; SBP, systolic blood pressure; DBP, diastolic blood pressure.

The PPS consists of all patients who (1) practiced yoga at least once a week for nine weeks or more and (2) had no change in medication during the study period

Table 7

Scores on stress (PSS), anxiety and depression (HAD) after intervention and adjusted mean change including per protocol set analysis

	Yoga group		Control group	
	OC, n=84	PPS, n=66	OC, n=86	PPS, n=77
PSS score				
Mean (SD)	19.7 (7.6)	19.2 (7.7)	18.6 (8.2)	18.1 (8.0)
Change from baseline	-1.8 (-3.1 to -0.7)	-1.5 (-2.8 to -0.2)	-1.3 (-2.7 to 0.1)	-1.6 (-3.0 to -0.2)
P-value	**0.002***	**0.028***	0.071	**0.030***
Difference vs. control	-0.4 (-1.9 to 1.6)	0.4 (-1.5 to 2.2)		
P-value	0.849	0.710		
HAD total score				
Mean (SD)	6.2 (4.8)	5.7 (4.5)	6.6 (6.1)	6.2 (5.5)
Change from baseline	-1.7 (-2.5 to -0.8)	-1.7 (-2.6 to -0.8)	-0.3 (-1.1 to 0.6)	-0.4 (-1.1 to 0.3)
P-value	**0.000***	**0.001***	0.534	0.286
Difference vs. control	-1.2 (-2.3 to -0.1)	-1.1 (-2.2 to -0.0)		
P-value	**0.036***	**0.042***		
HAD anxiety score				
Mean (SD)	4.4 (3.3)	4.1 (3.3)	4.1 (3.6)	3.8 (3.3)
Change from baseline	-0.9 (-1.5 to -0.3)	-0.8 (-1.6 to -1.1)	-0.5 (-1.0 to 0.1)	-0.6 (-1.1 to -0.1)
P-value	**0.006***	**0.024***	0.095	**0.013***
Difference vs. control	-0.2 (-1.0 to 0.5)	-0.1 (-0.9 to 0.7)		
P-value	0.531	0.854		
HAD depr. score				
Mean (SD)	1.8 (2.2)	1.6 (1.9)	2.5 (3.0)	2.4 (2.7)
Change from baseline	-0.8 (-1.1 to -0.4)	-0.8 (-1.2 to -0.5)	0.2 (-0.2 to 0.6)	0.2 (-0.3 to 0.6)
P-value	**0.000***	**0.000***	0.389	0.221
Difference vs. control	-0.9 (-1.5 to -0.4)	-1.0 (-1.5 to -0.5)		
P-value	**0.001***	**0.000***		

Complete case analysis. Notes: Means (CI) unless stated otherwise.

* Significant change from baseline

PSS, perceived stress scale; HAD, hospital anxiety and depression scale; OC, observed cases; PPS, per protocol set; SE, standard error of the mean; SBP, systolic blood pressure; DBP, diastolic blood pressure

The PPS consists of all patients who (1) practiced yoga at least once a week for nine weeks or more and (2) had no change in medication during the study period