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The Effect of Perioperative Music on Medication Requirement and Hospital Length of Stay

A Meta-analysis

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Objective: To assess and quantify the effect of perioperative music on medication requirement, length of stay and costs in adult surgical patients.

Summary Background Data: There is an increasing interest in nonpharmacological interventions to decrease opioid analgesics use, as they have significant adverse effects and opioid prescription rates have reached epidemic proportions. Previous studies have reported beneficial outcomes of perioperative music.

Methods: A systematic literature search of 8 databases was performed from inception date to January 7, 2019. Randomized controlled trials investigating the effect of perioperative music on medication requirement, length of stay or costs in adult surgical patients were eligible. Meta-analysis was performed using random effect models, pooled standardized mean differences (SMD) were calculated with 95% confidence intervals (CI). This study was registered with PROSPERO (CRD42018093140) and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines.

Results: The literature search yielded 2414 articles, 55 studies (N = 4968 patients) were included. Perioperative music significantly reduced postoperative opioid requirement (pooled SMD −0.31 [95% CI −0.45 to −0.16], $P < 0.001$, $I^2 = 44.3$, N = 1398). Perioperative music also significantly reduced intraoperative propofol (pooled SMD −0.72 [95% CI −1.01 to −0.43], $P < 0.00001$, $I^2 = 61.1$, N = 554) and midazolam requirement (pooled SMD −1.07 [95% CI −1.70 to −0.44], $P < 0.001$, $I^2 = 73.1$, N = 184), while achieving the same sedation level. No significant reduction in length of stay (pooled SMD −0.18 [95% CI −0.43 to 0.067], $P = 0.15$, $I^2 = 56.0$, N = 600) was observed.

Conclusions: Perioperative music can reduce opioid and sedative medication requirement, potentially improving patient outcome and reducing medical costs as higher opioid dosage is associated with an increased risk of adverse events and chronic opioid abuse.

Keywords: analgesia, medication requirement, music, opioids, perioperative patient care, propofol, sedation, surgery

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A majority of patients continues to experience moderate to severe postoperative pain,[1] which is a risk factor for delayed hospital discharge[2] and the occurrence of postoperative complications,[3,4] persisting chronic pain and the predominant factor for the immediate postsurgical quality of life.[5] Opioid analgesics are the primary treatment modality for acute postoperative pain, which is the second most common reason to prescribe opioids.[6] However, opioid-related side effects are common.[7,8] Opioid use is considered a risk factor for pruritus, nausea, vomiting, drowsiness, urinary retention and the development of delirium.[9] Higher opioid doses also increase the incidence of postoperative ileus and respiratory depression.[10,11] Moreover, persistent opioid use in surgical patients is quite prevalent. Earlier studies reported that 5.9% of patients still filled an opioid prescription 3 to 6 months after minor surgical procedures,[12] whereas over half of the patients receiving 90 days of continuous opioid medication still use opioid analgetics 1 year later.[13] Both opioid prescription dosage and duration of use are important predictors for chronic opioid use.[6] The concomitant use of benzodiazepines can potentially increase the risk of adverse effects, delirium, and prolonged opioid misuse even more.[11]

Despite these common adverse events and an increase in opioid-related deaths, opioid prescription rates have currently reached epidemic proportions.[6] Therefore, there is an increasing interest in nonpharmacological interventions to reduce both postoperative pain and opioid consumption. Recently, several studies have reported beneficial effects of perioperative music.[14–16] The purpose of this systematic review and meta-analysis is to assess and quantify the effect of perioperative music as a nonpharmacological intervention on medication requirement before, during and after invasive, surgical procedures. Secondary outcomes are the effect of perioperative music on length of stay and cost reduction.

METHODS

This systematic review and meta-analysis adheres to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines and has been registered with PROSPERO (CRD42018093140).

Literature Search Strategy

A literature search using the exhaustive literature search method was performed with a biomedical information specialist.[17] The databases Embase, Medline Ovid, Web-of-science, Scopus, Cochrane central, Cinahl, PsychINFO Ovid, and Google Scholar were searched from date of inception until January 7th, 2019. The full search terms and number of search results of each database are detailed in Appendix A, http://links.lww.com/SLA/C758. Also, manual cross-referencing of the included studies was performed.

Study Screening and Selection

Three reviewers (V.F., P.O., and V.E.) independently identified eligible studies using a 2-stage approach. First, title and abstract of all identified papers screened, followed by reading of the full text if eligibility criteria were matched. Inclusion criteria for this systematic review were all available, peer-reviewed, full-text articles of randomized controlled trials in the English language, containing adult patients 18 years old undergoing an inhospital or outpatient invasive,

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surgical procedure, investigating the use of recorded music before, during and/or after surgery with either medication requirement, hospital length of stay or direct medical costs as outcome measures. As these predefined outcome measures were often secondary outcomes and therefore not always mentioned in titles or abstracts, the 3 reviewers screened all studies full text for potential review inclusion if during the title and abstract screening process music as a perioperative intervention in adult patients was investigated. The music intervention was predefined as vocal sound, instrumental sound or both, containing the elements melody, harmony, and rhythm. Therefore, studies investigating solely nature sounds were excluded. Studies investigating live music with a music therapist were also excluded, because of the possibility that the effect is caused by the presence of the musical therapist and the irreproducibility of the study. Finally, studies investigating music with an additional, concomitant intervention were excluded, except if this additional intervention was used in both the intervention and control group (for example, the music intervention occurred during bed rest, and the control group received only bed rest). Disagreements between the investigators were resolved by referring to the supervisor (J.J.).

Data Extraction

Study data were independently extracted by the 3 reviewers (V.F., P.O., and V.E.) using a custom, predesigned Microsoft Excel 2010 document. Risk of bias was also independently assessed using the Cochrane Collaboration's tool for assessing risk of bias in randomized trials.[18] Authors of included studies were contacted for additional information if necessary. All data was mutually discussed and disagreements between the investigators were resolved by referring to the supervisor (J.J.).

Statistical Analysis

Data were analyzed with the open-source, meta-analysis software OpenMeta-Analyst, which uses R as the underlying statistical engine.[19] Random effect models were used, because heterogeneity between the included studies was assumed to be present. Standardized mean differences (SMD) and absolute mean differences were calculated with 95% confidence interval (CI). Studies were included for meta-analysis if mean values and standard deviations (SDs) of the outcome measures were reported. Opioid doses were converted to milligrams (mg) of morphine equianalgesic (ME), with 1 mg ME being equivalent to 1 mg parenteral morphine. If interquartile ranges or ranges were reported, an approximation of the SD was calculated by dividing the interquartile range by 1.35 and the range by 4. When the standard error of mean was reported, SDs were calculated by multiplying the standard error of mean with the square root of the number of patients.[18] Publication bias was visually assessed using funnel plots, if more than ten studies were included in the meta-analysis. Heterogeneity was analyzed using the I^2-test. Statistical significance was inferred at P-value <0.05.

If studies included several music groups, the means and SDs of the music groups were pooled to an approximated mean and SD of the entire group.[18] If this was not appropriate, the music group that offered patients the choice to select from a preselected music list was preferred for meta-analysis. Choosing music from a preselected playlist has been observed to have a more beneficial effect on postoperative pain, compared to the own favorite music of the patient or preselected music without offering any choice.[16] If studies included several control groups, only the group which resembled standard perioperative patient care the most was included for meta-analysis.

RESULTS

The literature search yielded 2414 results. A total of 1524 titles and abstracts were screened after removal of duplicates and 154 articles were assessed full text. Fifty-five studies (4968 patients) were included in the qualitative synthesis and 33 studies (2390 patients)[20–53] in the meta-analysis (Fig. 1). There was a high agreement rate of over 85% between the 3 reviewers on study inclusion, risk of bias assessment, and data extraction, and all disagreements could be resolved through mutual discussion.

Study Characteristics

A detailed overview of the study characteristics is presented in Table 1. The music intervention was assessed in a wide range of different surgical procedures. General anesthesia was the most commonly used anesthesia method during surgery in 36 studies (65%), whereas locoregional anesthesia was used in 8 studies (15%). Eight studies (15%) did not report the anesthesia method used and 3 studies (5.5%) contained different surgical procedures with different anesthesia methods. The moment of music intervention varied. Music was played solely preoperatively in 3 (5.5%), intraoperatively in 10 (18%), postoperatively in 25 (45%), and on multiple moments in 15 studies (27%). Two studies by the same author contained both an intraoperative music intervention group and a second music intervention group in which the intervention was solely applied postoperatively.

The music intervention was commonly described as soothing, relaxing, nonlyrical, instrumental music and was preselected by the research team in most studies (45 studies, 82%): patients could select music from a preselected list in 21 studies (38%), whereas no choice was offered in 24 studies (44%). The preferred music of the patient was used in 9 studies (16%), whereas 1 study (1.8%) did not elaborate on the exact music intervention. In a majority of studies, music delivery was achieved using a music player and headphones (41 studies, 75%). Other reported music delivery methods were a music pillow (3 studies, 5.5%), CD-player (3 studies, 5.5%), personal stereo (1 study, 1.8%), an integrated music system in the patient room (1 study, 1.8%), or not specified (6 studies, 11%). The control group consisted of standard care (26 studies, 47%), headphones without music (16 studies, 29%), headphones with white noise or recorded OR noise intraoperatively (5 studies, 9.1%), no music without further specification (3 studies, 5.5%), or an unspecified rest period (3 studies, 5.5%). Two studies (3.6%) had both a standard care and headphones without music group acting as control.

Risk of Bias Assessment

An overview of the risk of bias assessment is presented in Fig. 2 and a more detailed description in Appendix B, http://links.lww.com/SLA/C758. A potentially high risk of selection bias was present in several studies (8 studies, 15%),[24,29,47,54–58] as sequence generation was done using odd and even numbers, days of the week or hospital record number. Several studies provided insufficient details to assess selection bias (14 studies, 25%).[20,22,26–28,30,32,36,38,40,59–62] A moderate to high risk of performance bias was present, as blinding of patients for the music intervention is only possible when the intervention is performed solely intraoperatively during general anesthesia. Blinding of personnel can theoretically be achieved by using headphones for all patients, but is more difficult in practice when patients are free to change music tracks or adjust the volume. Five studies (9.3%) employed a study design in which patients, surgical personnel and outcome assessors were all blinded adequately.[38,41,46,63,64] The ''other risk of bias'' category was reported as unclear in more than half of the studies (36 studies, 65%), because one of the baseline characteristics age, sex, weight, or the duration of surgery, which can influence intraoperative and postoperative medication requirement, was not reported. There was a high risk of other bias because of significant difference in either surgery duration or age between the

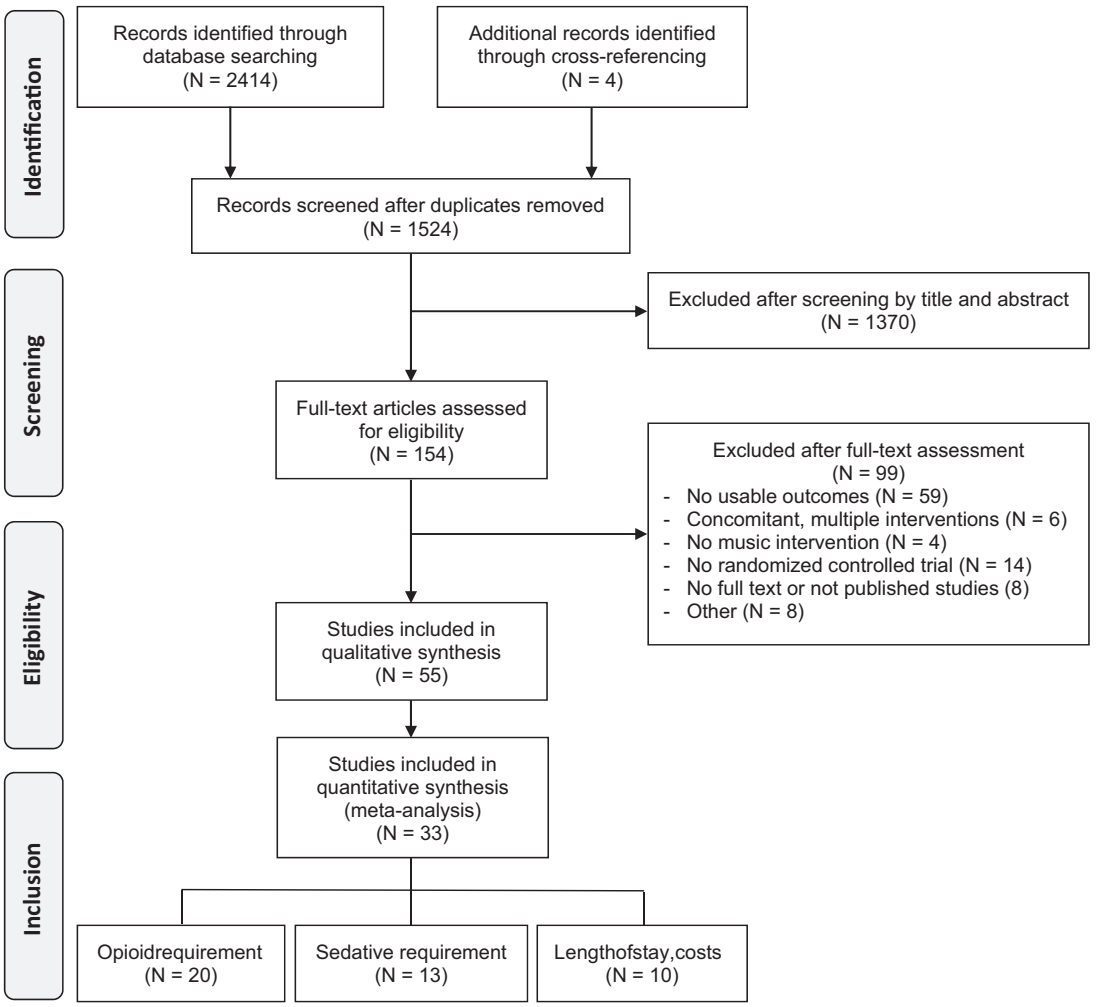

FIGURE 1. PRISMA Flow diagram. N indicates number of studies.

music and control group in 3 studies.[25,36,45] A funnel plot to investigate publication bias of studies assessing the effect of perioperative music on postoperative opioid requirement showed a near funnel-shaped plot, lacking a small number of studies in the lower-left corner which could be indicative of studies with relatively small samples sizes and small effect sizes being potentially absent (Appendix C, http://links.lww.com/SLA/C758).

Opioid Requirement

The effect of perioperative music on postoperative opioid requirement was assessed in 42 studies, of which 20[22–24,26–32,38,39,41–43,45,46,49,50] could be included in the meta-analysis. Thirteen studies presented the postoperative opioid dose requirement as morphine equivalents (ME) or parenteral morphine. In 3 studies, postoperative ketobemidone requirement was evaluated, which are equipotent to parenteral morphine (1 mg parenteral ketobemidone = 1 mg ME[65]). Postoperative parenteral tramadol requirement (10 mg parenteral tramadol = 1 mg ME[66]) was assessed in 3 studies and pethidine requirement in 1 study (10 mg pethidine = 1 mg ME[67]). Length of follow-up differed, as 5 studies assessed opioid requirement during the stay in the post-anesthesia care unit,[26,29,30,32,43] 3 within the first 2 postoperative hours[27,42,44] and 2 within the first 12 postoperative hours.[39,46] Ten studies (50%) assessed opioid requirement for minimally 24 hours after surgery or longer.[22–24,28,31,38,41,45,49,50] General anesthesia was used during surgery in all of these 20 studies.

Perioperative music significantly reduced postoperative opioid requirement (pooled SMD −0.31 [95% CI −0.45 to −0.16], $P < 0.001$, $I^2 = 44.3$, N = 1398 patients) (Fig. 3). The mean overall absolute reduction in postoperative opioid requirement of the 8 studies which measured postoperative opioid requirement during post-anesthesia care unit stay or within the first 2 postoperative hours was −1.0 mg ME (95% CI −1.6 to −0.49, $P < 0.001$, $I^2 = 10.5$, N = 698 patients). The mean absolute reduction in postoperative opioid requirement of the 10 studies which measured postoperative opioid requirement for at least 24 hours or more after surgery was −4.4 mg ME (95% CI −8.2 to −0.65, $P = 0.022$, $I^2 = 69.6$, N = 598 patients). The mean absolute reduction in 5 of these studies which measured opioid requirement for at least 3 postoperative days and involved major surgical procedures was −9.82 mg ME (95% CI −17.9 to −1.70, $P = 0.018$, $I^2 = 48.8$, N = 298 patients).[22–24,31,41] Intraoperative music during general anesthesia in 3 of the 20 studies in which the patients, surgical staff, and outcome assessors were all blinded did not significantly reduce postoperative opioid requirement

TABLE 1. Study Characteristics

Study ID	Surgical Procedure	Anesthesia	Intervention	Moment	Duration	N	Control	N	Outcome Parameters
Allred, 2010	Total knee arthroplasty	General or spinal with femoral block	Choice of easy listening, nonlyrical music	Postoperatively	POD 1, 20 min before and after first ambulation	28	Quiet rest period	28	Postoperative opioid requirement
Ames, 2017	Surgical procedures requiring ICU stay	General	MusiCure	Postoperatively	POD 1-2, 50 min, 1-8 times	20	50 min quiet rest	21	Postoperative opioid requirement
Ayoub, 2005*	Urological procedures	Regional	Own favorite music	Intraoperatively	Procedure duration	31	Headphones with operation noise recording	28	Intraoperative propofol requirement PACU length of stay
Bansal, 2010*	Abdominal, urological, or lower extremity surgery	Spinal	Choice of folk, classical, religious, soothing music	Intraoperatively	*Not specified*	50	Occlusive headphones	50	Intraoperative midazolam requirement
Binns-Turner, 2011	Mastectomy	General	Choice of classical, easy-listening, new age, inspirational music	Preoperatively Intraoperatively Postoperatively	*Not specified*	15	Blank iPOD with occlusive headphones	15	Intraoperative opioid requirement Postoperative opioid requirement PACU length of stay
Blankfield, 1995*	Coronary artery bypass surgery	General	Dreamflight II by Herb Ernst	Intraoperatively Postoperatively	Procedure duration and 2 × 30 min daily postoperatively	32	Blank tape intraoperatively and standard care postoperatively	29	Postoperative opioid requirement ICU length of stay Hospital length of stay
Chen, 2015*	Total knee replacement	*Not specified*	Chinese piano and violin music	Preoperatively Postoperatively	Total 120 min	15	Standard care	15	Postoperative opioid requirement
Ciğerci and Özbayir, 2016*	Coronary artery bypass surgery	General	Choice of Turkish classical and folk music	Preoperatively Postoperatively	90 min before surgery, after surgery 30 min in ICU and 30 min each day	34	Standard care	34	Postoperative opioid requirement
Cutshall, 2011*	Coronary artery bypass graft and/or cardiac valve surgery	General	Choice of 4 CD's	Postoperatively	2 × 20 min on POD 2–4, 120 min in total	49	Standard care with bed rest for 20 min	51	Postoperative opioid requirement Hospital length of stay
Dabu-Bondoc, 2010*	Outpatient surgery	General	Own favorite music	Preoperatively Intraoperatively	Preoperative 30 min, procedure duration	20	Intraoperatively headphones with white noise	20	Intraoperative propofol requirement Intraoperative opioid requirement Postoperative opioid requirement PACU length of stay
Easter, 2010	Elective outpatient surgery procedures	*Not specified*	Choice of easy-listening, country, gospel, rock	Postoperatively	During length of stay in PACU	111	No music	102	Postoperative opioid requirement PACU length of stay
Ebneshahidi and Mohseni, 2008*	Elective cesarean section surgery	General	Own favorite music	Postoperatively	30 min in the recovery room	38	Headphones without music	39	Postoperative opioid requirement
Finlay, 2016	Total knee arthroplasty	Spinal with nerve block	32 tracks with range of genres	Postoperatively	15 min	72	Headphones without music	17	Postoperative opioid requirement
Good, 1995*	Elective, open abdominal surgery	General	Choice of sedative nonlyrical piano, harp, synthesizer orchestral or slow jazz music	Postoperatively	60 min during the first 2 d after surgery	21	Standard care	21	Postoperative opioid requirement

TABLE 1. (*Continued*)

Study ID	Surgical Procedure	Anesthesia	Intervention	Moment	Duration	N	Control	N	Outcome Parameters
Good, 1999	Elective, open, major abdominal surgery	General	Choice of taped soothing music	Preoperatively Postoperatively	First 2 d after surgery	151	Standard care	152	Postoperative opioid requirement
Graversen and Sommer, 2013*	Laparoscopic cholecystectomy	General	Musicure using music pillow	Preoperatively Intraoperatively Postoperatively	Before surgery start until day care discharge	40	Standard care	35	Intraoperative propofol requirement Intraoperative opioid requirement Postoperative opioid requirement Day care unit length of stay
Heitz, 1992*	(Para)thyroidectomy or unilateral modified radical mastectomy	General	Choice of 3 instrumental classical tapes	Postoperatively	15 min after PACU arrival until discharge	20	Headphones without music	20	Postoperative opioid requirement
							Standard care	20	PACU length of stay
Hook, 2008*	Moderate or major elective surgery	General	Choice of Malay, Western, Chinese, soothing music	Preoperatively Postoperatively	60 min before and 180 min after surgery	51	Standard care	51	Postoperative opioid requirement
Iblher, 2011	Open heart surgery (coronary bypass, valvular transplant, or both combined)	General	Baroque organ, flute, string orchestra music with 60-80 bpm	Postoperatively	60 min after ICU admission	25	Standard care	25	Postoperative opioid requirement
					60 min after sedation stop	24			Postoperative catecholamine requirement
Ignacio, 2012	Elective spine, hip or knee surgery	General	*Not specified*	Postoperatively	2 × 30 min	12	No music	9	Postoperative opioid requirement
Ikonomodou, 2004*	Laparoscopic sterilization or tubal dyeing	General	Peaceful pan flute music	Preoperatively Postoperatively	30 min before and after surgery	29	Blank compact disk	26	Postoperative opioid requirement
Johnson, 2012	Gynaecological outpatient surgery	*Not specified*	Choice of soft country, classical/ new age and inspirational music	Preoperatively Intraoperatively Postoperatively	On average 212 min	43	Headphones without music	35	Postoperative opioid requirement
							Standard care	41	PACU length of stay
Kar, 2015*	Elective cardiac surgery under cardiopulmonary bypass	General	Raga therapy (Indian classical music)	Preoperatively Intraoperatively	30 min before surgery and procedure duration	17	Headphones without music	17	Intraoperative sedative requirement Intraoperative opioid requirement
Kliempt, 1999	Diverse range of surgical procedures	General	Classical music Adagio Karajan	Intraoperatively	Procedure duration	25	Headphones without music	26	Intraoperative opioid requirement
Koch, 1998*	Outpatient urological procedures	Spinal	Own favorite music	Intraoperatively	Procedure duration	19	Standard care	15	Intraoperative propofol requirement PACU length of stay
Koelsch, 2011*	Total hip arthroplasty	Spinal	Joyful instrumental music	Preoperatively Intraoperatively	120 min before surgery and procedure duration	20	Headphones with breaking sea waves noise	20	Intraoperative propofol requirement
Kumar, 2014	Hernia, breast, appendix and thyroid surgery	*Not specified*	Raga Ananda Bairavi (Indian classical music)	Preoperatively Postoperatively	At admission and POD 1–3	30	Standard care	30	Postoperative opioid requirement

TABLE 1. (*Continued*)

Study ID	Surgical Procedure	Anesthesia	Intervention	Moment	Duration	N	Control	N	Outcome Parameters
Laurion and Fetzer, 2003	Gynecological, laparoscopic outpatient day surgery	General	Piano music	Preoperatively Intraoperatively Postoperatively	2 times a day before surgery, procedure duration, PACU stay	28	Standard care	28	Postoperative opioid requirement PACU length of stay
Lepage, 2001*	Nononcologic, outpatient or short-stay surgery	Spinal	Choice of pop, jazz, classical, new age	Preoperatively Intraoperatively Postoperatively	Anesthesia induction until recovery	25	Standard care	25	Perioperative midazolam requirement
Liu and Petrini, 2015	Thoracic surgery	General	Soft, melodious music 60-80 bpm	Postoperatively	30 min daily on POD 1–3	56	Standard care	56	Postoperative patient-controlled analgesia requirement
Macdonald, 2003	Total abdominal hysterectomy	*Not specified*	Own favorite music	Postoperatively	2–6 h on day of surgery	30	Standard care	28	Postoperative patient-controlled analgesia requirement
Masuda, 2005*	Orthopedic surgery	General and spinal	Choice of Noh, Gagaku, classical or Enka music	Postoperatively	20 min	22	Standard care	22	Hospital length of stay
McCaffrey and Loscin, 2006	Elective hip or knee surgery	*Not specified*	Choice of CD's	Postoperatively	60 min 4 times a day	62	Standard care	62	Postoperative patient-controlled analgesia requirement
McRee, 2003	'Low risk' surgery	General, spinal, local and regional	Soft piano music	Preoperatively	30 min	13	Standard care	13	Postoperative opioid requirement
Migneault, 2004*	Gynaecological surgery	General	Choice of jazz, classical, popular new-age or piano music	Intraoperatively	Procedure duration	15	Headphones without music	15	Intraoperative end-tidal isoflurane Intraoperative fentanyl requirement Postoperative opioid requirement
Miladinia, 2017*	Abdominal surgery	General	Relaxing nonlyrical music with a bpm of 60–80	Postoperatively	3 × 10 min sessions on day of surgery	30	Standard care	30	Postoperative opioid requirement
Nielsen, 2018*	Unspecified orthopedic, urological, gynaecological and general surgery	Epidural, spinal and local	Musicure	Intraoperatively	Procedure duration	58	Standard care	44	Intraoperative fentanyl requirement Intraoperative propofol requirement
Nilsson, 2001*	Elective abdominal hysterectomy	General	Relaxing, calming music with sea waves sound	Intraoperatively	Procedure duration	30	Headphones with operation noise recording	28	Postoperative opioid requirement Hospital length of stay
Nilsson, 2003a*	Daycare surgery: varicose veins, open inguinal hernia repair	General	Soft, relaxing and calming classical music	Postoperatively	PACU arrival until patient chose to stop	62	Headphones without music	63	Postoperative opioid requirement
Nilsson, 2003b*	Daycare surgery: varicose veins, open inguinal hernia repair	General	Soft instrumental new-age synthesizer music	Intraoperatively	Procedure duration	51	Headphones without music	49	Postoperative opioid requirement
				Postoperatively	1 h after PACU arrival	51			
Nilsson, 2005*	Open hernia repair (Lichtenstein)	General	Soft, new-age synthesizer	Intraoperatively	Procedure duration	25	Headphones without music	25	Postoperative opioid requirement
				Postoperatively	1 h after PACU arrival	25			

TABLE 1. (*Continued*)

Study ID	Surgical Procedure	Anesthesia	Intervention	Moment	Duration	N	Control	N	Outcome Parameters
Nilsson, 2009a	Coronary artery bypass graft and/or aortic valve replacement	General	MusiCure using music pillow	Postoperatively	30 min on POD1	20	Standard care	20	Postoperative opioid requirement
Nilsson, 2009b*	Coronary artery bypass graft or aortic valve replacement	General	Soft, relaxing, new age style music using music pillow	Postoperatively	30 min on POD1	28	Standard care	30	Postoperative opioid requirement
Reza, 2007*	Elective caesean section	General	Soft, instrumental, Spanish style guitar music	Intraoperatively	Procedure duration	50	White music	50	Postoperative opioid requirement
Santhna, 2015	Total knee replacement surgery	*Not specified*	Choice of soothing and relaxing nonlyrical piano or violin music	Postoperatively	60 min, 4 times a day	20	Standard care	20	Postoperative opioid requirement
Schwartz, 2009*	Coronary artery bypass graft surgery	General	Light piano music	Postoperatively	Patient's choice in ICU	35	Standard care	32	ICU length of stay Hospital costs
Sen, 2009a*	Local urological procedures	Propofol PCS with local infiltration	Own favorite music	Intraoperatively	Procedure duration	30	Earphones without music	30	Intraoperative propofol requirement
Sen, 2009b*	Elective caesarian section	General	Own favorite music	Preoperatively	60 min	50	Headphones without music	50	Postoperative opioid requirement
Sen, 2010*	Elective caesarian section	General	Own favorite music	Postoperatively	60 min	35	No music	35	Postoperative opioid requirement
Szmuk, 2008	Laparoscopic hernia or cholecystectomy	General	Choice of pop-rock, classical or Israeli music	Intraoperatively	Procedure duration	20	Headphones without music	20	Intraoperative end-tidal sevoflurane Postoperative opioid requirement
Tse, 2005	Endoscopic sinus surgery or tubinectomy	*Not specified*	Choice of Chinese, Western or own favorite music	Postoperatively	2 × 30 min after surgery and on POD1	27	Standard care	30	Postoperative analgesic medication requirement
Vaajoki, 2012	Elective major abdominal midline incision surgery	General	Choice of 2000 popular music songs	Postoperatively	Total of 7 × 30 min	83	Standard care	85	Postoperative opioid requirement Hospital length of stay
Zhang, 2005*	Total abdominal hysterectomy	General with spinal or epidural	Own favorite music	Intraoperatively	Procedure duration	55	Headphones without music	55	Intraoperative propofol requirement
Zhou, 2011*	Radical mastectomy	General	Choice of 202 songs	Postoperatively	2 × 30 min daily	60	Standard care	60	Hospital length of stay
Zimmerman, 1996	Coronary artery bypass graft surgery	General	Choice of 5 soothing music tapes	Postoperatively	30 min daily during POD1-3	32	Scheduled rest of 30 min	32	Postoperative opioid requirement Hospital length of stay

*Denotes study included in meta-analysis.
CD indicates compact disk; ICU, intensive care unit; Min, minutes; N, number of patients; PACU, post-anesthesia care unit; PCS, patient-controlled sedation; POD, postoperative day; d, days; h, hours.

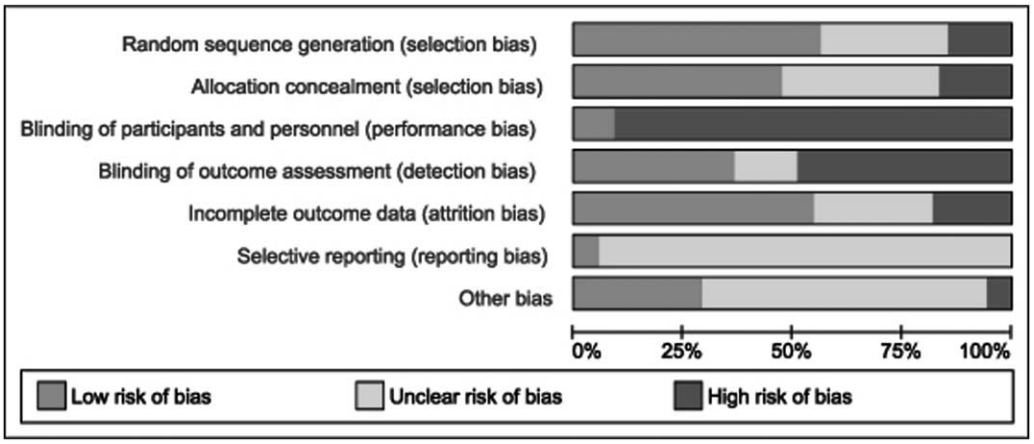

FIGURE 2. Risk of bias summary. Risk of bias summary graph.

(pooled SMD −0.16 [95% CI −0.63 to 0.31], $P = 0.49$, $I^2 = 57.1$, N = 188 patients).[38,41,46]

The effect of preoperative and/or intraoperative music on intraoperative opioid requirement was assessed in 7 studies.[23,26,29,33,38,40,63] Meta-analysis was not performed because of insufficient data presented, the broad variation in the types of surgery performed and difference in surgery duration.

Intraoperative Sedative Requirement

The effect of perioperative music on intraoperative sedative medication requirement was assessed in 13 studies (846 patients). Propofol requirement was assessed in 9,[20,26,29,33–35,40,48,51] midazolam requirement in 3,[21,33,36] and end-tidal inhalation anesthetics concentration in 2 studies.[38,64] In one of these aforementioned studies, both propofol and midazolam were administered intraoperatively for sedation.[33] Incremental intraoperative sedative medication doses were administered based on sedation depth, which was either assessed using a bispectral index monitor or a validated sedation scale. The infusion rate was patient-controlled in 4 studies.[20,34,36,48] The manner of sedation depth assessment and whether or not infusion rate was patient-controlled is specified in Fig. 4.

Perioperative music significantly reduced intraoperative propofol requirement (pooled SMD −0.72 [95% CI −1.01 to −0.43], $P < 0.00001$, $I^2 = 61.1$, N = 554 patients, 9 studies) (Fig. 4). All included studies evaluating the effect of music on propofol requirement, except 2[29,40] that did not specify the manner of sedation depth assessment, reported that the level of sedation did not differ between the music and control group. This reduction in intraoperative propofol requirement remained present when these 2 studies[29,40] were excluded from the analysis (pooled SMD −0.86, [95% CI −1.18 to −0.53], $P < 0.00001$, $I^2 = 54.9$, N = 377 patients, 7 studies), and when the 3 studies with patient-controlled propofol infusion rate were analyzed as a separate subgroup (pooled SMD −0.82 [95% CI −1.25 to −0.38], $P = 0.00025$, $I^2 = 40.1$, N = 153 patients). Perioperative music also significantly reduced intraoperative midazolam requirement (pooled SMD −1.07 [95% CI −1.70 to −0.44], $P < 0.001$,

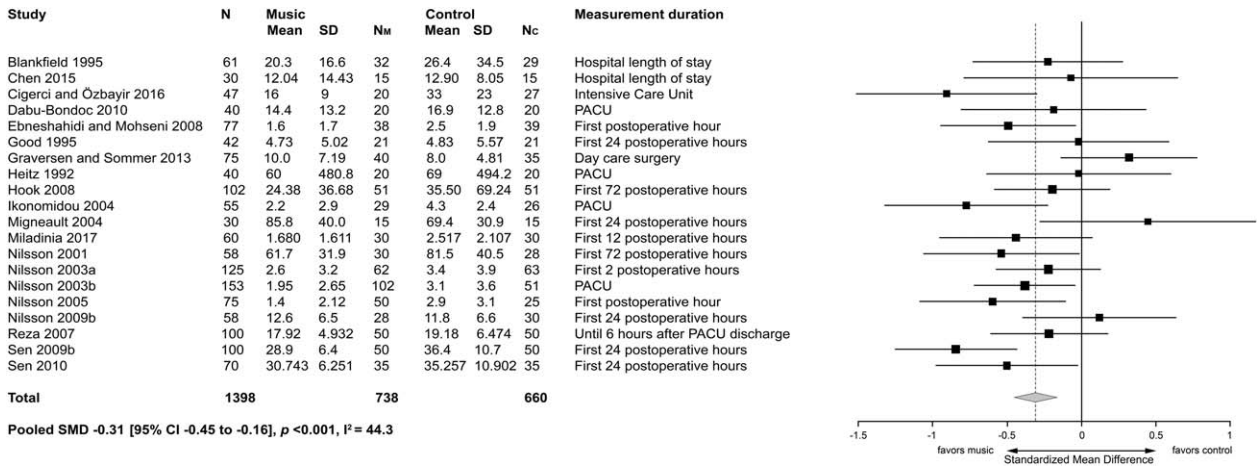

FIGURE 3. Effect of perioperative music on postoperative opioid requirement. Forest plot presenting the effect of perioperative music on postoperative opioid requirement (milligrams of morphine equianalgesics). CI indicates confidence interval; Mean, mean milligrams of morphine equianalgesics; N, total number of patients in study; N_C, number of patients in the control group; N_M, number of patients in the music group; PACU, post-anesthesia care unit; SD, standard deviation in milligrams of morphine equianalgesics; SMD, standardized mean difference.

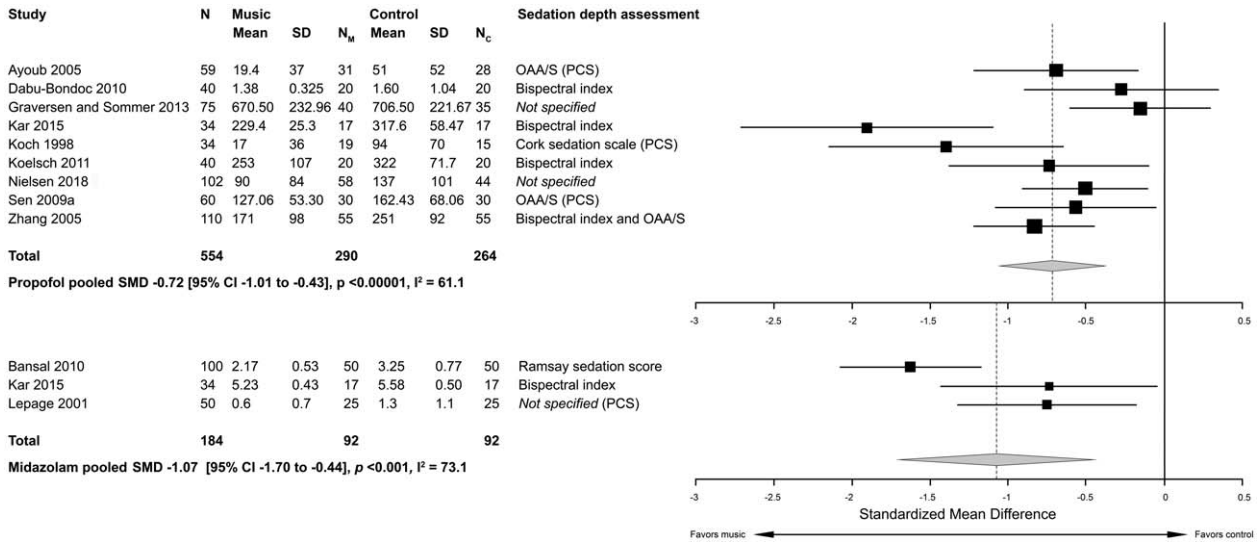

FIGURE 4. Effect of perioperative music on intraoperative sedative medication requirement. Forest plot presenting the effect of perioperative music on intraoperative propofol (above) and midazolam (below) medication requirement. CI indicates confidence interval; Mean, mean milligrams of propofol or midazolam; N, total number of patients in study; N_C, number of patients in the control group; N_M, number of patients in the music group; OAA/S, observer assessment of alertness/sedation scale; PACU, post-anesthesia care unit; PCS, patient-controlled sedation; SD, standard deviation in milligrams of propofol or midazolam; SMD, standardized mean difference.

I^2 = 73.1, N = 184 patients) (Fig. 4), while achieving the same sedation depth.

Length of Stay and Medical Costs

The effect of perioperative music on length of stay was assessed in 17 studies, of which 9 studies could be included in the meta-analysis. Total length of hospital stay of surgical inpatients was assessed in 4 studies,[22,25,37,52] length of stay in the post-anesthesia or day care unit of patients undergoing outpatient surgery in 4 other studies[20,26,29,34] and intensive care unit length of stay in 1 study.[47] Perioperative music did not significantly reduce length of stay (pooled SMD −0.18 [95% CI −0.43 to 0.067], $P = 0.15$, $I^2 = 56.0$, N = 600 patients) (Fig. 5). When analyzing the studies with outpatient surgical patients (pooled SMD −0.053 [95% CI −0.35 to 0.24], $P = 0.73$, $I^2 = 13.1$, N = 208 patients) and inpatient operations (pooled SMD −0.21 [95% CI −0.66 to 0.25], $P = 0.37$, $I^2 = 75.2$, N = 325 patients) separately, length of stay was also not reduced.

Intensive care unit costs tended to be lower in 1 pilot study [3911 (SD 1566) versus 4365 dollars (SD 2632), $P = 0.09$], as time spent in the intensive care unit was significantly reduced in the music group compared to the control group.[47] However, this did not reach statistical significance and overall direct medical costs during hospital length of stay did not differ significantly.

DISCUSSION

This systematic review and meta-analysis of 55 randomized controlled trials evaluates the effect of perioperative music on

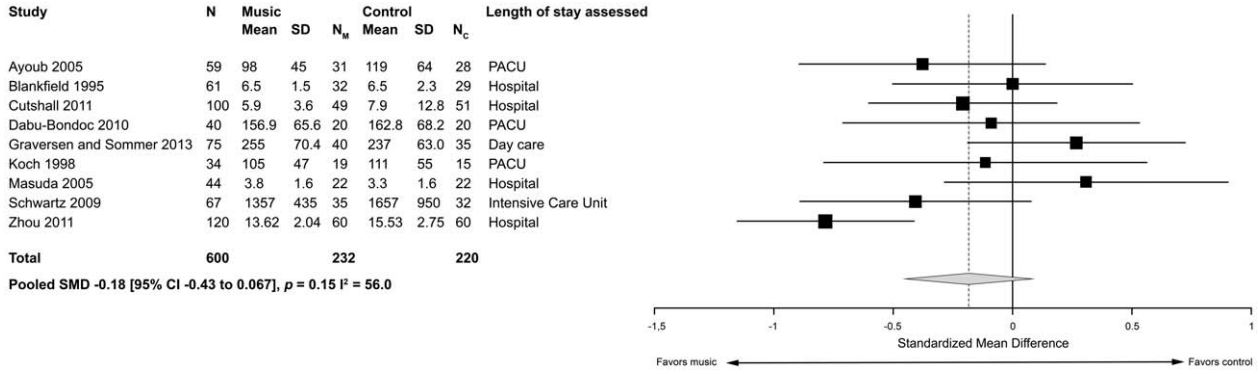

FIGURE 5. Effect of perioperative music on length of stay. Forest plot presenting the effect of perioperative music on length of stay. CI indicates confidence interval; Mean, mean length of stay; N, total number of patients in study; N_C, number of patients in the control group; N_M, number of patients in the music group; PACU, post-anesthesia care unit; SD, standard deviation; SMD, standardized mean difference.

intraoperative and postoperative medication requirement and length of stay. Because of the current opioid epidemic, which has increased opioid-related deaths and led to a substantial financial burden,[6,68] there is an increased interest in nonpharmacological interventions that can reduce both postoperative pain and opioid consumption. Perioperative music reduced opioid consumption by 4.4 mg ME in studies measuring opioid requirement for at least 24 hours or more after surgery. In studies measuring at least 72 hours or more after major surgical procedures, a reduction of 9.82 mg ME was observed. Opioid-related adverse effects have been observed to be dose-dependent and an increased requirement of 3 to 4 mg ME after surgery has been related to the occurrence of 1 additional, clinically meaningful, adverse event.[69] A maximum daily dose exceeding 2 mg of parenteral hydromorphone, equivalent to 10 to 14 mg ME,[70] were significantly associated with the development of postoperative ileus after colorectal surgery, increasing morbidity, length of hospital stay, and direct medical costs.[71] Both a higher daily opioid dose and a prolonged use in opioid-naive patients also increase the risk of chronic opioid use.[6] As more elderly patients are nowadays undergoing surgery, this group would be of particular interest to the use of perioperative music, as they have an increased risk of opioid-related adverse effects and chronic abuse because of polypharmacy and comorbidity.[72,73]

Perioperative music also significantly reduced both intraoperative propofol and midazolam requirement, whilst achieving the same sedation level. Midazolam is often used during locoregional anesthesia or as a preoperative anxiolytic, but is a risk factor for the occurrence of postoperative delirium.[74] A higher level of preoperative anxiety has been associated with a higher amount of intravenous sedation requirement to induce and maintain adequate sedation level during surgery.[75] Previous studies have reported a beneficial effect of perioperative music on anxiety levels,[14–16] which could theoretically explain the reduced sedation dosage needed. Although a dose-dependent relation of sedative medication and intraoperative hemodynamic changes has been observed,[76] the predictive outcome capabilities of intraoperative hemodynamics have only been investigated sparingly.[77]

No effect of perioperative music on length of stay was demonstrated. However, only 4 studies assessed total length of stay and organizational rather than patient factors are the most important predictors of delayed discharge.[78] Moreover, almost half of the studies (44%) that assessed length of stay did so in patients undergoing minor surgery in the outpatient setting, making it unlikely to find a clinically relevant difference. Even though opioids are relatively cheap, opioids accounted for 1% of total hospital costs in an observational study of patients undergoing joint replacement surgery.[79] As one of the most commonly performed procedures in the developed world, yearly costs in the United States alone amount to more than $20 billion.[80] It is therefore likely that the beneficial effects of perioperative music on mediation requirement will also be observed financially, especially when taking into account the costs that come with opioid-related adverse effects.[10]

This meta-analysis has several strong points. A comprehensive literature search was performed with a dedicated biomedical information specialist. A predefined definition of music was used and studies with live music, a music therapist and concomitant interventions were excluded. In comparison to earlier performed meta-analyses investigating the effects of perioperative music, our focus was solely on medication requirement and length of stay in adult surgical patients. Vetter et al did observe a significant reduction in pain medication requirement by perioperative music in fourteen studies, but this was not significant for the subgroup of patients who received general anesthesia in 9 studies.[15] The meta-analysis by Hole et al contained studies with both surgical and nonsurgical, diagnostic procedures leading to clinical heterogeneity, and did not differentiate between opioid, benzodiazepines, and sedative medication requirement.[14] Nevertheless, this meta-analysis has limitations as well. The included studies contained different surgical patients, surgical procedures, and follow-up duration of the outcome assessment. This was reflected in the moderate to high level of heterogeneity observed. Medication requirement can be influenced by factors such as age, body weight, and the duration of surgery. Some of these baseline characteristics were not reported in the included studies, potentially increasing the risk of bias in interpreting results. Therefore, it is not entirely clear whether perioperative music can have the same beneficial effect size on medication requirement for all surgical procedures. Measurement duration of postoperative opioid requirement in 15 of the 20 studies was 24 hours after surgery or less. Consequently, the mean absolute reduction in mg ME in the music group was relatively low and perhaps does not reflect the full beneficial effect of perioperative music on medication requirement. Although a meta-regression analysis could be performed with covariates such as music intervention duration, music exposure moment relative to the surgical procedure (ie, preoperatively, intraoperatively, postoperatively, or multiple moments), operative severity (ie, minor, moderate, or major surgery), and measurement duration, this was not deemed appropriate as at least ten studies for each co-variate are recommended.[18] Only postoperative opioids were assessed, as other analgesic medications were often not reported. Some included studies did report that perioperative music also reduced nonopioid analgesic requirement postoperatively.[24,49]

Our literature search did not include patient-reported outcome measures. However, it should be noted that patients in the included studies were extremely positive towards the use of perioperative music. Almost all patients (88% or higher) found perioperative music to be an enjoyable experience.[23,35,55,56,81–83] Likewise, a majority would opt for music again in the future,[21,25,28] even pro-actively asking for music in subsequent surgical procedures.[21] Patient satisfaction was also markedly increased in the music group,[48–51,56] with the only negative comments observed being from those who did not get music or related to the type of available music.[25,84] Although side-effects of perioperative music could theoretically occur, none of the included studies reported any adverse effects. Specifically, no cardiorespiratory depressions were observed,[34,51] while McCaffrey et al reported that perioperative music had a significant beneficial effect on delirium and confusion.[56,85] In some studies, care was taken to restrict music volume and adhere to the noise and hearing loss guidelines to prevent hearing damage,[86] whereas others allowed patients the option to adjust the music volume to their liking. The most well-known implemented nonpharmacological, multimodal interventions in surgical patient care are part of the guidelines collectively known as the Enhanced Recovery After Surgery protocols, which focus on reducing the physiological stress response to surgery by optimizing nutritional state, reducing opioid use and early mobilization.[87] Originally introduced in colorectal surgical patient care, it has subsequently been implemented in a wide range of different surgical specialties with surgery-specific variations. Likewise, the use of perioperative music should be adapted to fit into the operative procedure, individual clinical setting, and wishes and requirements of the medical team. Although it is difficult to draw a firm clinical recommendation based on the data in our meta-analysis, 75% of studies assessing opioid requirement exposed patients to a total of 120 minutes perioperative music on average or less, delivered either before, during and/or on the first 2 days after surgery. Therefore, it seems that a relatively short exposure to music can already be beneficial, with a majority of the studies using a music player and headphones to avoid disrupting communication of the medical staff. Further research could focus on the effect of

perioperative music on postoperative complications, clinical recovery, costs, and implementation.

CONCLUSIONS

Perioperative music can reduce postoperative opioid and intraoperative sedative medication requirement. Therefore, perioperative music may potentially improve patient outcome and reduce medical costs, as a higher opioid dosage is associated with an increased risk of adverse events and chronic opioid use. The use of perioperative music seems to be safe and patient-friendly, given the high patients satisfaction reported whilst no adverse effects were observed.

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