U wave inversion during attacks of variant angina

KUNIHISA MIWA, TOMOYUKI MURAKAMI, HIROFUMI KAMBARA, CHUICHI KAWAI

From Third Division, Department of Internal Medicine, Kyoto University; and the Cardiology Division, Takeda Hospital, Kyoto, Japan

SUMMARY Sequential 12 lead electrocardiograms were recorded during angina pectoris induced by ergonovine maleate in 38 patients with variant angina. Transient U wave inversion was observed in 17 patients with ST segment elevation in anterior chest leads, but in only three of 21 patients with ST segment elevation in the inferior leads associated with right coronary artery spasm. In the 17, all of whom had spasm of the left anterior descending coronary artery, the sensitivity of ST segment elevation in V5 was only 41%, and that of U wave inversion 71%. U wave inversion without ST segment elevation occurred during attacks in 35% of patients. During the recovery phase, the sensitivity of U wave inversion was 82% in V4 and 65% in V5, though ST segment elevation was absent in both V4 and V5. Thus, inverted U waves without ST segment elevation often appear in marginal ischaemic zones or during the time of recovery from temporary ischaemia. Detection of inverted U waves should aid in the diagnosis of variant angina when only lead V5 is used as a monitor and when electrocardiograms are recorded only during the recovery phase.

The electrocardiographic recording of ST segment elevation during attacks is essential for a diagnosis of variant angina.¹ Such recordings, however, are hampered as the duration of the attacks is often very short and the ST segment elevation is usually localised to a limited number of leads.

A negative U wave is also a sign of ischaemic heart disease,² but there are few published reports of U wave inversion during attacks in patients with variant angina. Accordingly, we examined the frequency of inverted U waves and compared our findings with those of ST segment elevation on 12 lead electrocardiograms in patients with a variant form of angina provoked by ergonovine maleate.

Subjects and methods

Standard 12 lead electrocardiograms taken during angina provoked by ergonovine maleate were reviewed in 38 successive patients with variant angina (35 men and three women; 37 to 71 years of age). All patients had angina at rest with typical chest pain and ST segment elevation on the electrocardiograms during spontaneous attacks or attacks induced by ergonovine. Patients with abnormal Q waves or T wave inversion on resting electrocardiograms were

excluded from the study. The ergonovine test was performed for the diagnosis of variant angina and for documentation of the spastic site in the coronary artery. Electrocardiograms recorded during the ergonovine test in another 29 patients with chest pain syndrome, with neither significant fixed coronary stenosis nor coronary spasm, were reviewed. All patients underwent cardiac catheterisation and coronary arteriography using Sones's method, and coronary spasm with angina was confirmed by ergonovine provocation in all of the former group.

Ergonovine maleate was given by intravenous bolus injection. An initial dose of 0.05 mg ergonovine maleate was given and then 0.05, 0.10, and 0.20 mg every three minutes until chest pain or electrocardiographic signs of myocardial ischaemia occurred. Twelve lead electrocardiograms using six channel electrocardiographic recorders, and aortic pressure, were constantly monitored during this procedure. X ray transparent carbon electrodes were used for anterior chest leads to record electrocardiograms constantly during coronary arteriography. After coronary arteriography during the anginal attack, glyceryl trinitrate was administered sublingually or in the artery.

ST segment shift and the appearance of negative U waves were assessed during the attack and in the recovery period, and leads with ST segment elevation and inverted U waves were examined. We defined "during the attack" as a period of ST segment eleva-

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tion over 2 mm, observed in any one of the 12 leads. The beginning of the recovery phase was defined as the time when the ST segment elevation first disappeared in one or more leads. ST segment elevation of over 1 mm compared with that of the resting electrocardiogram was considered positive, and inverted U waves were considered to be significant if there was a discrete, negative deflection more than 1 mm in depth within the TP segment. When positive U waves over 0.5 mm were observed on a resting electrocardiogram, U wave inversion with a negative deflection over 0.5 mm was considered to be significant. A terminal T wave dip was identified on the simultaneously recorded leads where U waves were not apparent. The QT interval was also determined to verify that a discrete negative deflection in the TP segment was not the result of negative terminal T waves. Statistical analysis was done using the χ^2 test with Yates's correction.

Before the catheterisation procedures, written informed consent was obtained from each patient and no untoward side effect was observed during or after the procedure.

Results

Anginal attacks induced by ergonovine maleate were accompanied by ST segment elevation over 3 mm in more than one of 12 leads in all 38 patients with variant angina. U wave inversion was observed during

the attacks in all 17 patients (100%) with ST segment elevation in the anterior chest leads, but in only three of 21 patients (14%) with ST segment elevation in the inferior leads due to right coronary artery spasm. Reciprocal electrocardiographic changes were discarded. Neither ST segment elevation nor U wave inversion was observed during the ergonovine test in any of the 29 patients with chest pain syndrome.

In all 17 patients with ST segment elevation in anterior chest leads, spasm of the left anterior descending coronary artery was shown angiographically during the anginal attacks. Clinical data and coronary arteriographic findings and electrocardiographic findings before and during attacks in these patients are listed in Table 1. The lead showing maximum ST segment elevation during attacks was V3 in 15 patients (88%), V2 in one patient (6%), and V4 in one patient (6%). The lead showing maximum inversion of the U wave was V3 in nine (53%), V4 in seven (41%), and V2 in one (6%). The sensitivity of each lead of ST segment elevation and U wave inversion is summarised in Table 2. The sensitivity of U wave inversion was 71% in V5, while the sensitivity of ST segment elevation was only 41% in the same lead. Isolated U wave inversion without ST segment elevation in V5 was observed in 35% during the attacks, and either ST segment elevation or U wave inversion in 76%. During the recovery phase, ST segment elevation was not present in leads V4 or V5, while U wave inversion without ST segment elevation was

Table 1 Clinical data and electrocardiographic findings in patients with spasm of left anterior descending artery

Case	Age and sex (y)	Coronary arteriogram (% stenosis)	Electrocardiogram at rest	Electrocardiogram at ergonovine provocation				
				Inv U preceding ST†	During attack ST†	Inv U	Recovery phase ST†	Inv U
1	56 M	90% LAD, 90% RCA	Normal, pos U in V2-4	+ V3-5	V1-5	V3-5	V1-3	V3-5
2	60 M	99% LAD	Normal	—	V1-4	V2-6	V1-3	V3-5
3	62 M	90% LAD, 75% LCX	Normal	+ V2-6	V1-5	V2-6	V1, 2	V2-6
4	69 M	99% LAD	Normal, pos U in V2	—	aVL, V1-4	V2, 6	V2-3	V2-6
5	56 M	99% LAD	Normal, pos U in V1	+ V3-5	aVL, V1-5	V3-5	V1, 2	V2-5
6	42 M	75% LAD	Normal	—	V1-4	V4, 5	V1-3	V5
7	37 M	Normal	Normal	+ V4-6	V1-3	V4-6	None	V4, 5
8	45 M	Normal	T flat in V5, 6	—	V1-5	V3-5	V1-3	V3-5
9	71 M	90% LAD	Normal, pos U in V2, 3	—	V1-5	V3-5	V2, 3	V3-5
10	40 M	Normal	Normal, pos U in V2-4	+ V3-5	V1-4	V3-5	V1-3	V4
11	62 M	90% LAD, 75% RCA	Normal	—	V1-4	V3, 4	V1-3	V3
12	67 M	Normal	Normal	+ V2-4	I, aVL, V1-6	V2-4	V2	V2-5
13	45 M	90% LAD	Normal	—	I, aVL, V1-4	V2, 3	aVL, V1, 2	V2-4
14	46 M	Normal	T biphasic in V3	—	I, aVL, V1-6	V3-6	V1, 2	V3, 4
15	61 F	90% LAD	Normal, pos U in V2-4	—	V1, 2	V2-4	None	V3, 4
16	60 M	99% LCX	T flat in V4, 5	—	V1-3	V2-4	V1, 2	V3
17	60 M	99% LAD, 75% LCX	T biphasic in V3	—	aVL, V1-4	V2-5	V1-3	V2-5

RCA, right coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery; Pos U, positive U wave; Inv U, inverted U wave; ST†, ST segment elevation.

Table 2 Sensitivity of ST segment elevation and U wave inversion during attacks in patients with spasm of left anterior descending artery by ergonovine provocation

Lead	Inverted U preceding	During attack		Recovery phase	
	ST segment ↑	ST segment ↑	Inverted U	ST segment ↑	Inverted U
V1	0	100	0	71	0
V2	12	100	47	88	35
V3	29	94	88	53	76
V4	35	82	94	0*	82*
V5	29	41	71	0*	65*
V6	12	12	29	0	12
I	0	18	0	0	0
aVL	0 (%)	35 (%)	0 (%)	6 (%)	0 (%)

* significantly different ($p < 0.01$), ST segment elevation VS inverted U.

Fig. 1. Case 2. Before: no abnormality before ergonovine provocation. Attack: typical ST segment elevation in V1-4 and U wave inversion in V2-6 were observed during attacks provoked by ergonovine. V5, though insensitive for ST segment elevation, was sensitive for U wave inversion during the attacks. Recovery: though only slight ST segment elevation was observed in V1-3, inverted U waves were apparent in V3-5.

Fig. 2. Case 12. Before: the resting electrocardiogram and normal findings. Pre-attack: U wave inversion in V2-4 preceded the appearance of ST segment elevation when the patient began to complain of mild chest discomfort. Attack: ST segment elevation in V1-6 and U wave inversion in V2-4 were observed during chest pain. Recovery: inverted U waves were present in V2-5 though ST segment returned to the baseline in V3-5 after glyceryl trinitrate administration.

present in 14 out of 17 (82%) in V4 and in 11 out of 17 (65%) in V5 (ST segment elevation vs U wave inversion: $p < 0.01$ in V4 and V5). In six patients (35%) inverted U waves appeared before ST segment elevation. Typical cases are shown in Fig. 1 to 3.

Discussion

The present study clearly showed inverted U waves in some of the 12 leads during chest pain in all patients with variant angina in whom spasm of the left anterior descending artery was induced by ergonovine. Inverted U waves never appeared in patients with chest pain syndrome but the exact specificity could not be determined in our patient population. Contrary

Fig. 3. Case 5. Before: electrocardiogram before ergonovine provocation. Pre-attack: inverted U waves preceded the ST segment elevation in V3-5 when the patient began to complain of slight dyspnoea. Attack: ST segment elevation in V1-5 and inverted U waves in V3, 4 were present during the attack. Recovery: there were prominent U waves during the recovery phase, a time when the ST segment had returned almost to the baseline.

to cases of spasm, the sensitivity of U wave inversion in the exercise stress test for the detection of significant fixed coronary stenosis is reportedly 21%, but the specificity is as high as 93%.³

In our patients with spasm of the left anterior descending artery, two markers of ischaemia, ST segment elevation and U wave inversion, occurred with variable frequencies in different leads and the variability was more pronounced during the recovery phase. Inverted U waves without ST segment elevation appeared in 35% of the cases in V5 during attacks, and much more frequently in V4 and V5 during the recovery phase.

The sensitivity of ST segment elevation is not high in V5 but the ambulatory electrocardiographic system (24 hour continuous monitoring) or the trans-telephonic system frequently monitors V5 or V6 and may miss ST segment elevation in patients with var-

iant angina caused by spasm of the left anterior descending artery. MacAlpin⁴ reported that V3 was the most sensitive and specific lead for ST segment elevation during attacks in those cases. Indeed, we have seen inverted U waves without ST segment elevation in modified V5 during anginal attacks, using 24 hour continuous monitoring. With twelve lead monitoring, ST segment elevation was noted in other chest leads. Matsuguchi *et al.*⁵ reported negative U waves without ST segment elevation during ergonovine induced angina. Here, only V5 was monitored during ergonovine provocation and the electrocardiogram during spontaneous attacks may have been taken during the recovery phase.

Lead V5, in which inverted U waves frequently appear without ST segment elevation, may be located in the marginal ischaemic area, not in the central ischaemic zone. Inverted U waves without ST segment elevation, therefore, may indicate marginal ischaemia or recovery from temporary ischaemia and may be related to the regional heterogeneity of recovery from transient ischaemia. Normal U waves have the same polarity as the T waves.⁶ The mechanism of U waves is poorly understood, but one theory is that these waves result from after-potentials related to stretch of myocardial fibres by rapid ventricular filling.⁷ Another proposal is that these waves relate to repolarisation of the ventricular Purkinje fibres.⁸ Fu *et al.*⁹ reported that post-ischaemic negative U waves appeared after the release of the ligation of the left anterior descending artery in canine hearts, and the nature and possible mechanism of the negative U waves were discussed.

That the U wave inversion in cases of spasm of the left anterior descending artery is very high and that this wave remains inverted in the recovery phase when the ST segment elevation has already subsided are clinically pertinent. These data may also be useful when attempting to detect U wave inversion preceding ST segment elevation in some cases, since complications of additional administration of ergonovine maleate can probably be avoided.¹⁰

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Requests for reprints to Dr Chuichi Kawai, Third Division, Department of Internal Medicine, Faculty of Medicine, Kyoto University, Sakyo-ku, Kyoto 606, Japan.