



Effects of Music on Pain and Autonomic Functions of Heart Rate, Blood Pressure, Nausea and Vomiting After Major Surgery—Meta-analysis

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Abstract

The aim of this study was to evaluate the effect of music on patients' heart rate, blood pressure, nausea and vomiting in the intraoperative and perioperative period. We searched randomised clinical trials (RCT) and controlled clinical trials and abstracts of major conferences comparing music with placebo from Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, PubMed, Google Scholar, Embase and Scopus using key words music, surgery, intraoperative, postoperative pain, heart rate, blood pressure, nausea and vomiting. Our last search was on 30th May 2020. We included patients of all ages admitted for any kind of surgery. Quality of trials was assessed using Cochrane collaboration tools. Results and data were screened and assessed independently. Outcome parameters were levels of pain, heart rate, systolic/diastolic blood pressure, nausea and vomiting during and after surgery.

We included 67 trials. Music reduced pain (mean difference random effects -0.72 , 95% CI -1.01 to -0.42) and heart rate (Std mean difference random effects -0.37 , 95% CI -0.66 to -0.08) compared to controls. However, there was no association between music and systolic/diastolic blood pressure, nausea or vomiting.

The reduction of pain sensation and heart rate in the perioperative period may indicate a positive effect of playing music to patients in a surgical setting. Further research is needed to specify how such measures could be best integrated into anaesthesiological procedures to alleviate stress for patients.

Keywords Music · Pain · Heart rate · Blood pressure · Nausea · Vomiting · Surgery

Introduction

The stress of undergoing surgery which is nature's way of survival could lead to homeostatic imbalance. Stress causes adverse effects such as hypertension, tachycardia,

hyperglycemia and immunosuppression. Symptoms related to anxiety which is a 'flight and fight' response are pain, nausea and vomiting.

Patients undergoing surgery experience pain of varying intensities and duration. Pain is a disturbing feature for the patient and can cause haemodynamic instability, cardiac overload, myocardial ischaemia reduce coughing capacity thereby increasing pulmonary infections and delays postoperative recovery which may escalate healthcare costs. Pain can result in increased opioid consumption.

Perioperative pain has psychological effects such as anxiety, mood disorders and delirium. Perioperative pain is often underestimated and undertreated. Pain is multifactorial with psychological, biological and social factors which explains the varied response between different individuals.

Heart rate variability is an autonomic response to nociceptive stimulation.

Nausea and vomiting are often experienced by patients postoperatively. Today as we move towards ambulatory surgery, we aim to discharge patients the same day. Presence

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of nausea and vomiting will delay discharges. The incidence of postoperative nausea and vomiting is estimated at 30% [1]. It has a much higher incidence of 80% in the high-risk groups such as those undergoing laparoscopy, tonsillectomy and strabismus surgery [2, 3].

It is important to reduce the stress and anxiety of patients undergoing surgery to maintain their comfort and stabilise them haemodynamically. Music has been found to be effective in reducing stress [4–6]. Music recruits neural systems of emotions and reward just like those of food, sex and drug abuse. Music reduced cortisol levels which cause increased heart rate and blood pressure, in participants who listened to music before or during medical interventions. Relaxing music decreases anxiety, blood pressure and heart rate in stress [7]. In coronary heart disease patients, music reduces heart rate and systolic blood pressure and pain [8]. Music can act as an analgesic relieving pain by releasing endorphins or changing catecholamine levels [9, 10]. Endorphins are chemicals which are produced by the body to relieve stress and pain and they work similar to opioids. Catecholamines (adrenaline and epinephrine) are mediated by changes in the sympathetic nervous system during stress. Activation of the analgesic mechanisms is the result of interaction between specific neurotransmitters, e.g. norepinephrine; mechanisms are the result of interaction between specific neurotransmitters, e.g. norepinephrine, serotonin and specific neurons transmitting pain. This is similar to how opioid drugs depress the release of transmitters associated with transmission of pain.

Catecholamines cause physiological changes that prepare the body for physical activity (flight or fight response) such as alterations in heart rate, blood pressure and blood glucose level. Music affects these activities of the sympathetic nervous system.

Our aim in this systematic review of randomised controlled trials (RCTs) and controlled clinical trials was to assess the effects of music compared to controls on alleviating pain, stabilising heart rate and blood pressure, reducing nausea and vomiting in patients undergoing surgery.

Methods

We included randomised control trials (RCTs) and controlled clinical trials (CCTs) published between 1995 through 2020. The study participants were patients of all ages who were admitted for all types of surgery for all types of anaesthesia (topical, loco-regional, general). Music which was the intervention was played before, during and after surgery. The outcomes studied were pain, heart rate, systolic and diastolic blood pressure, nausea and vomiting.

We identified relevant studies using the terms—music, surgery, intraoperative, postoperative pain, heart rate,

blood pressure, nausea and vomiting. The trial register was compiled from the Cochrane Central Register of Controlled Trials (CENTRAL) (updated each new issue of *The Cochrane Library*), MEDLINE, PubMed, Google Scholar, Embase and Scopus. We searched for unpublished work from abstracts of major conferences—World Music Therapy Conference, International Society Music Education World Conference, World Surgery Conference, International Congress on Surgery and World Psychiatry Conference. Our search was until 30th May 2020.

We conducted the systematic review according to PRISMA systematic review template. The eligibility of the studies was assessed and screened independently by the review authors (TT and ALA). The authors worked out disagreements via discussion and brain-storming sessions. Full texts in the English language were reviewed. Participants were human patients of all ages undergoing surgery.

The studies were independently selected by the authors. Disputes were settled by discussion among the authors.

Assessment of Risk of Bias in Included Trials

For each trial selected, the authors gauged the following systematic errors—random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias) and selective reporting (reporting bias). These risks of biases were classified as low risk, moderate risk, high risk or unclear risk.

Data Synthesis

We performed meta-analysis via the use of Review Manager Software (RevMan 2014) for the eligible studies. Fixed effects meta-analysis model was utilised for trials that were sufficiently similar with no significant heterogeneity. For studies with moderate and considerable heterogeneity, we carried out meta-analysis via the use of random effects model. Depending on the types of variables, we made use of odds ratio or mean differences or standardised mean differences as summary measures where applicable.

Assessment of Heterogeneity

We employed χ^2 test for heterogeneity (significance level $P < 0.1$) and estimated the degree of heterogeneity via the use of the I^2 statistic. I^2 value of 30% or more is deemed as having moderate heterogeneity.

Assessment of Reporting Bias

The authors made extensive and exhaustive searches to ensure minimal publication and reporting biases. Funnel plot analysis was utilised to assess for publication bias when there was sufficient number of trials with similar outcome measures.

Sensitivity Analysis

We performed sensitivity analysis by reanalyzing data using different statistical approaches via the use of either random effects model or fixed effects model. Sensitivity analysis was also utilised when there was ambiguity in including the study and also to explore the effects of the risk of bias of the trials (assessed by concealment of allocation, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting) and thereafter by excluding trials with a high risk of bias.

Results

Search Results

A total of 87 records were established through database searching via the following search engines—Cochrane Library, Google Scholar, MEDLINE and PubMed (Fig. 1). We did not identify additional record through other databases. We eliminated a total of 20 records from the list as the inclusion criteria were not fully fulfilled. As for the remaining 67 records, we obtained the full texts to enable full systematic review of these trials.

Included Studies

A total of 67 trials met our inclusion criteria ranging from publication year 1995 until 2020 [11–77].

All the trials were of randomised controlled trial in design with the intervention group listening to music and the control group not being exposed to music or additionally having a quiet rest or receiving usual care or receiving empty blank cassette with headphones. Most trials involved two groups—an intervention group and a control group. However, there were a total of 12 trials that involved three groups (intervention group, combination group, control group) [18, 24, 26, 44–46, 52–54, 62, 68, 75] and a further five trials utilising four groups [25, 28–30, 33].

Risk of Bias in Included Trials

The overall risks of bias for the 67 included trials are illustrated in Addendum.

The trials were classified as to whether they were having low risk bias (documented appropriate or adequate methodology), high risk bias (documented inappropriate methodology) or unclear risk of bias (methodology on the bias not found within the full text or undocumented) in the following selected biases—random sequence generation and allocation (selection bias), blinding (performance bias and detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias).

Random Sequence Generation and Allocation (Selection Bias)

A total of 37 trials (55% of total trials) reported the use of randomisation techniques and were therefore classified as having low risk of bias. However, only eight (12%) of the trials adequately described the use of allocation concealment in the methodology.

Blinding (Performance Bias and Detection Bias)

We observed a total of 20 (30% of the 67 trials) employing the use of double-blinding procedure to minimise performance and detection bias. The remaining 70% either did not provide details of the blinding procedure (48%) or were unclear in the methodology (22%) and were therefore categorised as having high risk and unclear risk of bias respectively.

Incomplete Outcome Data (Attrition Bias)

A total of 49 (73%) of the 67 trials had noted complete outcome data with at least 80% of the total original participants completing the study. We henceforth classified these trials as having low risk bias in this domain.

Selective Reporting (Reporting Bias)

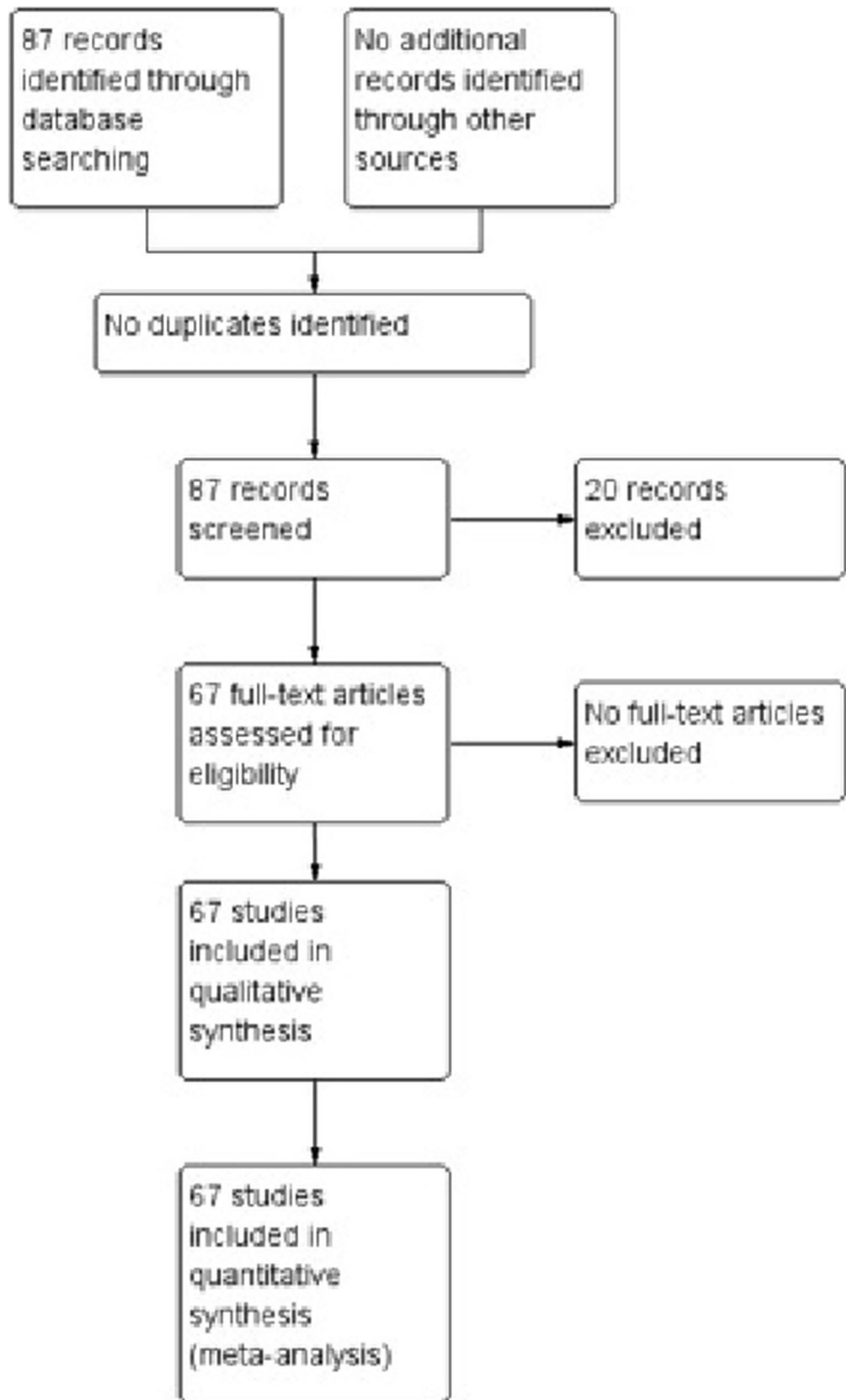
Of the 67 trials, 94% were noted to have low risk of reporting bias as these trials reported all outcome objectives in the results section.

Effects of Interventions

Pain Score (VAS Score)

A total of 42 trials were included in the meta-analysis of effects of music on pain score. Random effects model was utilised as heterogeneity was noted to be high with $I^2 = 90\%$. Overall, exposure to music during surgery was noted to significantly reduce the mean pain score (VAS) in comparison

Fig. 1 Flow chart—selection of studies for inclusion



to control (mean difference random effects -0.72 , 95% CI -1.01 to -0.42 ; Table 1 and Fig. 2). Funnel plot was

generated and produced symmetrical plot indicating no or minimal publication bias (not in figure).

Table 1 Effects on pain score (VAS), heart rate, systolic plus diastolic blood pressure, nausea and vomiting among those exposed to music and control

Trial	Music group	Control group	Mean difference random effects 95% CI
Effects on pain score (VAS)			
Allred 2010 [11]	28	28	−3.90 (−18.90, 11.10)
Baki 2018 [13]	25	25	−0.45 (−0.98, 0.09)
Belloeil 2020 [14]	74	77	0.30 (−0.34, 0.94)
Chen 2015 [18]	15	15	0.47 (−0.38, 1.32)
Chiodo 2019 [19]	25	25	−0.42 (−6.34, 5.50)
Choi 2018 [20]	26	26	−0.96 (−2.14, 0.22)
Dabu-Bondoc 2010 [21]	20	20	0.30 (−0.88, 1.48)
Ebneshahidi 2008 [22]	38	39	−19.00 (−28.83, −9.17)
Eren 2018 [23]	30	30	−0.47 (−1.76, 0.82)
Good 1998 [27]	13	21	−19.52 (−35.25, −3.79)
Good 1999 [28]	89	89	−4.00 (−11.49, 3.49)
Good 2002 [26]	73	72	−6.00 (−15.44, 3.44)
Good 2005 [25]	41	31	−7.00 (−17.26, 3.26)
Good 2010 [24]	96	103	−8.10 (−14.63, −1.57)
Graversen 2013 [31]	40	35	−1.00 (−1.38, −0.62)
Guerrero 2012 [32]	54	47	7.50 (−1.91, 16.91)
Hepp 2018 [35]	154	150	−0.49 (−0.83, −0.15)
Hogan 2015 [36]	12	13	−1.69 (−1.99, −1.39)
Ikonomidou 2004 [38]	29	26	−4.80 (−13.40, 3.80)
Kahloul 2017 [39]	70	70	−0.41 (−0.71, −0.11)
Kavakli 2019 [40]	32	32	0.20 (−0.29, 0.69)
Kim 2011 [41]	106	113	−0.20 (−0.47, 0.07)
Kongsawatvorakul 2016 [42]	36	37	−0.78 (−2.62, 1.06)
Kshetry 2006 [43]	53	51	−1.10 (−1.98, −0.22)
Kurdi 2018 [45]	63	63	−1.38 (−1.73, −1.03)
Laurion 2003 [46]	28	28	−0.40 (−1.09, 0.29)
Nilsson 2001 [52]	29	27	−0.90 (−1.29, −0.51)
Nilsson 2003b [53]	62	63	−2.80 (−3.31, −2.29)
Özer 2013 [56]	44	43	−0.17 (−0.35, 0.01)
Pellino 2005 [59]	33	32	0.32 (−0.66, 1.30)
Rafer 2015 [60]	28	28	1.07 (−1.10, 3.24)
Reza 2007 [61]	50	50	−0.20 (−1.24, 0.84)
Sandelbach 2006 [63]	50	36	−1.11 (−1.92, −0.30)
Shertzer 2001 [64]	56	41	−0.56 (−1.43, 0.31)
Simcock 2008 [65]	15	15	−1.62 (−3.31, 0.07)
Suresh 2015 [67]	18	19	−60.00 (−110.13, −9.87)
Taylor 1998 [68]	30	31	0.60 (−0.33, 1.53)
Tusek 1997 [69]	65	65	−45.00 (−53.02, −36.98)
Vaajoki 2012 b [71]	83	85	−0.50 (−0.96, −0.04)
Voss 2004 [72]	19	21	−26.00 (−38.94, −13.06)
Wang 2014 [73]	20	20	−1.35 (−2.09, −0.61)
Wang 2015 [74]	30	30	−0.60 (−0.69, −0.51)
Total (95% CI)	1902	1872	−0.72 (−1.01, −0.42)
Heterogeneity: $\tau^2=0.50$; $\chi^2=396.82$, $df=41$ ($P<0.00001$); $I^2=90\%$			
Test for overall effect: $Z=4.80$ ($P<0.00001$)			
Trial	Music group	Control group	Std mean difference random effects 95% CI
Effects on heart rate			
Allred 2010 [11]	28	28	−5.20 (−12.36, 1.96)

Table 1 (continued)

Trial	Music group	Control group	Mean difference random effects 95% CI
Baki 2018 [13]	25	25	- 10.36 (- 20.09, - 0.63)
Chen 2015 [18]	15	15	1.53 (- 6.02, 9.08)
Choi 2018 [20]	26	26	- 1.25 (- 2.06, - 0.44)
Ebneshahidi 2008 [22]	38	39	4.00 (- 2.48, 10.48)
Eren 2018 [23]	30	30	4.86 (- 2.05, 11.77)
Guerrero 2012 [32]	54	47	2.70 (- 1.82, 7.22)
Hepp 2018 [35]	154	150	- 2.54 (- 5.70, 0.62)
Kavakli 2019 [40]	32	32	0.00 (- 0.49, 0.49)
Kim 2011 [41]	106	113	- 0.32 (- 0.59, - 0.05)
Kshetry 2006 [43]	49	50	- 0.20 (- 0.59, 0.20)
Liu 2015 [48]	47	51	- 0.58 (- 0.98, - 0.17)
Özer 2013 [56]	44	43	- 0.16 (- 0.58, 0.27)
Wang 2015 [74]	30	30	- 0.69 (- 1.21, - 0.16)
Wiwatwongwana 2016 [75]	44	44	0.33 (- 0.09, 0.75)
Wu 2017 [76]	19	19	- 1.00 (- 1.67, - 0.32)
Total (95% CI)	741	742	- 0.37 (- 0.66, - 0.08)
Heterogeneity: $\chi^2 = 37.70$, $df = 15$ ($P = 0.0010$); $I^2 = 60\%$			
Test for overall effect: $Z = 4.17$ ($P < 0.0001$)			
Trial	Music group	Control group	Std mean difference random effects 95% CI
Effects on systolic blood pressure			
Choi 2018 [20]	26	26	2.44 (0.84, 4.04)
Ebneshahidi 2008 [22]	38	39	- 3.00 (- 10.38, 4.38)
Eren 2018 [23]	30	30	- 0.10 (- 6.05, 5.85)
Guerrero 2012 [32]	0	0	- 1.20 (- 6.02, 3.62)
Hepp 2018 [35]	154	150	- 0.36 (- 0.58, - 0.13)
Kahloul 2017 [39]	70	70	- 0.57 (- 0.91, - 0.23)
Kavakli 2019 [40]	32	32	- 0.02 (- 0.51, 0.47)
Kim 2011 [41]	106	113	0.06 (- 0.20, 0.33)
Kshetry 2006 [43]	49	50	0.33 (- 0.07, 0.73)
Liu 2015 [48]	47	51	- 1.32 (- 1.76, - 0.88)
Özer 2013 [56]	44	43	0.03 (- 0.39, 0.45)
Wang 2015 [74]	30	30	- 0.69 (- 1.21, - 0.16)
Wiwatwongwana 2016 [75]	44	44	0.41 (- 0.01, 0.84)
Wu 2017 [76]	19	19	- 1.16 (- 1.86, - 0.47)
Total (95% CI)	689	697	- 0.23 (- 0.56, 0.10)
Heterogeneity: $\tau^2 = 0.24$; $\chi^2 = 73.30$, $df = 13$ ($P < 0.00001$); $I^2 = 82\%$			
Test for overall effect: $Z = 1.37$ ($P = 0.17$)			
Trial	Music group	Control group	Std mean difference random effects 95% CI
Effects on diastolic blood pressure			
Chen 2015 [18]	15	15	- 0.07 (- 8.77, 8.63)
Choi 2018 [20]	26	26	1.69 (0.93, 2.45)
Ebneshahidi 2008 [22]	38	39	- 2.00 (- 7.59, 3.59)
Eren 2018 [23]	30	30	- 0.40 (- 5.61, 4.81)
Guerrero 2012 [32]	0	0	- 0.50 (- 3.90, 2.90)
Kavakli 2019 [40]	32	32	0.20 (- 13.65, 14.05)
Kshetry 2006 [43]	50	50	- 0.09 (- 0.48, 0.30)
Liu 2015 [48]	47	51	- 0.32 (- 0.72, 0.08)
Özer 2013 [56]	44	43	0.22 (- 0.20, 0.64)
Wang 2015 [74]	30	30	- 0.69 (- 1.21, - 0.16)

Table 1 (continued)

Trial	Music group	Control group	Mean difference random effects 95% CI
Wiwatwongwana 2016 [75]	44	44	0.20 (−0.22, 0.62)
Wu 2017 [76]	19	19	−1.16 (−1.86, −0.47)
Total (95% CI)	375	379	−0.07 (−0.50, 0.37)
Heterogeneity: $\tau^2=0.29$; $\chi^2=40.75$, $df=11$ ($P<0.0001$); $I^2=73\%$ Test for overall effect: $Z=0.29$ ($P=0.77$)			
Trial	Music group	Control group	Odds ratio Inverse variance, fixed effects 95% CI
Effects on nausea, vomiting			
Belloeil 2020 [14]	19	132	0.57 (0.21, 1.53)
Buehler 2017 [15]	23	112	1.45 (0.59, 3.57)
Cetinkaya 2019 [17]	8	59	0.13 (0.01, 1.12)
Dabu-Bondoc 2010 [21]	6	34	1.00 (0.18, 5.67)
Graversen 2013 [31]	2	75	0.88 (0.05, 14.51)
Ikonomidou 2004 [38]	7	48	1.23 (0.25, 6.08)
Kurdi 2018 [45]	63	63	1.16 (0.82, 1.63)
Laurion 2003 [46]	28	28	0.48 (0.16, 1.41)
Nilsson 2003b [53]	59	56	0.64 (0.30, 1.35)
Total (95% CI)	215	607	0.95 (0.73, 1.24)
Heterogeneity: $\chi^2=9.19$, $df=8$ ($P=0.33$); $I^2=13\%$ Test for overall effect: $Z=0.36$ ($P=0.72$)			

Heart Rate

For the meta-analysis of effects of music on heart rate, 16 trials were included. There was an overall significant reduction of heart rate among those exposed to music when compared to control (Std mean difference random effects -0.37 , 95% CI -0.66 to -0.08 ; Table 1 and Fig. 3).

Blood Pressure

Music was noted to have no significant effect on both systolic (Std mean difference random effects -0.23 , 95% CI -0.56 to 0.10 ; Table 1 and Fig. 4) and diastolic blood pressures (Std mean difference random effects -0.07 , 95% CI -0.50 to 0.37 ; Table 1 and Fig. 5) in comparison to the control group.

Nausea and Vomiting

The meta-analysis of nausea and vomiting involved 9 trials. There was no significant difference in the odds ratio of exposure to music and development of nausea and vomiting in contrast to the control group (odds ratio inverse variance fixed effects 0.95 , 95% CI 0.73 to 1.24 ; Table 1 and Fig. 6).

Discussion

We looked at music being played at any time starting from the induction room preoperatively, intraoperatively and in the recovery bay postoperatively with diverse methods of anaesthesia ranging from local to general anaesthesia.

We found that music reduced the sensation of pain which is the fifth vital sign among patients undergoing surgery. Other studies also support the view that music reduces pain in perioperative settings [78, 79].

Heart rate usually increases when there are stressful conditions such as surgical procedures but we found that listening to music reduced heart rate in patients undergoing surgery. In our study of 67 trials, we analysed 16 studies on heart rate variability of patients listening to music perioperatively. A Cochrane systematic review in patients with coronary heart disease undergoing surgery found that music reduces stress, anxiety and heart rate [80].

Elevated heart rate is associated with impaired cardiopulmonary performance. Music will be beneficial in surgical patients to reduce the heart rate and thereby prevent impaired cardiopulmonary function.

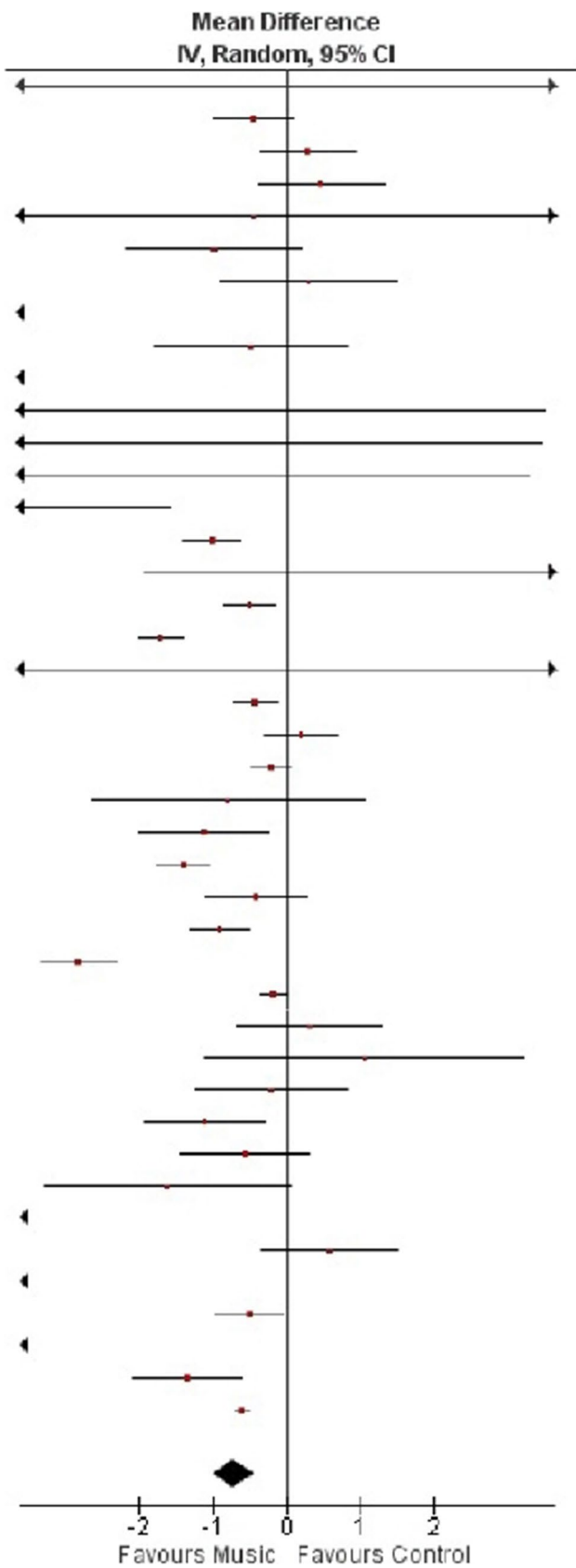


Fig. 2 Forest plot—mean difference of pain score (VAS) among those exposed to music and control

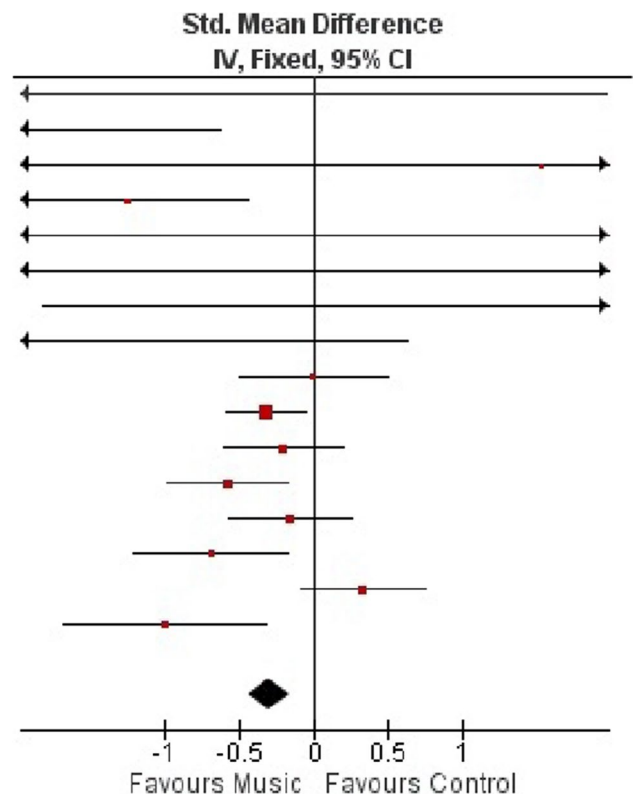


Fig. 3 Forest plot—mean difference of heart rate among those exposed to music and control

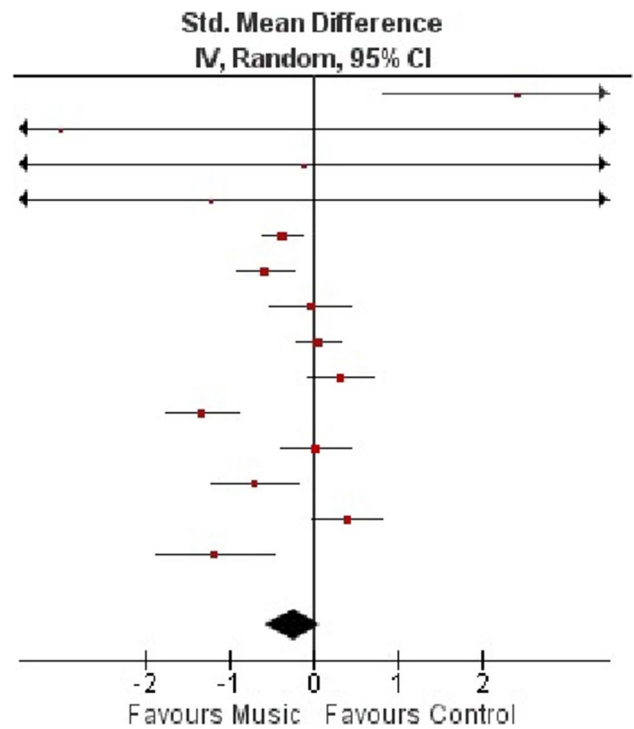


Fig. 4 Forest plot—mean difference of systolic blood pressure among those exposed to music and control

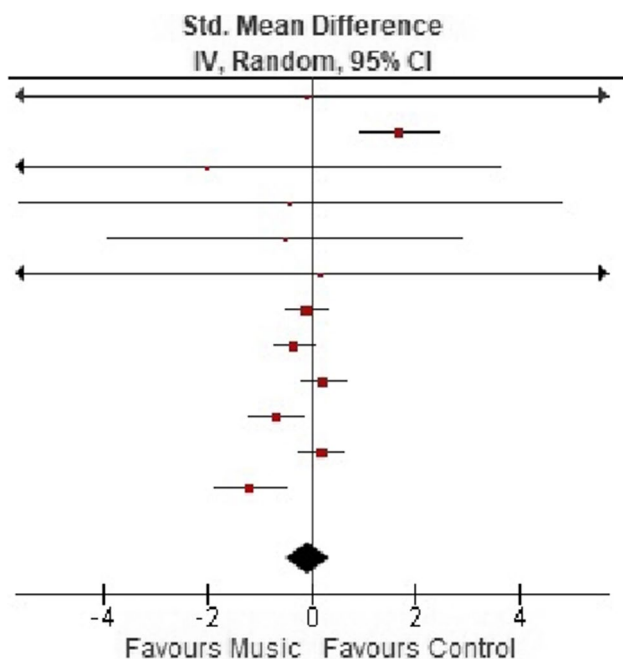


Fig. 5 Forest plot—mean difference of diastolic blood pressure among those exposed to music and control

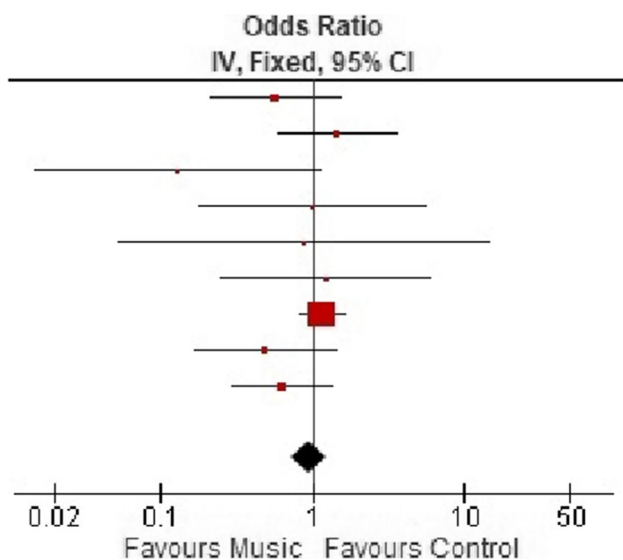


Fig. 6 Forest plot—odds ratio of presence of nausea and vomiting among those exposed to music and control

Music did not have any effect on either systolic or diastolic blood pressure among patients undergoing surgery.

Postoperative nausea and vomiting affect 20–40% of all patients undergoing surgery and 80% of those in the high-risk group [81, 82]. Music did not have an effect on nausea and vomiting in patients undergoing surgery. We did not find other review articles on the effects of music on nausea and vomiting perioperatively.

Music has been shown to have benefits in reducing pain and heart rate in patients undergoing surgery. However, we did not look at the types of music and the volume used. A study demonstrated that intuitive people such as surgeons appreciate a wide range of music [83]. Interestingly, exciting music increases heart rate whereas tranquilising music reduces heart rate [84].

Overall, the risk of bias was moderate with 55% describing the use of randomisation techniques, 12% describing adequate allocation method and 30% practicing double-blind technique. Majority

completed the study (73%) and reported all outcomes (94%). Though there was high level of heterogeneity (90%) which might be contributed to by the large variety of surgeries and anaesthesia used, sensitivity analysis via the use of both random and fixed effects models produced the same protective effect of music on pain. In addition, there was minimal publication bias as demonstrated by the generation of symmetrical funnel plot.

We looked at music in general and did not look at the type of music played. It will be interesting to conduct studies to compare the music played in the mother tongue of the patient which may be more familiar to the patient compared to music of the non-mother tongue. Further studies can be done to study the effects of these parameters using a variety of music ranging from classical, rock, pop, country, jazz and sentimental. The types of instruments ranging from keyboard to stings, brass and wind instruments and the effects on pain anxiety heart rate and blood pressure would be interesting so that positive findings of the research can be used in practice. The studies can also be categorised based on the era of music ranging from Baroque, Classical, Romantic to Contemporary. It is possible that the surgeons may not likely object to a wide variety of music played in the operating theatre [83]. A systematic review found that that the positive effects of music override the negative effects on surgeon's task performance [85]. In another study on perceptions of health staff, communication ($n = 400$, 80%) and concentration ($n = 384$, 77%) were affected by noise but not affected by music 385 (78%) [86].

This study looked overall at the effects of music on patients during the perioperative period. We recommend further studies to categorise the effects of music preoperatively, intraoperatively and postoperatively, to study the effects when the patient is being induced and coming out of anaesthesia as well. Further studies should be done to compare the effects of music on these parameters in elective and emergency surgeries so that music which does not have untoward effects can be used on patients in future.

Authors' Conclusions

This systematic review indicates that music may be advantageous to patients undergoing surgery for stress reduction as measured by reduction of the sensation of pain and decreased heart rate. Therefore, we conclude that presenting musical input to patients during interventions may effectively contribute to control pain and heart rate in patients undergoing surgery.

Author Contribution TT—Concept and design, acquisition of data, data analysis and interpretation, drafting of manuscript and critical revision, approval of final version of manuscript.

ALA—Concept and design, acquisition of data, data analysis and interpretation, drafting of manuscript and critical revision, approval of final version of manuscript.

UV—Drafting of manuscript and critical revision, approval of final version of manuscript.

Data Availability All data is made available.

Declarations

Consent for Publication We thank the DG of MOH Malaysia for granting permission to publish.

Conflict of Interest The authors declare no competing interests.

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