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Detection and evaluation of ventricular repolarization alternans: An approach to combined ECG, thoracic impedance, and beat-to-beat heart rate variability analysis

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ABSTRACT

Background and objective: Beat-to-beat alteration in ventricles repolarization reflected by alternans of amplitude and/or shape of ECG S-T,T segment (TWA) is known as phenomena related with risk of severe arrhythmias leading to sudden cardiac death. Technical difficulties have caused limited its usage in clinical diagnostics. Possibilities to register and analyze multimodal signals reflecting heart activity inspired search for new technical solutions. First objective of this study was to test whether thoracic impedance signal and beat-to-beat heart rate reflect repolarization alternans detected as TWA. The second objective was revelation of multimodal signal features more comprehensively representing the phenomena and increasing its prognostic usefulness.

Materials and methods: ECG, and thoracic impedance signal recordings made during 24 h follow-up of the patients hospitalized in acute phase of myocardial infarction were used for investigation. Signal morphology variations reflecting estimates were obtained by the principal component analysis-based method. Clinical outcomes of patients (survival and/or rehospitalization in 6 and 12 months) were compared to repolarization alternans and heart rate variability estimates.

Results: Repolarization alternans detected as TWA was also reflected in estimates of thoracic impedance signal shape and variation in beat-to-beat heart rate. All these parameters

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showed correlation with clinical outcomes of patients. The strongest significant correlation showed magnitude of alternans in estimates of thoracic impedance signal shape.

Conclusions: The features of ECG, thoracic impedance signal and beat-to-beat variability of heart rate, give comprehensive estimates of repolarization alternans, which correlate, with clinical outcomes of the patients and we recommend using them to improve diagnostic reliability.

1. Introduction

Visible ECG T-wave alternans (TWA), a beat-to-beat alternation in amplitude and/or morphology of the S-T segment and T wave, has been observed for over a century and was reported to be a predictor of sudden cardiac death [1]. The phenomenon occurs in association with life-threatening arrhythmias in patients with acute coronary syndrome and heart failure. Experimental [2,3] and clinical [4] studies indicate that TWA appears in cases of temporal–spatial heterogeneity of ventricular repolarization, which is a critical factor in arrhythmogenesis arising in different cardiac pathologies. The phenomena can establish the preconditions for conduction block, reentry, and life-threatening arrhythmias what may cause sudden cardiac death [5,6].

Detection and evaluation of TWA over the last two decades has evolved from visual inspection of the ECG to the use of computerized analytical methods for detection of non-visible TWA in the microvolt range. The variety of methods ranges from the widely-used spectral methods, e.g. [7], through correlation methods, e.g. [8], to sophisticated multivariate analysis methods including truncated representation of the signals by means of Karhunen–Loève transform [9] or Principal component analysis [10]. The review of methods for detection and evaluation of TWA is given in [11]. Clinical usefulness or predictive value of results obtained by particular method should be concerned as main estimate to evaluate quality of newly designed method. Gehi with co-authors [12] provides meta-analysis results about clinical usefulness of methods for detection and evaluation of TWA rising hesitations that unfortunately the results of existing methods did not reveal any incremental prognostic usefulness. Most of elaborated methods are tested on clinical recordings where TWA was evoked by atrial pacing or using recordings of healthy and ischemic patients. Such rough evaluation usually does not show any incremental prognostic usefulness and could be the main reason for hesitations expressed in [12]. On the other hand, ECG signals used in mentioned studies only partially reflect repolarization alternans. The mechanism of the phenomena primarily relates to abnormalities in intracellular calcium cycling between the sarcoplasmic reticulum and cytosol. It leads to alternation of cytosolic calcium and corresponding changes in action potential morphology via sarcolemmal calcium-sensitive ion channels [13,14]. The detailed electrophysiological and ionic mechanisms underlying TWA have been also reviewed in [5,15]. Calcium alternans also causes mechanical alternans that manifests as alternans of peak tension in in vitro papillary muscle preparations [16] or as pulse alternans in vivo [17]. Concurrent alternans in electrical and mechanical action of the heart is reported in [18]. Thoracic impedance signal (actually first derivative of it) registered during routine noninvasive investigations reflects mechanical action of the heart muscle. So it is expected that amplitude and/or morphological properties of this signal can reflect repolarization alternans.

Alternans in amplitude of peak arterial blood pressure was observed in association with beat-to-beat alternans of heart rate. The incidence of occurred alternans phenomena is associated with the severity of the impaired cardiac performance [19]. Voss and co-authors [20] showed that extended analysis of electrical, hemodynamical and heart rate alternans could be useful for enhanced characterization of patients with dilated cardiomyopathy. Appearance of microscopic systolic pressure alternans was found in episodes of TWA evoked by atrial pacing in cardiomyopathy patients analyzing finger pressure sensor and micro manometer-tipped catheter signals [21].

The aim of this study was to investigate possible reflection of repolarization alternans in thoracic impedance signal and beat-to-beat RR intervals, as alternatives to ECG analysis based detection of TWA. For investigation we used clinical recordings of patients in acute phase of myocardial, because it is reported that specific TWA is present in such cases [22]. We have all clinical records of these patients corresponding to recorded signals what allowed us to compare repolarization alternans estimates with clinical outcomes. We expect that combination of methods based on analysis of several alternative signals can give more comprehensive representation of repolarization alternans phenomena and reveal additional features increasing prognostic usefulness of the investigation.

2. Materials and methods

2.1. *Signals and patients*

Clinical recordings of the signals for investigation were taken from 24 h follow up of the patients hospitalized in the acute phase of myocardial infarction in Department of Cardiology of Lithuanian University of Health Sciences in Kaunas (Permission of Kaunas Region Ethics Committee for Biomedical Research Nr. 169/2004). Thoracic impedance signal together with one lead ECG was recorded by Heartlab^{TM} system [23] (certificate No. LS. August 2, 2002) using 12-bit resolution A/D conversion at 1000-Hz sampling rate. Recordings of 178 patients were selected for further analysis in regard to the quality of recorded signals and absence of frequent extrasystolic beats or arrhythmia episodes. Diagnosis was confirmed and clinical status of the patients was estimated by the concentration of troponin I, a biochemical marker, in blood and functioning of the coronary vessels estimated by coronary angiography test and classified as one-vessel disease, two-vessel disease, three-vessel disease, and main-stem disease. The status of patients was evaluated according to the Killip-Kimball classification: 50 patients were classified as class I; 109, as class II; 10, as class III; and 9, as class IV. A control set of 20 recordings was made from healthy young volunteers. Clinical outcomes were estimated using data about survival of the patient after 6 and 12 months together with data about rehospitalization of the patient within 6 and 12 months. Generalized estimate of clinical outcome (*CLO*) was calculated as following:

$$CLO = S_6 + S_{12} - \frac{R_6}{2} - \frac{R_{12}}{4} \tag{1}$$

where S_6 and S_{12} are equal to 1 if patient survived after 6 and 12 months respectively, otherwise equal to 0. R_6 and R_{12} are equal to 1 if patient was rehospitalized within 6 or 12 months respectively, otherwise equal to 0. So for the patients who survived after 12 months and were not rehospitalized maximal value of *CLO* estimate 2 was given.

2.2. Signal preprocessing

ECG signal pre-processing we started with detection of fiducial point of each cardiocycle – peak of R-wave. After preliminary detection, using filtered derivative of the ECG signal, final detection of peak of R-wave was found maximizing cross-correlation of the sliding in time R-wave template with the ECG signal. R-wave template was constructed from first 10 cardiocycles of the recording and updated after every processed cardiocycle. Heart rate estimates were obtained by measuring R–R intervals between these fiducial points. Main heart rate estimates were mean of R–R intervals and triangular heart rate variability index calculated according [24].

A mean value of 10 consequent samples in interval between the end of T-wave of preceding cardiocycle and beginning of P-wave of current cardiocycle was considered to be a baseline reference point of each cardiocycle. Bicubic spline interpolation using these reference points was used to calculate baseline wander component, which was subtracted from the original ECG signal.

First derivative of thoracic impedance signal (dZ/dt) was also not free from baseline wandering. We applied bicubic spline interpolation to determine this component. Two reference points of each cardiocycle (before and after first peak of dZ/dt) were used for this process.

Excerpts of ECG signal samples representing S-T,T complexes of each cardiocycle were taken for further analysis. Number of samples corresponding to 2/3 of mean length of RR intervals in the recording was considered as a length of interval of samples representing S-T,T complex. This interval was starting at the 100th sample after fiducial point of cardiocycle. The length of Q–T interval is varying in regard to heart rate. We applied time stretching of the ordinary Q–T interval to align it with the others using bicubic spline interpolation, maximizing cross-correlation with the template constructed from the first 10 cardiocycles. Estimated coefficients for Q–T interval time stretching were close to the values reported by [25], proposed as substitution of classical Bazett formula. Corrected (stretched) arrays of samples from each cardiocycle formed matrix of samples **X**, which was giving a redundant but comprehensive representation of variety of the shape of S-T,T complexes from the recording considered for analysis:

$$\mathbf{X} = \begin{bmatrix} x_{1,1} & x_{1,2} & \dots & x_{1,n} \\ x_{2,1} & x_{2,1} & \dots & x_{2,n} \\ \dots & \dots & x_{i,j} & \dots \\ x_{p,1} & x_{p,2} & \dots & x_{p,n} \end{bmatrix} \tag{2}$$

where $x_{i,j}$ is the *i*th sample of the *j*th cardiocycle.

Excerpts of dZ/dt signal, representing each cardiocycle were taken in the similar way. The interval was starting at 100th sample before fiducial point and interval length was 2/3 of mean length of RR intervals in the recording (the same as S-T,T complex) +500 samples. Alignment of arrays was done by time stretching procedure was also applied for dZ/dt signal excerpts using the same coefficient as for current cardiocycle of ECG signal. Similar matrix of samples was formed for all samples representing dZ/dt cardiocycles.

2.3. Multivariate analysis for signal shape evaluation

Multivariate analysis method Principal Component Analysis (PCA) was successfully used in detection and evaluation of TWA [10]. It was able to reveal and evaluate fine morphological changes in the signal representing phenomena. The similar method was used to detect episodes of TWA in the recordings of present study.

PCA was used to reduce dimensionality of redundant representation of S-T,T complexes and dZ/dt signals. The PCA transforms original data set into a new set of vectors (the principal components), which are uncorrelated, and each of them involves information represented by several interrelated variables in the original set. The calculated principal components are ordered so that the very first of them retain most of the variation present in all the original variables. Thus it is possible to perform a truncated expansion of S-T,T complexes or dZ/dt cardiocycles representing vectors by using only the first several principal components. Every vector $\mathbf{x}_i$ representing ordinary S-T,T complex or dZ/dt cardiocycle is then represented by linear combination of the principal components ϕ_k multiplied by coefficients $w_{i,k}$:

$$\mathbf{x}_i = \sum_{k=1}^{p} w_{i,k}\varphi_k \tag{3}$$

Variation of coefficients $w_{i,k}$ represents variation of the shape of S-T,T complexes or dZ/dt cardiocycles. It was shown in our previous works that TWA is usually represented by beat-to-beat alternans of one or at least few coefficients *w* [10].

Minimal yet sufficient number of principal components to be used for truncated representation of the signals was determined by Wold's criteria [26]:

$$PR(m) = \frac{PRESS(m)}{PRESS(m-1)} \tag{4}$$

where *PRESS(m)* is calculated as following:

$$PRESS(m) = \sum_{i=1}^{n}\sum_{j=1}^{p}({}_m\hat{x}_{ij} - x_{ij})^2 \tag{5}$$

where ${}_m\hat{x}_{ij}$ is the estimate of the original data set based not on all but the first *m* principal components; x_{ij}, the original data set. Final determination of number was done according to our experience; the detail description is given in [27].

2.4. Detection and evaluation of repolarization alternans

Detection of TWA was performed step by step in consequent intervals of the recordings. TWA was detected by two methods. First method uses normalized estimate of power spectral density of the coefficients w at the highest frequency. Episode of TWA was registered in case when this estimate at the highest frequency in 128 coefficients interval was at least two times bigger than mean of 10 neighboring lower frequency estimates [10]. Second method is based on the idea used in [28], that shape of S-T,T complexes in odd and even cardiocycles should be similar between each other in the groups and different between these groups. Unlike moving average complexes used by [28] we used groups of quantitative estimates of shape of the S-T,T complexes in odd and even cardiocycles – coefficients of principal components. The shape is optimally represented by several coefficients of principal components as a point in multidimensional orthogonal space. Performing the t test for means between such two coefficient sets formed from 32 odd and 32 even cardiocycles we can detect differences in their average shape. TWA was detected when means of two sets were statistically different at significance level of $P < 0.05$.

Final detection of TWA was performed consolidating results of these two methods, taking into account only episodes where results of methods coincided.

Relation between alternans in shape of S-T,T complexes and dZ/dt cardiocycles was evaluated by Spearman's rank correlation coefficients between arrays of coefficients of Principal Components representing them (MatLab™ function "corrcoef"). Relation of beat-to-beat alternans in heart rate to alternans in shape of S-T,T complexes and dZ/dt cardiocycles was investigated by evaluation of correlation between R–R intervals and coefficients of Principal Components. We used only the highest frequency component of these sequences extracted by hi-pass filter excluding impact of other factors then beat-to-beat alternans. Correlation coefficients were taken into account only in cases when probability of getting a correlation as large as the observed value by random chance, when the true correlation is zero, was less than 0.05.

3. Results

Analysis of the signals was started from establishment of minimal yet sufficient number of principal components to be used as quantitative estimates of shape variation in ECG S-T,T complexes and dZ/dt cardiocycles. Values of Wold's criteria PR and percentage of variation represented by corresponding number of first principal components are presented in Fig. 1. Specific brake-point in PR criteria values, according to our experience described in [27] suggested considering of first five principal components, representing more than 90% of variation in S-T,T complexes and more than 85% of variation in dZ/dt cardiocycles, as minimal yet sufficient set of principal components for truncated expansion of the signals. Coefficients of these 5 principal components to be used for optimal representation of shape of every S-T,T complex or dZ/dt cardiocycle were considered as quantitative estimates of their shape.

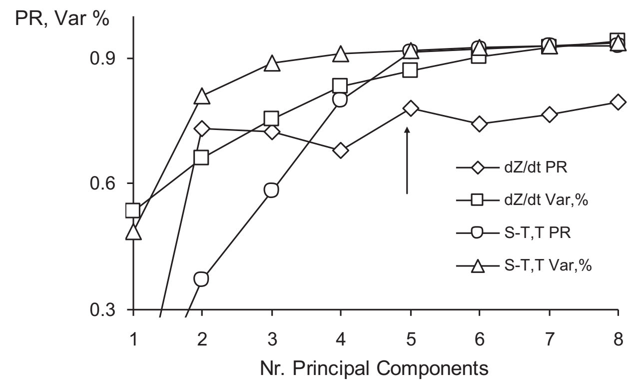

Fig. 1 – Wold's criteria PR and part of variation (Var%) represented (numeric values must be ×100 to get percentage) for determination of minimal yet sufficient number of principal components for truncated representation of dZ/dt (dZ/dt) cardiocycles and S-T,T complexes. A specific point in dependency of PR criteria is marked by an arrow.

Visually noticeable interrelated alternans of shape of S-T,T complexes, dZ/dt cardiocycles and beat-to-beat heart rate, represented by R–R intervals, was found in numerous episodes of the signals. Example is shown in Fig. 2.

Correlation coefficients between excerpts of estimates of shape of S-T,T complexes and dZ/dt cardiocycles (arrays of first 5 coefficients of principal components) taken around episode shown in Fig. 2, together with their significance levels are presented in Table 1. Statistically significant correlation ($P < 0.05$) was found in four pairs of coefficients: 1st representing S-T,T and 1st representing dZ/dt; 3rd S-T,T and 1st dZ/dt; 3rd S-T,T and 5th dZ/dt; 5th S-T,T and 5th dZ/dt (shown in bold in Table 1). Modest level of correlation, but between the first coefficients representing both signals is considered as substantial, because first principal components represent nearly 60% of variation in both signals (see Fig. 1). We selected only the largest statistically significant correlation coefficient representing relations between the shape estimates in every analyzed episode for further analysis. Median value of such selected biggest correlation coefficients was used as generalized measure representing certain group of the results, because the value of the correlation coefficient is not a linear function of the magnitude of the relation between the variables and correlation coefficients cannot simply be averaged. Median value of such biggest correlation coefficients in TWA episodes of all recordings was 0.66. Such measure but in TWA-free episodes of the recordings was 0.37. The difference was statistically significant (Wilcoxon Signed Ranks test, $P < 0.001$). In fact variation of amplitude/shape of S-T,T segment or dZ/dt cardio cycles is often noticeable in the recordings of myocardial infarction patients, however correlated alternans could be the indicator of repolarization alternans phenomena, what could have a special diagnostic value. We can expect more repolarization alternans episodes in the recordings of hardly affected heart muscle. The volume

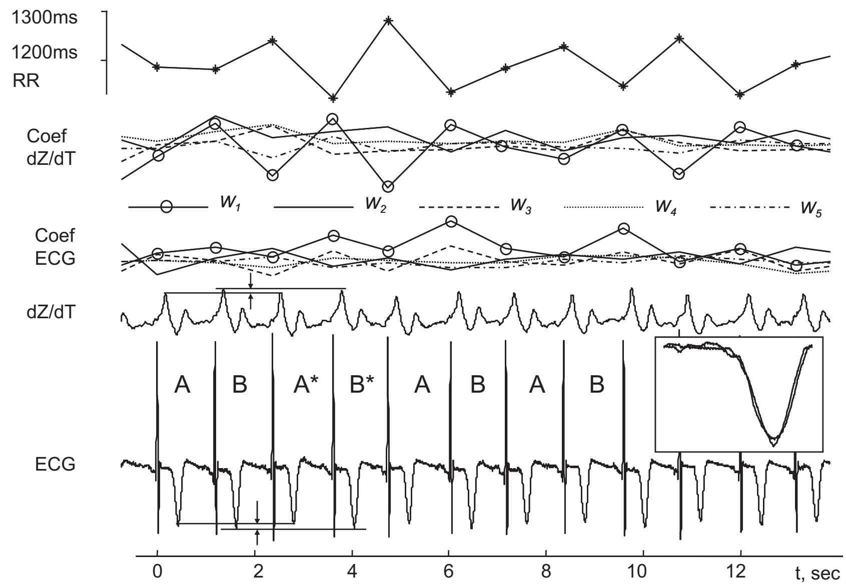

Fig. 2 – Coefficients of first five principal components representing dZ/dt cardiocycles (upper graph), ECG S-T,T complexes (second graph) together with synchronically recorded first derivative of thoracic impedance signal dZ/dt and ECG. Interrelated alternans in shape and amplitude of both signals is clearly visible. Inset graph represents enlarged S-T,T complexes of two neighboring cardiac beats marked with asterisk.

Table 1 – Correlation coefficients between coefficients of principal components representing ECG S-T,T complexes and dZ/dt cardiocycles in detected typical TWA episode.

$\rho_{S\text{-}T,T:dZ/dt}$		dZ/dt coefficients				
		1	2	3	4	5
S-T,T coefficients	1	**0.5695 (0.021)**	−0.1475 (0.586)	−0.0781 (0.774)	0.1572 (0.561)	0.4005 (0.124)
	2	−0.187 (0.488)	0.1716 (0.525)	0.3446 (0.191)	0.107 (0.693)	−0.3386 (0.199)
	3	**0.6367 (0.008)**	−0.3425 (0.194)	−0.3499 (0.184)	−0.2129 (0.429)	**0.6022 (0.014)**
	4	0.0419 (0.878)	−0.0705 (0.795)	−0.0554 (0.839)	0.064 (0.814)	−0.0026 (0.992)
	5	−0.2829 (0.289)	−0.1417 (0.601)	0.4682 (0.067)	0.1866 (0.489)	**−0.5696 (0.021)**

Significance level P is shown in brackets. Statistically significant correlation is given in bold.

of heart muscle injury is reflected by Troponin I concentration in the blood. It ranged from 0.2 ng/mL to 180 ng/mL in investigated patients. The fact that strength of correlation between alternans in shape of S-T,T complexes and dZ/dt cardiocycles inversely depends on volume of injury of heart muscle was supported by weak but statistically significant Spearman's rank correlation ($r = -0.372$, $P = 0.028$) between generalized measures of it and Troponin I concentration. We compared correlation between shape estimates (coefficients of principal components) in TWA and TWA-free episodes in recordings of patients with different number of malfunctioning coronary vessels. Bigger volume of heart muscle injury there was confirmed by bigger Troponin I concentration in blood of patients. The results shown in Fig. 3 and numeric values are shown in Table 3. We found statistically different values of correlation in regard to the number of malfunctioning coronary vessels (Kruskal–Wallis test, $P = 0.0021$ and $P = 0.005$ respectively). Significantly weaker correlation in TWA-free episodes in two vessel disease and main stem disease cases, also between one vessel disease and main stem disease cases (Dunn's post hoc test, $P < 0.05$). Modest, but statistically significant decay in biggest correlation coefficients in TWA episodes was observed only between one and two vessel disease cases (Dunn's post hoc test, $P < 0.05$). As reference to all mentioned above findings, biggest correlation coefficients of whole recordings of healthy persons are presented on the right side of Fig. 3. The median value of them was 0.308. Presented recordings of healthy patients were free from TWA episodes; therefore, there are no data of TWA episodes.

Correlation between alternans in R–R intervals, shape estimates of S-T,T complexes and dZ/dt cardiocycles in excerpt around the episode shown on Fig. 2 are presented in Table 2. Strong, statistically significant correlation was found between RR intervals and particular coefficients of principal components representing S-T,T complexes and dZ/dt cardiocycles, showing strong mutual correlation (shown in bold). However such strong correlation was found only in few recordings. As generalized measures of correlation between alternans of RR intervals and estimates of ECG S-T,T complexes or dZ/dt cardiocycles we used correlation coefficients between R–R intervals and particularly those coefficients of principal components which were already used as generalized measure of mutual correlation between alternans in ECG S-T,T complexes and dZ/dt cardiocycles. Significant difference found between median values of generalized measures of correlation

Fig. 3 – Summarized data about biggest correlation coefficients between shape estimates of ECG S-T,T segment and dZ/dt cardio cycles in TWA episodes (diamonds), TWA-free episodes (filled circles) of myocardial infarction patients and TWA-free episodes of healthy persons (triangles). Troponin I concentration in blood of myocardial infarction patients (filled boxes) indicates volume of heart muscle injury. The marker shows median value, vertical dimensions of the boxes indicate interquartile range (25%–75% of values) and whiskers show total range (min–max).

between alternans in R–R intervals and ECG S-T,T complexes in TWA episodes (median, 0.37) and (median, 0.32) in TWA-free episodes (Wilcoxon signed ranks test, $P < 0.001$). No significant difference found in case of median values of correlation coefficients between alternans in R–R intervals and dZ/dt cardiocycles in TWA episodes (median, 0.327), versus (median, 0.329) in TWA-free episodes (Wilcoxon Signed Ranks test, $P = 0.551$). No dependency of all these measures found on severity of disease (Kruskal–Wallis test, $P = 0.122$ and $P = 0.051$, respectively). Numerical values are presented in Table 3.

We found that correlation between alternans in R–R intervals and alternans in shape estimates of ECG S-T,T complexes is weakly but significantly dependent from heart rate variability. Weak, but significant Spearmen correlation ($r_{sp} = 0.344$, $P = 0.037$) found between triangular heart rate variability index and median values of correlation between R–R intervals and coefficients of principal components representing ECG S-T,T complexes in TWA episodes. The same measures in TWA-free episodes did not show any significant correlation.

Table 2 – Correlation coefficients between RR intervals and coefficients of principal components representing ECG S-T,T complexes and dZ/dt cardiocycles in detected typical TWA episode.

Coefficients of principal components	$r_{RR:S\text{-}T,T}$	$r_{RR:dZ/dt}$
1	**0.6619 (0.0052)**	**−0.8828 (<0.001)**
2	**−0.6747 (0.0041)**	0.2549 (0.3407)
3	**0.8395 (<0.001)**	0.2126 (0.4292)
4	0.2821 (0.2898)	0.1206 (0.6564)
5	−0.1972 (0.4642)	**−0.7319 (0.0013)**

Significance level P is shown in brackets. Statistically significant correlation is given in bold.

Magnitude of alternans in ECG S-T,T segment or thoracic impedance signal shape is represented by normalized estimate of power spectral density of the first principal components coefficients w at the highest frequency (the same estimate we used to detect TWA episodes by method [10]). Such estimate of power spectral density of second principal component coefficient of thoracic impedance signal shape showed significant correlation with clinical outcome estimates of patients. Most significant Spearmen rank correlation ($r_{sp} = -0.59$, $P = 0.02$) we found in patients having not maximal clinical outcome estimate (e.g. at least one rehospitalization). It means that less magnitude of alternans in fine shape structure (represented by second principal component) of thoracic impedance signal was corresponding to better clinical outcome.

4. Discussion

Observed correlation between alternans in shape estimates (coefficients of principal components) of S-T,T complexes and dZ/dt cardiocycles complies with the results published in [18]. Comparison of the results with parameters describing clinical status of the patient revealed dependency of such correlation on degree of injury of heart muscle. Interestingly only minor changes in regard to the degree of injury observed in correlation in TWA episodes. However significant decay in correlation in TWA-free episodes related with high degree of

Table 3 – Comparison of median values of correlation coefficients of generalized measures of correlation coefficients in regard to expected severity of cardiac muscle injury.

	Severity of injury				P value*
	One-vessel disease	Two-vessel disease	Three-vessel disease	Main stem disease	
$r_{S\text{-}T,T:dZ/dt}$ TWA episodes	0.69○	0.65○	0.66	0.64	0.021**
$r_{S\text{-}T,T:dZ/dt}$ TWA-free episodes	0.42△	0.45●	0.38	0.18△, ●	0.005**
$r_{RR:S\text{-}T,T}$	0.37	0.35	0.38	0.36	0.122
$r_{RR:dZ/dt}$	0.36	0.32	0.35	0.32	0.051

* Kruskal–Wallis test.
** Difference is significant at the 0.05 level (2-tailed).
Significant pairwise difference between values of correlation coefficients (multiple comparisons Dunn's test) is marked by ○, △ and ● respectively.

injury (three-vessel disease and main stem disease cases) results in significant difference of this measure between TWA and TWA-free episodes in more severe cases, what suggests its better diagnostic value. Reliable detection of alternans in electrical activity needs sophisticated methods to reveal fine changes indicating it, while mechanical activity is represented by more integral reflections of hemodynamics and in more cases could be observed even visually as reported in [18]. Therefore our results suggest inclusion of dZ/dt signal analysis into the methods of detection and evaluation of TWA.

Many factors are influencing mechanical functioning of the heart determining the shape of the dZ/dt signal. Repolarization alternans, when it takes part, covers only certain part of whole impact resulting modest values of correlation coefficients in TWA episodes. On the other hand we used only S-T,T complexes which represent repolarization of ventricles. Depolarization, reflected by QRS complex does play a significant role in determination of shape of the dZ/dt signal too, but combined investigation of its impact and interrelations with impact of alternans in repolarization processes could be a topic for next study.

We observed significant and nearly not changing correlation between alternans in S-T,T complexes and dZ/dt cardiocycles in TWA episodes in regard to severity of cardiac muscle injury, while significant decay in such correlation in TWA-free episodes in cases of severe heart muscle affection. Variation in shape of cardio cycles of both signals increases in more severe injury cases, but correlated alternans or variation could be a feature indicating real repolarization alternans episode.

Low heart rate variability is reported as related with most severe cases in risk determination in myocardial infarction patients [29]. Observed weak but statistically significant correspondence of triangular heart rate variability index with correlation between alternans in R–R intervals and shape estimates of ECG S-T,T complexes suggests possibility that certain increase in heart rate variability could be related with appearing repolarization alternans, what is indicator of increasing severity of clinical situation. Repolarization alternans results in beat-to-beat alternans of R–R intervals, so it is reflected only at highest frequency range when evaluated according to [24]. Not generalized, but only low frequency range heart rate variability measure is reported as most significant predictor of severe situations in myocardial infarction patients [30]. So detail time-frequency analysis of heart rate variability therefore is suggested to use for evaluation of situation.

Observed significant difference in correlation between alternans in R–R intervals and shape estimates of ECG S-T,T complexes in TWA and TWA-free episodes and absence of such difference in correlation between alternans in R–R intervals and shape estimates of dZ/dt cardiocycles could be considered as controversial result because mentioned difference of mutual correlation between shape estimates of ECG S-T,T complexes and dZ/dt complexes was also found. However, a modest level of correlation suggests that separate mechanisms could be acting and no mutual relation among all three measures could be found.

Observed significant correlation between magnitude of alternans in thoracic impedance signal shape and estimates of clinical outcomes shows importance of diagnostic features derived analyzing this signal.

Summarizing we can conclude that our results suggest recommendation to use combined ECG, thoracic impedance signal and beat-to-beat heart rate variability analysis for better diagnostic reliability.

5. Conclusions

Repolarization alternans detected by ECG signal analysis are reflected by alternans in mechanical function of the heart, which is estimated by morphological properties of thoracic impedance signal in patients in acute phase of myocardial infarction.

Not generalized, but only low frequency range heart rate variability measure should be used for status of myocardial infarction patient prediction in regard to possible increase of highest frequency variability due to repolarization alternans in critical situations.

It is recommended to evaluate ventricular repolarization alternans using combined ECG, thoracic impedance signal and beat-to-beat heart rate variability analysis for better diagnostical reliability.

Conflict of interest

The authors state no conflict of interest.

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