U Wave Features in Body Surface Potential Mapping in Post-Myocardial Infarction Patients

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Background: The data on U wave features in post-myocardial infarction (MI) remain sparse. We employed 120-lead body surface potential mapping (BSPM) to explore the U wave in patients with remote MI.

Methods: Sixty post-MI patients and 46 healthy controls were examined. After signal averaging, the polarity changes of U wave related to the T wave were analyzed, and the spatial and temporal U wave parameters were computed.

Results: Four types of patterns based on T and U polarity were recognized. A pattern with positive T and U waves was related to better ventricular function. The study groups did not differ as regards to Tend-Uapex and Tapex-Uapex intervals whereas Uapex-Uend was significantly longer in MI patients (110 ± 20 ms vs. 100 ± 13 ms, $P = 0.004$). MI patients had significantly higher U wave maximum amplitude (70 ± 30 μ V vs. 50 ± 20 μ V, $P < 0.001$), and U integral area (3.96 ± 1.50 μ V·s vs. 3.17 ± 0.99 μ V·s, $P = 0.002$), but lower corresponding T wave parameter values, thus resulting into higher U/T maximum amplitude and area ratios (0.16 ± 0.10 vs. 0.09 ± 0.04 , $P < 0.001$; and 0.13 ± 0.06 vs. 0.09 ± 0.03 , $P < 0.001$). In comparison to 12-lead ECG, BSPM covering the entire thorax enhanced the detection of U waves.

Conclusion: MI tends to increase the U amplitude and prolong the later part of U wave duration thus augmenting the U wave. The size and location of infarction were associated with specific T and U wave polarity patterns.

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U wave; body surface potential mapping; myocardial infarction; repolarization

INTRODUCTION

The features of U wave, defined as a small deflection after T wave in ECG, were first described in detail in different clinical conditions by Lepeschkin.¹ Since then, new data on the subject have been sparse mainly because U wave in conventional 12-lead ECG is hard to discern, especially in the presence of tachycardia or a notched T wave or biphasic T-U waves. However, it is conceivable that U waves may have a role

in the detection of repolarization abnormalities in various cardiac diseases. Therefore, it is necessary to employ more efficient methods to explore the normal and abnormal U wave.

So far, studies on “abnormal” U wave have focused on polarity changes at the acute phase of ischemic heart disease.^{2–4} Previous data have shown that abnormalities in the repolarization period, mainly represented by T wave variables, are associated with arrhythmia propensity in various cardiac pathologies including myocardial

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infarction (MI).^{5,6} In long QT syndrome (LQTS) U wave related to T wave amplitude parameter serves as a predictor of ventricular arrhythmias.⁷ Yet, the spatial and temporal features of U wave in post-MI patients remain unclear. The purpose of this study was to investigate the characteristics of U wave in post-MI patients applying 120-lead body surface potential mapping (BSPM). Conventional 12-lead ECG was registered for comparison.

METHODS

Study Population

Post Myocardial Infarction Patients

A total of 60 patients (10 females) with remote MI (≥ 6 months) were included in the study. Coronary arteriography was performed and left ventricular ejection fraction (LVEF) was obtained from cineangiograms. Patients with atrial fibrillation were excluded from the study. All antiarrhythmic medications were discontinued at least five half-lives before the BSPM registrations.

Healthy Controls

Healthy volunteers served as a control group ($n = 46$, 8 females), in which significant cardiovascular disease was excluded by a normal 12-lead ECG and a bicycle treadmill test.

All study individuals gave their written informed consent and the Institutional Ethical Review Board approved the study protocol. The study complies with the Declaration of Helsinki.

BSPM Recording and Signal Processing

BSPM recording was performed in sinus rhythm in supine position for 5 minutes at rest according to our practice.⁸ Both BSPM acquisition system and Ag-AgCl electrodes were custom-made by Department of Biomedical Engineering and Computational Science of Aalto University, Finland. In brief, 18 vertical strips containing 120 leads covering both anterior (63 leads) and posterior (57 leads) thorax were used (Fig. 1). The limb leads were recorded conventionally and Wilson's central terminal was taken as the reference point for all the chest leads. After band-pass filtering at 0.16–300 Hz, the signals were digitized with a sampling frequency of 1000 Hz.

Next, the data were transferred to a personal computer. An experienced cardiologist blinded to the clinical data analyzed the signals using custom-made software.^{9,10} Signal averaging of 100–150 sinus beats was performed to improve the signal-to-noise ratio. The beats were matched based on maximum cross correlation criteria between the beats and a selected template beat. During averaging, extremely noisy beats and ventricular extra beats were automatically rejected. After averaging, conventional 12-lead ECG leads not enclosed in the BSPM recording were derived by interpolation thus yielding a complete 12-lead ECG.

Next, the onset and offset of QRS together with T and U wave fiducial points (T and U wave apex, T and U wave end) were separately identified with an automated algorithm.^{10,11} U wave apex was determined as the peak of a parabola fitted to the highest amplitude deviation from the baseline after T wave. Similarly to T wave end, U wave end was defined as the intersection point of the steepest tangent fitted to the descending limb of U wave and U-P baseline. The onset of the U wave was determined as the nadir of the TU junction. U wave could be magnified by changing scale to clearly and repeatedly check the fiducial points to improve reliability. In addition, both tiled and overlapped layouts of the multiple BSPM channels could be displayed with the software thus facilitating the determination of the TU and UP junctions (Fig. 2). BSPM channels were excluded from further analyses if there was a biphasic U or T wave or if the U wave amplitude was $< 10 \mu\text{V}$. In addition, leads with the time interval from Tapex to Uapex was < 150 ms were rejected; in these cases the second deflection was recognized as the T_2 wave.¹² Study subjects with less than 10 accepted channels were not included in the final analysis.

T-U Morphology Analyses and Parameter Measurements

U wave morphology and polarity changes related to preceding T wave were examined in anterior precordium where both U and T waves present positive deflections and largest signals in healthy subjects according to previous data.¹³ The following parameters were computed:

Mean of cardiac cycle length (RR).

QU interval corrected to heart rate by Bazett formula (QUc).

Figure 1. BSPM electrode (channel) layout. Dark squares represent the sites of precordial leads of 12-lead ECG. The rectangle within dashed lines marks the area where U and T waves always present the same positive deflection in the healthy controls.

- Time interval from Tapex to Uapex (Ta-Ua).
- Time interval from Tend to Uapex (Te-Ua).
- Time interval from nadir of TU junction to Uend (U duration).
- Time interval from Uapex to Uend (Ua-Ue).
- Maximum absolute amplitude value of monophasic U wave (Umaxamp).
- Maximum absolute amplitude value of monophasic T wave (Tmaxamp).
- Mean of absolute integral area of monophasic U wave (Uarea).
- Mean of absolute integral area of monophasic T wave (Tarea).
- Ratio of Uarea to Tarea (U/Tarea ratio).
- Ratio of Umaxamp to Tmaxamp (U/Tmaxamp ratio).

The parameter values were computed as the average values of all the accepted channels.

Construction of Isovalue maps

Isovalue maps, representing the values over body surface, were constructed by setting the values measured in each unipolar lead to the corresponding position on the torso and the value in space between the measurement points after interpolation. In the present study, the isovalue maps were constructed from the voltage at the peak of the U and T waves.

Statistical Analysis

All continuous variables are presented as mean ± SD and discrete variables as frequencies and percentages. Comparisons of variables were performed using the Student's *t*-test (paired and unpaired), One-way ANOVA or chi-square test. Linear regression and correlation analyses were

Figure 2. Illustration of BSPM channels tiled layout (upper panel) and overlapped layout (lower panel). Onset and offset of QRS complex, fiducial points of T and U wave apex and end were separately identified by the vertical lines with the custom-made software. The channels with the crosses were rejected from the final U wave analysis. Arrow indicates the onset of U wave determined manually as the nadir of TU junction.

Table 1. Parameters in BSPM

Parameters	Control Group (n = 45)	MI Group (n = 56)	P-value
Accepted Channels (n)	39 ± 18	54 ± 15	<0.001
RR (ms) (minimum–maximum)	982 ± 128 (750–1290)	1012 ± 135 (770–1350)	0.25
Ta-Ua (ms)	213 ± 24	212 ± 29	0.85
Te-Ua (ms)	136 ± 25	134 ± 27	0.74
U duration (ms)	238 ± 27	243 ± 32	0.43
Ua-Ue (ms)	100 ± 13	110 ± 20	0.004
QUc (ms)	637 ± 29	650 ± 34	0.03
Umaxamp (μV)	50 ± 20	70 ± 30	<0.001
U/Tmaxamp ratio	0.09 ± 0.04	0.16 ± 0.10	<0.001
Uarea (μV·s)	3.17 ± 0.99	3.96 ± 1.50	0.002
Tarea (μV·s)	40.43 ± 16.20	35.27 ± 15.19	0.11
U/Tarea ratio	0.09 ± 0.03	0.13 ± 0.06	<0.001

Full name of the parameters see text.

used to study the relationships between the variables. A two-tailed P-value ≤ 0.05 was considered statistically significant. Statistical analyses were carried out with SPSS version 13.0 software package (SPSS Inc, Chicago, IL, USA).

RESULTS

Subjects Characteristics

One healthy control and four patients were excluded from the final analysis due to all of the U wave amplitudes $<10 \mu\text{V}$ (three cases) or the number of accepted channels less than 10 (two cases). Altogether, 101 subjects (56 patients and 45 controls) were eligible for U wave analysis. The groups were similar as regards to age (54 ± 13 vs. 59 ± 6 years old, $P = \text{NS}$) and gender. The LVEF was $34 \pm 9\%$ in MI patients. Twelve (21%) patients had suffered anterior, 16 (29%) inferior, and 28 (50%) both anterior and inferior MIs.

Observations of the U Wave and T-U Pattern in BSPM

Healthy Controls

U wave in BSPM was more prevalent in MI patients compared to healthy controls (54 ± 15 vs. 39 ± 18 channels, $P < 0.001$, Table 1). The U and T waves always presented the same positive direction in the area of strip row 4 to 5 of column 4 to 10 approximately corresponding to leads V_1 – V_4 in 12 lead ECG. The strongest U wave signals presenting positive deflections were generally located on the anterior left chest in strip rows 4 or 5 (Fig. 1), most frequently at channels 39 and 46. The

highest U and T waves were found in the same channel in only seven cases whereas in most cases they were in separate although closely located channels.

Post Infarction Patients

Based on the findings in healthy controls, four types of T-U patterns presenting in the precordial leads could be identified (Fig. 3):

- 1) Positive T and U wave pattern (T+U+) (n = 16);
2. TU negative pattern (T-U-) (n = 22): T wave with U wave gradually changing from positive to biphasic then to negative, resulting in TU negative concordance generally from lead 61 extending to left flank;
3. Negative T wave with positive U wave pattern (T-U+) (n = 12);
4. Positive T wave with negative U wave pattern (T+U-) (n = 6).

T+U- pattern was the least common and not observed in any patient with anterior infarction alone. In contrast, T-U- pattern was the most common and more often related to history of both anterior and inferior infarction.

Patients with T+U+ (n = 16) pattern had more preserved ventricular function with the LVEF of $38.9 \pm 9.2\%$ compared to others with $32.1 \pm 7.8\%$ in T-U+ pattern, $31.5 \pm 5.5\%$ in T+U- pattern, and $32.9 \pm 9.2\%$ in T-U- pattern, respectively ($P = 0.042$).

Time Interval and Amplitude Parameters

There were no significant differences in the time domain parameters except the later part of the

Figure 3. Demonstration of T-U wave pattern in MI patients. Isovoltage maps constructed from the voltage at the peak of the T wave (upper part of each left-hand panel) and U wave (lower part of each left-hand panel) and corresponding electrocardiographic illustration with overlapped layout (right-hand panel). Grey gradient ribbon displays the amplitude range of T and U wave, respectively. Dark squares represent the positions of the electrodes. Amplitude unit: mV. Electrocardiographic magnification 5 $\times$.

A: T+U+ pattern; B: T-U- pattern; C: T-U+ pattern; D: T+U- pattern.
Channel 39, 54, 68 and Channel 68.

U wave (Ua-Ue, $P = 0.004$) and QUC interval ($P = 0.03$) between the two groups (Table 1). Compared to healthy controls, MI patients had significantly higher Umaxamp ($70 \pm 30 \mu\text{V}$ vs. $50 \pm 20 \mu\text{V}$, $P < 0.001$) and Uarea ($3.96 \pm 1.50 \mu\text{V}\cdot\text{s}$ vs. $3.17 \pm 0.99 \mu\text{V}\cdot\text{s}$, $P = 0.002$). However, Tmaxamp and Tarea tended to be lower in MI patients, although not significantly. Accordingly, MI group showed higher U/Tmaxamp and U/T area ratios ($P < 0.001$ for both, Table 1).

Correlation analysis showed that Uarea was strongly correlated with Umaxamp ($r = 0.840$, $P < 0.001$), but not with Tmaxamp and Tarea. U amplitude parameters had no correlation with age in either control or patient group. In MI group, regression analysis showed that neither Umaxamp nor U duration had any relation with infarct location or LVEF.

BSPM vs. ECG

In 12-lead ECG, two more MI cases were excluded from the analysis because of low amplitude of U wave. However, these patients showed prominent U waves in BSPM in areas not covered by 12-lead. In general, BSPM displayed a wider distribution of the highest U waves in MI patients compared to controls and this difference could not be detected in 12-lead ECG.

In comparison between ECG and BSPM, the amplitudes of the highest U waves of the controls were significantly lower in ECG than in BSPM ($49 \pm 20 \mu\text{V}$ vs. $54 \pm 19 \mu\text{V}$, $P < 0.001$), but almost the same in MI group ($70 \pm 28 \mu\text{V}$ vs. $70 \pm 29 \mu\text{V}$, $P = 0.962$).

DISCUSSION

U Wave Morphology Features and T-U Pattern in BSPM Recordings

To the best of our knowledge, this is the first study to employ 120-lead BSPM to compare U wave features in healthy controls and in the chronic phase of ischemic heart disease where a more complicated U wave morphology variation and T-U pattern over the body surface can be expected. First of all, the findings in healthy controls provide the criteria for normality of the T and U wave polarities; both U and T waves present positive deflections in the leads corresponding to the area covered by leads V₁-V₄

of the ECG instead of all precordial channels, which is slightly at variance with the previous observations.^{1,13} This somewhat subversive finding may be due to individual variations in the distribution of U waves in body surface.

In MI patients, four types of "abnormal" U waves with respect to the preceding T wave were identified and labeled following the designation first introduced by Reinig et al.¹⁴ However, we found more complicated patterns with negative U waves especially in T-U- and T+U- types.

The most common pattern, T-U- pattern, is of particular interest due to a complicated U wave and T-U junction, in which a negative U wave combined with a negative T wave is generally located in the left flank channels (Fig. 3). Previous publications reported that U wave vector tends to be directed away from the site of an akinetic or dyskinetic region suggesting that U wave inversion could be due to asynchronous segmental early ventricular relaxation, which is closely linked with regional ventricular abnormality.¹⁵⁻¹⁷ Kanemodo et al. demonstrated that negative U waves in left precordial leads after anterior MI reflected a large infarct area.¹⁸ In this study, negative U waves in T-U- pattern were more often observed in patients with a history of both anterior and inferior infarction, which is consistent with their findings and might be one of the manifestations of extensive myocardial injury.

The T+U- pattern displays a negative U wave connected with positive T wave in a larger area from right precordial leads to left flank. It is better related with an inferior than anterior infarction and it is the only pattern not related to pure anterior infarction. Thus, a negative U wave is not specific for anterior infarction. It also implies a possibility of a U wave associating with right ventricular infarction since about 50% of inferior infarcts also involve the right ventricle and the U wave inversion exhibits in right precordial channels.^{19,20}

Some previous studies investigated the clinical significance of a negative U wave in patients with old MI focusing mainly on its relation with left ventricular function.^{18,21,22} Somewhat conflicting results led to contradictory conclusions, which is probably attributed to the isolated analysis of a negative U wave. Considering the association between a negative U wave and decreased ventricular function, the present study showed lower LVEFs in patterns with either negative U wave, negative T wave, or both. In contrast, the

pattern with positive T and U waves was associated with better ventricular function. This finding suggests that U wave analysis alone is not an indicator of cardiac function.

U Wave Parameters in BSPM Recording

In post infarction patients, U and T waves showed disparate behavior. The T wave amplitude decreased whereas U wave enlarged thus producing higher U/T amplitude ratio. Diverse factors, such as exercise, sympathomimetic stimulation, and antiarrhythmic drugs tend to increase the amplitude of the U wave and display the similar TU wave behavior in healthy population thus indicating that U wave is a distinct component of cardiac repolarization in both physiological and pathological conditions.^{1, 16, 23}

However, unlike the physiological augmentation of U wave in healthy individuals, the U time domain parameters with respect to T wave (Ta-Ua and Te-Ua) in post-MI patients remain unchanged at resting heart rates (Table 1). The temporal relation between T and U waves was not affected in this MI population. In contrast to positive inotropic action of exogenous catecholamines, infarcted myocardium shows impaired function (LVEF was $34 \pm 9\%$). It seems paradoxical that both enhanced and impaired ventricular contractility similarly enhance the U wave. However, during the process of structural remodeling after infarction, cardiac function may be initially protected and later detrimentally influenced by the remodeling of ion-channel and ion-transport functions. This disease-induced ion-channel remodeling including alterations in K^+ and Ca^{2+} currents finally results in the enhancement of early and delayed afterdepolarizations.²⁴ Even though the genesis of U wave is poorly understood, afterdepolarization is thought to be one of the mechanisms candidate, which probably explains the augmented U wave in post-MI patients. Thus, arrhythmia tendency in post-MI cardiac dysfunction could in part be attributed to enhanced early or delayed afterdepolarizations. From this point of view, the relevance of augmented U wave to ventricular arrhythmias in post-MI patients is worthy of further exploration.

We are aware of only one previous report associating MI and increased U wave, which was in the setting of a strictly posterior infarction.²⁵ In the present study, infarct location did not affect the results in this respect.

BSPM vs. ECG

As an extension of the 12-lead ECG, BSPM has been previously applied in the studies such as VT localization and detection of late potentials and ischemia. In the present study BSPM allowed more detailed detection of thoracic distribution of cardiac potentials and enhanced U wave detection, thus leading to more accurate recognition of the U wave distribution, U-T patterns, and U polarity changes (Figs. 2 and 3). In healthy controls, the different locations of the highest U and T waves demonstrate that the U wave vector is not identical to T wave vector. This is inconsistent with previous conclusions derived from 12-lead ECG data. In addition, lower U maximum amplitude value in ECG indicates that highest U wave is not always located at the area covered by 12-lead ECG. In MI patients, the highest U waves tended to display wide distribution extending to areas not covered by 12-lead ECG. In addition, isovalue maps constructed from the voltage at the peak of the U and T waves visually display the amplitude and polarity changes of the U and T waves over body surface (Fig. 3). In the present study, superimposition of multiple BSPM channels proved helpful in the identification of barely discernible U-waves. Thus, in the U wave analysis BSPM seems to have particular advantages compared to 12-lead ECG.

Study Limitations

The number of accepted channels in the control group was smaller than that in the patient group being mostly due to less discernible U waves in the back electrodes in control patients. The reason is not entirely clear but may be related to the overall tendency to larger (and thus more distinct) U waves in MI patients. However, the most prominent U waves were mostly located at the front left torso and therefore this difference on the number of accepted channels is not supposed to have a marked influence on the main findings.

We did not repeat the BSPM registrations and thus we have no data on the evolution of the U-wave in different phases after MI. The number of the studied individuals was relatively small and a study with a larger population is warranted to confirm the findings.

CONCLUSION

MI tends to increase the U wave amplitude and prolongs the later part of the U wave without changing the temporal relation between T and U waves at resting heart rate. U wave polarity should be analyzed with respect to the preceding T wave. Negative U wave combined with a positive T wave in the precordial leads is more likely associated with inferior than anterior infarction. T-U negative concordance is probably a manifestation of a large infarction. U wave features and T-U patterns in post infarction patients can be better displayed in BSPM compared to conventional ECG.

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