Complementary Therapies in Medicine 66 (2022) 102825

Contents lists available at ScienceDirect

Complementary Therapies in Medicine

journal homepage: www.elsevier.com/locate/ctim

Clinical effects of using a massage chair on stress measures in adults: A pilot randomized controlled trial☆

Ji Yeon Baek, Eunju Lee, Bora Gil, Hee-Won Jung *, Il-Young Jang *

Department of Geriatrics, Division of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

ARTICLE INFO

Keywords:
Massage chair
Cortisol
Stress hormone

ABSTRACT

Objective: Since the clinical benefits of a massage chair have not been fully elucidated, we aimed to assess the effects of the long-term use of a massage chair on stress measures in adults.
Design: Randomized controlled trial.
Setting: Community.
Interventions
In total, 80 adults aged 50–75 years were randomly assigned to the intervention group (n=41) and control group (n=39). The intervention group used the massage chair twice a day for 6 months. The control group was educated about lifestyle modification.
Main outcome measures: The primary outcome was the change in serum cortisol levels in the morning (8 a.m.) and afternoon (1 p.m.), and the secondary outcomes included changes in levels of dehydroepiandrosterone-sulfate (DHEA-S), serotonin, insulin-like growth factor, erythrocyte sedimentation rate, high sensitivity C-reactive protein, and natural killer cell activity, and results from a questionnaire on mood, cognition, and quality of life.
Results: The use of the massage chair was associated with a decreasing trend in serum cortisol levels at 1 p.m. (-2.68 ug/dL, $p = 0.059$). Serum DHEA-S levels significantly decreased with the intervention (-9.66 ug/dL, $p = 0.003$). In addition, the perceived rate of depression and health status considerably improved following the intervention.
Conclusions: Chronic stress in adults could be effectively managed using a massage chair.

1. Introduction

Stress can provoke biological responses, which could impend homeostasis both extrinsically and intrinsically.[1,2] Since stress response is the physiological interface of the organism interacting with the dynamically changing environment,[3] it might not lead to a significant adverse impact on human health if properly managed. However, severe and prolonged stress beyond an individual's threshold might result in adverse physiological changes. Stress response mainly exerts its effects through the autonomic nervous system and hypothalamic-pituitary-adrenal (HPA) axis, affecting vital organs and systems, such as the central nervous, circulatory, gastrointestinal, and immune systems.[2,4]

Stress and stress response could clinically result in various adverse health consequences. For example, coronary artery disease and arrhythmia are reportedly associated with psychosocial stress.[5,6] Intensive and long-term stress might result in cognitive problems, such as memory loss and increased risk of dementia.[7,8] Moreover, excessive stress reportedly might alter the immune function and increase the susceptibility to infectious diseases.[9,10] Furthermore, studies have shown that exposure to stressors might adversely affect the mood, quality of life, social functioning, and even increase the risk of death.[11,

Abbreviations: BEPSI-K, brief encounter psychosocial instrument; DHEA-S, dehydroepiandrosterone-sulfate; ESR, erythrocyte sedimentation rate; EQ-5D-5L, EuroQol-5 Dimensions-5 Levels; EQ-VAS, EuroQol-Visual Analog Scale; hsCRP, high sensitivity C-reactive protein; HPA, hypothalamic-pituitary-adrenal; IGF-1, insulin-like growth factor; IFN-γ, interferon gamma; NK, natural killer; PRO, patient-reported outcome; RIA, radioimmunoassay; RCT, randomized controlled trial; SGDS-K, short form of the geriatric depression scale.

☆ Clinical trial number: ClinicalTrials.gov (NCT03732729).

* Correspondence to: Division of Geriatrics, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Republic of Korea.
E-mail addresses: hwjung@amc.seoul.kr (H.-W. Jung), dr.onezero2@amc.seoul.kr (I.-Y. Jang).

https://doi.org/10.1016/j.ctim.2022.102825
Received 6 December 2021; Received in revised form 2 March 2022; Accepted 21 March 2022
Available online 24 March 2022

[12] Therefore, numerous strategies have been developed and studied to alleviate the possible adverse health effects of stress by effective management of stress through meditation, mindfulness, aromatherapy, and massage.[13–16]

Among the traditional methods for stress management, hand massage reportedly has diverse effects on the human body. The known effects of hand massage include alleviation of depression and pain,[17] improvement of sleep quality, and heart rate stabilization.[18] In addition, hand massage could modify the levels of several hormones, such as decreased serum cortisol and increased dopamine, serotonin, and oxytocin levels.[17,19,20] However, results from previous studies focusing on the changes in the hormone levels following hand massage were less reliable owing to limitations in the research settings and sample size.[17–20] Hence, these studies failed to elucidate the mechanism of biological response associated with hand massage.

Automated massage chair was invented in Japan in the 1950s and has gained popularity owing to the aging population and sedentary lifestyle. In Korea, the market size of massage chairs has increased steadily since the middle of the 2000s and reached 0.8 billion USD in 2019,[21,22] with demands across all age groups, for stress management. As modern society is characterized by rapid industrialization, intellectualization, and digitalization, a life of modern people is full of management and adaptation to new environmental changes causing a psychological stress. Hence, we focus on the way of managing stress regularly with convenience, having a massage by automated massage chair. Although several studies have evaluated the effect of massage chair on diverse parameters, such as pain control,[23] sleep quality, fatigue,[24] and physiological markers including heart rate and blood pressure,[25,26] none of the previous studies focused on the effect of massage chair on the stress hormones through a randomized controlled trial (RCT). There was the study investigating the serum cortisol level after the use of massage chair; however, it was limited to evaluate general stress responses by measuring a single stress-related hormone, the cortisol, in a short study period.[26] In this RCT, testing the hypothesis that the use of massage chair might reduce the subjective level of stress and modify the stress-related hormones, we aimed to assess the effects of the long-term use of massage chair in sedentary adults.

2. Material and methods

2.1. Trial population

In this trial, adults aged 50–75 years were considered eligible for participation. After assessing the baseline sociodemographic and physical parameters, and comorbidity status, participants were excluded if they were unable to sign their own informed consent, had any disability or limb damage, exercised regularly more than twice a week during the last 6 months, received regular massage during the last 6 months, were confirmed to have osteoporosis (bone mineral density T score < -2.5) or had a history of compression fracture, had clinical diagnosis of cortisol-metabolism disorder or other diseases that could affect the steroid levels, used any medicine related to steroid secretion or metabolism within the last 2 weeks, had life expectancy of less than 12 months (e.g., symptomatic heart failure, end-stage renal disease, and malignancy), and had a spouse already enrolled in this trial. The trial protocol, available at ClinicalTrials.gov (NCT03732729), was approved by the institutional review board of Asan Medical Center (IRB No. 2018-1204). The study registration following the enrollment of the participants started was delayed by a month since the preparatory process for trial registration took more time than anticipated. All ongoing and related trials for this intervention are registered. All the procedures adhered to the tenets of the Declaration of Helsinki, and all the participants provided written informed consent before participation in the study.

2.2. Randomization and trial intervention

Participants were randomly assigned, in a 1:1 ratio, to receive a massage chair in addition to lifestyle modification for stress management (intervention group), or lifestyle modification alone (control group). We employed a computed randomization method stratified by the participant's age (50–64 years or 65–75 years) and sex for allocation considering the age and sex effects on the level of stress-related hormones.[27,28]

We used a massage chair (Bodyfriend Inc., Seoul, Korea), which can massage the entire body with multiple massage balls, rollers, and airbags. In the intervention group, participants were asked to use this massage chair for 30 minutes, twice a day. The massage chair was delivered to the participant's home and collected at the end of the study. The total recommended period of use was 6 months and the participants were expected to respond to a telephone call to report the rate of compliance and adverse events, every month during this study period.

The trial was discontinued if the participants experienced any severe adverse events or had safety issues during the study period. In both the control and intervention groups, the participants received general education regarding diet, exercise, and mental health (lifestyle modification) by a geriatrician at baseline examination.

2.3. Measurement

Baseline serum white blood cell (WBC) counts (including neutrophils and lymphocytes) and hemoglobin and creatinine levels were measured at the beginning of the study. All the hormones and inflammatory markers, and natural killer (NK) cell activity were measured both, at the baseline and at the end of the study period.

A total of 15 ml blood samples were collected and distributed to different tubes: 2 ml in in ethylene diamine tetra-acetic acid (EDTA) for WBC and hemoglobin, 2 ml in clot activator and gel tube for chemistry (creatinine, albumin, alanine aminotransferase, and C-reactive protein), 10 ml in clot activator and gel tube for endocrine sampling (cortisol, dehydroepiandrosterone-sulfate [DHEA-S], serotonin, and insulin-like growth factor-1 [IGF-1]), and 1 ml in NK vue® tube with heparinization for measuring NK cell activity. Serum cortisol was measured by radioimmunoassay (RIA) using the Coat-A-Count® cortisol kit (Siemens Healthcare Diagnostics, Los Angeles, CA, USA). DHEA-S levels were determined by RIA using the Coat-A-Count® DHEA-SO4 kit (Siemens Healthcare Diagnostics, Los Angeles, CA, USA). Serotonin levels were measured by liquid chromatography-tandem mass spectrometry with a 1290 high performance liquid chromatography (Agilent, Santa Clara, CA, USA), Qtrap 5500 (ABSciex, Framingham, MA, USA) and a reverse phase column (Pursuit 5 C18 150 $\times$ 2 mm). Serum IGF-1 concentration was analyzed using commercially available kits for IGF-1, immunoradiometric assay A15729 (Immunotech, Prague, Czech Republic). Erythrocyte sedimentation rate (ESR) and high sensitivity C-reactive protein (hsCRP) rates were also measured. Normal serum hsCRP levels and ESR were considered as ≤ 0.6 mg/dL and ≤ 20 mm/h, respectively. NK cell activity was measured using NK Vue® kit (ATgen, Sungnam, Korea) as per the manufacturer's instructions. The principle of NK Vue® is to detect interferon gamma (IFN-γ) secreted by the NK cells by using an engineered recombinant cytokine, Promoca (ATgen), as a stimulant. Released IFN-γ was quantitatively measured using sandwich enzyme-linked immunosorbent assay.[29]

2.4. Questionnaires

Participants were asked to complete a series of questionnaires to evaluate the mood, cognitive function, and quality of life. For evaluating the cognitive performance, we used the Korean version of Mini-Mental Status Examination that included the cognitive domains of orientation, attention, memory, language, and visuoconstruction.[30] For evaluating the mood, we used the Korean version of the short form of the geriatric

depression scale (SGDS-K) comprising 15 items.[31] To assess the level of stress, we used the Korean version of brief encounter psychosocial instrument (BEPSI-K), comprising five items, with scores for each item ranging from 1 ("never") to 5 ("always"). The final score was calculated by dividing the sum of 5 items by 5.[32] For self-reported quality of life, we used the EuroQol-5 Dimensions-5 Levels (EQ-5D-5L), which is widely used for the overall measure of health status, comprising 2 parts. The first part evaluated 5 parameters of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) with scores ranging from level 1 ("no problem") to level 5 ("unable to/extreme problem").[33] EQ-5D index score was calculated as the weighted index number ranging from -0.148 (lowest) to 1 (healthy status).[34] The second part of the questionnaire was EuroQol-Visual Analog Scale (EQ-VAS), where participants were asked to rate their perceived health from 0 ("the worst imaginable health") to 100 ("the best imaginable health").

2.5. Outcomes

In this study, the primary outcome was serum cortisol level in the morning (8 a.m.) and afternoon (1 p.m.). Secondary outcomes were other serum hormone levels (DHEA-S, cortisol/DHEA-S, serotonin, and IGF-1), inflammatory markers (ESR and hsCRP), and NK cell activity. Moreover, the patient-reported outcomes (PROs), participants' perceived evaluation of mood, cognitive function, and quality of life were assessed as secondary outcomes. All the measures were evaluated at baseline and at 6 months of the trial.

2.6. Statistical analysis

On the basis of a previous report showing the change of serum cortisol level following hand massage,[20] we assumed the mean plasma cortisol level as 26 ug/dL (standard deviation 18 ug/dL) and estimated effect size as -12 ug/dL. Hence, we determined that a sample of 80 participants would offer 80% power to detect the change in cortisol levels at an alpha level of 5% when estimating a 10% follow-up loss during the study. We performed the per-protocol analysis as the primary analysis, which included participants whose rate of compliance with using the massage chair was above 80% to evaluate the true efficacy of using a massage chair.

Primary and secondary outcomes were analyzed by t-test for parametric variables and Mann–Whitney U test for non-parametric variables. The relationship between the primary outcomes and PROs was assessed using a linear regression model. The IBM SPSS Statistics for Windows, Version 23.0 (IBM corp., Armonk, NY, USA) was used for data analysis. We considered two-sided $p < 0.05$ as statistically significant.

3. Results

3.1. Population characteristics

From October 8, 2018 to August 29, 2019, a total of 105 participants were screened. After excluding 25 participants based on the predefined criteria, 80 participants were randomly assigned to the two groups; 41 in the intervention group and 39 in the control group. Subsequently, 3 participants in the intervention group withdrew from the study owing to failure of massage chair installation, consent withdrawn, and moving abroad. Four participants in the control group withdrew the consent of the study. Thus, 38 and 35 participants in the intervention and control groups, respectively were assessed for outcome measures. Among the 38 participants in the intervention group, 6 were additionally excluded owing to low compliance (< 80%), and finally, 32 and 35 participants in the intervention and control groups, respectively were included for the per-protocol analysis (Fig. 1).

Baseline characteristics of the participants did not show statistically

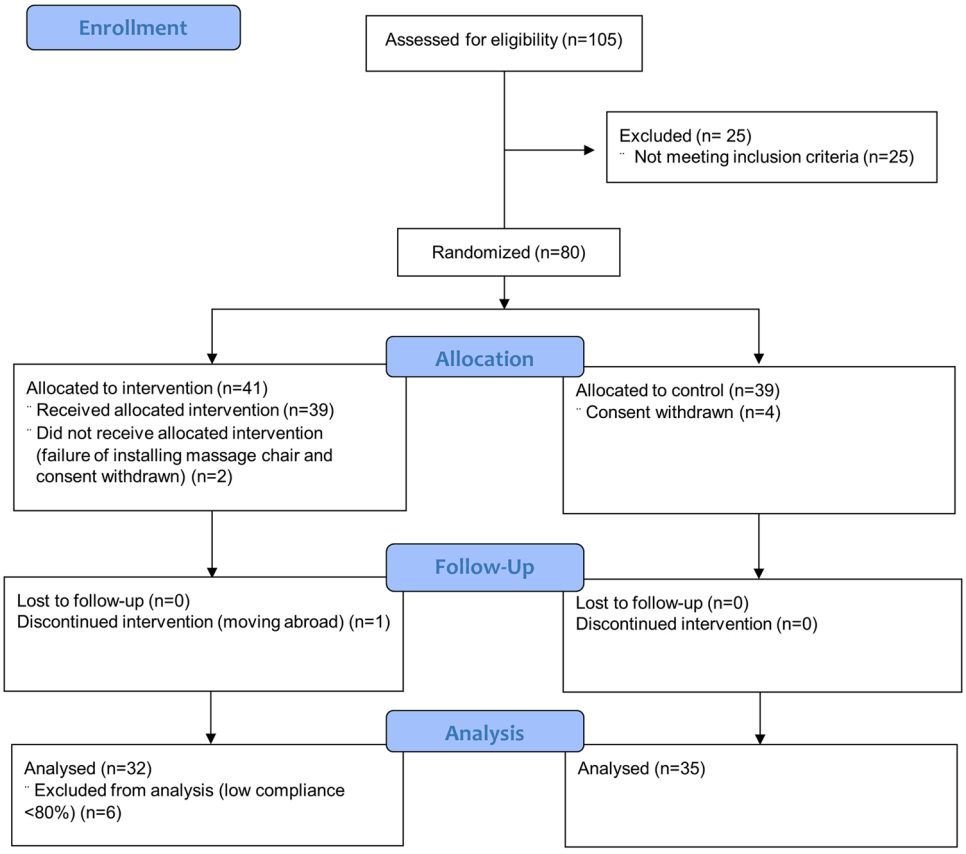

Fig. 1. Flow chart of the study design.

significant differences between the two groups in terms of anthropometric parameters (height, weight, body mass index), socioeconomic status, vital signs, comorbidities, and basic laboratory findings. The mean rate of compliance with the massage chair was 90.49% (standard deviation [SD] 8.28%) (Table 1).

3.2. Primary outcome

In the intervention group, the mean serum cortisol at 8 a.m. was 15.07 mg/dL (SD 4.09 mg/dL) at baseline and 12.96 mg/dL (SD 4.06 mg/dL) after the intervention, while in the control group, it was 15.48 mg/dL (SD 3.96 mg/dL) at baseline and 13.80 mg/dL (SD 4.77 mg/dL) at the end of the study, in the per-protocol population (Table 2). However, no further statistically significant reduction in the levels of cortisol in the intervention group was observed (p = 0.715). The mean serum cortisol at 1 p.m. in the intervention group was 11.58 mg/dL (SD 3.48 mg/dL) at baseline and 8.90 mg/dL (SD 2.80 mg/dL) after the intervention, whereas in the control group, it was 10.82 mg/dL (SD 2.57 mg/dL) at baseline and 9.97 mg/dL (SD 2.50 mg/dL) at the end of the study, in the per-protocol population. The difference in the cortisol level at 1 p.m. was significantly larger in the intervention group (-2.68 mg/dL, 95% confidence interval [CI] = -4.38 to -0.99) than that in the control group (-0.85 mg/dL, 95% CI = -1.87 to 0.16) (p = 0.059) (Table 2). Additional analyses in the modified intention-to-treat population are presented in Table S1.

Table 1
Baseline characteristics of the patients in the per-protocol population.

Characteristic	Massage Chair Group (n=32)	ControlGroup (n=35)	*p*-value
Male sex — n (%)	14 (43.8)	17 (48.6)	0.693
Age — years	60.19±5.96	60.71±5.24	0.702
Height — cm	162.64 ±8.35	164.30±7.58	0.398
Weight — kg	66.02±11.01	65.33±10.14	0.793
Body-mass index — kg/m^2	24.82±2.68	24.11±2.90	0.297
Compliance — %	93.26		
Companion			0.502
Yes — n (%)	30 (93.8)	34 (97.1)	
Decision maker			0.408
Oneself — n (%)	28 (87.5)	28 (80.0)	
Spouse — n (%)	4 (12.5)	7 (20.0)	
Education level			0.563
Less than middle school — n (%)	1 (3.1)	1 (2.9)	
Less than high school — n (%)	8 (25)	13 (37.1)	
University or more — n (%)	23 (71.9)	21 (60.0)	
Monthly household income[a]			0.486
100-199 — n (%)	9 (28.1)	13 (37.1)	
200-299 — n (%)	7 (21.9)	4 (11.4)	
300-399 — n (%)	3 (9.4)	6 (17.1)	
400-499 — n (%)	3 (9.4)	5 (14.3)	
500-599 — n (%)	10 (31.2)	7 (20.0)	
Systolic blood pressure — mmHg	128.66±11.74	128.57 ±14.25	0.979
Diastolic blood pressure — mmHg	75.41±7.73	75.34±8.51	0.975
Heart rate — bpm	75.34±9.49	74.20±8.76	0.61
Charlson Comorbidity Index (CCI)	1.66±0.6	1.83±0.79	
Myocardial Infarct — n	1	0	0.292
Ulcer Disease — n	0	0	NA
Mild Liver Disease — n	2	0	0.133
Diabetes (without complication) — n	0	3	0.09
Solid Tumor (non-metastatic) — n	0	2	0.17
Hemoglobin — g/dL	13.65±1.31	13.97±1.27	0.308
WBC — 10^3/uL	5.65±1.28	5.69±1.38	0.907
Neutrophil — %	51.19±8.72	49.77±7.58	0.48
Lymphocyte — %	38.28±8.25	39.23±7.66	0.628
Serum Creatinine — mg/dL	0.75±0.15	0.78±0.16	0.408
Serum Albumin — g/dL	4.03±0.23	4.04±0.21	0.914
ALT — IU/L	23.7±12.15	17.82±5.28	0.131

Values are presented as means±standard deviation or number (%), or only numbers. ALT = alanine aminotransferase; WBC = white blood cell; NA = not applicable.
[a] 10,000 won.

3.3. Secondary outcomes

The ratio of cortisol and DHEA-S (cortisol/DHEA-S) at 8 a.m. and at 1 p.m. did not show significant differences between the two groups in the per-protocol analysis (Table 3). Serum DHEA-S level was decreased by 9.66 ug/dL (95% CI = -19.27 to -0.05) following the use of a massage chair; however, the serum DHEA-S level was increased in the control group (p = 0.003) (Table 3).

Serotonin and IGF-1 demonstrated an upward trend following the use of the massage chair compared to the downward trend in the control group. However, the differences were not statistically significant (Table 3). The levels of the inflammatory markers (ESR, hsCRP level) did not significantly differ between the two groups. However, NK cell activity showed an increasing trend following the intervention, compared to the decreasing trend in the control group (Table 3). Additional analyses in the modified intention-to-treat population are presented in Table S1.

Among the PROs, there were significant changes in the depression (SGDS-K) and self-rated health status (EQ-VAS). In the intervention group, SGDS-K score decreased by 1.41 (95% CI = -2.1 to -0.71) from a mean of 3.69 (SD 2.72) to a mean of 2.28 (SD 2.05). However, in the control group, the SGDS-K score increased by 0.15 from a mean of 1.91 (SD 1.62) to 2.06 (SD 2.12) (Table 4). Additionally, the EQ-VAS score significantly increased by 3.91 (95% CI = -0.23 to 8.05) from a mean of 78.13 (SD 13.23) to 82.03 (SD 11.42) in the intervention group. While in the control group, the score decreased by 2.74 (95% CI = -6.76 to 1.27) from a mean of 85.37 (SD 9.59) to 82.63 (SD 9.81) (Table 4). Additional analyses in the modified intention-to-treat population are presented in Table S2.

3.4. Relationships between the changes in cortisol and PROs

Among the PROs, only EQ-VAS score showed a significant relevance with the cortisol levels (Fig. 2). In the intervention group, higher EQ-VAS score was related to low cortisol levels (p = 0.011 [8 a.m.], p = 0.046 [1 p.m.]).

3.5. Adverse events

Only one participant reported visual disturbance due to newly diagnosed cataract during the trial. However, its causal relationship with the intervention was determined to be weak by the researchers. There were no other adverse events reported during the trial.

4. Discussion

This study demonstrated that 6-month use of a massage chair resulted in a significant reduction in DHEA-S and a trend of decreasing serum cortisol levels measured at 1 p.m. Furthermore, there was a significant improvement in the depressive mood and subjective health status using a massage chair.

Despite the increasing trend of use of massage chairs in recent years, 22 scientific evidence illustrating the positive effects of massage chair on the human body is scarce. Previous studies demonstrated that massage chair was effective in improving the sleep quality, 24 fatigue, concentration, and memory[35] and in relieving pain.[23] While none of the previous studies attempted to correlate the use of massage chair with stress management, our study possesses the strength and novelty of

Table 2
Primary outcome in the per-protocol population.

	Measures				Changes		
	Massage Chair Group(n=32)		Control Group (n=35)		Massage ChairGroup(95% CI)	Control Group (95% CI)	*p*- value
	Baseline	6-month follow-up	Baseline	6-month follow-up			
Cortisol at 8 a.m. (ug/dL)	15.07 (4.09)	12.96 (4.06)	15.48 (3.96)	13.8 (4.77)	-2.11(-4 to -0.22)	-1.68(-3.16 to -0.19)	0.715
Cortisol at 1 p.m. (ug/dL)	11.58 (3.48)	8.90 (2.80)	10.82 (2.57)	9.97 (2.50)	-2.68(-4.38 to -0.99)	-0.85(-1.87 to 0.16)	0.059

Values are presented as mean with standard deviation, or changes with confidence intervals. CI = confidence interval.

Table 3
Secondary outcomes in the per-protocol population.

	Measures				Changes		
	Massage Chair Group (n=32)		Control Group (n=35)		Massage Chair Group (95% CI)	Control Group (95% CI)	*p*- value
	Baseline	6-month follow-up	Baseline	6-month follow-up			
Cortisol/DHEA-S at 8 a.m.	0.25 (0.19)	0.25 (0.21)	0.27 (0.18)	0.22 (0.13)	0.00(-0.07 to 0.07)	-0.05(-0.09 to 0.01)	0.205
Cortisol/DHEA-S at 1 p.m.	0.20 (0.18)	0.16 (0.11)	0.19 (0.14)	0.16 (0.10)	-0.04(-0.11 to 0.02)	-0.03(-0.07 to 0)	0.729
DHEA-S (ug/dL)	**86.55 (49.79)**	**76.89 (46.08)**	**83.01 (49.01)**	**89.75 (58.44)**	**-9.66(-19.27 to -0.05)**	**6.74(0.98 to 12.5)**	**0.003**
Serotonin (ng/mL)	103.41 (31.16)	107.21 (32.98)	124.06 (38.89)	121.78 (32.45)	3.79(-3.84 to 11.43)	-2.28(-9.95 to 5.39)	0.63
IGF-1 (ng/mL)	97.83 (34.71)	100.88 (34.25)	108.71 (37.80)	108.35 (32.25)	3.04(-9.1 to 15.19)	-0.36(-8.46 to 7.74)	0.257
ESR (mg/dL)	11.42 (9.24)	10.35 (6.52)	11.13 (6.79)	11.25 (7.91)	-1.06(-3.64 to 1.52)	0.12(-1.71 to 1.96)	0.444
hsCRP (mm/hr)	0.13 (0.23)	0.09 (0.09)	0.12 (0.25)	0.08 (0.08)	-0.04(-0.11 to 0.03)	-0.04(-0.11 to 0.02)	0.934
NK Cell Activity (IFN-γ)	4688.46 (5126.29)	4738.42 (6073.43)	4027.41 (3989.92)	4011.88 (4646.56)	49.96(-1815.18 to 1915.11)	-15.53(-812.52 to 781.46)	0.949

Values are presented as mean with standard deviation, or changes with confidence intervals. Significant changes ($p < 0.05$) are shown in bold type.
CI = confidence interval; DHEA-S = dehydroepiandrosterone-sulfate; ESR = erythrocyte sediment rate; hsCRP = high sensitivity C-reactive protein; IGF-1 = insulin-like growth factor 1; IFN-γ = interferon gamma; NK cell = Natural killer cell.

Table 4
Mood, cognitive function, and quality of life in the per-protocol population.

	Measures				Changes		
	Massage Chair Group(n=32)		Control Group (n=35)		Massage Chair Group (95% CI)	Control Group (95% CI)	*p*- value
	Baseline	6-month follow-up	Baseline	6-month follow-up			
K-MMSE	28.88 (1.58)	28.91 (1.40)	28.03 (2.12)	28.69 (1.37)	0.03(-0.54 to 0.6)	0.66(0.02 to 1.29)	0.142
SGDS-K	**3.69 (2.72)**	**2.28 (2.05)**	**1.91 (1.62)**	**2.06 (2.12)**	**-1.41(-2.1 to -0.71)**	**0.15(-0.46 to 0.76)**	**0.001**
BEPSI-K	21.94 (2.11)	22.44 (2.05)	23.29 (1.51)	23.00 (1.88)	0.50(-0.24 to 1.24)	-0.29(-0.76 to 0.19)	0.068
EQ-5D-5L	0.88 (0.08)	0.89 (0.08)	0.90 (0.68)	0.89 (0.08)	0.00(-0.01 to 0.02)	-0.01(-0.03 to 0.02)	0.526
EQ-VAS	**78.13 (13.24)**	**82.03 (11.42)**	**85.37 (9.59)**	**82.63 (9.81)**	**3.91(-0.23 to 8.05)**	**-2.74(-6.76 to 1.27)**	**0.022**

Values are presented as mean with standard deviation, or changes with confidence intervals. Significant changes ($p < 0.05$) are shown in bold type.
CI = confidence interval; BEPSI-K = Korean brief en-counter psychosocial instrument; EQ-5D-5L = Euroqol-5 dimensions-5 levels; EQ-VAS = Euroqol-visual analog scale; K-MMSE = Korean mini-mental status examination; SGDS-K = Korean short form of geriatric depression scale.

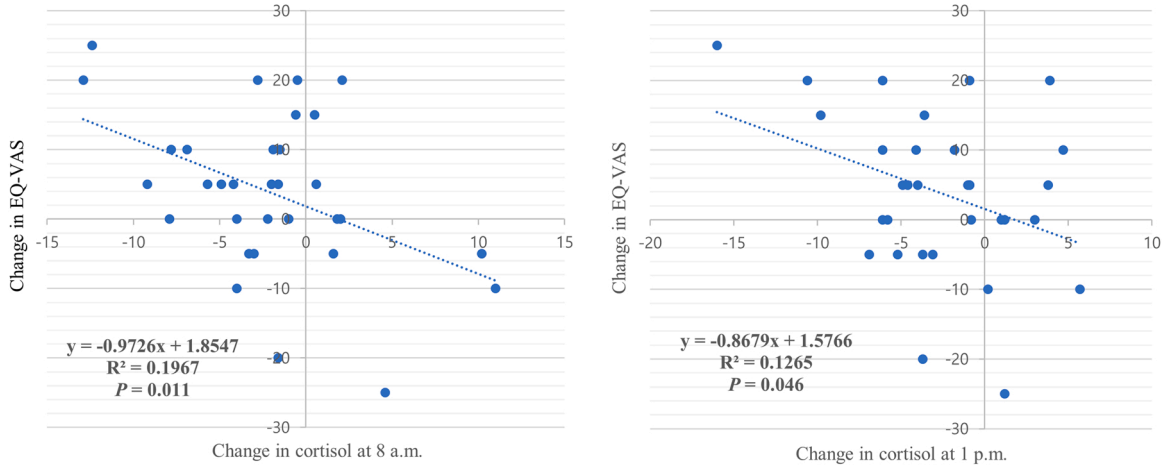

Fig. 2. Relationship between the changes in the EQ-VAS scores and the cortisol levels in the massage chair group. EQ-VAS = Euroqol-visual analog scale.

investigating the level of stress hormones as the main outcome; moreover, the study was a RCT.

Psychosocial stress causes various physiologic changes in the human body by activation of the sympathetic nervous system and HPA axis. In stress conditions, the adrenocorticotropic hormone, a typical hypothalamic hormone, stimulates the adrenal cortex and cortisol is secreted in the zona fasciculata and DHEA-S in the zona reticularis.[36] On the other hand, taking a massage activates parasympathetic nervous system leading to muscle and soft tissue relaxation, and reduction of anxiety.[37,38] Therefore, frequency and length of the massage affect the degree of stress alleviation. Also, it is known that systematic light touch with low intensity, or the use of muscle relaxation tape can have similar biologic actions like massage.[20,39] In this study, DHEA-S was significantly lower at follow-up in the intervention group than that in the control group. DHEA-S, which is a sulfate form of DHEA, has a longer half-life and narrower diurnal variation compared to DHEA. Both DHEA and DHEA-S are used to synthesize the precursors of sex hormones.[40,41] DHEA-S can affect cognitive function and mood by modulating the action of gamma-aminobutyric acid and N-methyl-D-aspartate receptors in certain parts of the brain,[42] and has been reported to be related to stress. DHEA-S increases not only during acute stress,[43] but also in chronic stress conditions, such as post-traumatic stress disorder.[44] A study by a Korean hospital reported that the level of chronic stress owing to one's job was closely related to the DHEA-S rather than cortisol levels.[45] Furthermore, a study from the United States on rhesus monkeys suggested DHEA-S as an important indicator of chronic stress.[41] Elevated cortisol caused by acute stress was gradually relieved as consecutive similar stress was applied in a rhesus monkey. However, increased serum DHEA-S levels were maintained throughout the repetitive stress condition. Consistent with these findings, a significant decrease in the DHEA-S level in our study suggests that chronic stress was relieved by using the massage chair.

Moreover, cortisol levels at 1 p.m. also showed a decreasing trend following the use of the massage chair (Table 2). Numerous studies have already reported that cortisol level was related to diverse stress conditions, such as hard work, unemployment, or divorce.[46–48] Owing to the diurnal pattern of cortisol secretion, the measurement time for assessing the HPA axis is challenging. It usually peaks at 30 minutes after awakening and undergoes two decline phases: the early decline phase, which lasts for 2 hours, and the late decline phase with a more gradual slope than that of the first decline.[49] A recent study demonstrated that the basal serum cortisol level measured between 9 a.m. and 1 p.m. was not inferior to the morning cortisol level measured at 8 a.m. as a single marker for evaluating adrenal insufficiency.[50] Moreover, basal serum cortisol can be considered as a first-line test for evaluating the HPA axis before pituitary surgery.[51] Considering these findings, a diminished level of cortisol at 1 p.m. in our study could indicate stress mitigation using the massage chair.

Despite its strengths, our study has several limitations. First, the relatively small population size and short duration of the study could be inadequate to draw a conclusion about the association between the use of the massage chair and the changes in several hormones. However, the RCT design stratifying age and sex from the allocation period is an obvious strength of the study. Since age and sex of participants can significantly affect not only the amplitude of the cortisol and DHEA-S,[27] but also the general stress response through the HPA axis,[27,28] adjusting these factors from the initial point could be advantageous. Since there is no prior pilot study on the association between the use of a massage chair and cortisol levels, our study should be evaluated as a pilot study for future research. Second, although study examiners who collected the blood samples were unaware of assigned group of the participants, blinding of the participants was impossible. Third, only one day measurement and insufficient sample points of cortisol level could be inaccurate. Since plasma cortisol shows diurnal variation and is easily affected by situational factors of individuals, multiple sampling of cortisol levels for at least 2 days before and after the intervention is recommended.[52] Likewise, NK cell activity measured by the level of IFN-γ, could be affected by this diurnal variation of serum cortisol, since stress response activates glucocorticoid receptors resulting in IFN-γ suppression.[53,54] Fourth, although the subjective stress level estimated by the BEPSI-K questionnaire showed no significant changes throughout the study in the intervention group, we did not consider the effects of the possible stress from venipuncture itself and the emotional pressure to use the massage chair twice a day on hormone levels, especially in adults with frailty. Lastly, the difference in individual personality and stress coping style could act as confounding variables in evaluation of stress status.

5. Conclusion

The 6-month use of a massage chair not only decreased the serum DHEA-S, but also improved the PROs, including mood and subjective health status. However, serum cortisol levels were not affected by the use of the massage chair. Massage by using an automated massage chair could effectively manage chronic stress. Future studies sampling serum cortisol levels for at least 2 days with a larger population in a more controlled stress condition are warranted for defining an obvious correlation of use of the massage chair with stress measures.

Ethical statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board of Asan Medical Center, Seoul, Korea (IRB No. 2018-1204).

CRediT authorship contribution statement

Ji Yeon Baek: Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **Eunju Lee**: Conceptualization, Funding acquisition, Writing – review & editing. **Bora Gil**: Data curation, Project administration, Writing – review & editing. **Hee-Won Jung**: Formal analysis, Methodology, Writing – review & editing. **Il-Young Jang**: Conceptualization, Funding acquisition, Project administration, Writing – review & editing.

Conflict of interest

Authors declare no conflict of interest.

Data Availability

Data that support the findings of the study are available from the corresponding authors upon reasonable request.

Acknowledgments

The authors thank all the participants for their active participation in the study. This research was funded by Bodyfriend Inc., Seoul, Republic of Korea (2018OM1204). The funder lent massage chairs for the study protocol. The funder played no role in the design, conduct, or reporting of this study. This study was also supported by a grant (2022IP0057) from the Asan Institute for Life Science, Asan Medical Center, Seoul, Republic of Korea.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ctim.2022.102825.

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