ORIGINAL ARTICLE

The Effect of Diuresis on the Paced QRS Complexes in Pacing-Dependent Patients with Heart Failure

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Background: Augmentation of the amplitude of QRS complexes with diuretic therapy for patients with congestive heart failure has been well documented. However, the effect of diuresis on the paced QRS complexes in pacing-dependent patients with heart failure is scarce.

Objective: To investigate the effect of diuresis on the paced QRS complexes in pacing-dependent patients with heart failure.

Method: Thirty-two consecutive pacing-dependent patients with heart failure were enrolled in this study. Before and after diuresis, the sums of paced QRS amplitude of leads I+II ($\Sigma pQRS_{I+II}$), six limb leads ($\Sigma pQRS_{6L}$), leads V₁–V₃ ($\Sigma pQRS_{V1-V3}$), leads V₄–V₆ ($\Sigma pQRS_{V4-V6}$), leads V₁–V₆ ($\Sigma pQRS_{V1-V6}$), and lead aVR ($pQRS_{aVR}$), paced QRS duration ($pQRS_d$), paced QT intervals (pQT) and the body weight of each patient were measured, then the % changes ($\Delta\%$) in paced electrocardiogram (ECG) variables and the $\Delta\%$ in body weight were evaluated.

Results: Compared with before diuresis, paced ECG variables significantly increased and body weight significantly decreased after diuresis, $\Delta\%$ in paced QRS amplitude(s) in all ECG variables ($\Sigma pQRS_{I+II}$, $\Sigma pQRS_{6L}$, $\Sigma pQRS_{V1-V3}$, $\Sigma pQRS_{V4-V6}$, $\Sigma pQRS_{V1-V6}$, and $pQRS_{aVR}$) correlated well with $\Delta\%$ in body weight ($r = 0.416$, $r = 0.849$, $r = 0.901$, $r = 0.371$, $r = 0.837$, $r = 0.619$, and $P = 0.018$, $P < 0.001$, $P < 0.001$, $P = 0.037$, $P < 0.001$, $P < 0.001$), while there was no correlation between $\Delta\%$ in $pQRS_d$ and pQT and $\Delta\%$ in body weight.

Conclusions: The changes in amplitude of paced QRS complexes may be useful for the monitoring of therapy of pacing-dependent patients with heart failure.

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diuresis; heart failure; electrocardiogram; pace

Increase in the amplitude of QRS complexes resulting from diuretic therapy for patients with congestive heart failure has been documented previously.^{1–5} However, the amplitude of QRS complexes mainly evaluated in these studies is the amplitude of intrinsic QRS complexes, but not the amplitude of paced QRS complexes. Although several previous studies have established limited data demonstrating the amplitude of paced QRS complexes can change in patients with pacemaker implantation under various edematous states,^{6,7} the effect of diuresis on the paced QRS complexes in pacing-dependent patients with heart failure is scarce. The aim of this study was to focus on the

effect of diuresis on the paced QRS complexes in pacing-dependent patients with heart failure.

METHODS

Study Patients

Thirty-two consecutive pacing-dependent patients with heart failure receiving diuresis were recruited in this study between January 2013 and November 2014. The enrollment criteria on admission included dyspnea at rest, pulmonary crackles on chest auscultation, peripheral edema on inspection and deep palpation of the lower

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extremities, and lung congestion on chest radiography. The exclusion criteria consisted of systolic blood pressure below 90 mmHg, serum creatinine above 2 mg/dL, and marked pleural effusion detected by echocardiography on admission, which would have confound the electrocardiogram (ECG)/body weight correlations.

Study Variables

Baseline clinical characteristics of all the participants were obtained. Additionally, parameters included in the study were systolic blood pressure, diastolic blood pressure, BUN, creatinine, electrolytes, hemoglobin (Hb), and hematocrit (Ht), brain natriuretic peptide (BNP) before and after diuresis (7 days diuretic therapy), weight (before and after diuresis), echocardiography (before and after diuresis), and a 12-lead ECG before and after diuresis. Patients were weighed wearing the same clothes both before and after diuresis. Hospital weight scales were calibrated daily for the purpose of this study. The corresponding percentage weight change was calculated as variables. Echocardiographic (Vivid 7 Dimension, GE Medical Systems, Horten, Norway) evaluation was performed with the patient in left lateral decubitus position before and after diuresis. Left ventricular end-systolic diameters (LVESD) and left ventricular end-diastolic diameters (LVEDD) were measured according to the standards of the American Society of Echocardiography.⁸ Left ventricular ejection fraction (LVEF) was measured in accordance with the Simpson's method.⁹

ECGs were recorded before and after diuresis, at paper speed of 25 mm/s and at 10 mm = 1 mV standardization. Measurements of the amplitude (highest positive + lowest negative) deflections of the paced QRS complexes in ECG leads to the nearest 0.5 mm were made by a single doctor blinded to the study, using calipers and a magnifying glass. Because serial ECGs monitoring of precordial leads QRS voltage changes have some potential shortcomings such as the difficulties in accurate placement of electrodes over chest at the same exact localizations every time,¹⁰ in order to overcome this shortcoming, we placed precordial leads via marked thoracic sites when serial ECGs were performed,¹¹⁻¹³ and the evidence that mere ΣQRS_{I+II} or ΣQRS_{6L} could have a role as a bedside index based on an "eye-balling" estimate of QRS amplitude changes in these leads in serial

ECGs obtained at different time points during follow-up of heart failure status in a patient.¹⁴⁻¹⁶ Therefore, before and after diuresis, $\Sigma pQRS_{I+II}$, $\Sigma pQRS_{6L}$, $\Sigma pQRS_{V1-V3}$, $\Sigma pQRS_{V4-V6}$, $\Sigma pQRS_{V1-V6}$, and $pQRS_{aVR}$ and corresponding $\Delta\%$ in $\Sigma pQRS_{I+II}$, $\Sigma pQRS_{6L}$, $\Sigma pQRS_{V1-V3}$, $\Sigma pQRS_{V4-V6}$, $\Sigma pQRS_{V1-V6}$, and $pQRS_{aVR}$ were evaluated for statistical analysis, at the same time, $pQRS_d$ and pQT were measured as previously described,¹⁷ and corresponding $\Delta\%$ in $pQRS_d$ and pQT were evaluated for statistical analysis too.

Diuresis Procedure

Intravenous furosemide was administered in all patients on admission at a dose of 80 mg daily, with a speed of 10 mg/h, and was substituted with oral furosemide 5.2 ± 0.7 days later. Serum level of potassium was monitored, if serum level of potassium was lower than normal, potassium was supplemented until it became normal.

This study is in accordance with the principles outlined in the Declaration of Helsinki and it was approved by local ethics committee. Written informed consent was obtained from all patients.

Statistical Analysis

Normal distributions of variables were tested by Kolmogorov-Smirnov test. Numerical variables with a normal distribution were presented as the mean $\pm$ standard deviation, numerical variables with a skewed distribution were presented as the median (minimum and maximum), categorical variables were expressed as percent (%). Numerical variables before and after diuresis were compared by using paired samples *t*-test or Wilcoxon signed ranks test according to normality test results. Relationships between the continuous variables were evaluated by Pearson's correlation analysis when data were normally distributed. A *P* value <0.05 was considered statistically significant. All statistical studies were carried out with SPSS program (version 17.0, SPSS, Chicago, IL, USA).

RESULTS

Representative ECG of a patient before and after diuresis is shown in Figure 1. The baseline clinical characteristics of the patients are summarized in Table 1. Routine laboratory data and echocardiographic data before and after diuresis

Figure 1. Representative electrocardiogram of a patient before (A) and after (B) diuresis.

are presented in Table 2. Body weight and the paced ECG variables and the corresponding $\Delta\%$ in body weight and $\Delta\%$ in paced ECG variables are shown in Table 3. Compared with before diuresis, the results in Table 3 showed that there was a significant decrease in body weight after diuresis, and there was a drastic increase in the paced ECG variables. Correlation between $\Delta\%$ in paced ECG variables and $\Delta\%$ in body weight is shown in Table 4. The results showed that $\Delta\%$ in $\Sigma pQRS_{I+II}$, $\Sigma pQRS_{6L}$, $\Sigma pQRS_{V1-V3}$, $\Sigma pQRS_{V4-V6}$, $\Sigma pQRS_{V1-V6}$, and $pQRS_{aVR}$ were significantly correlated with $\Delta\%$ in body weight ($r = 0.416$, $r = 0.849$, $r = 0.901$, $r = 0.371$, $r = 0.837$, $r = 0.619$, and $P = 0.018$, $P < 0.001$, $P < 0.001$, $P = 0.037$, $P < 0.001$, $P < 0.001$).

DISCUSSION

The main findings of this study were that the increased paced QRS amplitude(s) in all ECG variables and $pQRS_d$ and pQT consequent to body weight or fluid loss were found in pacing-dependent patients with heart failure after 7 days diuretic therapy, and $\Delta\%$ in paced QRS ampli-

Table 1. Baseline Characteristics of Study Patients

	Patients (n = 32)
Age (years)	72.3 $\pm$ 4.3
Gender (male, %)	22/32 (68.8)
Hypertension (n, %)	16/32 (50)
Diabetes (n, %)	13/32 (40.6)
Etiologies of recommendation for pacemaker implantation	
Sick sinus syndrome (n, %)	19/32 (59.4)
Third-degree atrioventricular block (n, %)	13/32 (40.6)
Duration for pacemaker implantation (years)	5.57 $\pm$ 0.48
Pacing mode	
VVI (n, %)	26/32 (81.3)
DDD (n, %)	6/32 (18.7)
Right ventricular pacing rate (%)	94.6 $\pm$ 3.4
Medications	
ACEI/ARB (%)	23 (71.9)
Calcium channel blockers (%)	10 (31.3)
β -blockers (%)	13 (40.6)
Diuretics (%)	15 (46.9)

tude(s) in all ECG variables were significantly correlated with $\Delta\%$ in body weight.

Increase in the amplitude of QRS complexes resulting from diuretic therapy for patients with congestive heart failure has been documented previously.¹⁻⁵ The mechanism of this phenomenon is not fully clarified, the most popular notion proposed to explain this phenomenon is that these ECG changes correlate with body weight or fluid loss resulting from diuretic therapy for patients with heart failure and are attributed to an increase in the transfer impedance of the ECG potentials mediated by the passive body volume conductor, consequent to fluid loss.¹⁸ In general, fluid loss through diuresis reduces transmissibility, since the fluid resistance is lower compared to the other body's constituents.¹⁹ Therefore, the transfer impedance increases due to withdrawal of fluid during diuresis and QRS amplitude increases, according to Ohm's Law. Based on the mechanism mentioned above, the reason for augmentation of QRS amplitude consequent to body weight or fluid loss in patients with heart failure receiving diuretic therapy is considered to be an extracardiac origin, which is further supported by the stability of the amplitude of intracardiac electrograms in patients with changes in their edematous states, while the voltage of the corresponding surface ECGs changes markedly.²⁰ Additionally, the data from another

Table 2. Laboratory Data and Echocardiographic Data before and after Diuresis

Variable	Before Diuresis	After Diuresis	P Value
Systolic BP (mmHg)	109.1 ± 8.3	108.8 ± 8.1	0.677
Diastolic BP (mmHg)	69.1 ± 4.8	68.8 ± 4.9	0.107
Potassium (mmol/L)	4.17 ± 0.45	4.12 ± 0.43	0.311
Creatinine (mg/dL)	1.62 ± 0.19	1.61 ± 0.19	0.165
Hemoglobin (g/L)	127.1 ± 9.9	128.6 ± 10.9	0.158
Hematocrit (%)	41.9 ± 3.2	42.1 ± 2.9	0.079
BNP (pg/mL)	3542(438–6532)	3501(388–6345)	0.298
LVEDD (mm)	41.1 ± 1.9	40.9 ± 1.9	0.134
LVEDD (mm)	58.6 ± 1.3	58.4 ± 1.2	0.211
LVEF (%)	40.3 ± 3.7	40.5 ± 3.8	0.206

BNP = brain natriuretic peptide; LVEDD = left ventricular end-diastolic diameter; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction.

Table 3. Body Weight and the Paced ECG Variables before and after Diuresis, and the Corresponding $\Delta\%$ in Body Weight and $\Delta\%$ in Paced ECG Variables

Variable	Before Diuresis	After Diuresis	Mean Difference	Percent Difference	P Value
$\Sigma pQRS_{I+II}$ (mm)	10.4 ± 1.4	16.1 ± 1.8	5.7 ± 0.9	54.9 ± 7.7	<0.001
$\Sigma pQRS_{6L}$ (mm)	43.0 ± 2.0	55.4 ± 2.9	12.4 ± 1.1	28.8 ± 1.9	<0.001
$\Sigma pQRSV_{1-3}$ (mm)	24.3 ± 2.1	30.1 ± 2.6	5.7 ± 0.6	23.6 ± 1.7	<0.001
$\Sigma pQRSV_{4-6}$ (mm)	23.7 ± 1.7	33.7 ± 2.5	10.1 ± 1.1	40.9 ± 8.1	<0.001
$\Sigma pQRSV_{1-6}$ (mm)	48.0 ± 2.6	63.8 ± 3.5	15.8 ± 1.4	32.9 ± 2.4	<0.001
$pQRS_{aVR}$ (mm)	5.52 ± 0.5	6.18 ± 0.1	0.67 ± 0.8	12.1 ± 1.2	<0.001
$pQRS_d$ (ms)	17.6 ± 1.5	22.7 ± 1.9	5.1 ± 0.9	28.7 ± 5.9	<0.001
pQT (ms)	457.5 ± 1.7	514.8 ± 18.8	57.3 ± 8.7	12.5 ± 1.8	<0.001
Body weight (Kg)	64.1 ± 4.6	58.1 ± 4.2	6.2 ± 0.9	5.9 ± 1.0	<0.001

$\Delta\%$ = percent changes after diuretic therapy; $\Sigma pQRS_{I+II}$ = the sum of paced QRS amplitude in leads I and II; $\Sigma pQRS_{6L}$ = the sum of paced QRS amplitude in all limb leads; $\Sigma pQRSV_{1-3}$ = the sum of paced QRS amplitude in leads V_1 – V_3 ; $\Sigma pQRSV_{4-6}$ = the sum of paced QRS amplitude in leads V_4 – V_6 ; $\Sigma pQRSV_{1-6}$ = the sum of paced QRS amplitude in leads V_1 – V_6 ; $pQRS_{aVR}$ = the amplitude of paced QRS in lead aVR; $pQRS_d$ = paced QRS duration; pQT = paced QT intervals.

Table 4. Correlation between $\Delta\%$ in Paced ECG Variables and $\Delta\%$ in Body Weight

Variables	R Value	P Value
$\Delta\%$ in $\Sigma pQRS_{I+II}$ vs $\Delta\%$ in body weight	0.416	0.018
$\Delta\%$ in $\Sigma pQRS_{6L}$ vs $\Delta\%$ in body weight	0.849	<0.001
$\Delta\%$ in $\Sigma pQRSV_{1-3}$ vs $\Delta\%$ in body weight	0.901	<0.001
$\Delta\%$ in $\Sigma pQRSV_{4-6}$ vs $\Delta\%$ in body weight	0.371	0.037
$\Delta\%$ in $\Sigma pQRSV_{1-6}$ vs $\Delta\%$ in body weight	0.837	<0.001
$\Delta\%$ in $pQRS_{aVR}$ vs $\Delta\%$ in body weight	0.619	<0.001
$\Delta\%$ in $pQRS_d$ vs $\Delta\%$ in body weight	0.128	0.485
$\Delta\%$ in pQT vs $\Delta\%$ in body weight	–0.107	0.560

$\Delta\%$ = percent changes after diuretic therapy; $\Sigma pQRS_{I+II}$ = the sum of paced QRS amplitude in leads I and II; $\Sigma pQRS_{6L}$ = the sum of paced QRS amplitude in all limb leads; $\Sigma pQRSV_{1-3}$ = the sum of paced QRS amplitude in leads V_1 – V_3 ; $\Sigma pQRSV_{4-6}$ = the sum of paced QRS amplitude in leads V_4 – V_6 ; $\Sigma pQRSV_{1-6}$ = the sum of paced QRS amplitude in leads V_1 – V_6 ; $pQRS_{aVR}$ = the amplitude of paced QRS in lead aVR; $pQRS_d$ = paced QRS duration; pQT = paced QT intervals.

study reported by Madias⁷ also supported this notion, in his study, the author found that there were differences in the amplitude of pacemaker stimuli of surface ECGs in patients with pacemaker implantation under various edematous states. As is well known, the output of pacemaker stimuli of

a pacemaker with normal function always keeps constant,⁷ hence, the reason leading to changes of the amplitude of pacemaker stimuli of surface ECGs in patients with pacemaker implantation under various edematous states should be an extracardiac origin. In this study, we found that

the paced QRS amplitude(s) in all ECG variables increased consequent to body weight or fluid loss in pacing-dependent patients with heart failure after diuresis, as already mentioned above, the output of pacemaker stimuli of a pacemaker with normal function always keeps constant,⁷ consequently, the ventricular activation stemming from the same pacemaker stimuli in pacing-dependent patients with heart failure might be the same before and after diuresis, therefore, the changes of paced QRS amplitude(s) in all ECG variables consequent to body weight or fluid loss in pacing-dependent patients with heart failure after diuresis implied that extracardiac origin was associated with these ECG changes.

What is novel about this study is that the increased paced QRS amplitude(s) in all ECG variables consequent to body weight or fluid loss were found in pacing-dependent patients with heart failure after diuresis, and $\Delta\%$ in paced QRS amplitude(s) in all ECG variables were significantly correlated with $\Delta\%$ in body weight. Although the amplitude of QRS complexes increased resulting from diuretic therapy for patients with congestive heart failure has been established previously,¹⁻⁵ the study patients in these studies were those who did not receive pacemaker implantation, and the amplitude of QRS complexes mainly evaluated was the amplitude of intrinsic QRS complexes, but not the amplitude of paced QRS complexes. In the present study, we found that the sums of $\Sigma pQRS_{I+II}$, $\Sigma pQRS_{6L}$, $\Sigma pQRS_{V1-V3}$, $\Sigma pQRS_{V4-V6}$, $\Sigma pQRS_{V1-V6}$, and $pQRS_{aVR}$ increased consequent to body weight or fluid loss in pacing-dependent patients with heart failure after diuresis, which was partially consistent with the results reported by Madias that the amplitude of paced QRS complexes can increase via hemodialysis or body weight loss in patients with pacemaker implantation,^{6,7} but the number of patients in his studies was very small and the effect of diuresis on the amplitude of paced QRS complexes was not evaluated.

There are other potential influences on the surface ECG in patients undergoing diuresis, which includes increase in Hb/Ht due to hemoconcentration, alleviation of cardiomegaly, and serum potassium changes. Both an increase in Hb/Ht and an alleviation of cardiomegaly are expected to be associated with a decrease in the amplitude of QRS complexes as shown in previous studies,^{21,22} the opposite of what was observed in this study. In addition, potassium changes are thought to have a number of influences on the ECG morphology,

mainly affecting the T waves and the ST segments. However, the Hb/Ht, cardiac volume indicated by LVESD and LVEDD, and serum potassium levels after diuresis all had no significant changes when compared with before diuresis, which implied that these factors were not the causes of increased paced QRS amplitude(s) in all ECG variables consequent to body weight or fluid loss in pacing-dependent patients with heart failure after diuresis. Based on $\Delta\%$ in paced QRS amplitude(s) in all ECG variables were significantly correlated with $\Delta\%$ in body weight, which suggested that the main reason for paced QRS amplitude increased with diuresis in pacing-dependent patients with heart failure was the loss of interstitial fluid and resultant body weight loss.

As mentioned above, the changes of the amplitude of QRS complexes in patients with heart failure may represent their various edematous states, therefore, a previous study has proposed the notion that the changes of the amplitude of QRS complexes may be as same sensitive as BNP for monitoring heart failure patients.¹³ However, in the present study, the paced QRS amplitude(s) in all ECG variables in our patients after diuresis increased significantly, the serum BNP in our patients after diuresis had no significant change when compared with before diuresis. Several reasons might be associated with no obvious change of serum BNP in our patients after diuresis. First, the study patients in our study are those who are pacing-dependent and with heart failure, which is different from the study patients in other studies, might contribute to no obvious change of serum BNP in our patients after diuresis. Another reason for no obvious change of serum BNP in our patients after diuresis was the relatively short duration of diuresis, because it has been reported that relatively long time is needed for serum BNP change in a hormone level secreted by the structural and functional changes in the geometry of ventricles.¹⁰

Additionally, similar to previous studies' results that the QRS duration and QT intervals increased as a consequence of increase in the amplitude of QRS complexes in heart failure patients with alleviation of edematous states,^{23,24} we found that the $pQRS_d$ and pQT increased along with the increase in paced QRS amplitude(s) in all ECG variables in pacing-dependent patients with heart failure after diuresis.

The present study has some limitations. First of all, the number of the patients in this study was

small, the results should be verified in large clinical trials. Second, the amplitude of pacemaker stimulus, which has been shown to have comparable changes similar to their corresponding amplitude of paced QRS complexes with perturbations of peripheral edema,⁷ was not evaluated in this study, because there was a great deal of "overshooting" of pacemaker stimulus in recorded ECGs, which would have an effect on accurate measurement of the amplitude of pacemaker stimulus. Finally, we did not use automated ECG measurements with computerized algorithms due to the inconvenience of the software used in our ECG recorder in determining the amplitude of paced QRS complexes, undoubtedly automated ECG measurements would probably more precise than time-consuming manual measurements employed in this study.

In conclusion, the increased paced QRS amplitude(s) in all ECG variables and pQRS_d and pQT consequent to body weight or fluid loss were found in pacing-dependent patients with heart failure after 7 days diuretic therapy, and $\Delta\%$ in paced QRS amplitude(s) in all ECG variables were significantly correlated with $\Delta\%$ in body weight, which suggests that the changes in amplitude of paced QRS complexes may be useful for the monitoring of therapy of pacing-dependent patients with heart failure.

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