

The Second International Conference  
Psychology and Music – Interdisciplinary Encounters  
(PAM-IE Belgrade 2022)

Main Conference Program, October 26–29, 2022

Parallel Conference Program, October 27, 2022

Main Organizer

Faculty of Music, University of Arts in Belgrade

Co-organizers

Institute of Psychology, Faculty of Philosophy, University of Belgrade

Psychology of Music Section, Serbian Psychological Society

Regional Network Psychology and Music (RNPaM)

**How to cite this volume**

Bogunović, B., Nikolić, S., & Mutavdžin, D. (Eds.). (2023). *Proceedings of the PAM-IE Belgrade 2022*. Faculty of Music, University of Arts in Belgrade.

Proceedings of the Second International Conference  
Psychology and Music – Interdisciplinary Encounters, Belgrade 2022

*Editors*

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*Publisher*

Faculty of Music, University of Arts in Belgrade, Kralja Milana 50, Belgrade

*For publisher*

Faculty of Music  
Ljiljana Nestorovska

*Editor-in-Chief of the Faculty of Music Publications*

Gordana Karan

*Cover design*

Stefan Ignjatović

*Technical Editor and Pre-Press*

Dušan Ćasić

ISBN-978-86-81340-59-2

PAM-IE Belgrade 2022 Conference and this publication were supported by  
the Ministry of Science, Technological Development and Innovation of the Republic of Serbia.

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**PROCEEDINGS**

Editors

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Faculty of Music, University of Arts in Belgrade, 2023

# Music Therapy in Patients with Hypertension: Eighteen-Year Experience

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## Abstract

The effect of music on blood pressure has been a constant theme throughout the medical history. Music can be used as medication in patients with heart disease or hypertension. Music can help in the treatment of these patients by improving endothelial function. This study aimed to evaluate the music therapy treatment for blood pressure reduction in patients with hypertension (HT). All 580 patients (pts) with HT between 2002 and 2021 were divided into 2 groups: a group with music therapy (MT Group) – 242 pts and a control group of 338 pts, without music therapy – non-MT Group. MT Group received sedative music without strong rhythm, with a rate of 60–80 beats/minute, and instrumental music with sustained melody. The protocol for listening to music was to sit on a chair, using soft open-air headphones (allowed outside sounds) and a CD player with closed eyes. They listened to selected music for 30 minutes twice a day. The music was chosen for each patient specifically. The preferred music genre was defined through interviews with patients. Baseline data collected included age, traditional coronary risk factors (RF), number of RF, previous organ damage, cardiovascular disease, chronic kidney diseases, and the number of Grades  $\geq 2$  HT episodes/pts in the last 6 months. Endothelial function was estimated by measurement of circulating blood markers (nitric-oxide – NOx, dimethylarginine – ADMA, symmetric dimethylarginine – SDMA, and xanthine-oxidase – XO). The follow-up period was 6 months. Standard statistical analysis was used for data analysis. There were no differences between the 2 groups in all baseline data. In the 6-month follow-up period, there were statistically significant differences between the 2 groups in the number of Grades  $\geq 2$  HT episodes/pts ( $p = .04$ ), in all 6 months of the follow-up period. This decrease was highest in the first month of the follow-up period. After 6-month NOx ( $p = .01$ ), ADMA ( $p = .04$ ), and SDMA ( $p = .04$ ) increased in the MT Group significantly in comparison to the non-MT Group. The value of XO was significantly lower in the MT Group

( $p = .04$ ) than in the non-MT Group. To conclude, in pts with HT listening to their favorite music together with standard medical therapy improves endothelial function, expressed through a significantly higher increase of NOx, decreasing of ADMA, SDMA, and XO than standard medical therapy alone. This improvement in endothelial function is associated with significant improvement in blood pressure reduction.

## Introduction

A particular hypothesis is that people with known diseases respond to music in a way that is mediated by that disease. Because of that, it is very important to moderate the musical parameters restricted by this disease (Aldridge, 1994). In patients with heart disease or hypertension, music can be used as medication (Mitrović et al., 2018). The way that music can help in the treatment of these patients can be by improving endothelial function.

Music produces physiological and psychological effects, such as changing skin conductance, brain activity, endothelial function, heart rate, and blood pressure, and affects our outlook on life and health. The impact of music on blood pressure has been a repeating theme throughout history. In one of the first issues of the medical journal *Lancet*, Vincent and Thompson (1929) discovered the influence of listening to the gramophone and radio music on blood pressure.

## Aim

The aim of this study was to evaluate music therapy treatment for the reduction of blood pressure in patients with hypertension (HT).

## Material and Methods

**Study design and patients.** Data from 580 patients (pts) diagnosed with HT at the Emergency Hospital, Cardiology Clinic, University Clinical Centre of Serbia between 2002 and 2021 were prospectively collected. The first criteria for inclusion in the study was to have systolic blood pressure (SBP) > 140 mmHg, and/or diastolic blood pressure (DBP) > 90 mmHg, more than 6 months before inclusion. All pts were divided into 2 groups: Group with music therapy (MT Group) – 242 pts and a control group of 338 pts, without music therapy – non-MT Group.

**Music therapy sessions’ protocol.** Patients in MT Group listened to sedative music without emphasized rhythm, with a 60–80 beats/minute rate, and instrumental music with a sustained melody. All pts in MT Group received instruction for listening to music and about the procedure that was planned. They listened to therapeutic music to relax. The protocol for listening to music was to sit on a chair and use soft open-air headphones and CD player, with closed eyes. Patients listened to music for 30 minutes twice a day. The music was selected for each patient, specifically. The music genre was defined after the interview with a patient. All patients chose music genres by themselves (classical, pop, rock, instrumental, jazz, evergreen, landscape, and folk music). Baseline data collected included age, traditional coronary risk factors (RF; e.g., smoking, diabetes mellitus, hyperlipidemia, obesity, and family history), number of RF, previous organ damage, cardiovascular disease, chronic kidney diseases, and the number of Grades  $\geq 2$  HT episodes/pts in last 6 months.

**Endothelial function.** Endothelial function was estimated by measurement of circulating blood markers (the stable end product of nitric-oxide [NOx], dimethylarginine [ADMA], symmetric dimethylarginine [SDMA], and xanthine-oxidase [XO]).

**Follow-up period.** All patients returned to our institution for follow-up 2 weeks after

discharge, after an additional 2 weeks, and thereafter every month. The control protocol was identical in both groups (standard cardiology ambulatory examination and patients being interviewed about medically documented Grade  $\geq 2$  HT episodes in the previous follow-up period). The duration of follow-up in both groups was 6 months. Endpoints were death (sudden, non-sudden cardiac, non-cardiac). Sudden death was defined as death within 1 hour of the onset of symptoms or unexpected death during sleep.

**Statistical analysis.** In this study, continuous variables were expressed as median values, and categorical variables were presented as a percent. For the comparison of categorical variables, Chi-square or Fisher exact test was used, and for continuous variables, the Student’s *t*-test.

## Results

In the study period (2002 to 2021), 242 (41.7%) out of 580 consecutive patients with HT were exposed to music therapy interventions.

**Baseline characteristics.** The clinical characteristics of the pts in both groups are shown in Table 1.

**Table 1. Baseline clinical characteristics in the two study groups.**

	MT Group (n = 242)	non-MT Group (n = 338)	<i>p</i>
Age (years)	57.4 ± 6.7	59.4 ± 7.4	.82
<b>Coronary risk factors</b>			
Smoking	83 (34.1%)	113 (33.4%)	.83
Diabetes mellitus	68 (28.2%)	112 (33.0%)	.20
Family history	83 (34.1%)	122 (36.0%)	.65
Total cholesterol (mmol/liter)	6.4 ± 0.8	6.1 ± 0.6	.73
HDL cholesterol (mmol/liter)	1.2 ± 0.4	1.3 ± 0.7	.48
Triglycerides (mmol/liter)	2.4 ± 1.1	2.5 ± 1.2	.32

Body mass index (kg/m <sup>2</sup> )	25.0 ± 2.0	26.4 ± 3.2	.12
<b>No other RF</b>	167 (69.1%)	226 (66.8%)	.58
1-2 RF	56 (23.0%)	88 (26.1%)	.43
≥ 3 RF	19 (7.9%)	24 (7.1%)	.73
<b>HT therapy</b>			
Ca antagonists	116 (48.0%)	175 (51.9%)	.36
ACE inhibitors	162 (67.0%)	206 (60.9%)	.14
Beta-blockers	68 (28.2%)	115 (34.1%)	.13
Diuretics	43 (17.9%)	78 (23.1%)	.12
Sartans	24 (9.9%)	27 (7.9%)	.42
<b>Previous angina</b>	56 (23.0%)	91 (26.9%)	.30
<b>Previous infarction</b>	34 (13.9%)	61 (18.1%)	.20
<b>Organ damage</b>	29 (11.9%)	54 (15.9%)	.17
<b>Chronic kidney disease stage ≥ 3</b>	10 (4.0%)	20 (6.0%)	.34
<b>OD, CKD stage 3 or diabetes</b>	38 (15.9%)	71 (20.9%)	.11
<b>Symptomatic CVD, CKD stage ≥ 4 or diabetes with OD/RFs</b>	17 (7.1%)	30 (9.0%)	.42
<b>No. of Grade ≥ 2 HT episodes/pts (in last 6 months)</b>	150 (61.9%)	197 (58.2%)	.37

Note. RF = risk factor; OD = organ damage; CKD = chronic kidney disease; CVD = cardiovascular disease; HT = hypertension.

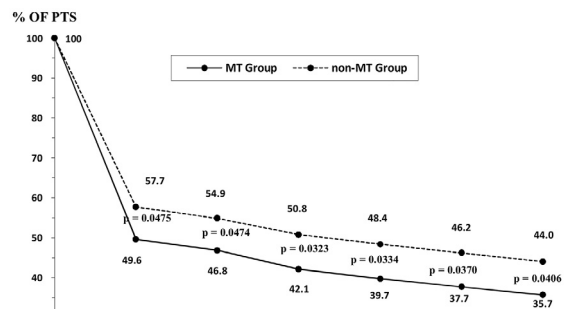
**Table 2. Endothelial function in the 6-month follow-up period.**

	MT Group (n = 242)		p	non-MT Group (n = 338)		p
	Before	After		Before	After	
NOx (μmol/l)	30.1 ± 6.2	50.2 ± 6.9	.001	32.0 ± 6.7	35.1 ± 6.0	.33
ADMA (ug/l)	0.98 ± 0.10	0.75 ± 0.09	.04	0.81 ± 0.07	0.88 ± 0.10	.88
SDMA (ug/l)	0.96 ± 0.25	0.82 ± 0.18	.05	0.85 ± 0.09	0.83 ± 0.12	.32
XO (nmol O <sub>2</sub> /ml)	2.68 ± 1.20	1.40 ± 1.18	.04	2.31 ± 1.12	2.28 ± 0.62	.74

Note. NOx = nitric-oxide; ADMA = dimethylarginine; SDMA = symmetric dimethylarginine; XO = xanthine-oxidase.

There were no differences between the 2 groups in age, coronary RF, number of RF, HT therapy, previous coronary vascular disease (CVD), organ damage (OD), chronic kidney disease (CKD), and the number of Grade ≥ 2 HT episodes/pts in last 6 months.

**Follow-up period.** In the 6-month follow-up period, the 2 groups had statistically significant differences in the number of Grades ≥ 2 HT episodes/pts (Figure 1).



**Figure 1. Number of Grades ≥ 2 HT episodes/pts in the 6-month follow-up period.**

Patients in the MT Group had a statistically significant decrease in the number of Grades ≥ 2 HT episodes/pts, in all 6 months of the follow-up period, compared to the control, non-MT Group. This decrease was highest in the first month of the follow-up period (Figure 1).

After 6-month NOx significantly increased in the MT Group ( $p = .001$ ) and did not increase significantly in the non-MT Group ( $p = .33$ ; Table 2).

The value of ADMA ( $p = .04$ ) and SDMA ( $p = .05$ ) significantly decreased in the MT Group, and there were no significant changes in the non-MT Group, in the 6-month follow-up period (Table 2).

The value of XO was significantly lower in the MT Group ( $p = .04$ ) than it was in the non-MT Group ( $p = .74$ ).

## Discussion

To examine the effects of musical treatment on psychological and physiological responses in patients with coronary heart disease (CHD), Bradt et al. (2013) showed that music treatment had a small beneficial effect on psychological distress in people with CHD. Studies that used music therapy with patients with myocardial infarction pointed out reduced anxiety ( $p < .0001$ ) as a consequence of the treatment (Roy et al., 2009). Then studies that used patient-selected music showed a greater reduction of anxiety ( $p = .001$ ; Good, 1995). As in our study, these studies indicated that listening to music reduces heart rate ( $p = .01$ ), respiratory rate ( $p < .0001$ ), and systolic blood pressure ( $p < .001$ ). Only one study considered hormone levels and quality of life as outcome variables (White, 1999). This study presented the value of enzymes and hormones that influenced endothelial function (which is correlated with blood pressure).

In our study, we also presented the value of enzymes that influenced endothelial function. All these parameters were significantly different in the group of patients who listened to sedative music without emphasized rhythm and instrumental music with a sustained melody, improving endothelial function. White (1999) suggested music may benefit systolic blood pressure, heart rate, quality of sleep, respiratory rate, and pain in persons with CHD.

Bradt et al. (2013) examined the effects of music therapy combined with standard care of patients and only standard care on preoperative anxiety in surgical patients. They included 26 trials (2051 participants). All patients used to listen to pre-recorded music. The results suggested that music therapy may have a benefi-

cial effect on preoperative anxiety. Specifically, music listening reduced anxiety ( $p < .001$ ). One analyzed study by Bradt et al. (2013) found that music therapy was more effective than sedative medications in reducing preoperative anxiety and equally effective in reducing physiological responses. This systematic review indicates that music therapy may have a beneficial effect on preoperative anxiety reduction.

Another study was conducted to assess psychological and physical outcomes in cancer patients when music therapy and standard medicine interventions were applied in 22 new trials (Levison, 2009). The evidence of Gomez's and Danuser's review (2004) rests on 52 trials with a total of 3731 participants. They included music therapy interventions offered by trained music therapists and music medicine interventions, defined as listening to pre-recorded music offered by medical staff. They categorized 23 as music therapy trials and 29 as music medicine trials. The results suggest that music therapy may have a beneficial effect on anxiety in patients with cancer ( $p < .001$ ). Results also suggested a moderately strong, positive impact on depression ( $p = .02$ ). Music therapy may lead to small reductions in heart rate, respiratory rate, and blood pressure. They found a large pain-reducing effect ( $p = .001$ ). Music therapy had a small to moderate treatment effect on fatigue ( $p = .03$ ).

Koelsch and Lutz (2015) showed that the anxiety-reducing effects of music are probably also associated with (small) reductions in BP. Music has been used in hypertensive patients to lower BP by controlled breathing. The music had effects on BP. Meta-analytic data indicated (small) reductions of RR and BP in patients due to music interventions. The conclusion was that music has effects by the findings that HR and RR are higher (and HRV lower) during exciting music compared with tranquilizing music. Heart rate (and RR) increased during musical frissons, especially when associated with piloerection. Compared with silence, music increased HR and RR, and HR and RR are higher during pleasant than unpleasant music. Data

analysis suggested that music also has effects on the regional activity of the heart, as well as in changes in ECG amplitude. Music can reduce pain, anxiety, and BP and RR reductions (Gaston, 1951). The use of music for intervention and therapy is a low-cost and safe adjuvant. But there is a pressing need for high-quality systematic research on the effects of music on the heart in both healthy individuals and patients.

## Conclusion

In patients with HT listening to preferred music together with standard medical therapy, improves endothelial function, expressed through a higher increase of NOx, and decrease of ADMA, SDMA, and XO, compared to standard medical therapy alone. This improvement in endothelial function is associated with significant improvement in blood pressure reduction.

**Acknowledgements.** This study was partially supported by the Ministry of Science and Technological Development and Innovations of the Republic of Serbia (Grant No. 175084) and The Belgrade Cardiology Club.

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