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*Editorial Comment*

# Thrombolytic Therapy, Infarct Vessel Patency and Late Potentials: Can the Arrhythmic Substrate Be Altered?*

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**Historical background.** More than 15 years have passed since localized epicardial electrical signals beyond ventricular activation were recorded in dogs with ventricular arrhythmias after experimental myocardial infarction (1) and subsequently termed "late potentials." These observations became the basis for catheter and intraoperative electrical mapping in humans with sustained ventricular tachyarrhythmias following myocardial infarction to enable curative endocardial resection (2). During the past decade, signal-averaged surface electrocardiography has demonstrated the ability to record such late potentials noninvasively. Correlations between late potentials detected on the signal-averaged electrocardiogram (ECG) and spontaneous or induced sustained ventricular tachyarrhythmias in a variety of clinical states have been reproducibly confirmed. Thus, late potentials have been referred to as markers of an electrical substrate capable of sustaining malignant ventricular arrhythmias.

Concomitantly, a decade of clinical investigations with administration of various thrombolytic agents during the evolutionary phase of acute myocardial infarction has proved fruitful. When administered within several hours after the onset of symptoms, thrombolytic agents have demonstrated improvement in the preservation of left ventricular function and survival. Successful reperfusion has been associated with spontaneous ventricular arrhythmias, most notably accelerated idioventricular rhythms. Decreased frequencies of ventricular premature beats have been reported after successful thrombolytic therapy. However, no substantial data have been reported concerning the impact that coronary artery reperfusion has had on the occurrence of significant ventricular tachyarrhythmic events after the early postmyocardial infarction period.

**Signal-averaged electrocardiography after myocardial infarction.** Of all available noninvasive approaches explored thus far, an abnormal signal-averaged ECG represents the strongest predictor of a sustained ventricular tachyarrhythmia after myocardial infarction (3–5). The effect of thrombolytic therapy on late potentials may provide useful prognostic data regarding future arrhythmic events. In this issue of the Journal, Turitto and colleagues (6) evaluated the effect of thrombolytic therapy administered within 6 h of the onset of myocardial infarction on the signal-averaged ECG. Their data revealed no significant differences in the presence of any abnormal signal-averaged variables (evaluated in the time domain mode) whether analyzed individually or in any possible combination. This finding held whether or not infarct-related vessel patency was present.

**Thrombolytic therapy and late potentials.** Despite their origin in a well designed study, these findings need to be interpreted with great caution. True trends were present with respect to more abnormal quantitative and qualitative signal-averaged variables in patients who did not receive thrombolytic therapy or whose coronary angiogram did not demonstrate patency of the infarct-related vessel. Most notably, the quantitative root mean square voltage of the terminal 40 ms of the signal-averaged vector complex was significantly more abnormal in these patients. This finding could suggest that the cellular and stromal changes required for the development of an arrhythmic substrate and late potentials are lessened with thrombolytic therapy. Because the left ventricular ejection fraction was higher in patients receiving thrombolytic agents, the higher root mean square voltages of the terminal 40 ms and of the entire QRS vector complex may have reflected preservation of greater myocardial tissue.

**Comparative studies of thrombolytic therapy and signal-averaged electrocardiography.** Given that the conclusions of this report (6) are not conclusive, the contrasting findings that Gang and colleagues (7) recently reported must also be looked on with a degree of skepticism. Although Gang and colleagues compared patients who had successful reperfusion with those who had unsuccessful thrombolytic therapy, important differences existed that could account for the different findings. Furthermore, these differences raise issues that need to be resolved:

1. Patients were considered for thrombolytic therapy if they were seen within 4 h of symptom onset in the study of Gang et al. (7), whereas enrollment required treatment within 6 h in the present study. Thus, does the time of

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administration of thrombolytic agents alter the heterogeneity of myocardial injury and the subsequent recording of late potentials to different degrees?

2. The thrombolytic agents used were predominantly urokinase in the present study, whereas Gang et al. used only recombinant tissue-type plasminogen activator (rt-PA). Thus, is the development of postinfarction late potentials somehow related to the thrombolytic agent used?

3. Characteristics of vessel patency also differed between the two studies: Thrombolysis in Myocardial Infarction (TIMI) trial grade 2 or better in the present study and TIMI grade 3 in the study of Gang et al. (7). Thus, one must ask whether late potential development is at all dependent on the extent of perfusion and collateral vessel development. To this end, suggestions have been made that collateral blood vessels to an infarct-related artery may be more common in patients with than in those without sustained ventricular tachycardia (8).

4. As Turitto et al. (6) point out, the optimal time for recording a signal-averaged ECG is from 48 h to 2 weeks after myocardial infarction. In their study, the results were analyzed in terms of signal-averaged ECGs obtained 13 ± 2 days after myocardial infarction, whereas they were obtained within 48 h in the study of Gang et al. (7). This difference may, in part, explain the discordance of results between the two studies because reanalysis of the previously reported results of Gang et al. on the basis of signal-averaged ECGs obtained later has an adverse effect on the study's statistical significance.

5. Differences in the signal-averaged techniques and definitions of abnormal results in the two studies may have participated in the discrepant results and need to be resolved. Many investigators still use the normal values for signal-averaged ECG variables originally proposed by Simson (3), whereas few have established norms for their patient populations. Even in the only two comparative studies on the effect of thrombolytic therapy on signal-averaged recordings (6,7), differences in the accepted normal QRS duration of the vector complex exist. In addition, the precise signal-averaged variables defining as abnormal ECG differed between the two studies. Yet even when a signal-averaged ECG was defined as abnormal on the basis of abnormalities of all three variables, as in the report of Gang et al. (7), the present study still falls shy of revealing a statistical difference associated with infarct vessel patency.

**Recommendations for future studies.** Thus, as signal-averaged electrocardiography becomes more widely employed, absolute criteria should be proposed for abnormal signal-averaged ECG. Even with the inconsistencies noted, the clinical implication of signal-averaged electrocardiography for risk stratification after myocardial infarction in patients with nonsustained ventricular tachycardia and in patients with syncope of unknown etiology has become widely accepted.

In the present study, no follow-up data are provided with respect to the development of subsequent malignant ventricular tachyarrhythmias or sudden death. However, if the incidence of arrhythmic events turns out to be as low as that in the study of Gang et al. (7) (that is, 1 of 62 or 1.5% of patients with an abnormal signal-averaged ECG at 6 months), one must question whether signal-averaged electrocardiography after thrombolytic therapy may lose some of its predictive ability for a postinfarction arrhythmic event. Alternatively, the lower incidence could be due to the relatively preserved left ventricular ejection fractions reported in both studies.

Further studies are needed to evaluate the impact of thrombolytic therapy on late potentials, both as a marker of infarct vessel patency and as a marker of future malignant ventricular tachyarrhythmias. However, such studies should be large cooperative efforts, like the numerous thrombolytic trials. Consistent methodologies should be used to reconcile the discrepancies pointed out here, as well as others that may not have been mentioned.

## References

1. Scherlag BJ, El-Sherif N, Hope R, Lazzara R. Characterization and localization of ventricular arrhythmias resulting from myocardial ischemia and infarction. Circ Res 1974;35:372–83.

2. Josephson ME, Horowitz LN, Farshidi A. Continuous local electrical activity: a mechanism of recurrent ventricular tachycardia. Circulation 1978;57:659–65.

3. Simson MB. Use of signals in the terminal QRS complex to identify patients with ventricular tachycardia after myocardial infarction. Circulation 1981;64:235–42.

4. Kuchar DL, Thorburn CW, Sammel NL. Prediction of serious arrhythmic events after myocardial infarction: signal-averaged electrocardiogram, Holter monitoring and radionuclide ventriculography. J Am Coll Cardiol 1987;9:531–8.

5. Gomes JA, Winters SL, Stewart D, Horowitz S, Milner M, Barreca P. A new noninvasive index to predict sustained ventricular tachycardia and sudden death in the first year after myocardial infarction: based on signal-averaged electrocardiogram, radionuclide ejection fraction and Holter monitoring. J Am Coll Cardiol 1987;10:349–57.

6. Turitto G, Risa AL, Zanchi E, Prati PL. The signal-averaged electrocardiogram and ventricular arrhythmias after thrombolysis for acute myocardial infarction. J Am Coll Cardiol 1990;15:1270–6.

7. Gang ES, Lew AS, Hong M, Wang FZ, Siebert CA, Peter T. Decreased incidence of late potentials after successful thrombolytic therapy for myocardial infarction. N Engl J Med 1989;321:712–6.

8. Atie J, Brugada P, Smeets JLRM, et al. Incidence of collateral blood supply to the infarcted area in patients with ventricular tachycardia after myocardial infarction (abstr). Circulation 1989;80(suppl II):II-325.