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Investigation of heart rate variability and heart rate turbulence in chronic hypotensive hemodialysis patients

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Abstract

Background Sudden cardiac death is the leading cause of cardiac-related death in hemodialysis patients. Hypotensive episodes in pre-, intra-, and post-dialytic periods can present serious clinical challenges that affect a patient's quality of life and prognosis. The aim of the present study was to evaluate cardiac autonomic control and arrhythmogenic risk by analyzing 24-h heart rate variability (HRV) and heart rate turbulence (HRT) in hypotensive hemodialysis patients.

Methods A total of 79 patients on maintenance hemodialysis treatment, 39 normotensive and 40 with frequent hypotension episodes during non-dialysis periods, were included in the study. Dialysis-free periods were recorded with a 24-h Holter rhythm and ambulatory blood pressure monitor device. The time-domain parameters of HRV and HRT, including turbulence onset (TO) and turbulence slope (TS), were calculated.

Results Values for SDNN (105.5 ± 7.02, 127.6 ± 6.2 $p < 0.001$), SDANN (95.1 ± 5.9, 111.8 ± 5.01 $p < 0.001$), and SDNN index (50.04 ± 2.7, 55.6 ± 3.7 $p = 0.03$), in the hypotensive group were significantly lower than in the normotensive group, respectively. Values for RMSSD (26.5 ± 2.5, 27.3 ± 2.7 $p = 0.178$), pNN50 (17 ± 1.7, 55.6 ± 3.7 $p = 0.03$), and Tİ (35.1 ± 3.1, 34.7 ± 2.6 $p = 0.542$) in both groups were not significantly different; however, there was a significant difference between HRT parameters, TO (-1.8 ± 0.37, -2.4 ± 0.39 $p < 0.001$) and TS (6.9 ± 0.71, 8.2 ± 0.97 $p < 0.001$), respectively, hypotensive and normotensive group.

Conclusion Dialysis patients that experience frequent hypotensive episodes may also undergo significant changes in HRT and HRV which may be indicative of serious cardiac sequela. Thus, in such cases, a complete cardiologic evaluation is warranted.

Keywords Arrhythmia · Hemodialysis · Hypotension · Heart rate variability · Heart rate turbulence

Background

Hemodialysis (HD) is a life-sustaining procedure for more than 2.6 million people worldwide [1]. Other than renal replacement, HD is the most common treatment option for patients with end-stage renal disease (ESRD), and without it, most would die within a few weeks [2]. Sudden cardiac death is the main cause of death in the HD population and arrhythmia is considered the main trigger factor for this cohort [3, 4] which has many risk factors for cardiac death. Determining all factors which may lead to cardiac-related death in HD patients is critical. Reliable data have shown that preventing or at least trying to treat arrhythmias might prolong survival in the case of HD patients.

Assessment of the autonomic modulation of the cardiovascular system can be done through the use of several approaches. An example of a non-invasive method for assessment is heart rate variability (HRV). This method evaluates

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heart rate regulation by looking at parasympathetic and sympathetic divisions of the autonomic nervous system to detect changes in the sinus rate. Studies have shown that lower HRV corresponds with greater sympathetic tone, and that higher variability is related with vagal tone [5]. A considerable amount of research has been conducted on HRV in cardiac patients, particularly those who have survived an acute myocardial infarction and those with congestive heart failure and left ventricular dysfunction [6]. Another example of a method for assessment is heart rate turbulence (HRT), which evaluates the physiologic changes that occur in sinus rate following ventricular premature beats (VPBs) to identify baroreflex sensitivity [7]. HRT is measured by examining the impact of turbulence onset (TO) on the initial acceleration of heart rate following a premature beat and of the turbulence slope (TS), which demonstrates subsequent deceleration of heart rate [8]. Numerous studies have indicated there to be a relationship between impaired HRT and mortality in cardiovascular diseases [9].

Intradialytic hypotension occurs during 10–30% of treatments and ranges from asymptomatic episodes to marked compromise of organ perfusion resulting in myocardial ischemia, cardiac arrhythmias, vascular thrombosis, loss of consciousness, seizures, or death [10]. Recurrent HD-induced ischemic cardiac injury (myocardial stunning) is a prominent cause of intradialytic hypotension and is more common at higher ultrafiltration rates and less frequent with longer and more frequent dialysis treatments [11]. In addition, rapid electrolyte changes, heart failure, and autonomic dysfunction may contribute to hypotensive episodes [12]. Like intradialytic hypotension and post-dialysis orthostatic hypotension, myocardial stunning is an independent risk factor for mortality [13]. The hypotensive course persists after HD in many patients which tend to be hypotensive or at the lower limit of the normal range of blood pressure during pre-dialysis periods. Hypotensive episodes lead to a vicious circle of "hypotension-HD and inadequacy-hypervolemia". Each of these factors strongly impacts mortality in HD patients; however, the causative factor for this hypotension is not clear.

In many studies, a relationship between hypotension during dialysis and autonomic dysfunction has been shown; however, there is little data in the literature related to chronic renal failure patients with hypotension during non-dialysis periods. Therefore, we aimed to evaluate cardiac autonomic functions using 24-h HRV and HRT analysis in hypotensive HD patients.

Methods

This study was performed at the Afyonkarahisar Health Science University, Kırıkkale University and Yozgat State Hospital between October 1, 2017 and July 1, 2018, in the Departments of Cardiology and Nephrology. Patients were included in the study from three dialysis units. The study was designed as a cross-sectional study. A total of 89 patients with ESRD, 42 normotensive and 47 with frequent hypotensive episodes who were on maintenance HD treatment (a 4-h HD session, 3 times a week), were enrolled in the study. Patients who had frequent hypotensive attacks were selected from those who had experienced hypotensive episodes at least two times in the last week. Hypotensive episodes were defined as together blood pressure below < 90/60 mmHg (systolic/diastolic) with related symptoms. Patients who were noted as "symptomatic hypotensive" by experienced hemodialysis physicians, were accepted for 24-h ambulatory blood pressure monitoring to determine symptomatic or asymptomatic hypotensive periods in their dialysis-free periods. Ten patients were excluded due to a lack of data and exclusion criteria. Two patients with atrial fibrillation, three patients with severe infection, and five patients using blood pressure or antiarrhythmic drugs were excluded. Also, they were monitored with 24-h Holter to evaluate concomitant rhythm status. The study was approved by the Institutional Local Ethics Committee and all individuals signed an informed consent. The flowchart of our study is given in Fig. 1.

Patients in need of frequent medical and nursing services because of low blood pressure were selected for further evaluation using 24 h ABPM and Holter rhythm monitoring. Our aim was to investigate the contribution of frequent hypotensive status to the cardiac arrhythmic status and autonomic functions in the non-dialysis period. Symptomatic hypotensive episodes were investigated from dialysis registries of patients. Hypotension was defined as the presence of symptoms related to impaired perfusion of vital organs and blood pressure below 90/60 (systolic/diastolic) mmHg. Symptoms associated with hypotension; were defined as dizziness, blackout, fainting, weakness, fatigue, exertional dyspnea, and palpitation. These symptoms were recorded in the patients' files. Patients with hypotension at least twice weekly were included in the study and were selected from patients with signs of hypotension during the non-dialysis period.

In the selection of patients, we largely depended on whether the patients have symptoms, which occurred after a remarkable blood pressure reduction. To exclude the presence of hypotension during dialysis, 24-h rhythm Holter and ABPM were performed during the non-dialysis period. The schedule of hemodialysis of patients' who accepted to join the study was modified according to 24-h rhythm Holter and 24-h ABPM studies' time; the dialysis sessions of patients on the Schedule of "Monday-Wednesday-Friday" were adjusted as Monday–Wednesday–Saturday for once and patients were invited Friday for studies of 24-h rhythm Holter and 24-h ABPM. Also, patients on the Schedule

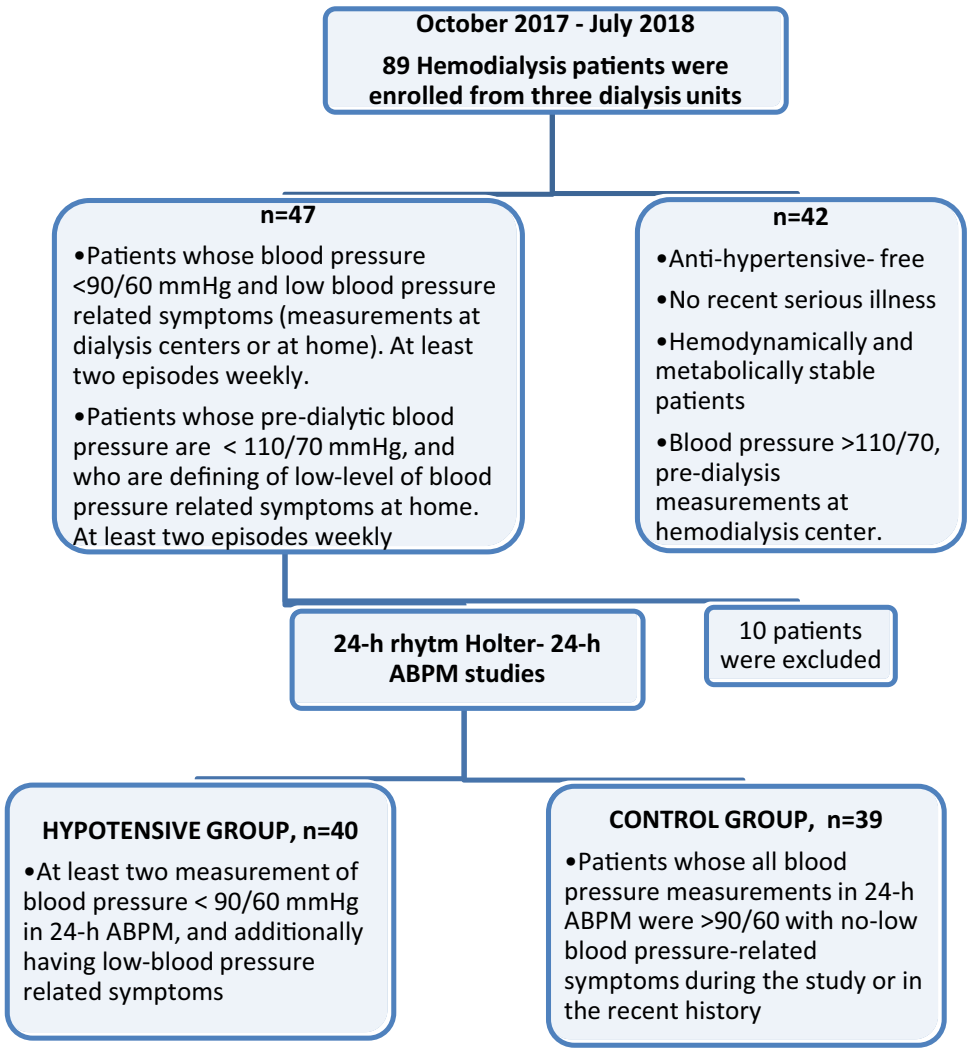

Fig. 1 Study of flowchart. *HD* hemodialysis, *n* number

of "Tuesday-Thursday-Saturday" were invited to study on Monday. All hemodialysis centers were belonged to the state and are a part of the State hospital. Therefore, the practicers of the study were able to have enough time to put off the devices just before the normal sessions. All patients underwent a 24-h ABPM monitoring (CardioSoft Diagnostic Ambulatory Blood Pressure System, General Electric, Boston, USA). Also, laboratory measurements were performed in the interdialytic period together with HRV and HRT measurements.

Exclusion criteria

Patients with thyroid disorders, other hormonal disorders, pregnancy, hypertension, atrial fibrillation, disorders of the autonomic nervous system, patients with severe illnesses which were effecting their appetite, serious infection and neurological diseases were excluded. Patients using drugs such as b-blockers, antihypertensives, antiarrhythmic agents and nitrates that affect heart rate and blood pressure were excluded from the study.

HRT and HRV analysis

All patients underwent a 24-h course of Holter monitoring (Pathfinder Holter Software Version 8.255 of Reynolds Medical, England), after which all Holter recordings were examined and any artifacts the program indicated to be VPBs were rejected. Since the long interdialytic period may be affected the measurements, HRV and HRT measurements were performed during interdialytic period (all tests were performed in between dialysis days). A software program capable of calculating HRT measures, TO and TS were used (HRT analysis program, version 0.60-0.1 of HRT Software, Munich, Germany). TO shows early sinus acceleration and TS, late sinus deceleration following a VPB. In this study, the percent changes in the means of two RR intervals preceding and following a VPB were calculated to determine TO, each of which were calculated separately for all VPBs

before being averaged. To determine TS, for any sequence of five successive RR intervals within the first 20 sinus rhythm intervals following a VPB, the maximum positive slope of a regression line obtained was identified. The value of TS ≤ 2.5 ms/RR and TO ≥ 0% was considered abnormal [14].

For all patients, recordings from their 24-h Holter monitoring were used to calculate the HRV measures, as laid out in the recommendations provided by the North American Society of Pacing and Electrophysiology and the European Society of Cardiology [15]. The data used for time-domain measures of heart rate variability are given in Table 1.

Generally, extremely low values indicate autonomic dysfunction for HRV measures. SDNN reflects all 24-h variability components and circadian rhythms liable for the variability during the recording period. SDANN is a sensitive index of low frequencies such as physical activity, changes in position, and circadian rhythm and provides 24-h variability data. The most common parameters based on interval differences are RMSSD and pNN50. These means to short-term HRV changes and are not related to day/night variations [15, 16]; they reflect alterations in autonomic tone that are predominantly vagally mediated. Compared to pNN50, RMSSD appears more stable and as such should be preferred for clinical use.

Statistical analysis

Statistical analyses were conducted using the SPSS software version 23.0. The variables were analyzed using visual and analytical methods to determine of normally distributed. The mean and standard deviation or median and interquartile ranges were used for descriptive statistics. The Chi-square test was used to compare nominal and categorical variables (gender, hypertension, diabetes, and hyperlipidemia). Parametric data were compared using *t* tests and nonparametric data with Mann–Whitney *U* tests. Based upon a power analysis performed using the Piface application developed by Russel Lenth, we determined that at least 68 patients were required to achieve 95% strength and 5% type 1 error level. To determine the sample size, SD value of the SDNN and SDANN was used in the study of Kida et al. [17]. Correlation analysis was applied using Spearman and Pearson tests. A p value < 0.05 was considered statistically significant.

Results

Demographic characteristics and laboratory results of study participants are shown in Table 2. There were no significant differences in age, gender, or concomitant diseases among the two groups. The only significant difference found between the groups involved HD volume removed which was significantly lower in the hypotensive group ($p < 0.001$).

Patients classified as hypotensive HD were normotensive in 24-h ABPM studies. In addition, this group was substantially non-dipper and most HRV and HRT values were significantly different, compared to normotensive HD patients (Table 3). A dipper pattern (≥ 10% decrease in systolic blood pressure at night) was detected more frequently in the normotensive HD group ($p = 0.01$).

Significantly significant differences were found in SDNN, SDANN index, and SDANN between the hypotensive and normotensive HD groups ($p < 0.001$, $p = 0.003$ and $p < 0.001$, respectively; Table 3). No significant difference was found in the other HRV parameters. HRT parameters TO and TS were calculated in both groups with 24-h Holter recordings showing at least five VPBs appropriate for HRT analysis. Values of TO and TS were significantly lower in the hypotensive HD group ($p < 0.001$, $p < 0.001$, respectively; Table 2).

A significant correlation between HRV and HRT parameters with blood pressure values was determined as shown in Table 4.

Table 1 Time-domain measures of heart rate variability

Variables	Definition	Clinical use
SDNN ms	Standard deviation of all normal to normal intervals	Estimates total HRV
SDANN ms	Standard deviation of the averages of normal to normal intervals in all 5 min segments of the entire recording	Estimates 24 h components of HRV
RMSSD ms	The square root of the mean of the sum of the squares of differences between adjacent normal to normal intervals	Estimates short-term components of HRV
pNN 50%	The number of pairs of adjacent normal to normal intervals differing by more than 50 ms divided by the total number of all NN intervals	Estimates short-term components of HRV
Triangular index	Total number of all normal to normal intervals divided by the height of the histogram of all normal to normal intervals measured on a discrete scale with bins of 7.8125 ms (1/128 s)	Estimates total HRV

Table 2 Baseline demographic and clinical characteristics of study groups

Variables	Hypotensive HD (*n*: 40)	Normotensive HD (*n*: 39)	*p* value
Age (years)	56.95 ± 6.9	57.67 ± 11.4	0.737
Women *n* (%)	17 (42.5%)	21 (53.8%)	0.313
BMI (kg/m^2)	24 ± 2.5	24.7 ± 3	0.229
Diabetes mellitus *n* (%)	19 (47.5%)	18 (46.1%)	0.905
Hyperlipidemia *n* (%)	17 (42.5%)	16 (41%)	0.894
CAD *n* (%)	23 (57.5%)	15 (38.4%)	0.90
Stroke or TİA *n* (%)	7 (17.5%)	5 (12.8%)	0.562
Neuropathy *n* (%)	16 (40%)	13 (33.3%)	0.539
HD duration (years)	9.3 ± 3.6	8.4 ± 2.8	0.209
HD time (h)	3.9 ± 0.17	3.8 ± 0.14	0.732
HD volume removed UFR (ml/h/kg)	6.6 ± 1.5	6.79 ± 1.21	0.534
EF (%)	53.5 ± 6.5	53.6 ± 4.9	0.898
Fasting glucose (mg/dl)	131.2 ± 30.5	134.8 ± 25.1	0.57
Creatinine (mg/dl)	6.5 ± 1.9	6.8 ± 1.8	0.577
Sodium (mmol/dl)	136 ± 2.5	137 ± 2.6	0.136
Potassium (mmol/dl)	4.8 ± 0.81	4.9 ± 0.57	0.955
Calcium (mg/dl)	8.3 ± 0.6	8.2 ± 0.3	0.218
Hemoglobin (mg/dl)	11.3 ± 0.9	11.6 ± 1.6	0.885

HD hemodialysis, *n* number, *BMI* body mass index, *CAD* coronary artery disease, *TİA* transient ischemic attack, *EF* ejection fraction, *UFR* ultra filtration rate

Values are mean ± SD, $p < 0.05$ is significant

Discussion

The association between hypotension and cardiac autonomic functions in HD patients has not been broadly investigated. The current literature focuses on intradialytic hypotension. The evaluation of hypotensive episodes which occur during dialysis-free days has been neglected. Our study aimed to investigate the cardiac autonomic functions of HD patients with frequent hypotensive findings during non-dialysis periods. We found that cardiac autonomic functions deteriorated in HD patients with hypotensive episodes compared to normotensive subjects.

The predictive value of 24-h HRV in HD patients has been demonstrated in a number of studies [18, 19]. For example, in a 5.8-year prospective study conducted by Oikawa et al. with 383 HD patients, it was reported that SDNN < 75 ms independently predicted all-cause and cardiovascular mortality [18]. However, Suzuki et al., in an 87-month follow-up study of 281 HD patients, showed that SDNN had no significant predictive power [20]. The conflicting results could be attributed to differences in the timing of the evaluated 24-h electrocardiography recordings (i.e., over the HD period in the study by Oikawa et al., and between HD sessions in the Suzuki et al. study). Moreover, considering that the daytime–nighttime difference in heart rate strongly impacts the 24-h SDNN [15], this too may be influenced by HD. In cases where there is hemodynamic instability, SDNN has been shown to decrease with HD. Our results revealed SDNN values to be significantly lower in the hypotensive group during non-dialysis times.

Sympathetic overactivity and depressed vagal modulation have been reported in patients with ESRD and those requiring maintenance dialysis [20]. Furthermore, decreased HRV has been demonstrated to be an independent predictor of mortality and sudden death in maintenance HD patients [18, 21, 22]. İn our study, both HRV (SDNN, SDANN, and SDNN index) and HRT (TO and TS) values deteriorated in the hypotensive HD group. Since our patients were identified as having greater impaired cardiac autonomic function outside of dialysis, the probability existed that these patients would be at risk for more pronounced hypotension during dialysis. Hence, HRV and HRT measurements may provide risk-stratification values for early identification of high-risk patients.

Decreases between time interval (SDNN and TI) and frequency-domain HRV measurements have been identified as important predictors of cardiac death, independent of all known death risks for chronic HD patients [22]. Rubinger et al. showed that autonomic control is disrupted in patients with uremic heart injury, strongly associated with hemodynamic imbalance, decreased HRV, and impaired sympathetic balance [23]. Due to the frequency-domain analysis used in their studies, we cannot compare the results, but we can say that our HRV parameters showed similar deterioration. The HRV during 24-h Holter monitoring was lower in our HD patients and demonstrating impaired autonomic function, in agreement with previous studies [18, 21, 23, 24].

Our outcomes show that a significant correlation between lower blood pressure and SDNN–SDANN in HD patients. This finding reinforces the hypothesis that a reduction in blood pressure is strongly associated with the presence and severity of autonomic disfunction. Being non-dipper (ND) is a mortality factor both in general chronic kidney disease patients and the HD population [25–27]. Hypervolemia and autonomic dysfunction can cause a loss of the circadian rhythm of blood pressure in patients undergoing HD. Cardiovascular survival was reported in one study to be poorer in patients who had the ND pattern compared to that of patients who had the dipper pattern, and the study further reported that there was a relationship between high 24-h pulse pressure and nighttime systolic blood pressure and cardiovascular mortality [28]. In a prospective study involving the comparison of ND patients with D patients going through HD, the former was shown to have higher rates of cardiovascular mortality and coronary artery stenosis [29].

Table 3 ABPM and HRV–HRT analysis of study groups

Variables	Hypotensive HD (*n*: 40)	Normotensive HD (*n*: 39)	*p* value
ABPM day S (mmHg)	104.8 ± 1.4	124.5 ± 2.2	0.009*
ABPM day D (mmHg)	65 ± 0.98	79.4 ± 1.9	0.042*
ABPM night S (mmHg)	97 ± 1.5	106.4 ± 2.4	0.160
ABPM night D (mmHg)	61 ± 0.99	68.9 ± 1.6	0.127
ABPM 24 h S (mmHg)	100 ± 1.4	115.3 ± 2.3	0.098
ABPM 24 h D (mmHg)	63 ± 0.91	74.7 ± 1.7	0.011*
Dipper/non-dipper	12/28	23/16	0.010*
Frequency of hypotension in HD, *n* (%)	33/82.5%	25/64.1%	0.064
Pre HD S/D (mmHg)	96/61	125/76	< 0.001*
Post HD S/D (mmHg)	85.5/53	105/67	< 0.001*
Heart rate, beats/min	78 ± 1.07	76 ± 0.85	0.839
SDNN, ms	105.5 ± 7.02	127.6 ± 6.2	< 0.001*
SDNN index, ms	50.4 ± 2.7	55.6 ± 3.7	0.003*
SDANN, ms	95.1 ± 5.9	111.8 ± 5.01	< 0.001*
RMSSD, ms	26.5 ± 2.5	27.3 ± 2.7	0.178
pNN50, %	17 ± 1.7	17.5 ± 2.4	0.288
Triangular index	35.1 ± 3.1	34.7 ± 2.6	0.542
Turbulence onset, %	− 1.8 ± 0.37	− 2.4 ± 0.39	< 0.001*
Turbulence slope, ms/RR	6.9 ± 0.71	8.2 ± 0.97	< 0.001*

HD hemodialysis, *n* number, *ABPM* ambulatory blood pressure monitoring, *HRV* heart rate variability, *HRT* heart rate turbulence, *S* systole, *D* diastole, *$p < 0.05$ statistically significant, *SDNN* standard deviation of all normal to normal intervals, *SDANN* standard deviation of the averages of normal to normal intervals in all 5 min segments of the entire recording, *RMSSD* the square root of the mean of the sum of the squares of differences between adjacent normal to normal intervals, *pNN50* the number of pairs of adjacent normal to normal intervals differing by more than 50 ms divided by the total number of all normal to normal intervals

Table 4 Correlation analysis of HRV–HRT values

SDNN	SDANN	SDANN index	TO	TS
UFR (*r*: 0.102, $p < 0.185$)	UFR (*r*: 0.080, $p < 0.241$)	ABPM day S (*r*: 0.238, *p*: 0.034)	BMI (*r*: − 0.245, *p*: 0.03)	UFR (*r*: 0.162, *p*: 0.444)
ABPM day S (*r*: 0.466, $p < 0.001$)	ABPM day S (*r*: 0.450, $p < 0.001$)	ABPM day D (*r*: 0.227, *p*: 0.044)	UFR (*r*: − 0.24, $p < 0.416$)	ABPM day S (*r*: 0.419, $p < 0.001$)
ABPM day D (*r*: 0.445, $p < 0.001$)	ABPM day D (*r*: 0.488, $p < 0.001$)	Potassium (*r*: 0.233, *p*: 0.039)	ABPM day S (*r*: − 0.335, *p*: 0.003)	ABPM day D (*r*: 0.362, *p*: 0.001)
ABPM night S (*r*: 0.223, *p*: 0.048)	ABPM night S (*r*: 0.229, *p*: 0.042)		ABPM day D (*r*: − 0.345, *p*: 0.002)	ABPM night S (*r*: 0.264, *p*: 0.019)
ABPM night D (*r*: 0.327, *p*: 0.003)	ABPM night D (*r*: 0.345, *p*: 0.002)		ABPM 24/h D (*r*: − 0.258, *p*: 0.022)	ABPM night D (*r*: 0.273, *p*: 0.015)
ABPM 24/h S (*r*: 0.366, *p*: 0.001)	ABPM 24/h S (*r*: 0.357, *p*: 0.001)		Non-dipper (*r*: − 0.286, *p*: 0.011)	ABPM 24/h S (*r*: 0.323, *p*: 0.004)
ABPM 24/h D (*r*: 0.429, $p < 0.001$)	ABPM 24/h D (*r*: 0.449, $p < 0.001$)		Creatinine (*r*: − 0.233, *p*: 0.038)	ABPM 24/h D (*r*: 0.358, *p*: 0.001)
Sodium (*r*: 0.273, *p*: 0.015)	Sodium (*r*: 0.315, *p*: 0.005)			

HD hemodialysis, *HRV* heart rate variability, *HRT* heart rate turbulence, *BMI* body mass index, *SDNN* standard deviation of all NN intervals, *SDANN* standard deviation of the averages of NN intervals in all 5 min segments of the entire recording, *TO* turbulence onset, *TS* turbulence slope, *ABPM* ambulatory blood pressure monitoring, *S* systole, *D* diastole, *H* hour, *r* Pearson correlation coefficient, *UFR* ultra filtration rate

$p < 0.05$ statistically significant

In our study, the majority of hypotensive HD patients were non-dippers. Based on these study results, we surmise that worsened daily blood pressure rhythm in HD patients parallels autonomic dysfunction.

The frequent occurrence of VPBs in HD helps to compute parameters of HRT. HRT measurements refer to a short-term fluctuation in heart rate, triggered by a single VPB [30]. Corrupted heart rate turbulence reflects autonomic dysfunction and is associated with a lot of different situations. Several studies have showed HRT as one of the most potent risk predictors of mortality following acute myocardial infarction [9]. HRT is viewed to be a marker of vagal activity and an independent indicator of total mortality by the European Society of Cardiology [31]. TO and TS values have been shown to be heavily associated with certain HRV parameters, such as SDNN, RMSSD, and TI [9]. In the case of HD patients, it is safe to suggest that HRT provides clinically important information, as autonomic neuropathy has been shown to correspond to a pronounced drop in blood pressure in the course of HD [31]. We found no other investigations to date which have addressed the significance of HRT parameters in hypotensive HD patients. In our study, we determined a correlation between TO and TS with the volume of dialysis and blood pressure and found significant differences between the hypotensive and normotensive HD groups related to these parameters.

Over the years, although there has been clear improvement, the mortality rate for patients undergoing long-term HD has shown little change as a result of the rise in the prevalence of cardiac complications. Therefore, it is important that new diagnosis tests be developed for patients identifying especially high risk for cardiac death. Determining a decrease in HRV may provide unique and clinically useful information for identifying those with an increased risk of cardiac death in this high-risk population with an adverse prognosis. Chronic hypotensive condition in HD patients can be responsible for myocardial ischemia and ischemic cerebrovascular events. We found that evaluation of autonomic function, with easy to apply, might help predict the occurrence of hypotension interdialytic period, thereby defining a high-risk patient group.

Finally, hypotensive episodes in extradialytic periods may be a sign of serious arrhythmias or worse prognosis. In our observations, these patients were able to tolerate HD; however, a deep cardiologic evaluation is mandatory for extended survival.

Study limitation

Our study has some limitations. Primarily, and most significant, was the study's small sample size, an issue that resulted from the challenge of finding PVBs suitable for analysis, a regularly seen problem in HRT studies. We recorded Holter electrocardiography between HD sessions. In general, cardiac arrhythmias occur more frequently during and after HD. Next, it is possible that autonomic functions have an influence on coronary artery disease and diabetes, and given that these pathologies sometimes accompany or often can be caused by ESRD, finding an ESRD population that does not have these diseases, so that the effect of ESRD only on HRV and HRT can be evaluated, is hard. İn addition, this study is not mortality or morbidity work. Therefore, it is needed to check by another work the long-term results of patients who have impaired cardiac autonomic functions. Besides, it is well known 10–15% of hypotensive episodes are the consequence of a neurological event. Our study design is far away to evaluate the patients for further neurologic evaluation. Lastly, false-negative results can occur from non-invasive risk predictors of arrhythmias, such as HRV and HRT.

Conclusion

This study shows the potential value of HRV and HRT evaluation in predicting impaired cardiac autonomic functions in chronic hypotensive HD patients. In our evaluation of HRT and HRV analysis, we found that cardiac autonomic functions deteriorated in chronic hypotensive HD patients compared to normotensive HD patients.

Author contributions ZY: concept and design of study, analysis and interpretation of data, drafting and critical revision of the article. ZY, MED, SA and ÇA: critical revision of the article. ZY and MED: concept and design of study, interpretation of data, critical revision of the article, responsible for the integrity of the data acquired, its analysis and interpretation. All authors read and approved the final manuscript.

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Availability of data and material The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Conflict of interest The author(s) declare(s) that they have no conflicts of interest regarding the publication of this paper.

Ethics approval and consent to participate The study protocol complied with the ethical principles of the Declaration of Helsinki and received full approval from the institutional review boards of Afyonkarahisar Healty Sciences University Ethics Committee (no.2019/284). Under this approval, informed consent was waived.

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