Wavelet transformation analysis shows differences between impaired LVEF patients and healthy individuals

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INTRODUCTION

Heart failure (HF) is a global pandemic. It affects 64 million people worldwide, with steadily increasing incidence, morbidity, mortality, and economic burden [1]. Forecasts indicate continued rising prevalence, especially among the elderly and in low-to-middle socio-demographic index regions [2]. Left ventricular ejection fraction (LVEF) significantly impacts HF treatment and prognosis [3]. The sequence of physiological changes related to reduced LVEF remains uncertain, and only limited research has explored these mechanisms. This study employed wavelet transformation (WT) to investigate oscillatory interactions, exploring aging and decreased LVEF effects on cardiovascular dynamics. We analyzed central (electrocardiogram [ECG]) and peripheral (blood pressure [BP]) measurements, hypothesizing modified wavelet quantities in HF patients compared to healthy individuals.

METHODS

Subjects

In our study, we examined two groups of volunteers: a patient group and a control group.

Patient group: The study included 16 individuals. Inclusion criteria: compensated ischemic HF with LVEF ≤50% treated as per current guidelines and sinus rhythm. Exclusion criteria: age <18, history of sustained ventricular tachycardia, permanent supraventricular arrhythmia, paced rhythm, clinical instability within three months, incomplete or recent (<3 months) revascularization, II/III atrioventricular block and neuropathy.

The study group overwhelmingly consisted of males (94%), with an average age of 62 (6) years and a BMI of 29.1 (3.8) kg/m^2 (age and BMI expressed as mean [standard deviation]). Most patients had a history of myocardial infarction (88%), hypertension (75%), hypercholesterolemia (69%), and were active smokers (75%). Diabetes was present in 25% of cases, and paroxysmal atrial fibrillation was also present in 25% of participants. Pharmacotherapy details indicated widespread use, including beta-blockers (94%), angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (88%), statins (94%), antiplatelet drugs (88%), mineralocorticoid receptor blockers (50%), and diuretics or anticoagulants (25%). Patients were treated according to current HF management guidelines, with any instances of treatment omission attributable to contraindications or adverse effects. This study adhered to the Declaration of Helsinki and we obtained approval from the Ethics Committee of the Medical University of Gdansk (NKBBN/864/2022-2023).

Control group: 10 control participants (nine males and one female, age 28.5 [9.1] years, BMI = 24.1 [1.2] kg/m^2). Inclusion criteria: healthy individuals, age >18, non-smokers and having no chronic or acute illness. Exclusion criteria: pregnant women and those with a history of drug or alcohol abuse. The Ethics Committee of the University of Regina, Canada (REB#2017-013) approved this study and the experimental protocol. All control and patient participants provided signed informed consent forms.

Participants abstained from alcohol for 24 hours, and from tea, coffee, nicotine, cocoa, and methylxanthine-containing items for 12 hours prior to the experiment. Intense exercise was not allowed for 6 hours before testing. Before each procedure, participants rested quietly for 10 minutes.

The experiments for the patient group were conducted at the Department of Cardiology and Electrotherapy, Medical University of Gdansk, Poland and for the control group at the Faculty of Kinesiology and Health Studies, University of Regina, Canada. The recruitment period for the patient group was February 25, 2015, to July 28, 2018, and for the control group it was from June 1, 2019, to November 1, 2019. Researchers in Poland and Canada utilized a Finometer (Finapres 2300, Ohmeda) to measure participants' BP, employing a finger-cuff for beat-to-beat BP monitoring from the left middle finger. Additionally, ECG signals were recorded using the Finometer device, which incorporates ECG electrodes for simultaneous electrocardiogram signal measurement alongside BP readings. Pre-processing steps included detrending and normalization [4].

Wavelet transformation

We used wavelet analysis to identify and study the physiological mechanisms behind cardiovascular system oscillations [5]. Further details on WT and related measures such as wavelet amplitude and phase coherence are available in [4].

Statistical analysis

Non-parametric statistical tests, specifically the Wilcoxon rank sum test, were employed to compare the median values of wavelet amplitude and phase between the control and patient groups due to the non-normal distribution of the data. For the body mass index (BMI) comparison (Supplementary material, *Table S1*), a t-test was used, as the BMI values in both groups followed a normal distribution. We determined statistical significance of phase coherence using surrogate data testing [6].

RESULTS AND DISCUSSION

Figure 1 compares the frequency content of control and patient groups using median time-averaged amplitude of WT across four frequency intervals [4]. Intervals I and II (0.6–2 Hz and 0.145–0.6 Hz) relate to cardiac and respiratory function, while interval III (0.052–0.145 Hz) pertains to smooth muscle cell activity, and interval IV (0.021–0.052 Hz) reflects smooth muscle autonomic innervation [7].

We noticed a significant decrease in ECG wavelet amplitude (Figure 1A) within the cardiac frequency range in patients, linked to impaired LVEF. Similarly, a decline in phase coherence between BP and ECG signals (Figure 1C) was observed in patients within this frequency range. Phase coherence was significant if it exceeded the 95th percentile of 120 inter-subject surrogates (generated from 2-permutations of 16 subjects). BP-ECG phase coherence provides insights into dynamic heart electrical activity and cardiovascular hemodynamics interactions. Reduced coherence indicates cardiovascular dysfunction due to impaired LVEF, affecting BP. Conversely, in healthy individuals, BP-ECG coherence remains stable.

Our study found significant differences in interval III for BP signals (Figure 1B) between the control and patient groups. This may explain impaired myogenic activity in patients, suggesting increased vessel stiffness in older individuals [8].

Our observation of a notable decrease in BP signal wavelet amplitude in interval IV for the patient group (Figure 1B) is consistent with Bernjak et al. [7]. They noted reduced absolute spectral amplitude of laser Doppler flow signals in HF patients compared to healthy controls, indicating impaired smooth muscle autonomic innervation in those with impaired LVEF.

WT shows significant potential in cardiovascular medicine by analyzing complex physiological signals such as ECG and BP signals in both time and frequency domains simultaneously. It aids in detecting and diagnosing various cardiovascular conditions by extracting relevant features such as patterns associated with arrhythmias or ischemia in ECG signals [11]. Additionally, wavelet analysis helps in risk stratification for cardiovascular events by analyzing subtle variations and patterns in physiological signals [12]. Continuous monitoring of physiological signals through WT offers insights into cardiovascular disease progression and aids in predicting patient outcomes.

Limitations

Our patient group exhibited a higher BMI than our control group. Elevated BMI significantly affects heart function and cardiovascular health, correlating with a heightened risk of heart diseases such as coronary artery disease, HF, and atrial fibrillation [9, 10]. The varied drug regimens in our study pose challenges in evaluating their relative efficacy in treated patients. Additionally, 75% of the patient group were active smokers, and 25% had diabetes, potentially impacting the sympathetic nervous system (Figure 1B). Furthermore, limitations and sources of uncertainty regarding the Finometer include calibration, movement artifacts and processing algorithms, necessitating user awareness for reliable BP measurements. A final limitation was the small number of patients.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/polish_heart_journal.

Article information

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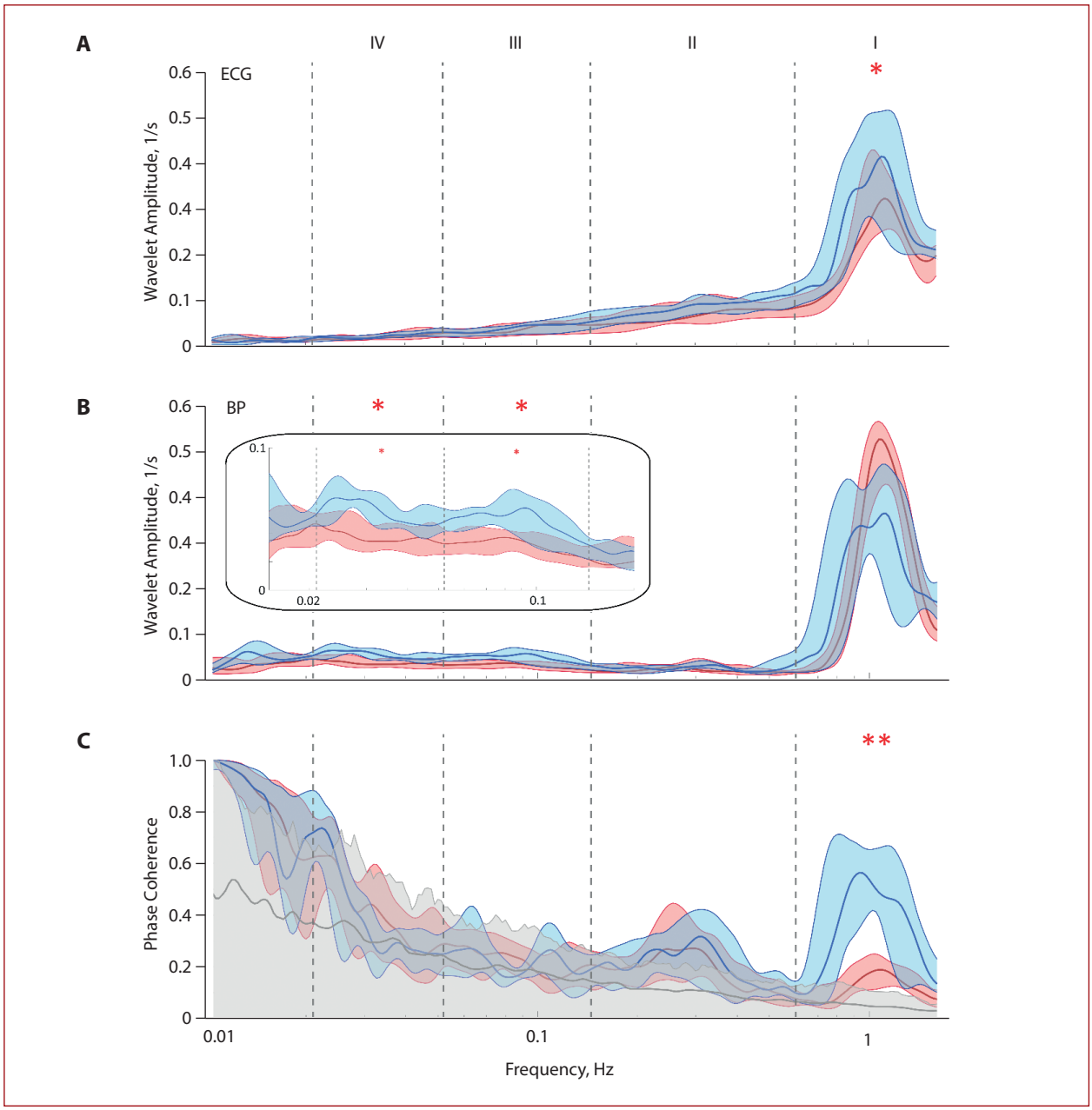

Figure 1. A–B. Displays median time-averaged wavelet transformation for signals recorded from patient and control groups, respectively. Thick red and blue lines represent patient and control groups, with shaded areas indicating interquartile range (25th to 75th percentiles). **A.** Shows electrocardiogram (ECG) signal results, while **B.** Shows BP signal results. **B.** Statistically significant frequency intervals III and IV were enlarged. **C.** Shows median wavelet phase coherence between blood pressure and ECG. Thick colored lines represent median values, with colored shading indicating interquartile range (25th to 75th percentiles). Coherence below 95th percentile of surrogates is not significant (light gray line/shading). Significant group differences are denoted by asterisks: **P* <0.05; ***P* <0.01

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