The Effect of Aromatherapy with Rose and Lavender on Anxiety, Surgical Site Pain and Extubation Time after Open Heart Surgery: A Double-center Randomized Controlled Trial

Hossein Babatabar Darzi,[1] Amir Vahedian-Azimi,[1]* Saeed Ghasemi,[1] Abbas Ebadi,[2] Thozhukat Sathyapalan[6,] Amirhossein Sahebkar[3,4,5]*

[1]Trauma Research Center, Nursing Faculty, Baqiyatallah University of Medical Sciences, Tehran, Iran.

[2]Behavioral Sciences Research Center, Life style institute, Nursing Faculty, Baqiyatallah University of Medical Sciences, Tehran, IR Iran.

[3]Halal Research Center of IRI, FDA, Tehran, Iran

[4]Neurogenic Inflammation Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

[5]Biotechnology Research Center, Pharmaceutical Technology Institute, Mashhad University of Medical Sciences, Mashhad, Iran

[6] Academic Diabetes, Endocrinology and Metabolism, University of Hull

Correspondence: amirvahedian63@gmail.com; sahebkara@mums.ac.ir; amir_saheb2000@yahoo.com

Running title: Aromatherapy after open heart surgery

This is the peer reviewed version of the following article: Babatabar Darzi, H., Vahedian-Azimi, A., Ghasemi, S., Ebadi, A., Sathyapalan, T., & Sahebkar, A. (in press). The effect of aromatherapy with rose and lavender on anxiety, surgical site pain, and extubation time after open-heart surgery: A double-center randomized controlled trial. Phytotherapy Research, which has been published in final form at https://doi.org/10.1002/ptr.6698 . This article may be used for non-commercial purposes in accordance With Wiley Terms and Conditions for self-archiving.

Abstract

Objective: To determine the effect of aromatherapy with rose and lavender on the patient outcomes after open heart surgery.

Methods: In the clinical-trial patients were randomized to four groups. One group received routine care, the placebo group received a cotton swab soaked in water and the other two groups received either a cotton swab containing 3 drops of rose or lavender essence (0.2 mL).

Results: A total of 160-patients were randomized into four groups. Intergroup anxiety was not significantly different; however, the reciprocal time-group effect was significant among the four groups. The extubation time was significant among the four groups which related to rose essence group compared with the control Group ($P<0.001$) and placebo group ($p=0.029$). The surgical site pain was significant in the rose essence and lavender groups compared to the control group.

Conclusion: Aromatherapy can reduce extubation time, surgical site pain severity, and anxiety in patients undergoing open heart surgery.

Clinical trial identifier: IRCT201510012730N9

Key Words: Airway extubation, Anxiety, Aromatherapy, Coronary artery bypass surgery, Lavender oil, Pain, Rose.

Introduction

Cardiovascular diseases (CVDs) are the most common, chronic and life-threatening disorders world wide.[1] [2] They are projected to be the leading cause of mortality in the world by 2020. [3] The American Heart Association (AHA) speculates that life expectancy would increase in the USA by 7 years if mortality due to CVDs are removed. [4] CVD is the leading cause of mortality in England accounting for 16000 cases of death per year. [5] CVD is also increasing in epidemic proportion in Japan. [6] A study in Finland found that 9.1% of men and 4.9% of women are affected with angina pectoris. [7] Similar to other countries, the CVDs are the major cause of mortality and the lost years of life in Iran. [8] Among the CVDs, the coronary artery disease (CAD) is the leading cause of mortality and 1.5 million people are affected with myocardial infarction (MI) leading to more than 600,000 deaths per year. [9]

Advancements in innovative treatments like thrombolytic treatment, balloon angioplasty, laser therapy and arterectomy have improved the medical management of cardiovascular patients. [10] However, cardiac surgery (CS) is still the mainline treatment for many patients with CVDs. The coronary artery bypass graft (CABG) surgery has been performed for about 35 years through out the world. [11] CABG is used for the management of 26.79% in North America, 0.72% in Asia, 17.94% in Western Europe, and 18.14% in other parts of the world [12] CVD patients. Also, 60% of open heart surgeries (OHSs) in Iran are by CABG surgery. [13] Following CABG surgery, the patients are managed in cardiac care unit (CCU) and mechanical ventilation is one of the most common postoperative treatments for all of these patients [13-14]

The process of weaning the patients from mechanical ventilation is of utmost importance for CABG patients [15] since the long-term use of mechanical ventilation may not only increase the healthcare costs, but also may result in various adverse outcomes.[16,17] There is a strong correlation between “intubation time” and “postoperative bleeding, readmission to the operating room, congestive heart failure, cardiac arrest, and hypotension” after the patient’s condition has stabilized. [18] Hence, the reduction of intubation time would lead to reduced complications. [19]

Moreover, physiologic responses to CABG will lead to stress, anxiety, and restlessness in CS patients predisposing to insomnia, increased oxygen consumption by myocardium, increased workload of the sympathetic system, tachypnea, tachycardia, neurohormonal

responses and hypertension, all of which make the extubation difficult. [20] Consequently, most CS patients receive sedatives and analgesics to diminish pain, stress and anxiety and to facilitate mechanical ventilation. [21] The pharmacological management with sedatives and analgesics are often accompanied by complications such as hypotension, suppressed vital functions such as respiration and heart rate, drowsiness, nausea, vomiting, constipation, drug dependence and tolerance, delayed extubation, [22] anaphylactic reaction, and even shock. In addition to numerous physical and mental complications, they also impose high healthcare cost to the economy. [23]

Non-pharmaceutical methods have been increasingly recognised in recent years to reduce the extubation time and stabilize the vital signs. [24] These non-pharmaceutical procedures such as music therapy [24-25] and educational interventions [26] offers a relatively simple, cheap, noninvasive and low-complication option compared to the pharmaceutical medications. [27]

Aromatherapy is one of the non-pharmaceutical option to manage peri-operative patients. It is classified as a branch of alternative or complementary medicine. It involves the use of volatile herbal oils like essences to improve the psychosomatic health. It is used to relieve pain, anxiety, depression, insomnia, fatigue and exhaustion, asthma, and even self-confidence, success, and creativity. [28] These oils can be used through inhalation, bath, or massage. The most common method used in aromatherapy is massage. [28]

It is believed that the aroma activates the olfactory neurons leading to stimulation of the limbic system; as a result, various neural transmitters are released depending on the type of aroma. These transmitters include enkephalin, endorphin, noradrenaline and serotonin. [28] One of the aromas with a tranquilizing effect is lavender with the scientific name *Lavandula stoechas (Lavandula angustifolia)* of the *Labiatae* family (mints). Linalool and linalyl acetate are the active componenets of this herb. Linalool acts as a tranquilizer by affecting gamma amino butyric acid (GABA)) receptors in the central nervous system (CNS) and linalyl acetate exerts a narcotic effect. Another aroma is the rose aroma that affects the CNS, especially the brain. The two constituents “citronelool” and “2-phenyl ethyl alcohol” in rose possess anxiolytic effects. [29]

There are a few studies on aromatherapy in open heart sugergy (OHS) patients such as cryotherapy and inhalation of rose aroma in reducing pain during extubation, [30] rose aroma on diminishing sternotomy site pain and the reduced need for analgesics, [31] rose aroma inhalation on stress and vital signs, [32] and rose aroma on vital signs. [33] To the best of our

knowledge, no study has so far compared the efficacy of rose and lavender aromas in reducing surgical site pain, anxiety and extubation time. Hence, this study aimed at determining the effect of aromatherapy with rose and lavender aromas on reducing extubation time, surgical site pain and anxiety in patients undergoing OHS.

2. Material and Methods

2.1 Design

The study was a double-center randomized clinical trial.

2.2. Participants

The study was conducted in the CCU of Baqiatallah-e A'zam Hospital and Jamaran Hospital in Tehran, capital of Iran, in 2016. Patients were eligible for study participation if they had the following qualifications: (1) Being a candidate of OHS, (2) willing to participate, (3) age of >18 and <70 years, (4) heartbeat of >60 bpm, (5) systolic BP of >90 mmHg and (6) OHS for the first time. Exclusion criteria were (1) emergency OHS, (2) coagulation disorders activated clotting time (ACT <2.5), (3) allergy to any of the aromas used (on the basis of patient self-report or incidence of symptoms after use), and (5) the need for postoperative intra-aortic balloon pump.

2.3 Randomization

Convenience sampling method was used first, followed by random assignment with octad blocks in four groups (two intervention groups, one control group, and one placebo group). To perform the random assignment with octad blocks, the letter A was allocated to lavender group, B to rose group, C to placebo group, and D to control group. Using the letters A, B, C, and D in octad groups, 8 possible combinations of AABBCCDD, BBAACCDD, ABABCCDD, BABACCDD, ABBACDDC, BAABDCCD, AABBDCDC, and CDDCBAAB were recorded on separate sheets and cast in a box. One of these sheets was drawn out of the box randomly, the letters combination on it was written down again, and was recast in the box. Since the sample size was 180 in this study, this lottery was repeated 23 times and each time the new letters combination and the previous letters combination were noted. Then, a number ranging from 1 to 180 was allocated sequentially to each letter in the successive combinations. Subsequently, each letter was put in an opaque envelope on which numbers

1-180 were written. Each time a patient was selected, one of these pockets was opened on the basis of the number on it and this determined the group to which the patient ought to be assigned. The essence used for the intervention groups was volatile and could penetrate in the surrounding space interfering with other aromas. If both intervention groups were drawn out simultaneously in the lottery in the same day, the manipulation for the intervention groups was performed in separate hospitals to avoid the interference of aromas between the two groups.

2.4 Intervention

In intervention groups, having obtained the permission of the university authorities, the researchers presented to Baqiatallah-A'zam Hospital and Jamaran Hospital in Tehran and explained the research goals and procedures to the head nurse in charge. The samples who qualified for inclusion as participants were selected in the hospital setting the day before surgery. Informed written consent was obtained from each patient. The demographic and clinical information questionnaire was completed by the patients and in some cases by the use of their medical records. At the completion of surgery, the patients were admitted to the CCUs. After transferring to the CCU, the first basic vital signs were recorded from the monitor for the four groups before dripping rose and lavender essence or the placebo immediately after the first triggered inspiration by the ventilated patient or the spontaneous respiration by the patient. The main components of rose and lavender oils were citronellol (41.23%) and ceineole (21.33%), respectively. After triggering of the first inspiration, a cotton swab soaked in three drops of rose or lavender essence (0.2 mL) was placed on the patient's chest for 15 min. Then, the vital signs were recorded half-hourly before extubation and quarterly after extubation for 1 h. The frequency of vital signs recording differed from patient to patient depending on their extubation time. The patient's anxiety level was measured preoperatively and immediately after entrance to the operation room using Spielberger anxiety questionnaire. It was also reexamined postoperatively and after transference to the CCU with the patients being awake. The surgical site pain after wheeling into CCU was investigated with a visual analogue scale while the patient is awake.

In placebo group, the procedure was exactly similar to that of the intervention groups except that a cotton swab soaked in water was placed on the patient's chest. In control

group, the procedure was exactly similar to that of the intervention and placebo groups except that this group received just routine care with no intervention.

2.4 Outcomes and relevant measures

The primary outcome was determining anxiety and the secondary outcomes were surgical site pain and extubation time after OHS.

2.4.1 Demographic and clinical information questionnaire

Demographic and clinical information questionnaire included quantitative demographic variables (age, gender, body mass index (BMI), ventricular ejection fraction (VEF), number of grafts, and the heart-lung machine time), qualitative demographic variables (education and occupation), and comorbid conditions (diabetes, hypertension, pulmonary pathologies and smoking). This form was developed and validated for content through review of literature and expert opinion (two fellowship cardiologists, two fellowship cardiac internists, five CCU nurses, and five nursing faculty clinicians with CCU work experience).

2.4.2 Physiological indices sheet

The sheet included systolic pressure, diastolic pressure, heart rate, respiration rate, and arterial blood oxygen saturation at various time intervals. These indices were measured by vital signs monitoring system (Dotex, General Electric Company, USA). The cardio respiratory and pulse oximetry monitoring device was calibrated first by the medical engineering of the center on the basis of manufacturer's guidelines and its accurate functioning was ascertained. The extubation time was measured with a standard chronometer (Saba Iran Co., Iran).

2.4.3 The visual analog scale (VAS)

The VAS was used to measure surgical site pain. This scale is a 10-cm ruler ranging from 0-10 cm. In this scale, 0 represents no pain and 10 indicate intolerable pain. [34, 35] The reliability coefficient of this tool was estimated as ICC=0.91 using test-retest reliability coefficient and Cronbach's α =0.93.

2.4.4 Spielberger standard 20-item questionnaire

This questionnaire was used to examine anxiety. This inventory uses a 4-point Likert scale with a score ranging from 4 to 80. Higher scores indicate more severe anxiety. [36] The

reliability coefficient of the anxiety questionnaire was estimated as ICC=0.92 using test-retest method and Cronbach's α=0.94.

2.5 Sample size estimation

The sample size was estimated to be 36 patients in each group using Altman nomogram with type I error of 0.05, test power of 90%, and effect size of 0.9 on the basis of Kavehee et al.'s study. [37] Considering a subject attrition rate of 10%, 40 patients were assigned to each group adding up to 160 patients in all.

2.6 Ethical Considerations

This double-center randomized clinical trial was approved by the Committee of Ethics in Human Research at Baqiatallah University of Medical Sciences with ethical code: IR.BMSU.REC.1394.141 and registered in the Iranian Registration of Clinical Trials under code: IRCT201510012730N9 dated 22.1.2016. The researcher explained the research goals and procedures in the orientation session. Informed written consent was obtained from all of the participants. They were assured that their lack of inclination for participation did not affect the course of their treatment. They were free to leave the study at any stage.

2.7 Statistical analysis

All analyses were conducted using SPSS 23 (SPSS Inc., IL, Chicago, USA) and GraphPad Prism 5© (Graph Pad Software Inc., La Jolla, CA) at α=.05 significance level. Data were presented using mean (SD) for normal numeric variables and frequency (Percentage) for categorical variables. Normality was assessed via Shapiro-Wilk test. Numeric and categorical variables were compared using t-test and Chi-Square and Fisher's exact test, where appropriate. Two-way analysis of variance (ANOVA) with repeated measures (RMANOVA) was conducted on anxiety to assess the main and interaction effects for unadjusted and adjusted results, respectively; age, gender, marital status, qualification, history of diabetic, pulmonary disease, hypertension, hospitalization period, and smoking, and body mass index were adjusted for. Univariate and multivariate ordinal logistic regression was utilized to compare pain severity in the rose, lavender, placebo, and control groups of patients under CABG surgery for unadjusted and adjusted results, respectively; age, gender, marital status, qualification, history of diabetic, and smoking were adjusted for. Odds ratios (ORs) and 95% confidence interval were presented in the analyses. Extubation time in the rose, lavender,

placebo, and control groups of patients under CABG surgery was compared according to the ANOVA in the unadjusted analysis and analysis of covariance (ANCOVA) adjusted for pump time, graft number, ventricular ejection fraction, age, history of smoking and pulmonary disease, and finally all measured vital signs in 13 times (pulse and respiratory rate, systolic and diastolic pressures, and SPO_2.

3. Results

3.1 Characteristics of the patients

A total of 200 patients' under CABG surgery consented to participate; 160 were included in the final analysis. Fourty patients' under CABG surgery were excluded due to emergency CS (n=6), CS more than one time (n=3), intra-aortic ballon pump after surgery (n=3), coagulating problems (n=5) and declined to participate (n=3) (Figure 1). Mean age of the patients in the rose, lavender, placebo and control groups were 60.50 ± 5.26, 58.05 ± 5.26, 62.27 ± 6.49, and 57.50 ± 7.43 years respectively with male predominance 62.5%, 70.0%, 47.5%, and 62.5%, respectively in four groups (Table 1). The results of the variables showed there were no significant differences among the socio demographic, background diseases, and CS variables (All p values >0.05) (Table 1).

3.2 Non adjusted and adjusted analyses of states anxiety

The results of two-way ANOVA with repeated measures on anxiety indicated a significant interaction between time and groups in the unadjusted and adjusted analyses representing a different time dependency in anxiety among groups in before and after measurements, after adjusting for age, gender, marital status, qualification, having history of diabetes, pulmonary disease, smoking, hypertension, hospitalization period, and BMI. Unadjusted and adjusted between group comparisons by utilizing ANOVA, did not showed significant differences in state anxiety in the rose, lavender and placebo groups compared to the control group ($p > 0.05$). Additionally, the results of within group comparisons did not showed significant differences in state anxiety in all groups ($p > 0.05$) (table 2).

3.4 Non adjusted and adjusted ordinal logistic regression of pain

The results of unadjusted ordinal logistic regression showed significant lower pain severity in the rose and lavender groups compared to the placebo and control groups. The lowest

pain severity was seen in the rose and lavender, respectively; although the severity did not show significant differences between the placebo and control but the severity was more in the placebo than control group. In the adjusted analyses the pain severity was significantly lower in the rose and the lavender groups compared to the placebo and control group after adjusting for age, gender, marital status, qualification, diabetic and smoking history; The lowest pain severity was seen in the rose and lavender, respectively; although the severity did not show significant differences between the placebo and control but the severity was more in the placebo group than control (table 4 and figure 3).

3.3 Non adjusted and adjusted analyses of extubation time

The results of one way ANOVA showed a significant difference among groups ($p > 0.0001$). Also the results of tukey post hoc tests indicated significant differences between the rose and placebo groups ($p=0.029$) and between the rose and the control groups ($p<0.0001$). Also the results of ANCOVA after adjusting for pump time, graft number, ejection fraction, age, smoking, respiratory disease, and pulse rate, respiratory rate, systolic and diastolic blood pressure, and SPO_2 in 13 times showed significant differences among the groups ($p<0.0001$). Also the results of tukey post hoc tests indicated significant differences between the rose and placebo groups ($p=0.041$) and between the rose and the control groups ($p=0.012$) (table 3 and figure 2).

4. Discussion

Given the increasing role of non-pharmaceutical interventions and complementary medicine in the nursing profession, this study compared the effect of aromatherapy with rose and lavender essences on reducing surgical site pain, anxiety, and especially extubation time in patients undergoing OHS. The findings of the pairwise comparisons of the four groups demonstrated that aromatherapy with rose and lavender essence exerted no significant effect on the rate of anxiety among the groups in the adjusted and non-adjusted analyses; however, there was a significant difference in time-group effect in the adjusted and non-adjusted analyses. The pain severity was significantly reduced in the rose and lavender groups in the adjusted and non-adjusted analyses compared to the control and placebo groups; yet, there was no significant difference in pain severity between the control and placebo groups. The pain intensity was lower in the control group compared to the placebo

group. There was a significant difference in extubation time among the groups in the adjusted and non-adjusted analyses that pertained to the rose group compared with control and placebo groups. The results showed that demographic information (age, gender, BMI, education, marital status and smoking) and underlying diseases (a history of hypertension, diabetes, repeated hospitalization, and pulmonary and coagulation problems) were the same among the four groups before intervention while variables pertaining to OHS (cardiac pump time, VEF and number of grafts) were the same after intervention among the four groups (Table 1).

The results of surgical site pain in present study was similar to the study by Heidari Gorji et al., [31] but different from the results of Salamati et al. study that showed that the inhalation of lavender essence exerted no significant effect on decreasing pain after OHS. This difference may be attributed to method, type, and time of intervention or the mean age of the patients. Salamati et al.'s study included one group with a mean age of 50 years in which aromatherapy was done for 10 min. [38]

For anxiety, the results of Babayii et al., [39] and Muzzareli et al. [40] studies were similar to the pairwise intergroup comparisons of the present study. The study by Babayee et al. did not compare the reciprocal time-group effect of intervention; nevertheless, this comparison was significant in our study; in other words, time changes among the groups were not the same after intervention and were significantly different. [39] Moreover, the results of Wilkinson et al. revealed that the patients who received aromatherapy massage had improved anxiety and depression levels compared to those who received merely ordinary care during 10 weeks. This is consistent with the intergroup results of the present study; however, it has been effective two weeks after intervention which is consistent with the reciprocal time-group effect of the present study. [41] Furthermore, Cho et al., results are not consistent with the intergroup results of our study; yet, it is consistent with the reciprocal time-group effect of our study. The difference may be due to the different nature of the samples under study (Percutaneous Coronary Intervention) and difference in the type of essences (aromatherapy with essences of lavender, matricaria, and orange blossoms). [42]

Our findings indicated that aromatherapy with essences of rose and lavender induced a significant effect on reducing extubation time. The extubation time was reduced in the rose group in both adjusted and non-adjusted analyses compared to the control and placebo groups. Since early extubation is done in almost all cardiovascular surgery centers round the

globe due to its numerous advantages, and given that reduced extubation time results in greater rehabilitation and earlier discharge from CCUs that prevents the numerous complications of mechanical ventilation, the reduction in extubation time is important. Korhan et al. demonstrated that the reflexive plantar massage induced tranquility and reduced the need for analgesics in ventilated patients through suppressing the physiological symptoms of anxiety, ultimately leading to reduced mechanical ventilation time. [43] The study by Ebadi et al. investigating the effect of reflexive plantar massage on physiologic indices and extubation time in OHS patients, showed no effect on these indices; yet, it exerted an effect on reducing extubation time, a finding which is consistent with the present study. [44] Apart from the promising effects of aromatherapy in these patients, other factors including medication adherence, [45,46,47] health literacy, [48] and self-care behaviors [49,50,51] in the patients with CVDs have protective effects.

There are certain limitations for this study. The researchers tried their best to reduce the effects of their presence on the participants (observer paradox). These included any uncontrollable environmental noises in the ward that could influence the aromatherapy process, the physical, mental, and personality structure of the individuals which were not identifiable and could cause differences in the effect of aromatherapy on patients, though the patients were randomly assigned to the four groups. The extubation process was commenced by the CCU nurse in charge, there were some differences in nurses' performance that could cause differences in the results, though an orientation session was held to homogenize the nurses' performance in the intended wards. Completing some tasks such as taking X-rays and moving the patients sometimes awakened them leading to the the administration of narcotics.

5. Conclusion

Aromatherapy with rose and lavender resulted in a significant difference in anxiety in the reciprocal time-group effect in the adjusted and non-adjusted analyses among the groups under study. The extubation time was significantly different among the groups in the adjusted and non-adjusted analyses which pertained to the rose group compared to the control and placebo groups. The severity of pain was less in the two intervention groups compared to the control and placebo groups, though albeit it was less in the control group than in the plcebo group. It could be possibly asserted that aromatherapy is a useful nursing

intervention in reducing pain severity and extubation time after CS. It is a cheap and complication-free procedure that can promote healthcare level and increase patient conveneince at the critical time after OHS. Also, given the contradictory results of the related studies, it is recommended that more extensive studies be carried out in future on the effect of aromatherapy on patients' anxiety level.

Consent for publication

Informed consent was obtained from the patient, legal guardian or healthcare surrogate and allowed for both study participation and publication of de-identified aggregate results.
There is no data contained within the manuscript from which individual patients or participants may be identified.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interests

None.

References

Figure legends

Figure 1: CONSORT 2010 Flow Diagram.

Figure 2: Extubation time in four groups Lavender, Rose, Placebo, and Control.

Figure 3: Pain score in four groups Lavender, Rose, Placebo, and Control.

Table 1 Socio demographic, background diseases, and cardiac surgery variables

	Variable		Rose group	Lavender group	Placebo group	Control group	P Value #
Sociodemographic variables	**Age**, Mean (SD)		60.50 (5.26)	58.05 (5.26)	62.27 (6.49)	57.50 (7.43)	0.11
	Body Mass Index, Mean (SD)		26.58 (2.72)	26.21 (2.60)	26.06 (3.47)	26.41 (2.71)	0.86
	Gender	**Male**, n (%)	25 (62.5)	28 (70)	19 (47.5)	25 (62.5)	0.21
		Female, n (%)	15 (37.5)	12 (30)	21 (52.5)	15 (37.5)	
	Qualification	**Middle school**, n (%)	5 (12.5)	3 (7.5)	7 (17.5)	6 (15)	0.37
		High school, n (%)	17 (42.5)	11 (27.5)	13 (32.5)	8 (20)	
		Diploma, n (%)	18 (45)	23 (57.5)	19 (47.5)	24 (60)	
		Higher diploma, n (%)	0 (0)	3 (7.5)	1 (2.5)	2 (5)	
	Smoking history	**Yes**, n (%)	12 (30)	16 (40)	11 (27.5)	9 (22.5)	0.96
		No, n (%)	28 (70)	24 (60)	29 (72.5)	31 (77.5)	
	Marital status	**Married**, n (%)	40 (100)	38 (95)	40 (100)	39 (97.5)	0.37
		Single, n (%)	0 (0)	2 (5)	0 (0)	1 (2.5)	
Background disease	**Hypertension history**	**Yes**, n (%)	35 (87.5)	27 (67.5)	31 (77.5)	35 (87.5)	0.09
		No, n (%)	5 (12.5)	13 (32.5)	9 (22.5)	5 (12.5)	
	Diabetic history	**Yes**, n (%)	22 (55)	21 (52.5)	23 (57.5)	21 (52.5)	0.96
		No, n (%)	18 (45)	19 (47.5)	17 (42.5)	19 (47.5)	
	Pulmonary disease history	**Yes**, n (%)	10 (25)	6 (15)	9 (22.5)	7 (7.5)	0.66
		No, n (%)	30 (75)	34 (85)	31 (77.5)	33 (82.5)	
	Coagulation problem history	**Yes**, n (%)	2 (5)	1 (2.5)	0 (0)	4 (10)	0.15
		No, n (%)	38 (95)	39 (97.5)	40 (100)	36 (90)	
	Hospitalization history	**Yes**, n (%)	10 (25)	6 (15)	9 (22.5)	7 (17.5)	0.66
		No, n (%)	30 (75)	34 (85)	31 (77.5)	33 (82.5)	
Cardiac surgery variables	**Pump time**	Mean (SD)	50.37 (29.28)	50.20 (15.09)	52.05 (16.08)	48.75 (12.05)	0.90
	Ventricular Ejection Fraction	Mean (SD)	42.87 (5.04)	44.12 (5.87)	43.62 (5.18)	43.75 (7.65)	0.82
	Graft number	Mean (SD)	2.75 (0.92)	2.80 (0.68)	2.95 (0.74)	2.82 (0.81)	0.71

ANOVA, Chi-Square/Fisher's exact test for numeric and categorical variables, respectively

Table 2 State anxiety in the Lavender, Rose, Placebo, and Control groups of patients under coronary artery bypass graft surgery

Variables	Time	Lavender (n=40) Mean ± SD	Rose (n=40) Mean ± SD	Placebo (n=40) Mean ± SD	Control (n=40) Mean ± SD	Unadjusted between group Comparisons @	Unadjusted Interaction #	Adjusted between group comparisons $	Adjust Intera $
State Anxiety	Before	44.10±7.60	45.70 ± 4.67	43.00 ± 6.55	44.92 ± 5.05				
	After	42.57±5.93	42.55 ± 5.63	44.60 ± 5.32	44.27 ± 5.59	P = 0.499	P = 0.049	P=0.548	0.0
	Pvalue *	0.477	0.233	0.496	0.172				

* Within group comparisons in repeated measures ANOVA

@ Between group comparisons in repeated measures ANOVA

Time-group interaction in repeated measures ANOVA

$ Between group comparisons in repeated measures ANCOVA adjusting for age, gender, marital status, qualification, having history of diabetic, pulmonary disease, smoking, hypertension, hospitalization period, and Body Mass index.

Table 3 Extubation time in the Lavender, Rose, Placebo, and control groups of patients under coronary artery bypass graft surgery

Variable	Groups	Procedure time (Minute)	Unadjusted P-value #	Adjusted P-value #
		Mean ± SD		
Extubation time	Lavender group (n=40)	431.37 ± 32.73	<0.0001	<0.0001
	Rose group (n=40)	422.00 ± 19.18		
	Placebo group (n=40)	437.87 ± 26.95		
	Control group (n=40)	442.17 ± 25.17		

According to the analysis of covariance (ANCOVA) adjusted for pump time, graft number, ejection fraction, age, smoking, respiratory disease, and pulse rate, respiratory rate, systolic and diastolic blood pressure, and SPO_2 in 13 times.

Table 4 Pain severity according to the Visual analog scale in the rose, lavender, placebo, and control groups of patients under coronary artery bypass graft surgery

Pain	**Unadjusted**				**Adjusted#**			
	OR	L	U	P-Value	OR	L	U	P-Value
Groups								
Control	Reference group	-----	-----	-----	Reference group	-----	-----	-----
Placebo	1.574	0.694	3.572	0.278	1.936	0.8269	4.5323	0.128
Lavender	0.141	0.059	0.338	**<0.0001**	0.136	0.055	0.337	**<0.0001**
Rose	0.046	0.0177	0.121	**<0.0001**	0.049	0.0181	0.1298	**<0.0001**

OR: Odds Ratio; L: Lower bound of 95% CI; U: Upper Bound of 95% CI;

According to the multivariate ordinal logistic regression adjusted for age, gender, marital status, qualification, diabetic and smoking history.

References:

1. Vahedian Azimi, A.; Sadeghi, M.; Movafegh, A.; Sorouri Zanjani, R.; Hasani, D.; Salehmoghaddam, A.; Kashshsfi, M., The relationship between perceived stress and the top five heart disease characteristics in patients with myocardial infarction. *J Adv Med Biomed Res* **2012,** *20* (78), 100-112.
2. Mathers, C. D.; Loncar, D., Projections of global mortality and burden of disease from 2002 to 2030. *PLoS medicine* **2006,** *3* (11), e442.
3. Pozo, L.; Bello, F.; Suarez, A.; Ochoa-Martinez, F. E.; Mendez, Y.; Chang, C. H.; Surani, S., Novel pharmacological therapy in type 2 diabetes mellitus with established cardiovascular disease: Current evidence. *World journal of diabetes* **2019,** *10* (5), 291-303.
4. Jauch, E. C.; Saver, J. L.; Adams, H. P., Jr.; Bruno, A.; Connors, J. J.; Demaerschalk, B. M.; Khatri, P.; McMullan, P. W., Jr.; Qureshi, A. I.; Rosenfield, K.; Scott, P. A.; Summers, D. R.; Wang, D. Z.; Wintermark, M.; Yonas, H., Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* **2013,** *44* (3), 870-947.
5. Kass-Hout, T. A.; Stevens, L. M.; Hall, J. L., American Heart Association Precision Medicine Platform. *Circulation* **2018,** *137* (7), 647-649.
6. Yano, Y.; Reis, J. P.; Lewis, C. E.; Sidney, S.; Pletcher, M. J.; Bibbins-Domingo, K.; Navar, A. M.; Peterson, E. D.; Bancks, M. P.; Kanegae, H.; Gidding, S. S.; Muntner, P.; Lloyd-Jones, D. M., Association of Blood Pressure Patterns in Young Adulthood With Cardiovascular Disease and Mortality in Middle Age. *JAMA cardiology* **2020**.
7. Lumme, S.; Manderbacka, K.; Keskimaki, I., Trends of relative and absolute socioeconomic equity in access to coronary revascularisations in 1995-2010 in Finland: a register study. *International journal for equity in health* **2017,** *16* (1), 37.
8. Dastoorpoor, M.; Sekhavatpour, Z.; Masoumi, K.; Mohammadi, M. J.; Aghababaeian, H.; Khanjani, N.; Hashemzadeh, B.; Vahedian, M., Air pollution and hospital admissions for cardiovascular diseases in Ahvaz, Iran. *The Science of the total environment* **2019,** *652*, 1318-1330.
9. Xu, X.; Li, S. X.; Lin, H.; Normand, S. L.; Lagu, T.; Desai, N.; Duan, M.; Kroch, E. A.; Krumholz, H. M., Hospital Phenotypes in the Management of Patients Admitted for Acute Myocardial Infarction. *Medical care* **2016,** *54* (10), 929-36.
10. Persell, S. D.; Liss, D. T.; Walunas, T. L.; Ciolino, J. D.; Ahmad, F. S.; Brown, T.; French, D. D.; Hountz, R.; Iversen, K.; Lindau, S. T.; Lipiszko, D.; Makelarski, J. A.; Mazurek, K.; Murakami, L.; Peprah, Y.; Potempa, J.; Rasmussen, L. V.; Wang, A.; Wang, J.; Yeh, C.; Kho, A. N., Effects of 2 Forms of Practice Facilitation on Cardiovascular Prevention in Primary Care: A Practice-randomized, Comparative Effectiveness Trial. *Medical care* **2019**.
11. Rocha, E. A. V., Fifty Years of Coronary Artery Bypass Graft Surgery. *Brazilian journal of cardiovascular surgery* **2017,** *32* (4), II-III.
12. Mary, A., Prevention of 30-Day Readmission After Coronary Artery Bypass Surgery. *Home healthcare now* **2017,** *35* (6), 326-334.
13. Bashar, F. R.; Vahedian-Azimi, A.; Farzanegan, B.; Goharani, R.; Shojaei, S.; Hatamian, S.; Mosavinasab, S. M. M.; Khoshfetrat, M.; Khatir, M. A. K.; Tomdio, A.; Miller, A. C., Comparison of non-invasive to invasive oxygenation ratios for diagnosing acute respiratory distress syndrome following coronary artery bypass graft surgery: a prospective derivation-validation cohort study. *Journal of cardiothoracic surgery* **2018,** *13* (1), 123.
14. Barzanji, A.; Zareiyan, A.; Nezamzadeh, M.; Mazhari, M. S., Evaluation of Observational and Behavioural Pain Assessment Tools in Nonverbal Intubated Critically Adult Patients after Open - Heart Surgery: A Systematic Review. *Open access Macedonian journal of medical sciences* **2019,** *7* (3), 446-457.
15. Elgebaly, A. S.; Sabry, M., Sedation effects by dexmedetomidine versus propofol in decreasing duration of mechanical ventilation after open heart surgery. *Annals of cardiac anaesthesia* **2018,** *21* (3), 235-242.
16. Borges, L. G. A.; Savi, A.; Teixeira, C.; de Oliveira, R. P.; De Camillis, M. L. F.; Wickert, R.; Brodt, S. F. M.; Tonietto, T. F.; Cremonese, R.; da Silva, L. S.; Gehm, F.; Oliveira, E. S.; Barth, J. H. D.; Macari, J. G.; de Barros, C. D.; Vieira, S. R. R., Mechanical ventilation weaning protocol improves medical adherence and results. *Journal of critical care* **2017,** *41*, 296-302.
17. Burns, K. E. A.; Wong, J. T. Y.; Dodek, P.; Cook, D. J.; Lamontagne, F.; Cohen, A.; Mehta, S.; Kho, M. E.; Hebert, P. C.; Aslanian, P.; Friedrich, J. O.; Brochard, L.; Rizvi, L.; Hand, L.; Meade, M. O.; Amaral, A. C.; Seely, A. J., Frequency of Screening for Weaning From Mechanical Ventilation: Two Contemporaneous Proof-of-Principle Randomized Controlled Trials. *Critical care medicine* **2019,** *47* (6), 817-825.

18. Yousefshahi, F.; Samadi, E.; Paknejad, O.; Bastan Hagh, E.; Aminzadeh, S., Effect of Hypoxemia in the Determination of Short-Term Prognosis of Coronary Artery Bypass Graft Patients: A Prospective Study. *Anesthesiology and pain medicine* **2019,** *9* (1), e81785.
19. Goodwin, M. J.; Bissett, L.; Mason, P.; Kates, R.; Weber, J., Early extubation and early activity after open heart surgery. *Critical care nurse* **1999,** *19* (5), 18-26.
20. Hetland, B.; Lindquist, R.; Weinert, C. R.; Peden-McAlpine, C.; Savik, K.; Chlan, L., Predictive Associations of Music, Anxiety, and Sedative Exposure on Mechanical Ventilation Weaning Trials. *American journal of critical care : an official publication, American Association of Critical-Care Nurses* **2017,** *26* (3), 210-220.
21. Arroliga, A.; Frutos-Vivar, F.; Hall, J.; Esteban, A.; Apezteguia, C.; Soto, L.; Anzueto, A., Use of sedatives and neuromuscular blockers in a cohort of patients receiving mechanical ventilation. *Chest* **2005,** *128* (2), 496-506.
22. Lee, O. K.; Chung, Y. F.; Chan, M. F.; Chan, W. M., Music and its effect on the physiological responses and anxiety levels of patients receiving mechanical ventilation: a pilot study. *Journal of clinical nursing* **2005,** *14* (5), 609-20.
23. Bashar, F. R.; Vahedian-Azimi, A.; Salesi, M.; Hajiesmaeili, M.; Shojaei, S.; Farzanegan, B.; Goharani, R.; Madani, S. J.; Moghaddam, K. G.; Hatamian, S.; Moghaddam, H. J.; Arrascaeta-Llanes, A.; Miller, A. C., Spiritual Health and Outcomes in Muslim ICU Patients: A Nationwide Cross-Sectional Study. *Journal of religion and health* **2018,** *57* (6), 2241-2257.
24. Lee, C. H.; Lai, C. L.; Sung, Y. H.; Lai, M. Y.; Lin, C. Y.; Lin, L. Y., Comparing effects between music intervention and aromatherapy on anxiety of patients undergoing mechanical ventilation in the intensive care unit: a randomized controlled trial. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation* **2017,** *26* (7), 1819-1829.
25. Lee, C. H.; Lee, C. Y.; Hsu, M. Y.; Lai, C. L.; Sung, Y. H.; Lin, C. Y.; Lin, L. Y., Effects of Music Intervention on State Anxiety and Physiological Indices in Patients Undergoing Mechanical Ventilation in the Intensive Care Unit. *Biological research for nursing* **2017,** *19* (2), 137-144.
26. Lee, C. H.; Liu, J. T.; Lin, S. C.; Hsu, T. Y.; Lin, C. Y.; Lin, L. Y., Effects of Educational Intervention on State Anxiety and Pain in People Undergoing Spinal Surgery: A Randomized Controlled Trial. *Pain management nursing : official journal of the American Society of Pain Management Nurses* **2018,** *19* (2), 163-171.
27. Avazah, A.; Khosh Fetrat, M.; Rahimi Bashar, F., Effect of progressive muscle relaxation on the vital signs and oxygenation indexes in patients under coronary artery bypass graft surgery: A triple blinded randomized clinical trial. *koomesh* **2019,** *21* (3), 423-436.
28. Hur, M. H.; Song, J. A.; Lee, J.; Lee, M. S., Aromatherapy for stress reduction in healthy adults: a systematic review and meta-analysis of randomized clinical trials. *Maturitas* **2014,** *79* (4), 362-9.
29. Dehkordi, A. K.; Tayebi, A.; Ebadi, A.; Sahraei, H.; Einollahi, B., Effects of aromatherapy using the damask rose essential oil on depression, anxiety, and stress in hemodialysis patients: a clinical trial. *Nephro-Urology Monthly* **2017,** *9* (6).
30. Hasanzadeh, F.; Kashouk, N. M.; Amini, S.; Asili, J.; Emami, S. A.; Vashani, H. B.; Sahebkar, A., The effect of cold application and lavender oil inhalation in cardiac surgery patients undergoing chest tube removal. *EXCLI journal* **2016,** *15*, 64-74.
31. Heidari Gorji, M. A.; Ashrastaghi, O. G.; Habibi, V.; Charati, J. Y.; Ebrahimzadeh, M. A.; Ayasi, M., The effectiveness of lavender essence on strernotomy related pain intensity after coronary artery bypass grafting. *Advanced biomedical research* **2015,** *4*, 127.
32. Bikmoradi, A.; Seifi, Z.; Poorolajal, J.; Araghchian, M.; Safiaryan, R.; Oshvandi, K., Effect of inhalation aromatherapy with lavender essential oil on stress and vital signs in patients undergoing coronary artery bypass surgery: A single-blinded randomized clinical trial. *Complementary therapies in medicine* **2015,** *23* (3), 331-8.
33. Salamati, A.; Mashouf, S.; Mojab, F., Effect of Inhalation of Lavender Essential Oil on Vital Signs in Open Heart Surgery ICU. *Iranian journal of pharmaceutical research : IJPR* **2017,** *16* (1), 404-409.
34. Chen, Y. P.; Huang, Y. Y.; Wu, Y.; Kuo, Y. J.; Lin, C. Y., Depression negatively affects patient-reported knee functional outcome after intraarticular hyaluronic acid injection among geriatric patients with knee osteoarthritis. *Journal of orthopaedic surgery and research* **2019,** *14* (1), 387.
35. Chen, Y. P.; Wang, S. M.; Wu, Y.; Lin, H. Y.; Wu, C. C.; Chuang, T. Y.; Ho, W. P.; Kuo, Y. J.; Leu, T. H.; Lin, C. Y., Worsen depression after viscosupplementation treatment for geriatric people with knee osteoarthritis? *International journal of clinical and health psychology : IJCHP* **2019,** *19* (1), 31-40.
36. Vahedian-Azimi, A.; Miller, A. C.; Hajiesmaieli, M.; Kangasniemi, M.; Alhani, F.; Jelvehmoghaddam, H.; Fathi, M.; Farzanegan, B.; Ardehali, S. H.; Hatamian, S.; Gahremani, M.; Mosavinasab, S. M.; Rostami, Z.; Madani, S. J.; Izadi, M., Cardiac rehabilitation using the Family-Centered Empowerment Model versus

home-based cardiac rehabilitation in patients with myocardial infarction: a randomised controlled trial. *Open heart* **2016,** *3* (1), e000349.
37. Kavei, P.; Ebadi, A.; Saeed, Y.; Moradian, S. T.; Sedigh Rahimabadi, M., Effect of foot reflexology on anxiety and agitation in patients under mechanical ventilation after open heart surgery: A randomized clinical trial study. *Journal of Clinical Nursing and Midwifery* **2015,** *4*.
38. Salamati, A.; Mashouf, S.; Sahbaei, F.; Mojab, F., Effects of Inhalation of Lavender Essential Oil on Open-heart Surgery Pain. *Iranian journal of pharmaceutical research : IJPR* **2014,** *13* (4), 1257-61.
39. Babaii, A.; Abbasinia, M.; Hejazi, S. F.; Seyyed Tabaei, S. R.; Dehghani, F., The effect of listening to the voice of Quran on anxiety before cardiac catheterization: a randomized controlled trial. *Health, Spirituality and Medical Ethics* **2015,** *2* (2), 2-7.
40. Muzzarelli, L.; Force, M.; Sebold, M., Aromatherapy and reducing preprocedural anxiety: A controlled prospective study. *Gastroenterology nursing : the official journal of the Society of Gastroenterology Nurses and Associates* **2006,** *29* (6), 466-71.
41. Wilkinson, S. M.; Love, S. B.; Westcombe, A. M.; Gambles, M. A.; Burgess, C. C.; Cargill, A.; Young, T.; Maher, E. J.; Ramirez, A. J., Effectiveness of aromatherapy massage in the management of anxiety and depression in patients with cancer: a multicenter randomized controlled trial. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* **2007,** *25* (5), 532-9.
42. Cho, M. Y.; Min, E. S.; Hur, M. H.; Lee, M. S., Effects of aromatherapy on the anxiety, vital signs, and sleep quality of percutaneous coronary intervention patients in intensive care units. *Evidence-based complementary and alternative medicine : eCAM* **2013,** *2013*, 381381.
43. Akin Korhan, E.; Khorshid, L.; Uyar, M., Reflexology: its effects on physiological anxiety signs and sedation needs. *Holistic nursing practice* **2014,** *28* (1), 6-23.
44. Ebadi, A.; Kavei, P.; Moradian, S. T.; Saeid, Y., The effect of foot reflexology on physiologic parameters and mechanical ventilation weaning time in patients undergoing open-heart surgery: A clinical trial study. *Complementary therapies in clinical practice* **2015,** *21* (3), 188-92.
45. Lin, C. Y.; Ganji, M.; Griffiths, M. D.; Bravell, M. E.; Brostrom, A.; Pakpour, A. H., Mediated effects of insomnia, psychological distress and medication adherence in the association of eHealth literacy and cardiac events among Iranian older patients with heart failure: a longitudinal study. *European journal of cardiovascular nursing : journal of the Working Group on Cardiovascular Nursing of the European Society of Cardiology* **2019**, 1474515119873648.
46. Lin, C. Y.; Ou, H. T.; Nikoobakht, M.; Brostrom, A.; Arestedt, K.; Pakpour, A. H., Validation of the 5-Item Medication Adherence Report Scale in Older Stroke Patients in Iran. *The Journal of cardiovascular nursing* **2018,** *33* (6), 536-543.
47. Lin, C. Y.; Yaseri, M.; Pakpour, A. H.; Malm, D.; Brostrom, A.; Fridlund, B.; Burri, A.; Webb, T. L., Can a Multifaceted Intervention Including Motivational Interviewing Improve Medication Adherence, Quality of Life, and Mortality Rates in Older Patients Undergoing Coronary Artery Bypass Surgery? A Multicenter, Randomized Controlled Trial with 18-Month Follow-Up. *Drugs & aging* **2017,** *34* (2), 143-156.
48. Lin, C. Y.; Brostrom, A.; Griffiths, M. D.; Pakpour, A. H., Psychometric Evaluation of the Persian eHealth Literacy Scale (eHEALS) Among Elder Iranians With Heart Failure. *Evaluation & the health professions* **2019**, 163278719827997.
49. Lin, C. Y.; Brostrom, A.; Arestedt, K.; Martensson, J.; Steinke, E. E.; Pakpour, A. H., Using extended theory of planned behavior to determine factors associated with help-seeking behavior of sexual problems in women with heart failure: a longitudinal study. *Journal of psychosomatic obstetrics and gynaecology* **2019**, 1-8.
50. Lin, C. Y.; Pakpour, A. H.; Brostrom, A.; Fridlund, B.; Arestedt, K.; Stromberg, A.; Jaarsma, T.; Martensson, J., Psychometric Properties of the 9-item European Heart Failure Self-care Behavior Scale Using Confirmatory Factor Analysis and Rasch Analysis Among Iranian Patients. *The Journal of cardiovascular nursing* **2018,** *33* (3), 281-288.
51. Saffari, M.; Lin, C. Y.; Brostrom, A.; Martensson, J.; Malm, D.; Burri, A.; Fridlund, B.; Pakpour, A. H., Investigating sexual problems, psychological distress and quality of life in female patients with Takotsubo cardiomyopathy: A prospective case-control study. *European journal of cardiovascular nursing : journal of the Working Group on Cardiovascular Nursing of the European Society of Cardiology* **2017,** *16* (7), 614-622.