T Wave Alternans and Acute Ischemia in Patients Undergoing Angioplasty

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Abstract

Electrical T-wave alternans (TWA) has been recognized as a marker of electrical instability, and has been shown to be related with patients at increased risk for ventricular arrhytmias. In this paper we have studied the presence of TWA on 83 patients undergoing percutaneous transluminal coronary angioplasty (PTCA). Two ECG recordings of each patient, a control recording before PTCA and the PTCA recording, were analyzed using a new robust TWA detector based on the GLRT for Laplacian noise distribution. 27 out of 83 patients (32.5%) showed TWA episodes, with highest prevalence on LAD artery occlusion subgroup (48.1%). In the study group, TWA appears always during the occlusion interval, generally after the first minute of occlusion, and its amplitude grows up as occlusion time increases. The lead profiles of the TWA and the alternant waveforms showed different distributions depending on the occluded artery. All these results suggest that TWA during angioplasty is related to the increasing electrical instability produced by the occlusion and that TWA in acute ischemia is a localized and transient phenomenon dependent on the occluded artery.

1. Introduction

T wave alternans (TWA) is a transient phenomenon appearing in the surface electrocardiogram (ECG) as beat-to-beat changes in the repolarization morphology (ST segment and T wave) on an every-other-beat basis. TWA has been reported in a wide range of clinical and experimental situations including long QT syndrome, myocardial infarction, Printzmetal angina, acute ischemia, etc [1].

Although visible TWA is an infrequent phenomenon, in recent years, computerized analysis of digital ECG recordings allowed the identification of subtle (microvolt) TWA, much more common than visible TWA. Recently, several studies showed that TWA is related to cardiac instability and high risk for malignant ventricular arrhythmias and sudden cardiac death [2]. Thus the importance of studying the mechanisms of TWA and understanding its relationship to the sources which origin the electrical instability.

TWA associated with ischemia has been explained by the failure of the ischemic area to depolarize on alternate beats because of variations in conduction and refractoriness, and also by the alternation of repolarization phases of action potentials due to abnormal electrolyte flux in the ischemic cell [3]. Recent studies [4] have supported the hypothesis that in order for TWA to occur, a large amount of ischemic myocardium must be present.

Percutaneous Transluminal Coronary Angioplasty or PTCA can be used as a good model to investigate the electrophysiological changes of acute ischemia, since the coronary occlusion is perfectly defined both in time (period of occlusion) and in space (occlusion site).

The aim of this study was to gain insight on the temporal and spatial relationship between TWA and ischemia.

2. Materials and methods

2.1. Study population

The study group consisted on 83 patients (55 males) from the STAFF III database undergoing elective PTCA in one of their major coronary arteries. The average duration of the occlusion period was 4' 26", considerably longer than that of usual PTCA procedures because the treatment protocol included a single prolonged occlusion rather than a series of brief occlusions.

The location of the 83 balloon inflations were: left anterior descending artery (LAD) in 27 patients, right coronary artery (RCA) in 38 patients and left circumflex artery (LCX) in 18 patients. Nine standard leads (V1-V6, I, II and III) were recorded using equipment by Siemens-Elema AB (Solna, Sweden) and digitized at a sampling rate of 1 kHz with amplitude resolution of 0.6 μV.

For each patient in the study group two recordings were considered: the control ECG recorded just before angioplasty and the PTCA recording. The control interval usually was 5 minutes long, in the same order as the average inflation time.

2.2. Analysis method and parameters

The control and the PTCA recordings were analyzed lead by lead using a new robust detector based on the GLRT for Laplacian noise distribution. This detector is presented in another paper in these proceedings [5]. All detected TWA

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episodes were visually inspected in order to reject false positive detections due to frequent ectopic beats or high noise levels.

Three different outputs of the detector were considered in each lead: the TWA episodes, the alternant waveform (i.e. how the amplitude is distributed during the repolarization phase of the cardiac cycle), and the RMS value of the TWA amplitude in each beat. In this fashion, we can study the TWA amplitude distribution on three different dimensions: the beat-to-beat course of the TWA along the occlusion, the temporal distribution of the TWA within the repolarization phase (alternant waveform) and the spatial distribution in the different leads of the ECG (lead profile). The first one gives an idea of the temporal evolution of the TWA amplitude, while the other two distributions are related to the spatial localization of the affected myocardial region. Actually, the lead profile shows how the alternant component is projected into the different leads, and the alternant waveform informs about the location of the electrically unstable region in the propagation path of the repolarization. An example of the outputs that can be obtained in each lead from every TWA episode is given in Figure 1.

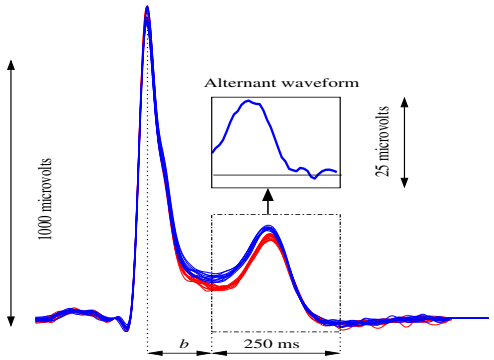


Figure 1. Superposition of beats during TWA and alternant waveform. The analysis window starts $b = 40 + 1.3RR_k^{1/2}$ ms after the QRS fiducial point.

Since in PTCA recordings the occlusion interval is known, we analysed how the TWA is related to the occlusion timing (time course analysis).

The region of the myocardium affected during acute ischemia depends on the occluded artery. In PTCA, the balloon position is known, an thus, we divided our study group in three subgroups classified according to the occluded coronary artery, in order to study how the balloon location is related to the TWA spatial features on the ECG. We did this in two ways: first, we analysed how the TWA amplitude is distributed on the ECG leads (the lead profiles), and second, we studied the alternant waveform, or equivalently how the alternans component is distributed on the repolarization phase.

For each subgroup, the mean lead profile and alternant waveform were computed. To obtain the mean lead profiles, we averaged the alternant amplitude in 11 beats around the peak of TWA at the time instant within repolarization phase where the TWA amplitude was maximum. Once obtained a lead profile for each recording, all of them were normalized in energy and averaged. The alternant waveform was calculated in each recording by averaging in 11 beats around the peak of TWA on the lead with maximum TWA amplitude. Afterwards, the waveforms were normalized and averaged for every subgroup.

3. Results

3.1. Episodes of TWA

Thirty TWA episodes were detected in 29 patients (34.9%). Out of them, no episodes were found during the control recordings. All episodes appeared on the PTCA recording, 27 of them during the balloon occlusion and 3 after the balloon release. About these TWA episodes appearing during the reperfusion, it is difficult to make conclusions, as a contrast was injected to the patients during the reperfusion and the ECG was significantly altered. Taking out the episodes during reperfusion, we present in Table 1 the number of patients showing TWA for the total study population and several subsets defined by the sex and the occluded coronary artery. It is interesting to note that the prevalence of TWA is higher for patients with LAD occlusion (48.1% of patients) than in the other subgroups.

Table 1. Patients with detected TWA episodes according to occluded artery and sex.

	# patients	# male	# LAD	# RCA	# LCX
Total	83	55	27	38	18
with TWA	27	19	13	9	5
% with TWA	32.5%	34.5%	48.1%	23.7%	27.7%

3.2. Time course analysis

In the 27 TWA episodes occurring during PTCA, the onset time ranged from 24" to 4'37" after the balloon inflation (m±std: 2'12"±1'05"). The final of the episode ranged from 2'07" to 5'17" after inflation (4'06±1'03"). Episodes were found with durations between 20" and 4'26" (1'53"±1'13"). The end time of the episodes relative to the balloon release ranged from 2'34" before the release to 30" after it (-0'42"±42").

Figure 2 shows the average of the normalized TWA amplitude time-course during PTCA. The time origin corresponds to the balloon inflation, and for each time, it is shown the average TWA amplitude for all the recordings in which the balloon is still inflated at that time. In the upper panel, the number of recordings with occlusion and with TWA at a given time is given.

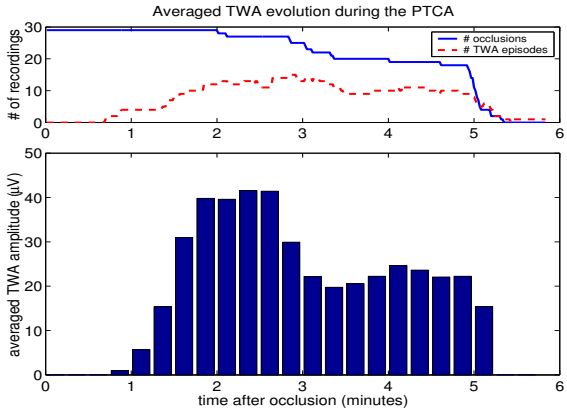


Figure 2. The upper panel shows the number of recordings with occlusion and with TWA for a given time after the beginning of PTCA. The lower panel shows the averaged time-course of TWA amplitude.

As we found TWA episodes of very variable amplitudes, the time course of high amplitude episodes can mask those of very small amplitudes when averaging directly the TWA amplitudes. Thus, we show in Figure 3 an alternative representation: the average of the normalized time courses of the TWA episodes, where all episodes were nomalized to have maximum amplitude of 1.

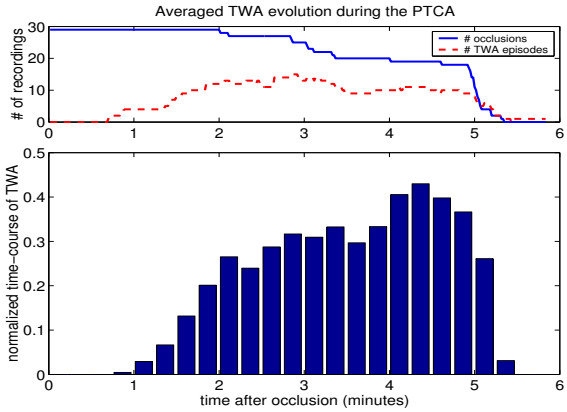


Figure 3. Similar to Figure 2, but normalising the time course before averaging.

From both figures, it can be seen that there are hardly any episodes in the first minute after occlusion. The results also show that the TWA amplitude grows in average, as the occlusion time increases. Note that the averages after the fifth minute have little significance as the number of averaged recordings declines quickly around that time.

3.3. Spatial analysis

Figure 4 shows the mean and standard deviation of the normalized lead profiles for the three subgroups. In LAD subgroup, TWA was predominant at chest leads V2-V4; in RCA subgroup in V1-V2 (and also V5, V6, II and III), while in LCX group, it was in V4-V6, giving an idea of the location of the ischemic region.

In Figure 5 we present the results of the alternant waveform. The frequency content of the waveforms is very similar to that of the T wave. However the waveform is advanced with respect to the T-wave, as can be seen in Figure 1. In LAD and LCX, TWA was concentrated in the beginning of the repolarization (in the first 250 ms, corresponding to the ST segment and the beginning of the T wave). Nevertheless, in RCA, TWA was more spread during the total repolarization interval. The inter-subject variability is greater than for the lead profiles, but differences can still be noted among the subgroups.

4. Discussion and conclusions

In this work we studied the relationship between TWA and acute myocardial ischemia. For this purpose, we selected a group of patients undergoing PTCA.

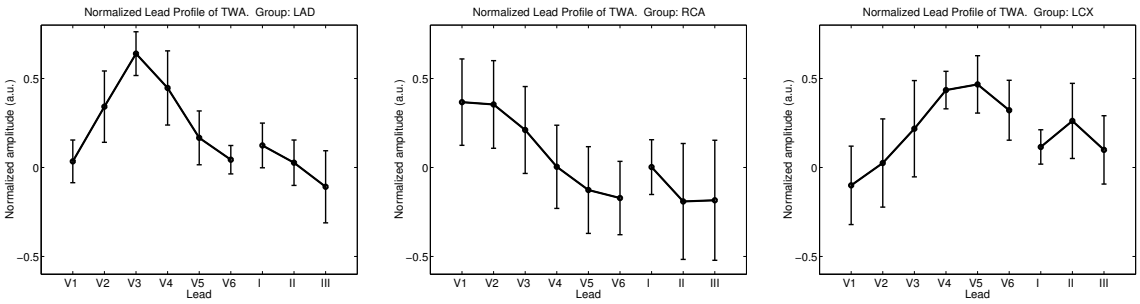
From our study group of 83 patients, about one third (32.5%) of the patients presented TWA during PTCA. None of them presented TWA in the control ECG recorded before the angioplasty. The greatest prevalence (48.1%) was observed on patients with the balloon inflated in the LAD artery. As this artery perfunds generally a wider myocardial region than the others, this result may support the hypothesis that to observe TWA in surface ECG, a large region of the myocardium must be affected.

It is also worthy to note that the standard 12-lead configuration used in this study performs a good mapping of the anterior and lateral walls of the heart, which are the areas supplied by LAD and partly by LCX. The inferior region of the myocardium, irrigated mainly by RCA and LCX arteries is not so well represented in the standard 12-lead ECG. If the ischemic region produced by the occlusion is mainly at the inferior wall of the myocardium, ECG signals from electrodes placed on the back of the patients, or body surface potential maps could give more representative results.

The study of the time course of TWA during the dilation yields the idea that TWA amplitude grows up as the time of occlusion increases, indicating a progressive growing of electrical instability within the myocardium. Also, most of TWA episodes finish around the end of the occlusion, when the affected cells are perfunded again.

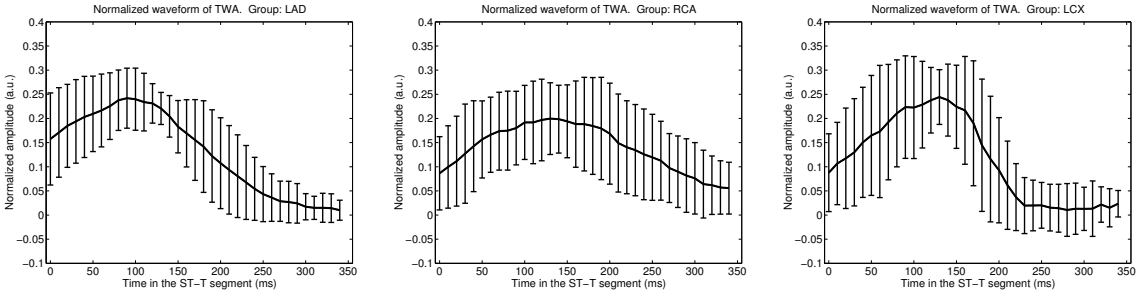
The average lead profile is different for the three subgroups. The chest leads with maximum alternant amplitude correspond with the ones that are near the region of the myocardium irrigated by the arteries: V2-V4 for LAD, V4-V6 for LCX, and V1-V2 ; V5-V6 and II, III for RCA.

The average TWA waveform analysis shows that the



(a) LAD artery (b) RCA artery (c) LCX artery

Figure 4. Mean and standard deviation of the lead profiles in the study subgroups.



(a) LAD artery (b) RCA artery (c) LCX artery

Figure 5. Mean and standard deviation of the alternant waveforms in the study subgroups.

TWA in subgroups LAD and LCX is limited to the first 250 ms of the ST-T complex, which corresponds to the ST segment and the beginning of the T wave. On the other hand, the TWA produced by RCA occlusion was not so concentrated, but more spread during the repolarization interval.

The spatial analysis of the TWA episodes presents some limitations: the anatomy of the coronary arteries and collateral circulation shows a clear inter-subject variation and some parts of the myocardium can be supplied by more than one artery. Thus, the affected regions are not necessarily the same in subjects with the same balloon location. Nevertheless, the results indicate that the observed TWA has a dependence on the location of the balloon, which may determine the TWA sources.

The analyses of lead profiles and alternant waveforms were considered separately. Thus, for averaging waveforms, the maximum TWA amplitude lead was chosen for each recording, and therefore waveforms in different leads were averaged. For a better analysis, the localization of TWA should be studied simultaneously in both dimensions.

Acknowledgments

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References

[1] Verrier RL, Zareba W, Nearing BD. T-wave alternans monitoring to assess risk for ventricular tachycardia and fibrilation. In Moss AJ, Stern S (eds.), Noninvasive Electrocardiology. Clinical Aspects of Holter Monitoring. London, UK: W. B. Saunders Company Ltd, 1996; 445–464.

[2] Rosenbaum DS, Jackson LE, Smith JM, Garan H, Ruskin JN, Cohen RJ. Electrical alternans and vulnerability to ventricular arrhythmias. The New England Journal of Medicine January 1994;330(4):235–241.

[3] Surawicz B, Fisch C. Cardiac alternans: Diverse mechanisms and clinical manifestations. Journal of the American College of Cardiollogy August 1992;20:483–499.

[4] Kwan T, Feit A, Alam M, Afflu E, Clark LT. ST-T alternans and myocardial ischemia. Angiology March 1999;50(3):217–222.

[5] Martínez JP, Olmos S. A robust T-wave alternans detector based on the GLRT for Laplacian noise distribution. In Computers in Cardiology 2002. IEEE, 2002; In these proceedings.

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