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Effect of music on patients with cardiovascular diseases and during cardiovascular interventions

A systematic review

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Summary

Background The therapeutic effects of music have been known for thousands of years. Recently, studies with music interventions in patients with cardiovascular diseases yielded controversial results. The aim of this review is to provide an overview of the effects of receptive music intervention on the cardiovascular system.

Methods We searched in PubMed, SCOPUS and CENTRAL for publications between January 1980 and May 2018. Primary endpoints were heart rate, heart rate variability and blood pressure. Secondary endpoints comprised respiratory rate, anxiety and pain. The quality of the studies was assessed by using the CONSORT statement and the Cochrane risk of bias assessment tool. A meta-analysis and subgroup analyses concerning music style, gender and region were planned.

Results A total of 29 studies comprising 2579 patients were included and 18 studies with 1758 patients investigated the effect of music on patients undergoing coronary angiography or open heart surgery. Other studies applied music to children with congenital

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C.-Y. Ho Liechtensteinstr. 8/12, 1090 Vienna, Austria heart diseases, pregnant women with hypertension or patients with unstable angina. Due to high methodological study heterogeneity, a meta-analysis was not performed. The study quality was assessed as medium to low. In ten studies with higher quality comprising 1054 patients, music intervention was not associated with significant changes in the cardiovascular endpoints compared to the control group. The subgroup analyses did not demonstrate any relevant results.

Conclusion Currently no definite effect of receptive music intervention on the cardiovascular system can be verified. Further research is needed to assess music as an inexpensive and easy applicable form of therapy.

Keywords Receptive music intervention \cdot Blood pressure \cdot Heart rate \cdot Coronary angiography \cdot Cardiac surgery

Introduction

The therapeutic effects of music have been known for thousands of years [1]; however, it remains unclear how music affects the human body. Most hypotheses assume that music, in addition to its conscious perception, influences the autonomic and central nervous system at subcortical levels and that the limbic system plays a crucial role in the processing of musical elements [2]. The influences on the limbic system also explain the strong effect on mood which may result in changes of cardiovascular parameters mediated by the autonomic nervous system.

The majority of previous studies focused on the anxiolytic and stress-reducing effects of music rather than on the direct impact on cardiovascular outcomes [3], although it is well acknowledged that a close connection exists between the psychological processes and functional parameters, such as blood pressure,

heart rate and heart rate variability. Therefore, the application of music as an adjuvant therapy for various diseases has been expanded over the past few years [4]. The aim of this review is to specifically focus on the effect of music in patients with cardiovascular diseases and during cardiovascular interventions.

Methods

Two reviewers (CH and CS) independently searched three electronic databases (PubMed, SCOPUS, CENTRAL) between June 2018 and February 2019 for the following predefined terms: "influence of music", "music, cardiovascular system", "music, heart", "music, cardiac", "music, hypertension", "music, heart rate", "music, newborns", "arrhythmia, music", "music, catheterization", "music, coronary angiography", "music, myocardial infarction", "music, cardiac surgery", "music, sudden death", "music, coronary artery disease", "music, catheter ablation", "music, coronary intervention", "music, pacemaker", "music, defibrillator", "music, congenital heart disease". A screening of the titles and abstracts of the publications between 1 January 1980 and 31 May 2018 was performed according to predefined inclusion and exclusion criteria (Table 1). Studies with one or more exclusion criteria and those that did not meet all inclusion criteria were excluded. To identify further publications, bibliographic lists of relevant studies or reviews were searched.

The primary outcomes were heart rate, heart rate variability and blood pressure. The secondary outcomes included respiratory rate, oxygen saturation, skin temperature, hormone levels, and psychological parameters (anxiety, stress, depression, pain, quality of life).

The following data were extracted: general information (title and author of the study, year and country of publication), information on study design, type of

| Table 1 | Inclusion | and | exclusion | criteria |
|---------|-----------|-----|-----------|----------|
| | | | | |

| Inclusion criteria | Exclusion criteria |
|--|--|
| The study investigates the effect of music | The study only |
| on the cardiovascular system by measuring | investigates the |
| the changes in at least one cardiovascular | influence of music |
| parameter (e.g. heart rate, blood pressure) | on psychological |
| or symptoms of cardiovascular diseases (e.g. | parameters (e.g. |
| angina). | anxiety, depres- |
| The study explores the influence of music | sion). |
| during cardiovascular interventions/cardiac | – The study includes |
| surgery or the effect of music on patients with | active music play- |
| cardiovascular diseases. | ing. |
| Patients undergoing receptive music therapy/ | The study explores |
| intervention, defined as listening to music for | the effects of music |
| therapeutic purposes. | on doctors, nurses |
| The patients are not exposed to any further | and other health- |
| stress test. | care workers. |
| Randomized controlled trial design. The study was published between 1 lanuary | Studies with ani- mala |
| 1980 and 31 May 2018. The article is written | Nonrandomized or |
| in German or English. | retrospective trial |

design.

randomization, music intervention, duration of music exposure, music genre, control intervention, setting, participants (number of patients, gender, age, ethnicity) and the outcome parameters.

The consolidated standards of reporting trials (CONSORT) checklist was used to assess the quality of randomized controlled trials [5]. The risk of bias (RoB), which is classified into selection, attrition, detection, performance and reporting bias, was assessed as low risk, high risk, or unclear risk by using the Cochrane risk of bias assessment tool [6].

Discrepancies concerning the results of the search as well as the quality assessment were carefully documented.

Statistical analyses were performed and graphics were generated by using the software Review Manager 5.3 of the Cochrane Collaboration [7]. Additional subgroup analyses were carried out by gender, age, cardiovascular diseases/interventions or cardiac surgery, time of the music intervention, music selection, setting, region, study duration and type of music.

This review was completed as part of a diploma thesis. The institutional review board of the community of Vienna considered no necessity of an approval for the present study.

Results

Results of the search

The search of the electronic databases PubMed, SCOPUS and CENTRAL delivered a total of 20,910 results. After the exclusion of double entries (n=16,688), 38 potentially relevant publications were identified from the remaining 4222 papers (Fig. 1). Searching the reference lists of the included studies did not reveal any additional studies. Attempts were made to access the full text of nine of these 38 publications that were not readily available and five authors immediately replied providing the full text. The remaining four studies were excluded as no full text was available. Five further publications were excluded as indicated in Fig. 1. There were no discrepancies between both reviewers with respect to the screening and inclusion of the studies.

Included studies

A total of 29 studies were selected for inclusion in this review, reporting a total of 2579 patients (Table 2; [8–36]). The sample size varied between 30 and 240 patients and the duration of each music intervention between 15 min and 1h. The majority of studies (n=20) examined the influence of music within a single intervention. Kunikullaya et al. [24] conducted a study for three months, representing the study with the longest duration and eight other publications applied more than one single music intervention [12, 13, 16, 19, 31, 32, 34, 35].

review article



Fig. 1 Flow Diagram of Literature Search and Selection Process

A total of 18 studies were found, comprising 1758 patients undergoing elective coronary angiography, coronary artery bypass grafting (CABG) and/or aortic valve replacement (AVR) [9–12, 14, 15, 17, 18, 20, 21, 23, 26–29, 31, 33]. Music was applied to pregnant women in three [16, 32, 35] and to children with congenital heart diseases in two further studies [8, 22]. Three further studies investigated the changes in physiological parameters in (pre)hypertensive patients [13, 24, 34], two studied the effect of receptive music intervention in patients with unstable angina [19] or acute myocardial infarction [36]. In one study, music had been applied during coronary computed tomography (Table 2; [25]).

A great variety of music styles was used in the studies, including Turkish [13, 35], Indian [24], classical [19, 22, 34, 36] and relaxing music [10, 18, 21, 26–28, 30, 32] as well as nature-based sounds [9, 23, 29]. In 11 studies, the music applied was not transparent [8, 11, 12, 14–17, 20, 25, 31, 33]. Overall, only ten studies provided a clear description of the musical structures such as rhythm, tempo and melody [18, 21–23, 26–28, 31, 34, 36].

Quality assessment

The included studies fulfilled between 24% and 69% of the criteria of the CONSORT statement (Table 2). None of the studies could achieve more than 75% of the CONSORT aspects. For ten studies, the percentage of fulfilled CONSORT aspects was below 50%.

Overall, 21 discrepancies with respect to the assessment based on the CONSORT statement (mostly regarding the aspects abstract, eligibility criteria and discussion) were resolved through discussion between the two reviewers.

Concerning the RoB, only two studies with a low RoB were identified (Figs. 2 and 3; [8, 9]). The highest RoB was found in the study by White [36]. Performance bias and detection bias of subjective outcomes (anxiety, pain) were found to be particularly high. In contrast, attrition and detection bias of objective outcomes (heart rate, blood pressure, heart rate variability) were assessed as low risk in most cases. Overall, a predominance of studies with high or unclear RoB was found.

A statistical analysis and graphical depiction of publication bias could not be performed due to miss-

| Table 2 | Overview of 1 | the included | studies, CONS | SORT assess | ment | | | |
|----------|----------------------------|---------------------------|--|--------------------|---|--|---|------------------------------|
| No | Study | Number of participants | Type of inter- vention/disease | Age (years) | Duration of the music intervention | Type of music | Results | CONSORT assessment (%) |
| <u>©</u> | Abd-Elshafy et al. 2015 | 20 | Congenital heart disease | 7.3 | Intraoperative and postoperative (until extubation) | Songs preferred by the child | Nonsignificant: HR, MAP, SpO ₂ , ST Significantly lower blood cortisol levels intraoperative and postopera- tive in the music group vs. control Significantly lower blood glucose levels intraoperative and postopera- tive in the music group vs. control Significantly lower pain and need for analgesics in the music group vs. control | 37 |
| 6 | Aghaie et al. 2014 | 120 | CABG | 57.3 | During the wean- ing off mechanical ventilation | Nature-based sounds | Significantly lower anxiety and agitation levels in the music group vs. control Nonsignificant: BP, RR, HR, SpO2, MAP | 64 |
| [10] | Argstatter et al. 2006 | 06 | Elective coro- nary angiogra- phy | 66.5 | Periprocedural | "Relaxation" by M. Rummel | Nonsignificant: HR, SBP, DBP Significantly greater reduction of STAI-S scores in the music group vs. control | 48 |
| Ξ | Bally et al. 2003 | 113 | Elective coro- nary angiogra- phy | No data | About 45 min | Softer, more relaxing music | Nonsignificant: HR, BP, STAI, VAS | 67 |
| [12] | Barnason et al. 1995 | 96 | CABG | 67 | 30 min × 2 ses- sions | "Country Western Instrumental, Fresh Aire" by M. Steamroller, "Winter into Spring" by G. Win- ston, "Prelude" and "Comfort Zone" by S. Halpern | Nonsignificant: anxiety, mood, HR, SBP, DBP | 43 |
| [13] | Bekiroğlu et al. 2013 | 60 | Elderly patients with hyperten- sion | No data (70–79) | 25 min × 28 days | Turkish classical music | Nonsignificant: HAM-A, SBP, DBP | 46 |
| [14] | Buffum et al. 2003 | 170 | Vascular an- giography | 6.8 | 15 min | Classical music, jazz, rock, coun- try western, easy listening | Nonsignificant: RR, SBP, DBP Significant reduction of anxiety in the music group vs. control Significant reduction of HR in the music group vs. control | 52 |
| [15] | Cadigan et al. 2001 | 140 | Elective coro- nary angiogra- phy | 62.2 | 30 min | Symphonic music, nature-based sound | Nonsignificant: HR, VAS, ST Significant reductions of BP and RR in the music group vs. control | 45 |
| [16] | Cao et al. 2015 | 60 | Pregnant women with PIH | 29.6 | 30–60 min. × 2 times per day × 4 weeks | Folk music, symphonies by L. v. Beethoven, F. Schubert, P. I. Tchaikovsky | Significant reduction of BP in both groups Significant reductions of HAM-A und HAM-D scores in the music group vs. control Significantly higher Ool in the music group vs. control | 31 |

| Table 2 | (Continued) | | | | | | | |
|---------|----------------------------|---------------------------|---|---------------------------------|---|--|---|------------------------------|
| No | Study | Number of participants | Type of inter- vention/disease | Age (years) | Duration of the music intervention | Type of music | Results | CONSORT assessment (%) |
| [17] | Chan 2007 | 20 | Elective coro- nary angiogra- phy | No data | About 45 min | Soft, slow music | Nonsignificant: DBP Significant reductions of SBP, HR, RR, SpO ₂ in the music group vs. control Significant reduction of pain in the music group vs. control | 20 |
| [18] | Chang et al. 2011 | 54 | Elective coro- nary angiogra- phy | 61.9 | 30 min | Soft melodies, played on piano, harp orchestral music, jazz, Chinese orchestra, synthesizer | Nonsignificant: HR, ST, HRV Significant reduction of anxiety in the music group vs. control | 55 |
| [19] | Elliott et al. 1994 | 56 | Unstable angina or acute MCI | 9.09 | 30 min × 2–3 ses- sions | Nonlyrical light classical music | Nonsignificant: HR, SBP, DBP, STAI, HADS, LAAS | 36 |
| [20] | Forooghy et al. 2015 | 64 | Elective coro- nary angiogra- phy | 58.4 | 20-40 min | Light instrumental music, compo- sitions by J.S. Bach, M. Makino | Nonsignificant: SBP, DBP, HR, SaO ₂ , RR Significant reduction of anxiety in the music group vs. control | 69 |
| [21] | Hamel 2001 | 101 | Elective coro- nary angiogra- phy | No data | 20 min | "Trance-Zendance" by S. Halpern | Nonsignificant: HR, DBP Significant reduction of SBP in the music group vs. control Significant reduction of anxiety in the music group vs. control | 35 |
| [22] | Hatem et al. 2006 | 84 | Congenital heart disease | No data (1 day– 16 years) | 30 min | "The Four Seasons (Spring)" by A. Vivaldi | Nonsignificant: ST, SaO ₂ , MAP, SBP, DBP Significant reduction of anxiety in the music group vs. control Significant reductions of HR and RR in the music group vs. control | 52 |
| [23] | Heidari et al. 2015 | 60 | CABG | 58.6 | 30 min | Nature-based sounds | Nonsignificant: HR, SBP, DBP, MAP Significant reduction of anxiety in the music group vs. control | 69 |
| [24] | Kunikullaya et al. 2015 | 100 | (Pre)hyper- tension | 46.7 | At least 15 min × 5 days per week × 3 months | Indian raga bhimpalas | Nonsignificant: HPV between group 1 (music + lifestyle) and group 2 (lifestyle modification) Significant reduction of anxiety in both groups Significant reduction of SBP in group 2 vs. group 1 Significant reduction of DBP in both groups Significantly increased parasympathetic and lower sympathetic pa- rameters (HRV) in groups 1 and 2 males and females of group 2 | 89 |
| [25] | Ng et al. 2016 | 197 | CCTA, PVCT, CCS | 56 | Preprocedural/ periprocedural | Relaxing music (Classical music, new age, jazz) | Nonsignificant: HR, STA | 60 |

| Mesno 2006Cudes and c61.5On muSuft relating musci, low ApieReprintent: H, Pado, Sado, MW, FR, anothy constrained and the manusci intervention, monoprillerat after arobits.Monoclasme | ole 2 | (Continued) Study | Number of participants | Type of inter- vention/disease | Age (years) | Duration of the music intervention | Type of music | Results | CONSORT |
|---|-------|------------------------------|---------------------------|---|----------------|--|---|---|-----------|
| IndextIndex | | Nilsson 2009 | 60 | CABG and/or AVR | 66.5 | 30 min | Soft, relaxing music, New Age | Nonsignificant: HR, PaO ₂ , SaO ₂ , MAP, RR, anxiety Significantly lower blood cortisol levels in the music group vs. control | (%) 62 |
| manutos or or manutos or | | Mileson 2000 | UV | CARG and/or | ה ה ה | 30 min | MusiPura® Cafion Bacords (coff | 30 min after the music intervention, nonsignificant after another 30 min Nonsionificant: UB_MAD_SaC | ž |
| Nisson et al.240Electrice corce payrangoga payrangoga by payrangogaNonsjonterant: STA, NRS (angla)66Bejer et al.130Electrice corce payrangoga phy61.720ninNature-besed sounds softificant reductions of analytin the music groups control softificant reductions of same phy66Bejer et al.130Electrice corce phy61.720ninNature-besed sounds softificant reductions of same phy61Bejer et al.100Electrice corce phy61.320ninx 2 three some control80Nature-besed sounds some control80Bejer et al.100Electrice corce phy61.320Nature-besed sounds some control8080StatisElectrice corce phy61.320Nature-besed sounds some control808080StatisElectrice corce phy61.320Nature-besed sounds some control808080StatisElectrice corce61.320Nature-besed sounds808080StatisElectrice corce81.32020808080StatisElectrice corce81.32010081.480StatisElectrice corce81.481.4Nature-Statis8080StatisElectrice corce81.481.480808080StatisElectrice corce81.481.480808080StatisElectrice corce <t< td=""><td></td><td></td><td>5</td><td>AVR</td><td>00.0</td><td></td><td>musicul e°, aeriori recorus (suri, relaxing music)</td><td>Nouseprimetant: mr, MMP, Sade Significantly higher PaO2 in the music group vs. control Changes of oxytocin (increase in the music group, decrease in the control group) statistically significant between the groups, but not over time in subjects of each group</td><td>0</td></t<> | | | 5 | AVR | 00.0 | | musicul e°, aeriori recorus (suri, relaxing music) | Nouseprimetant: mr, MMP, Sade Significantly higher PaO2 in the music group vs. control Changes of oxytocin (increase in the music group, decrease in the control group) statistically significant between the groups, but not over time in subjects of each group | 0 |
| Bejeh et al. 2016130Bechre oorto paragroups617OminNature based sounds significant reduction of anxiety. In the music group s. control sounding s. control67Mip/ et al. 201410Elective corp phy62±8Peproedural pertoreduralMusicuree, Gefion Records soft, anti- music group s. control sounding s. control67Mip/ et al. 20150Elective corp phy62±8Peproedural pertoreduralMusicuree, Gefion Records soft, hort music group s. control of sominant increase of Soft, in the music group s. control soluticant journes and soluticant increase of Soluticant journes and soluticant increase of Soluticant journes and soluticant journes and soluticant increase and soluticant increase and soluticant increase and soluticant increase and soluticant soluticant increase and soluticant journes and soluticant increase and soluticant increase and soluticant soluticant and soluticant increase and soluticant increase and soluticant | | Nilsson et al. 2009 | 240 | Elective coro- nary angiogra- phy | No data | About 45 min | MusiCure®, Gefion Records (soft, relaxing music) | Nonsignificant: STAI, NRS (angina) | 66 |
| Ripleyet al.70Elective coro- pay anglogra- pay anglogra- pay anglogra- pay anglogra- bay anglogra- bay anglogra- bay anglogra- bay anglogra- bay anglogra- | | Rejeh et al. 2016 | 130 | Elective coro- nary angiogra- phy | 61.7 | 20 min | Nature-based sounds | Significant reduction of anxiety in the music group vs. control Significant reductions of SBP, DBP, MAP, HR, RR in the music group vs. control Significant increase of Sp02 in the music group vs. control | 67 |
| Sendelbach60CABG and/or63.3±13.520min × 2 timesEasy listening, classical music, ser day × 3 daysNonsignificant H, SPP, DPP, opioid usage45Sundar et al. 20030Prehyper- tension0 data15 min × 3 ses- sionsBelaxing instrumental music, slonin x played on plano, guitar, futueNonsignificant H, SPP, DPP, API in the music group ws. control32Taylor-Piliae54Prehyper- tension58.2 ± 9.615-20 min talm x sloped on plano, guitar, futueNonsignificant reductions of SPP, PIP in the music group ws. control32Taylor-Piliae54Electwe coro- phy58.2 ± 9.615-20 min talm x slopedChinese and Western instrumen- talm x slopedNonsignificant reductions of SPP, PIP in the music group ws. control32Taylor-Piliae5415-20 min phyBelaxing instrumental music, talm x slopedNonsignificant R-M, SAI61Taylor-Piliae30Hypertension81.4 ± 815-20 min talm x slopedNonsignificant R-M, SAI61Taylor Piliae30Hypertension81.4 ± 8Bech, "Andante" by.J.Nonsignificant R-M, R-M, R-M, R-M, R-M32Tange et al.30Hypertension81.4 ± 8Bach, "Andante" by.J.Nonsignificant R-Buchon of SPP in the music group ws. control24Toker et al.8Boch, "Andante" by.J.Nonsignificant reduction of SPP in the music group ws. control24Under et al.8Boch, "Andante" by.J.Nonsignificant reduction of SPP in the music group ws. control24Under et al. | | Ripley et al. 2014 | 70 | Elective coro- nary angiogra- phy | 62±8 | Preprocedural/ periprocedural | MusiCure®, Gefion Records (soft, relaxing music) | Nonsignificant: SBP, DBP, HR, STAI, RHI | 55 |
| Sundar etal.60Prehyper- tensionNo data15 min × 3 ses.Relaxing instrumental music, played on piano, guitar, fluteSignificant reductions of SP, DB', Hi in the music group ws. control32Taylor-Pillae54Elective coro- puy80.2 ± 9.615 - 20 minChinese and Western instrumen.Nonsignificant reductions of SP, DB', Hi in the music group ws. control32Taylor-Pillae54Elective coro- puy80.2 ± 9.615 - 20 minChinese and Western instrumen.Nonsignificant RB, HR, SAI61Teng et al. 200290Hypertension81.4 ± 825 min per"Arin G" by J. S. Bach. "CanonNonsignificant RB, HR, SAI61Teng et al. 200710Hypertension81.4 ± 825 min per"Arin G" by J. S. Bach. "Andante" by J.2024Teng et al. 2007810Nonsignificant reduction of SBP in the music group ws. control24Teng et al.84Wentershole"Nonsignificant reduction of SBP in the music group ws. control24Toker et al.84PreclampisNonsignificant reduction of SBP in the music group ws. control24Under teal.84Nonsignificant reduction of SBP in the music group ws. control59Vint 199240Acute MCI55.7 ± 7.5ZminClassical musicNint 199240Acute MCI55.7 ± 7.5ZminSignificant reductions of HR and RP in the music group ws. control27 | | Sendelbach et al. 2003 | 86 | CABG and/or AVR | 63.3±13.5 | $20 \text{ min} \times 2 \text{ times}$ per day $\times 3 \text{ days}$ | Easy listening, classical music, jazz | Nonsignificant: HR, SBP, DBP, opioid usage Significantly lower STAI score und pain in the music group vs. control | 45 |
| Taylor-Piliae64Elective coro- phy58.2±9.615–20 min tal musicChinese and Westerm instrumen- tal musicNonsignificant: Rh, H, SAI61Teng et al. 200230Hypertension81.4±825 min per day × 4 weeks"Air in G" by J. S. Bach, "Canon Sinfificant reduction of SPP in the music group vs. control Sinfificant reduction of SPP in the music group vs. control24Teng et al.30Hypertension81.4±825 min per day × 4 weeks"Air in G" by J. S. Bach, "Andante" by J. S. Bach, "Andante" by J. P. I. TchaikveskyNonsignificant: DBP Sinfificant reduction of SPP in the music group vs. control Sinfificant reduction of SPP in the music group vs. control24Unite 199240Acute MCI55.7 ± 7.525 minClassical musicSinfificant reduction of SPP in the music group vs. control59White 199240Acute MCI55.7 ± 7.525 minClassical musicSinfificant reduction of anviety in both groups27 | | Sundar et al. 2015 | 60 | Prehyper- tension | No data | 15 min × 3 ses- sions | Relaxing instrumental music, played on piano, guitar, flute | Significant reductions of SBP, DBP, HR in the music group vs. control | 32 |
| Tengetal. 30 Hypertension 81.4±8 Z5min per day × 4 weeks "Air in G" by J. S. Bach, "Canon Nonsignificant: DBP 24 2007 2007 81.4±8 1n0" by Pachelbel, "Flute con- certo in A minor, Andante" by J. Significant reduction of SBP in the music group vs. control 24 2007 1 84 4 weeks in D" by Pachelbel, "Flute con- certo in A minor, Andante" by J. Significant reduction of SBP in the music group vs. control 24 1 Toker et al. 84 Pie celampsia 30.6±5.8 30 min × 7 days Turkish classical music Nonsignificant: reduction of SBP in the music group vs. control 59 2017 84 Note MCI 55.7±7.5 25 min Classical music Significant reduction of Bn in the music group vs. control 59 White 1992 40 Acute MCI 55.7±7.5 25 min Classical music Significant reduction of An idth groups 27 | | Taylor-Piliae et al. 2002 | 54 | Elective coro- nary angiogra- phy | 58.2±9.6 | 15–20 min | Chinese and Western instrumen- tal music | Nonsignificant: RR, HR, SAI | 61 |
| Toker et al.84Preeclampsia 30.6 ± 5.8 $30 \text{ min} \times 7 \text{ days}$ Turkish classical musicNonsignificant: STAI, RR, HR, Hetal HR5920172017Significant reduction of BP in the music group vs. controlSignificant reduction of BP in the music group vs. control59White 199240Acute MCI 55.7 ± 7.5 25 minClassical musicSignificant reduction of anxiety in both groups27White 199240Acute MCI 55.7 ± 7.5 25 minClassical musicSignificant reduction of anxiety in both groups27 | | Teng et al. 2007 | 30 | Hypertension | 81.4±8 | 25 min per day×4 weeks | "Air in G" by J. S. Bach, "Canon in D" by Pachelbel, "Flute con- certo in A minor, Andante" by J. S. Bach, "Andante cantabile" by P. I. Tchaikovsky | Nonsignificant: DBP Significant reduction of SBP in the music group vs. control | 24 |
| White 1992 40 Acute MCI 55.7 ± 7.5 25 min Classical music Significant reduction of anxiety in both groups 27 Nhite 1992 40 Acute MCI 55.7 ± 7.5 25 min Classical music Significant reduction of Anxiety in both groups 27 | | Toker et al. 2017 | 84 | Preeclampsia | 30.6 ± 5.8 | 30 min×7 days | Turkish classical music | Nonsignificant: STAI, RR, HR, fetal HR Significant reduction of BP in the music group vs. control | 59 |
| | | White 1992 | 40 | Acute MCI | 55.7±7.5 | 25 min | Classical music | Significant reduction of anxiety in both groups Significant reductions of HR and RR in the music group vs. control | 27 |

Fig. 2 Risk of bias graph: authors' judgements about each risk of bias item, presented as percentages across all included studies; low risk green, high risk red, unclear risk yellow



ing data (e.g. missing mean values and standard deviations of the reported outcomes) and extensive methodological heterogeneity among the studies (e.g. different patient groups and the great variety of music selected in the experiments).

Study results and meta-analysis

Overall, 11 studies of higher quality, defined as publications that achieved more than 50% of the aspects in the CONSORT statement and were assessed with a high RoB in three or less categories, were identified [9, 11, 18, 23–28, 30, 35]. Only one of these 11 studies reported a significant reduction of blood pressure in the music group compared to the control arm [35]. In the remaining ten studies of higher quality comprising 1054 patients, music intervention was not associated with significant changes in the cardiovascular endpoints compared to the control group (Table 2; [9, 11, 18, 23–28, 30]). In three of these ten studies, though, heart rate and blood pressure demonstrated a decreasing trend in the music group [18, 23, 27]. Interestingly, Kunikullaya et al. observed significant reductions of diastolic blood pressure only in both the interventional and control group as well as an increasing trend in parasympathetic parameters of heart rate variability, although not statistically significant [24]. Regarding the psychological outcomes, significantly greater anxiolytic effects in the music group compared to the control arm were found in three studies [9, 18, 23]. Kunikullaya et al. reported a reduction of anxiety in both the intervention and control group, indicating that both lifestyle modification and music intervention have anxiety relieving effects in patients with hypertension [24]. Furthermore, although psychological outcomes were not statistically significant in six studies [11, 25, 26, 28, 30, 35], two studies reported that the music intervention had a calming effect on and was highly appreciated by the patients during the procedure [11, 25].

However, due to the high methodological heterogeneity mentioned above, it was difficult to compare the study results in general. A statistical meta-analysis was, therefore, considered as inappropriate and was not performed.

Results of subgroup analyses

The studies were classified into subgroups by gender, age, cardiovascular diseases/interventions or cardiac surgical procedures, time of the music intervention, selection of music, setting, region, study duration and type of music. For each of these subgroup analyses, only the findings of those 11 studies with higher quality were summarized [9, 11, 18, 23–28, 30, 35].

The detailed results of the subgroup analyses are presented in Table 3. Due to the small number of studies of comparatively higher quality in each subgroup, no relevant information could be derived to answer the questions regarding choice of music, time of music intervention, patient group and gender-specific differences.

Discussion

According to the CONSORT statement and the risk of bias assessment, the overall quality of the studies was perceived as medium to low. An analysis of the studies with higher quality, defined as publications that fulfilled more than 50% of the aspects in the CONSORT statement and were assessed with a high RoB in three or less categories, revealed that most of the publications could not demonstrate any statistically significant changes in the physiological and psychological parameters. Some studies, however, showed a decreasing trend in heart rate or blood pressure in the music group [18, 23, 27], or reported that the music was positively accepted by the patients in the intervention group [11, 25] indicating that there still might be an effect which was not significant due to low statistical power; however, the great methodological variety and the small number of included studies led to difficulties in comparing the study results in general. In order to verify the significant findings of individual experiments, such as the anxiolytic or blood pressurereducing effects of music [18, 23, 35], further studies of high quality are needed.

Besides low statistical power, the study duration could be another important aspect that accounts for the predominantly insignificant results. Whether the length and number of music interventions have an

impact on the cardiovascular system remained unanswered as only nine of the included 29 studies with more than one single music intervention or a music exposure longer than 1h were found [12, 13, 16, 19, 24, 31, 32, 34, 35]. It is possible that the effect of music arises only after a certain period of time. The longterm effect should thus be examined in more detail when exploring the influence of music on chronic cardiovascular diseases; however, a single application of music as a therapeutic agent may be sufficient when the focus is on the (acute) effect in the context of cardiovascular examinations and/or interventions.

Another aspect that needs to be discussed is the way music is applied. The patients listened to music via headphones [8-13, 15-25, 29, 31, 33-36], speakers [14, 28] or music pillows [26, 27, 30] in the included studies. The advantage of headphones is that the participants are not distracted by the noise from medical devices. On the other hand, the question arises whether prerecorded music has a different impact than live music. Thus, it would be interesting to measure the changes in cardiovascular parameters in patients who listen to music which is performed live using an instrument. The implementation of such a music intervention during cardiovascular procedures could pose a challenge, though. To our knowledge, this has not been investigated in previous studies.

Furthermore, it is crucial to consider the type of music. The music applied in the studies included Turkish [13, 35], Indian [24], classical [19, 22, 34, 36] and relaxing music [10, 18, 21, 26-28, 30, 32] as well as nature-based sounds [9, 23, 29]. A clear description of the musical structures was only found in ten studies [18, 21-23, 26-28, 31, 34, 36]. Different cultural backgrounds, early experiences and generational influences by which personal preferences for a certain type of music is shaped must be taken into consideration. Listening to one's favorite music can trigger different changes in the human body in comparison to unfamiliar melodies that could implicate a lower patient adherence, reducing the possible therapeutic effects of music. For instance, in two of the included studies it was reported that patients withdrew from the intervention for dislike of the preselected music [17, 21]. On the other hand, Chang et al. found that a higher music preference was associated with lower posttest anxiety [18]. Preexisting moods and different personalities pose further challenges to the selection of the appropriate music. In addition, a general distinction must also be made between ergotropic and trophotropic types of music. It can be reasonably assumed that relaxing music has a calming effect during cardiac catheterization (directly or indirectly through anxiolytic processes) and therefore leads to reductions of blood pressure and/or heart rate. On the other hand, encouraging rhythms could facilitate faster mobilization e.g. after myocardial infarction [37]; however, since none of the studies to our knowledge has



Fig. 3 Risk of bias summary: authors' judgements about risk of bias item for each included study; *green encircled* +: low risk; *red encircled* -: high risk; *yellow encircled* ?: unclear risk

| 1 | Gender: female vs. male | Two studies investigated gender-specific differences of music intervention. Nilsson et al. did not show any significant results nor gender-specific differences in the music group vs. control [28]. Kunikullaya et al. [24] demonstrated significantly increased parasympathetic and lower sympathetic parameters (heart rate variability) in males of group 1 (music intervention + lifestyle modification) and group 2 (lifestyle modification only) and females of group 2. |
|-----------------|---|--|
| 1 | Age: newborns/ children vs. adults | The only two studies in newborns/children did not fulfill the defined criteria for studies of comparatively higher quality [8, 22]. Eleven studies in adults were assessed with higher quality (compared to the other included studies) [9, 11, 18, 23–28, 30, 35]. Ten of them comprising 1054 patients did not show any significant changes in cardiovascular outcomes in the music group compared to the con- trol group [9, 11, 18, 23–28, 30]. A significant reduction of blood pressure in the experimental group vs. control was only demonstrated in one study [35]. Kunikullaya et al. reported significant reductions of blood pressure in both group 1 (music intervention + lifestyle modifica- tion) and group 2 (lifestyle modification only) [24]. A significant reduction of anxiety in the music group vs. control was reported in three studies [9, 18, 23]. Kunikullaya et al. observed a significant reduction of anxiety in both the intervention and control group [24]. |
| | Cardiovascular diseases vs. cardiovascular interventions vs. cardiac surgical procedures | Cardiovascular diseases: only two studies of higher quality [24, 35] than the remaining four studies [13, 16, 32, 34] on patients suffering from hypertension were included. While Toker et al. found significant reductions of blood pressure in the music group vs. control [35], Kunikullaya et al. reported significant reductions of blood pressure in both the intervention and control group [24]. Additionally, an anxiolytic effect was reported in both the experimental group and the control arm in the study by Kunikullaya et al. [24]. The only two studies in patients with myocardial infarction [36] or unstable angina [19] did not fulfill the defined criteria for studies of comparatively higher quality. Cardiovascular interventions: the four studies of higher quality [11, 18, 28, 30] than the remaining eight studies [10, 14, 15, 17, 20, 21, 29, 33] on patients undergoing coronary angiography did not demonstrate any significant changes in cardiovascular outcomes in the music group vs. control. Only Chang et al. observed an anxiolytic effect in the music group vs. control [18]. Cardiac surgical procedures: Four studies of higher quality [9, 23, 26, 27] than the remaining four studies [8, 12, 22, 31] on patients undergoing cardiac surgical procedures were identified. The findings concerning cardiovascular outcomes were not significant. In two studies, a significant reduction of anxiety in the music group vs. control [9, 23]. |
| - | Time of the music intervention: preprocedural vs. periprocedural vs. postprocedural | Preprocedural music intervention: Chang et al. [18] represented the only study with higher methodological quality than the other four studies [14, 21, 29, 33] that performed preprocedural music interventions. No significant results concerning cardiovascular outcomes were found. With respect to the psychological endpoints, a significant reduction of anxiety in the music group vs. control was reported [18]. Periprocedural music intervention: two studies with higher quality [9, 28] than the remaining three trials [10, 17, 20] on patients listening to music during cardiovascular interventions or cardiac surgical procedures were identified. The findings concerning cardiovascular parameters were not significant in both studies [9, 28]; however, Aghaie et al. reported significantly lower anxiety and agitation levels in the music group compared to the control arm [9]. Postprocedural music intervention: three of seven studies [12, 15, 22, 23, 26, 27, 31] that performed postprocedural music interventions were of comparatively higher quality [23, 26, 27]. No significant changes in cardiovascular parameters were reported in any of these three studies. Regarding psychological outcomes, only Heidari et al. showed a significant reduction of anxiety in the music group vs. control [23]. Bally et al. presented the only study that applied music before, during and after coronary angiography [11]. The results were not significant. Overall, two studies that performed preprocedural and periprocedural music interventions were identified [25, 30]. Both studies were of comparatively higher quality and did not report any significant results. On estudy with periprocedural and postprocedural music intervention was found [8]; however, the publication did not fulfill the defined criteria for studies of comparatively higher quality. |
| | Selection of mu- sic: patient-selected vs. investigator- selected | Patient-selected music: in nine studies [8, 9, 11, 12, 14, 17, 18, 29, 33], the patients were allowed to choose the music according to their preferences, from which three trials were of comparatively higher quality [9, 11, 18]. In all studies the results of cardiovascular outcomes were not significant [9, 11, 18]. Anxiolytic effects in the music group vs. control were observed in two studies [9, 18]. Investigator-selected music: eight studies of higher quality [23–28, 30, 35] than the remaining 12 studies [10, 13, 15, 16, 19–22, 31, 32, 34, 36] with investigator-selected music were identified. Six of the eight studies of comparatively higher quality lid not show any significant changes in cardiovascular outcomes between the music group and the control [23, 25–28, 30]. Toker et al. found significant reductions of blood pressure in the music group vs. control [35], while Kunikullaya et al. reported similar findings in both the intervention and control group [24]. |
| ; ; (| Setting: inpatient vs. outpatient | Inpatient setting: 26 studies [8–12, 14–23, 25–33, 35, 36] were carried out in an inpatient setting, from which ten studies were of com- paratively higher quality [9, 11, 18, 23, 25–28, 30, 35]. A significant reduction of blood pressure was only reported in one study [35]. The remaining nine studies did not demonstrate any significant results concerning cardiovascular outcomes [9, 11, 18, 23, 25–28, 30]. Anxiolytic effects in the music group vs. control were observed in only three studies [9, 18, 23]. Outpatient setting: Kunikullaya et al. [24] presented the only study with higher quality compared to the remaining two studies [13, 34] that was conducted in an outpatient setting. Significant reductions of blood pressure and psychological outcome parameters were observed in both the experimental and control group. |

Table 3 Results of the subgroup analyses in detail

made such distinctions, no conclusions could be derived.

There are several studies that specifically investigated the effect of different styles of music on the cardiovascular system, mostly in healthy volunteers. Trappe and Voit conducted a randomized controlled trial with 120 healthy subjects who listened to music by Wolfgang Amadeus Mozart, Johann Strauss Jr. and ABBA [38]. Reductions of blood pressure and heart rate were reported when listening to Mozart or Strauss whereas the music by ABBA did not lead to any significant results. In the study by Bernardi et al. 24 healthy subjects were included and exposed to different styles of music [39]. A crescendo in music was associated with vasoconstriction and an increase in heart rate

Table 3 (Continued)

| Region: Europe vs. Asia vs. America vs. Africa vs. Aus- tralia | Europe: three of four studies [10, 26–28] that were published in Europe were of comparatively higher quality [26–28]. The results of primary endpoints were not significant in all three studies. The only significant results were reported by Nilsson in 2009, showing a higher PaO ₂ level in the music group vs. control [27]. The changes of oxytocin (increase in the music group, decrease in the control group) were statistically significant between the groups, but not over time in the subjects of each group. In a previous study by Nilsson in the same year, an initially lower blood cortisol level in the music group vs. control, 30 min after the music intervention, was reported [26]; however, the value proved to be nonsignificant after another 30 min. Asia: 12 studies were conducted in Asia [9, 13, 16–18, 20, 23, 24, 29, 32, 34, 35] from which five studies were of comparatively higher quality [9, 18, 23, 24, 35]. A significant reduction of blood pressure in the experimental group vs. control was only demonstrated in one study [35]. Kunikullaya et al. reported similar findings in both the intervention and control group [24]. Chang et al. and Heidari et al. only observed an anxiolytic effect in the music group vs. control [18, 23]. America: three of 11 studies [11, 12, 14, 15, 21, 22, 25, 30, 31, 33, 36] that were published in America were of comparatively higher quality [11, 25, 30]. In all three studies the results were not statistically significant. The studies in Africa [8] and Australia [19] did not fulfill the defined criteria for studies of comparatively higher quality. |
|--|--|
| Study duration: one single music intervention vs. several music therapy sessions vs. intervention/ follow-up > one week | One single music intervention: nine studies of higher quality compared to the remaining 11 studies [8–11, 14, 15, 17, 18, 20–23, 25–30, 33, 36] that performed one single music intervention were identified [9, 11, 18, 23, 25–28, 30]. None of the nine studies reported any significant changes in cardiovascular outcomes. Anxiolytic effects were demonstrated in three studies [9, 18, 23]. Intervention/follow-up > one week: Kunikullaya et al. reported the only study which conducted the music intervention for three months, thereby representing the longest study duration [24]. Significant reductions of blood pressure and psychological outcome parameters were observed in both the experimental and control group. Toker et al. presented the only study that was conducted over one week [35]. Significant reductions of blood pressure in the music group vs. control were reported. The remaining outcomes (anxiety, respiratory rate, [fetal] heart rate) were nonsignificant. The studies with more than one music therapy session [12, 19, 31, 32] or a study duration of exactly four weeks [13, 16, 34] did not fulfill the defined criteria for studies of comparatively higher quality. |
| Type of music: Indian vs. Turkish vs. Classical vs. Relaxing music vs. Nature-based sounds | Indian music: Kunikullaya et al. presented the only study that played Indian raga bhimpalas [24]. Significant reductions of blood pressure and psychological outcome parameters were observed in both the experimental and control group. Turkish music: two studies were identified [13, 35] that played Turkish music, from which only one publication fulfilled the defined criteria for studies of comparatively higher quality [35]. Significant reductions of blood pressure in the music group vs. control were reported while the remaining outcomes (anxiety, respiratory rate, [fetal] heart rate) remained nonsignificant. Relaxing music: eight studies that exposed the patients to relaxing music were identified [10, 18, 21, 26–28, 30, 32]. Five of these eight studies were of comparatively higher quality and did not report any significant changes in cardiovascular outcomes [18, 26–28, 30]. An anxiolytic effect was only documented by Chang et al. [18]. Nature-based sounds: overall, three studies applied nature-based sounds as the music intervention [9, 23, 29]. Two of them were as- sessed with comparatively higher quality and showed a significant reduction of psychological outcome parameters [9, 23]. The results concerning hemodynamic variables were not significant in both studies. The studies that used classical music [19, 22, 24, 36] did not fulfill the defined criteria for studies of comparatively higher quality. |

whilst uniform music induced vasodilatation and reductions of heart rate and blood pressure.

It can be concluded that the great variety of music with its complex elements which trigger different effects poses a great challenge to selecting the "right" music and that the fact that only ten studies provided a clear description of the music applied explains the difficulties in identifying homogeneous comparable trials. Therefore, an interdisciplinary cooperation between music therapists/musicologists and physicians is necessary. On 1 July 2009, the Austrian government officially recognized the music therapy profession by passing the Music Therapy Law [40], supporting the importance of incorporating musical specialists with their expertise into the studies.

Finally, it is important to underline that only studies which primarily investigated the cardiovascular system were included. Several literature reviews concluded that music might lead to a reduction of anxiety and pain [41–46]. Similar findings were reported in three of the included studies [9, 18, 23]. Therefore, it can be hypothesized that the focus of therapeutic effects of music is not on the cardiovascular system, but on psychological parameters; however, these effects might account for the subsequent changes in cardiovascular parameters.

Implications for further research

To minimize performance and detection bias, blinding is necessary. Headphones should be used for the experiments as they not only minimize the noise and distraction from outside, but also allow the blinding of the investigators and study participants during an intervention with the patient under general anesthesia or intubated patients in the intensive care unit who are not aware of the music played. This would therefore allow an objective analysis of the subconscious effects of music. Additionally, physiological changes are continuously measured in these settings and can be directly documented, thereby minimizing detection bias. In the case that double blinding is not possible, single blinded studies should still be preferred.

A further interesting field of investigation would be to examine patients with cardiac arrhythmia as nowadays arrhythmias can be easily detected by wearables, loop recorders or a 24-h electrocardiogram [47]. Patients could be continuously monitored on an outpatient basis to investigate the influence of music on the occurrence of atrial fibrillation or other types of arrhythmia.

As the influence of music is modified by personal preferences, it would be interesting to perform studies on newborns who might not have yet developed

personal tastes and thus could provide information that helps us to discern biological from cultural effects. Since it is presumed that music might only have an effect on cardiovascular diseases when applied with a certain regularity and length, future studies should also consider performing a series of music interventions with several follow-up sessions; however, as mentioned earlier, these questions regarding the choice of music as well as the length and number of music sessions should rather be discussed with music therapists/musicologists and documented in the study protocol. Moreover, the cooperation with music specialists helps defining and including a clear classification of the music style in the study protocol. This would result in more homogeneous studies and enable meta-analyses.

Finally, a careful and precise documentation of the patient's medical history and the music interventions can minimize confounders, such as underlying diseases and medication administered; however, obtaining a statistically significant number of homogeneous patients for an interindividual comparison indeed poses a great challenge. Focusing on the analysis of intraindividual changes over several music interventions can be perceived as a further approach to investigating music and its efficacy as an adjuvant therapy in medicine.

Limitations

One limitation is that only publications in English or German were searched. Another limitation involves the issue that only studies with receptive music intervention were included. Music therapy that incorporates active participation of the patient by singing, dancing, clapping and musical improvisation has not been explored in the present review. It is conceivable, though, that active music therapy induces greater effects compared to the passive form since a close connection between music and movement has been described in the literature [48].

Moreover, the number of analyzed studies was relatively low, mostly explained by the strict inclusion criteria. In addition, the number of comparable findings was further reduced due to high methodological heterogeneity among the studies. Thus, generalizability of the trial results remains unclear.

Conclusion

This review included 29 studies with 2579 patients. An extensive full text and subgroup analysis as well as a precise quality assessment revealed that currently no definite effect of receptive music intervention on the cardiovascular system can be verified; however, it cannot be ruled out that music during medical interventions for instance can contribute to a relief of anxiety and tension by reducing the stress response of the autonomic nervous system. The world of music and its connection to medicine remains an interesting topic. Further research is needed to assess music as an inexpensive and easy applicable form of therapy.

Conflict of interest C.-Y. Ho, P. Wexberg, B. Schneider, and C. Stöllberger declare that they have no competing interests.

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