

Effect of Listening to Intraoperative Hemispheric Synchronized Sounds on Postoperative Cognitive Function after Coronary Artery Bypass Graft Surgery: A Randomized Controlled Trial

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ABSTRACT

Objective: This study aimed to evaluate the effect of listening to hemispheric synchronized sounds during surgery on postoperative cognitive function, delirium, and pain scores in patients undergoing coronary artery bypass graft (CABG) surgery.

Material and Methods: This prospective, randomized study was conducted in Songklanagarind Hospital; from February 2021 to December 2022. A total of 70 patients having undergone CABG surgery, were divided into two groups: the “music” group (37 patients) and the control group (33 patients). In the operating room, all patients wore headphones connected to an MP3 player; hemispherical synchronization sounds were played in the music group, beginning immediately after sedation and continuing until the end of surgery. No sounds were played in the control group. Preoperative and postoperative Mini-Mental State Examination (MMSE), Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) 7, and Verbal Numerical Rating Scale pain scores were evaluated in all patients in the first 24 hr after extubation. **Results:** Preoperative MMSE scores (26 [interquartile range, IQR: 24,28] vs. 27 [IQR: 23,29], p-value=0.78), postoperative MMSE scores (27 [IQR: 23,29] vs. 27 [IQR: 24,29], p-value=0.42), and CAM-ICU 7 scores (0 [0,1] vs. 0 [0,1], p-value=0.69) did not differ between the control and music groups. However, the maximum pain score (7.6 [1.2] vs. 5 [1.3], p-value<0.001) and postoperative opioid consumption (61.1 [11.8] vs. 31.9 [11.3], p-value<0.001) were higher in the control group than in the music group.

Conclusion: Listening to hemispheric synchronized sounds during an operation did not affect postoperative cognitive dysfunction and delirium. However, music therapy decreased the level of pain and the need for analgesic drug intake postoperatively.

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INTRODUCTION

Postoperative cognitive dysfunction (POCD) and delirium are common complications following cardiac surgery, and are particularly serious in the geriatric surgical population. The possibility of developing cognitive dysfunction is highest after 7 days of surgery: accounting for 50–70%. Two months after operation, this percentage decreases to 30 to 50%¹. Open heart surgery is generally related to long-term morbidity; as it is considered a cause of POCD².

The effect of music therapy on POCD, delirium, anxiety, pain scores, and opioid consumption has been studied in both cardiac and non-cardiac surgeries^{3–7}. McCaffrey et al.⁴ reported that listening to music during hip or knee surgery may decrease the rate of POCD and postoperative delirium. However, the mechanisms underlying the effects of music therapy on cognitive dysfunction and delirium have seldom been discussed. Four main mechanisms have been proposed: neuroplasticity, neurogenesis and regeneration, neuroendocrine, and neuropsychiatric mechanisms⁸.

Hemispheric synchronized sounds, or binaural beats, are a type of music intervention developed by the Monroe Institute. Hemispheric synchronized sounds are produced when two audible stimuli at slightly different frequencies (1–30 Hz) are delivered separately to each ear at the same time. These sounds generate a brainstem reaction in the superior olivary nucleus in both cerebral hemispheres⁹. Chaieb et al. reviewed auditory beat stimulation and its effects on cognition and mood states. Their findings indicated that binaural beats improved verbal memory recall and performance in thinking processes. Additionally, they significantly decreased anxiety scores, tension, confusion and negative mood¹⁰. Kliem et al.¹¹ demonstrated that listening to hemispheric synchronized sounds under general

anesthesia significantly decreased fentanyl requirement compared with patients listening to classical music or a blank tape.

However, the effect of music therapy on cognitive outcomes remains a subject of debate. For example: while postoperative music listening has shown promise in reducing delirium in hip and knee surgery patients, other trials (using different protocols) have failed to replicate these effects on global cognitive scores; such as the Mini-Mental State Examination MMSE. These discrepancies are often managed in the literature by highlighting differences in intervention timing (intraoperative vs. postoperative) and the potential learning effect associated with repeated neuropsychological testing^{4,11}. Herein, we hypothesized that listening to music during surgery could decrease the incidence of POCD and postoperative delirium in patients undergoing coronary artery bypass graft (CABG) surgery.

MATERIAL AND METHODS

This randomized control study was conducted in Songklanagarind Hospital, and approved by the institutional ethics committee (EC 6350381). All patients provided informed consent. The study was prospectively registered in the Thai Clinical Trial Registry (TCTR 20201216005). We recruited patients over 50 years of age and scheduled them for on-pump CABG; from February 2021 to December 2022. Patients having vision or hearing loss, psychiatric disorders, cognitive impairment; dementia, a history of stroke or transient ischemic attack, chronic pain, drug addiction, American Society of Anesthesiologists classification >3; emergency surgery, and those who were on a mechanical ventilator preoperatively or with whom communication was difficult were excluded. This latter is because, the MMSE and pain scales require active verbal and written participation; hence, excluding those

with significant communicative barriers was necessary to prevent baseline sensory or language deficits from confounding the postoperative cognitive results. Withdrawal criteria were conversion to off-pump CABG, requirement for re-operation, prolonged postoperative intubation for more than three days, postoperative stroke or transient ischemic attack, or music interruption during surgery.

The patients were randomized into two groups, via computer-generated numbers: a “music” group (group M) and a control group (group C). All patients were evaluated using the Mini-Mental State Examination (MMSE) the day before surgery (baseline score), by a person not involved in anesthesia or surgery. Patients in both groups wore disposable headphones connected to an MP3 player in the operating room. Hemispherical synchronization sound was played, at a volume of 50 to 60 dB, in the music group after sedation with fentanyl and midazolam for arterial line insertion. The audio played from anesthesia induction until the end of the surgery. Anesthesia induction and maintenance protocols were the same for all patients. Anesthesia was induced using fentanyl 1–2 µg/kg, midazolam 0.02–0.04 mg/kg, and propofol 1–2 mg/kg. After titration, rocuronium 0.6–1.0 mg/kg was administered to facilitate intubation. The anesthesia level was maintained using desflurane in a mixture of 50% oxygen and 50% air. The depth of anesthesia was monitored via the bispectral index (BIS), maintaining a BIS of 40 to 60 throughout the surgery. Standard monitoring was performed every 5 min. During the cardiopulmonary bypass period, the mean arterial blood pressure, hematocrit, and blood sugar levels were maintained between 60 and 70 mmHg, above 20%, and between 80 and 180 mg%, respectively. Temperature management was performed using the alpha stat technique. After surgery, all patients were transferred to the intensive care unit for close monitoring. Within the first 24 hr, all patients were evaluated using the MMSE and the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) 7 in addition to Verbal Numerical

Rating Scale scores. The evaluation was performed by the same examiner that recorded baseline MMSE scores, so as to reduce individual bias and variations. Patients in both groups received control analgesia after surgery. Total postoperative opioid consumption was recorded 24 hr after surgery.

The primary outcome was the incidence of POCD after CABG surgery. POCD was defined as a decrease in postoperative MMSE scores by one standard deviation or 20% relative to the preoperative MMSE scores¹². Secondary outcomes were the incidence of postoperative delirium, as assessed using the CAM-ICU 7 score, postoperative pain scores, and total postoperative opioid consumption 24 hr after surgery.

Statistical analysis

In a previous study, the incidence of cognitive dysfunction varied considerably; however, it may be as high as 50 % to 70 % at 1 week after surgery¹. In this study, we assumed that music therapy could decrease the incidence of cognitive dysfunction by 50%. We thus used two independent formulas (without continuity correction), indicating that 31 patients per group would be required to achieve a power of 80% in detecting cognitive dysfunction: a type I error rate of 0.05. We assumed a withdrawal rate of 20%; hence, a total of 40 patients per group was required.

Statistical analysis was performed using R version 4.0.2. Continuous variables are presented as the mean and standard deviation (S.D.) or median and interquartile range (IQR). Categorical variables are presented as frequencies and percentages. The association between categorical variables and outcomes was determined using the Chi-squared test or Fisher's exact test. Continuous variables were analyzed using Student's t-test or the Wilcoxon rank-sum test. The Wilcoxon signed rank test was used to compare the preoperative with the postoperative MMSE scores. A P-value less than 0.05 was considered statistically significant.

RESULTS

Between February 2021 and December 2022, 70 patients met the inclusion criteria and were invited to participate in this study: as shown in the consort diagram in Figure 1. All patients consented to participate, from which 37 patients were transferred to the music group and 33 patients to the control group. The incidence of POCD was 11.4%. Patient characteristics and intraoperative data are presented in Tables 1 and 2, respectively. These parameters did not differ between the groups (p -value>0.05).

We used MMSE scores to determine the cognitive dysfunction of patients (Table 3). We observed no significant differences between preoperative (26 [IQR: 24, 28] vs. 27

[IQR: 23, 29], p -value=0.781) and postoperative MMSE scores (27 [IQR: 23,29] vs. 27 [IQR: 24, 29], p -value=0.416) in the control or music groups, respectively. Table 4 shows the postoperative outcomes. CAM-ICU 7 scores between the two groups did not differ (0.2 [S.D.: 0.5] vs. 0.3 [S.D.: 0.6], p -value=0.626). However, the control group had a significantly higher maximal pain score than the music group (5 [S.D.: 1.4] vs. 7.6 [S.D.: 1.2], p -value<0.001). Furthermore, postoperative opioid consumption in the control group was higher than that in the music group (61.1 [S.D.: 11.8] vs. 31.9 [S.D.: 11.3], p -value<0.001). Intraoperative awareness was not recorded in this study.

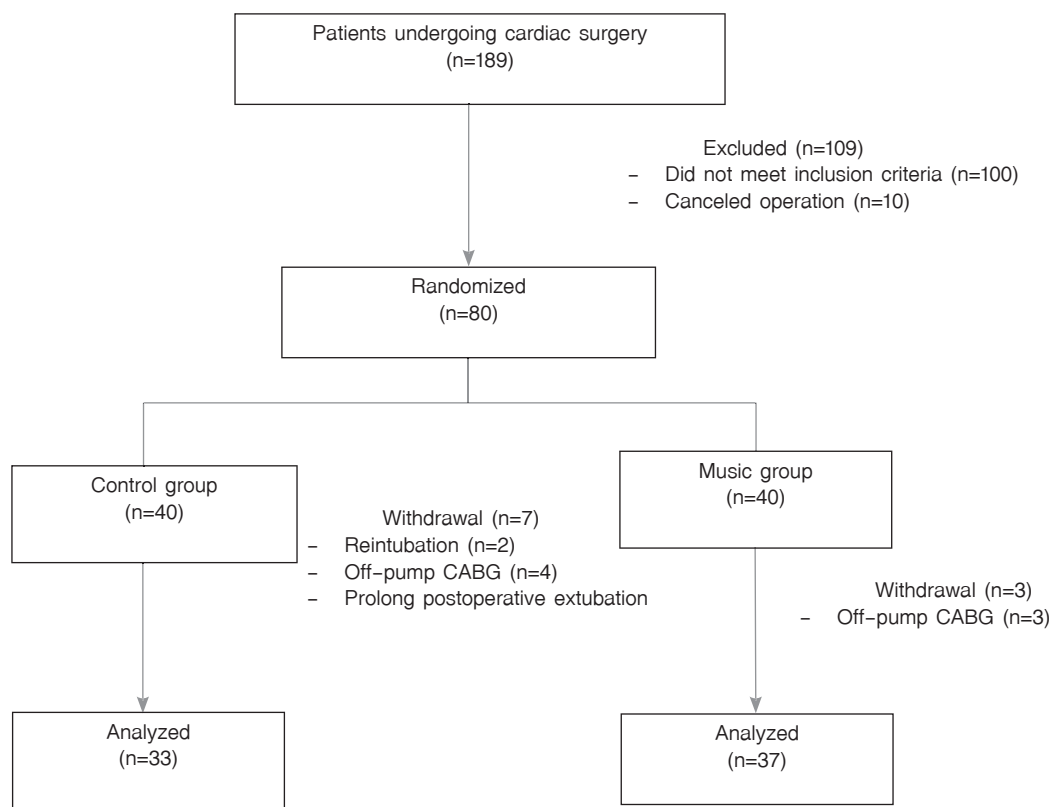


Figure 1 Study flow (CONSORT) chart showing patients allocated into either the control group or music group

Table 1 Baseline demographic characteristics of the control and music groups

Characteristics	Control (n=33)	Music (n=37)	p-value
Age (years), mean (S.D.)	61.9 (6.3)	63.8 (6.4)	0.214
Gender			0.774
Male	26.0 (78.8)	27.0 (73.0)	
Female	7.0 (21.2)	10.0 (27.0)	
BMI, mean (S.D.)	26.5 (3.3)	25.8 (3.5)	0.402
Comorbid disease	19 (90.5)	23 (100)	0.222
Diabetic mellitus	10 (52.6)	12 (52.2)	1.000
Hypertension	18 (94.7)	17 (73.9)	0.105
Dyslipidemia	12 (63.2)	16 (69.6)	0.913
Alcohol drinking	5 (15.2)	6 (16.2)	1.000
Education status			0.436
No education	2 (6.1)	0 (0)	
Elementary school	13 (39.4)	12 (32.4)	
High school	8 (24.2)	13 (35.1)	
Bachelor degrees	10 (30.3)	12 (32.4)	
Marital status			0.172
Single	0.0 (0.0)	2.0 (5.4)	
Married	31.0 (93.9)	35.0 (94.6)	
Divorced	2.0 (6.1)	0.0 (0.0)	

Values are means (standard deviation, S.D.); number (%); BMI=body mass index

Table 2 Comparison of the intraoperative period between the control and music groups

	Control (n=33)	Music (n=37)	p-value
Duration of surgery (min), mean (S.D.)	302 (74.8)	319.9 (65.9)	0.291
Cardiopulmonary bypass time (min), median (IQR)	89 (77,130)	110 (80,134)	0.317
Aortic cross clamp time (min), median (IQR)	64 (42, 92)	73 (48.5, 104.5)	0.209
Inotropic scores, median (IQR)	16 (8.5,22)	15 (7.2, 34.8)	0.651
Intraoperative vasodilator drug use	14 (42.4)	16 (43.2)	1
Intraoperative complication	17 (51.5)	12 (32.4)	0.169
DTX pre cardiopulmonary bypass (mg%), mean (S.D.)	117.2 (22.8)	117.5 (23.5)	0.957
DTX post cardiopulmonary bypass (mg%), mean (S.D.)	176.3 (40.4)	185.1 (41.4)	0.376

Values are means (standard deviation, S.D.); number (%) or median (interquartile range)

Table 3 Preoperative and postoperative MMSE scores of the control and music groups

Cognitive domains	Preoperative period			Postoperative period		
	Control (n=33)	Music (n=37)	p-value	Control (n=33)	Music (n=37)	p-value
MMSE scores, median (IQR)	26 (24, 28)	27 (23, 29)	0.781	27 (23,29)	27 (24,29)	0.416
Orientation for time, median (IQR)	5 (5,5)	5 (5,5)	0.175	5 (4,5)	5 (5,5)	0.04
Orientation for place, median (IQR)	5 (5,5)	5 (5,5)	0.348	5 (5,5)	5 (5,5)	0.13

MMSE=mini-mental state examination; IQR=interquartile range

Table 3 (continued)

Cognitive domains	Preoperative period			Postoperative period		
	Control (n=33)	Music (n=37)	p-value	Control (n=33)	Music (n=37)	p-value
Attention/calculation, median (IQR)	5 (2,5)	5 (1,5)	0.655	5 (1,5)	5 (1, 5)	0.625
Recall, median (IQR)	2 (1,3)	2 (0,3)	0.494	2 (1,3)	3 (2,3)	0.333
Naming, median (IQR)	2 (2,2)	2 (2,2)	1	2 (2,2)	2 (2,2)	1
Repetition, median (IQR)	1 (0,1)	1 (0,1)	0.965	1 (0,1)	1 (0,1)	0.905
Verbal Command, median (IQR)	3 (3,3)	3 (3,3)	0.26	3 (3,3)	3 (3,3)	0.492
Written Command, median (IQR)	1 (1,1)	1 (1,1)	0.26	1 (1,1)	1 (1,1)	0.067
Writing, median (IQR)	1 (0,1)	1 (0,1)	0.881	1 (0,1)	1 (0,1)	0.395
Visuoconstruction, median (IQR)	1 (1,1)	1 (0,1)	0.457	1 (0,1)	1 (0,1)	0.702

MMSE=mini-mental state examination; IQR=interquartile range

Table 4 Postoperative outcome (ICU stay, postoperative pain scores, opioid consumption, postoperative complication, CAM-ICU 7 score) of the control and music groups

Postoperative outcomes	Control (n=33)	Music (n=37)	p-value
Days in ICU (days), mean (S.D.)	5.1 (6.1)	4 (2.2)	0.301
Duration of mechanical ventilator (min), mean (S.D.)	689.9 (432.5)	505.6 (375.5)	0.061
Maximum pain score in 24 hr, mean (S.D.)	7.6 (1.2)	5 (1.3)	<0.001
Minimum pain score in 24 hr, mean (S.D.)	0.2 (1)	0.2 (0.6)	0.782
Equivalent dose of morphine (mg), mean (S.D.)	61.1 (11.8)	31.9 (11.3)	<0.001
Cardiac complication	7 (21.9)	4 (10.8)	0.356
Respiratory complication	3 (9.1)	1 (2.7)	0.337
CAM-ICU7 Delirium severity scale, median (IQR)	0.2 (0.5)	0.3 (0.6)	0.626
Total days of admission (days), median (IQR)	11.6 (6.4)	10 (4.2)	0.229

ICU=intensive care unit; IQR=interquartile range; S.D.=standard deviation; hr=hour

DISCUSSION

It was found that listening to hemispheric synchronized sounds was not associated with the incidence of POCD and delirium in patients having undergone CABG surgery. These results contrast with those of McCaffrey et al.⁶, who showed that patients that listened to music after hip or knee surgery had significantly higher postoperative MMSE scores than patients that did not. Listening to music also decreased the incidence of acute confusion after surgery⁶. However, music intervention in that study was performed postoperatively; additionally, patients were awake and could choose the type of music they preferred.

We chose hemispheric synchronized sounds in our study, because Chaieb et al. reported these sounds to have a positive effect on cognitive function and mood, improve memory recall and thinking processes, and significantly decrease anxiety and confusion¹⁰. Hemispheric synchronized sounds are created when two sounds of slightly different frequency are delivered to each ear simultaneously. Erhan et al. showed that listening to hemispheric synchronized sounds during general anesthesia improved the quality of awakening from anesthesia, lowered pain scores, increased satisfaction rates and decreased intraoperative remifentanyl consumption⁷. However, no study has investigated the

effects of listening to hemispheric synchronized sounds on POCD and postoperative delirium in patients undergoing general anesthesia.

Our study demonstrated that mean postoperative MMSE scores, which reflect cognitive function after CABG surgery, did not differ between the music and control groups. This result was probably owing to evaluation of postoperative MMSE scores 24 hr after extubation; i.e., approximately 1 to 3 days after surgery. However, POCD after cardiac surgery commonly occurs between 7 days and 3 months post surgery; hence, we may have missed patients that could have developed POCD later. Furthermore, mean postoperative MMSE scores were higher than preoperative MMSE scores in both the music and control groups. This outcome may be due to a learning effect resulting from the repeated administration of the MMSE¹³.

The incidence of postoperative delirium is notably high in older patients (70 years of age or older) undergoing cardiac surgery¹⁴. Our study indicated that the severity of delirium, determined by CAM-ICU 7 scores, did not differ between the music and control groups; no patients had postoperative delirium. This may have been due to the fact that patients in our study were mostly 60 years of age or younger.

Listening to hemispherical synchronized sounds decreased Visual Analog Scale scores for pain in previous studies^{7,15}. These results echo those of our study, indicating that listening to hemispherical synchronized sounds during general anesthesia has a significantly positive effect on postoperative pain and reduced opioid requirement within the first 24 hr after surgery. The underlying mechanism may involve an attenuating effect on the physiologic stress response to surgery and stress hormone levels¹⁶.

The strengths of this study were its prospective, randomized control and double-blind design; as this minimized the potential bias introduced by the anesthesiologist and the examiner that evaluated preoperative and postoperative MMSE scores. Moreover,

listening to sounds is a cheap, time-effective, and non-invasive intervention; furthermore, and no complications from music intervention were observed in this study.

However, this study also had some limitations. We studied patients older than 50 years that generally do not have a high incidence of neuropsychiatric complications after cardiac surgery. Moreover, we performed postoperative neuropsychological tests in the period with a low prevalence of POCD. Finally, the lack of follow-up may have resulted in the underestimation of patients that developed delayed postoperative cognitive impairment.

CONCLUSION

Listening to hemispheric synchronized sounds during CABG surgery did not affect the incidence of POCD and delirium within 24–72 hr. However, music therapy decreased the pain level and the need for postoperative analgesic drug intake. Further studies should involve a larger sample size and other types and timings (preoperative or postoperative) of sound/music intervention.

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