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ORIGINAL PAPER

Impact of shock wave lithotripsy on heart rate variability in patients with urolithiasis

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Abstract The physiological response of the cardiac autonomic nervous system during shock wave lithotripsy (SWL) remains unclear. Heart rate variability (HRV) is an index of cardiac autonomic balance. This study aimed to analyze HRV during SWL in patients with urolithiasis. Electrocardiograms of patients who underwent SWL were obtained. Recordings were obtained before and after SWL. For each time point, the recordings were obtained continuously for 6 min, after which R wave-to-R wave (RR) intervals were extracted. The time digital sequence derived from RR intervals was the HRV signal. Time-domain analysis revealed that the mean of RR intervals (MRR) and standard deviation of normal beat-to-normal beat (NN) intervals (SDNN), but not the square root of the mean squared difference of successive NNs (RMSSD) or triangular interpolation of NN intervals (TINN), significantly increased during SWL. The increase in SDNN persisted after SWL but MRR returned to the initial level. Frequency-domain analysis revealed that very low frequency (VLF), low frequency (LF), and LF/high frequency (HF) ratio significantly increased after SWL, while there was no statistically significant difference in HF. Thus, the patients had significantly high MRR and SDNN during SWL and significantly high SDNN, VLF, LF, and LF/HF ratio after SWL. SWL could alter the functioning of the cardiac autonomic nervous system, resulting in reduction in

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sympathetic activity and increase in parasympathetic activity. Further studies with larger samples are required to confirm these findings and understand the underlying mechanisms.

Keywords Cardiac autonomic system · Electrocardiogram · Shock wave lithotripsy · Heart rate variability · Urolithiasis

Introduction

As a stable, noninvasive, and cost-effective treatment of choice for urolithiasis, shock wave lithotripsy (SWL) has evolved with the development of third-generation electromagnetic lithotripters since Chaussy et al. [8] introduced the first-generation lithotripters in 1984. Although the devices use an R wave synchronous mode to avoid the influence of shock waves on heart rate (HR) during treatment, as high as 80% incidence of dysrhythmia had been observed in the beginning of the SWL era [16, 38]. Thereafter, development of new-generation lithotripters effected a gradual decline in the incidence of dysrhythmia to 8.8%, and no interruption of treatment was needed [40]. In the study of Küfer et al., no macroscopic or microscopic mechanical change was observed in implantable cardioverter-defibrillators (ICDs) exposed to shock waves. Thus, SWL seems to exert a minimal effect on cardiac function. Although deactivation of ICDs is not mandatory, Küfer et al. [22] suggested the application of the R wave synchronous mode during SWL to avoid pacing failure by artifact oversensing . However, some unknown impact of SWL on HR remains to be elucidated.

Heart rate variability (HRV) is measured by the variation in RR intervals; it is the average of variations in beat-to-beat RR intervals on an electrocardiogram (ECG) in a certain period [17, 18, 28]. The autonomic nervous system regulates HR via sympathetic and parasympathetic nerve impulses [15]. HRV represents beat-to-beat variability during a special condition, including physiological and pathological statuses [6]. Furthermore, HRV can be affected by various treatments, namely, Valsalva maneuver, or physiological conditions such as aging, deep breathing, postural changes, and day/night time [17, 19, 36]. Systemic evaluation of alterations in HRV has been performed in clinical settings. Reduction in HRV may imply a poor prognosis in patients with myocardial infarction [6], chronic kidney disease [7, 31], congestive heart failure [12, 24], coronary arterial disease [27], and diabetic neuropathy [32].

Many clinical conditions are associated with either increased or decreased HRV, including different treatments/conditions, such as hemodialysis [11, 14], lower urinary tract symptoms [10], percutaneous transluminal coronary angioplasty [5], mobile phone position [35], bilevel positive airway pressure [29], and transcutaneous electrical stimulation of acupoints [9]. However, no information is available about the interference between new-generation lithotripters and HRV; SWL has been reported to exert a minor effect on dysrhythmia [20, 41], but vague information is available about its effect on HRV. In addition, physiological responses to different levels of SWL remain to be clarified. HRV reflects the cardiac autonomic nerve function; examination of the effect of SWL on HRV may help to elucidate the effect of SWL on cardiac autonomic balance. Therefore, the aim of the present study was to noninvasively evaluate the cardiac autonomic nervous system control of HR by examining HRV during SWL and to correlate alterations in HRV with the physiological measurements. The present study tested the hypothesis that SWL can affect HRV in patients with calculi and the physiological variables can modulate alterations in HRV. To the best of our knowledge, this is the first survey on the effect of SWL on the cardiac autonomic nervous system. Our results showed that SWL could alter the functioning of the cardiac autonomic nervous system, resulting in an increase in sympathetic activity and decrease in cardiac autonomic balance.

Materials and methods

Recruited patients of this study

The 84 patients of the present study were recruited from the 26 to 80-year-old patients with urolithiasis and were indicated to be treated by SWL in a general hospital. Patients with history of severe illness such as stroke, dysrhythmia, congestive heart failure, coronary heart disease, coagulopathy, chronic kidney disease, use of β-blocker, digitalis and diabetes mellitus were excluded from this study. All patients agreed this study and signed an informed consent before the treatment. This study was approved by the Institutional Review Board (IRB) of the China Medical University Hospital (IRB No. 99-017).

SWL processing and data recording

Patients underwent shockwave treatment were asked to follow the standard procedure of operation which including fasting at midnight, complete blood count test, serum biochemical study, chest X-ray, and complete ECG record. Before treatment, patients lay down in a supine position on the treatment table at least for 10 min. An intravenous infusion with normal saline was set up. Patients underwent shockwave treatment were under an escalating stepwise increase of voltage according to the description of Demirci et al. [13] which were subjected to gradually increased (with every 500 shocks) output voltage as 11, 12, and 13 kV, respectively. The maximal of shockwave number was limited to 2,500 for renal stone and 3,000 for upper ureteral stone to limit tissue damage. The lithotripter used was Compact Delta lithotripter with Software 2.1X (Dornier MedTech, Munich, Germany). During shockwave treatment, patients were treated by one intravenous injection of 50 mg pethidine in every treatment whenever an intolerable pain occurred. Three leads of ECG recording were placed over patient's chest wall. The ECG signals were captured by a 3-channel portable device (MSI E3-8010) at 500 Hz sampling rate. Recording points were 10 min before treatment, 5 min after start of treatment; shockwave number reached 2,000 shocks, 5 min before the end of treatment, and 10 min after the end of treatment. ECG has been recorded continuously for 5 min on each point. And then RR intervals were extracted. The time digital sequence made from RR intervals was HRV signal.

The interpretation of HRV

The ECG signals were captured by a 3-channel portable device (MSI E3-8010) at 500 Hz sampling rate. Data were analyzed and monitored in real time and stored in a computer. RR intervals were detected from the ECG, and ectopic beats were identified and excluded from the calculations. The RR time series were obtained as the time intervals between consecutive R peaks. We calculated the mean of R wave-to-R wave intervals (MRR), standard deviation of all the normal to normal (NN) intervals (SDNN), square root of the mean squared difference of successive NNs (RMSSD), and triangular interpolation of NN intervals (TINN) as previously described [25]. R_i: RR length of the i heart beat, n: total numbers of RR intervals [2, 4, 36].

$$\text{mean} = \frac{\sum_{i=1}^{n} R_i}{n}\text{ms}$$

$$\text{SD} = \sqrt{\frac{\sum_{i=1}^{n} (R_i - \text{mean})^2}{n}}$$

$$\text{CV} = \frac{\text{SD}}{\text{mean}} \times 100\%$$

$$\text{rmsSD} = \sqrt{\frac{\sum_{i=1}^{n-1} (R_i - R_{i+1})^2}{n-1}\text{ms}}$$

Frequency-domain methods apply the fast Fourier transform to the RR-interval sequence to develop a power spectral density that describes how the variance of the signal (i.e., power) is distributed as a function of frequency. Four main spectral components have been identified: (1) very low frequency (<0.04 Hz), (2) low frequency (LF) 0.04–0.15 Hz, and (3) high frequency (HF) 0.15–0.40 Hz, and (4) ratio of LF/HF.

Statistical analysis

All data regarding RR intervals of heart rate recording are expressed as mean ± SD, and were analyzed using the Student's t test of normal distribution values. Nonparametric tests including Mann–Whitney and paired Wilcoxon signed rank test were used in case of non-normal distribution variables. Calculation was made by compared each patient's data before and after treatment. A P value of <0.05 denotes the presence of statistical significance. The software used for analysis was the Statistical Package for the Social Science (SPSS® for Windows, release 15.0, SPSS Inc., Chicago, IL, USA).

Results

Baseline characteristics of the 84 patients are given in Table 1. There were 57 males and 27 females with the mean age of 48.6 ± 12.5 years (range 26–80 years). Among the total number of patients, 66 had calculi in the kidney [left/right (L/R) = 46/20] and 18 had calculi in the ureter (L/R = 14/4).

The HRV parameters in patients during SWL are shown in Table 1. In the time-domain analysis, we found that MRR and SDNN were significantly increased during SWL, but this was not the case with RMSSD or TINN. The increase in SDNN persisted after SWL but MRR returned to the initial level.

In the frequency-domain analysis, a progressive increase (but not statistically significant) was noted in VLF, LF, and HF during SWL. After SWL, VLF, LF, and LF/HF ratio were significantly increased, while there was no statistically significant difference in HF. Thus, the patients had significantly high MRR and SDNN during SWL and significantly high SDNN, VLF, LF, and LF/HF ratio after SWL.

Discussion

SWL has been reported to exert a minor effect on dysrhythmia [14, 28], but vague information is available about its effect on HRV. In the present study, we provided the first evidence that SWL resulted in a significant increase in MRR and SDNN during the treatment. In the frequency-domain analysis, increase was noted in VLF, LF, and HF; however, the change was not statistically significant. After SWL, SDNN, VLF, LF, and LF/HF ratio were significantly increased. These results suggest that SWL could alter the

Table 1 Heart rate variability measures in patients during extracorporeal shock wave lithotripsy

	Pre-treatment	5 min after treatment start	ESW 2,000 times	5 min before end of treatment	Post-treatment	*P* value[#]
Time domain						
MRR (ms)	908 ± 123	929 ± 141*	927 ± 142*	935 ± 134*	910 ± 127	<0.001
SDNN (ms)	279 ± 105	292 ± 58*	295 ± 52*	299 ± 58*	298 ± 51*	0.011
RMSSD (ms)	276 ± 93	296 ± 60	301 ± 59	307 ± 70	301 ± 55	0.055
TINN (ms)	1291 ± 780	1401 ± 747	1420 ± 724	1286 ± 788	1211 ± 773	0.351
Frequency domain						
VLF (ms^2)	756 ± 725	771 ± 715	814 ± 630	917 ± 868	1274 ± 1126*	<0.001
LF (ms^2)	334 ± 318	370 ± 332	464 ± 436	469 ± 453	555 ± 573*	0.013
HF (ms^2)	333 ± 303	392 ± 435	478 ± 425	489 ± 445	405 ± 346	0.122
LF/HF ratio	1.00 ± 1.04	0.94 ± 0.76	0.97 ± 1.02	0.95 ± 1.01	1.37 ± 1.41*	0.034

Data represent mean ± S.D

[#] Calculated by one way repeated measures analysis of variance with Bonferroni post hoc test

* $P < 0.05$ compared with pretreatment

functioning of the cardiac autonomic nervous system, resulting in an increase in sympathetic activity and decrease in cardiac autonomic balance.

HRV is measured by the variation in RR intervals; the autonomic nervous system regulates heart rate via sympathetic and parasympathetic nerve impulses. Many clinical conditions are associated with either increased or decreased HRV. The present study evaluated the cardiac autonomic nervous system control of HR by examining HRV during SWL and to correlate alterations in HRV. Our results showed that SWL could alter the functioning of the cardiac autonomic nervous system, resulting in an increase in sympathetic activity and decrease in cardiac autonomic balance. Each heartbeat has its own R wave peak, and the time and frequency intervals between successive R wave peaks can be measured from an ECG. HRV is a measure of change in time and frequency intervals between R waves within a certain period. Thus, a series of data can be obtained from HRV by frequency- and time-domain analyses. In time-domain analysis, the average, maximum, and minor RR intervals are measured. In frequency-domain analysis, short-term recording (5 min) of LF power, HF power, and LF/HF ratio are measured. Stable HRV reflects a good balance between the functioning of the cardiovascular and autonomic nervous systems [37]. Heart failure is associated with the autonomic dysfunction, which can be quantified by measuring HRV. A reduction in SDNN identifies patients at a high risk of death [26, 39]. In outpatients with congestive heart failure, reduction in SDNN has been shown to be a more powerful predictor of the risk of death from progressive heart failure than other conventional clinical measurements [26]. Thus, our finding of increased SDNN persisting after SWL might have important clinical implications in patients with cardiovascular diseases. Further studies should be conducted for the observation of cardiac function during SWL.

Our results showed that the frequency-domain HRV parameters LF and LF/HF ratio, which mainly reflect vagal tone, were increased in patients during and after SWL. Some investigators have reported changes in HRV during clinical treatments, such as angioplasty in coronary artery disease [1, 3]. Vagal activity is a major contributor to the HF component [30]. On the other hand, some researchers consider the LF component as a marker of sympathetic nerve activity, while others consider it as a result of both sympathetic and vagal influences [33]. Many investigators consider that analysis of the LF/HF ratio rather than the individual components better reflects the sympathovagal balance [1]. In the present study, the balance between sympathetic nerve activity and vagal activity (LF/HF ratio) significantly showed sympathetic predominance immediately after SWL. These results indicate that LF is increased, which implies sympathetic predominance and parasympathetic withdrawal. Thus, we propose that autonomic imbalance may be associated with SWL in patients with urolithiasis. In addition, our data showed that VLF significantly increased after SWL. However, the physiological explanation of the VLF component is less well defined, and the existence of a specific physiological process contributing to these changes in the heart period remains questionable [1].

Because of the noninvasive nature of our study, several methodological aspects need further clarification. We measured the cardiac autonomic nervous system control of HR by analyzing HRV, which is a noninvasive measurement. Nonetheless, this important tool has previously been validated by pharmacological blockade [23, 33]. Another important issue is the time for which SWL was performed in the present study. In clinical settings, reduction in HRV may imply a poor prognosis in patients with myocardial infarction, chronic kidney disease, congestive heart failure, coronary arterial disease, and diabetic neuropathy. Our study results were limited to short-term application of shock waves, which allowed us to evaluate only the acute effects of this modality. However, it would be interesting to investigate the long-term effects of different levels of SWL on the cardiac autonomic nervous system. We expect that the long-term effects would be different from those observed in the present study. Moreover, we only studied subjects without cardiovascular disease. Hence, we cannot completely extrapolate our results to patients with cardiovascular disease, whose HRV responses may be different from those with "normal" clinical conditions. Nevertheless, our study intended to clarify SWL-induced physiological responses, e.g., variation in HR, considering its impact on the cardiac autonomic nervous system. In this context, we wanted to reinforce the importance of the level of SWL and the care required for each clinical condition. In addition, since HRV reflects the cardiac autonomic nerve function and SWL may influence the cardiac autonomic balance. We suggest the SWL should be temporarily interrupted when abnormal cardiac rhythm was found.

This study had some limitations. Owing to the ethical issue, we did not obtain the HRV data for patients only given anesthesia without any intervention. Therefore, the effect of anesthesia could not be measured definitively. We attempted to eliminate the effect of anesthesia by measuring HRV 5 min after SWL and hypothesized that anesthesia exerted a minor effect. However, the actual effect of anesthesia might be greater than that hypothesized by us. Discomfort and pain could be confounding factors in the study; the increase in LF percentage and LF/HF ratio with the decrease in HF indicated augmented sympathetic and attenuated parasympathetic drive. The second problem was a relatively wide age range of patients with urolithiasis who underwent SWL. During enrollment, we chose relatively healthy patients with urolithiasis, who did not have any major medical illness—especially cardiovascular disease, hypertension, arrhythmia, etc. This non-randomized study was an effort to decrease the effect of age on HRV. However, age-related physical status may affect HRV to some extent. We attempted to decrease the age range or divide patients on the basis of sex and re-analyze the data; however, no significant differences were found because of the small number of patients and large variation in the HRV data. Nevertheless, our study was designed as a within-subject study, and within-subject designs are often called repeated measures designs since within-subject variables always involve taking repeated measurements from each subject. We wish the study design could represent the apparent changes in HR parameters during lithotripsy in a general cohort.

In summary, SWL could alter the functioning of the cardiac autonomic nervous system, as well as physiological variables, in patients with urolithiasis. Changes in the vagal or sympathetic tone of HR, as assessed by HRV analysis, have been associated with mortality, arrhythmias, and sudden cardiac death, particularly after acute myocardial infarction and heart failure [21, 26, 34, 39]. Long-term studies with larger samples are necessary to evaluate whether these findings have clinical implications regarding mortality and morbidity.

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