Relationship between Arterial Pressure and Negative U Waves in Electrocardiograms

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Although Hypertension is a common pathologic condition associated with negative U waves in the electrocardiogram, their clinical significance and relationship to arterial pressure have not been adequately established.

Kemp et al.1 have described a correlation between negative U waves in left precordial leads and malignant hypertension with congestive heart failure. Reversal of the waves from negative to positive or isoelectric has been noted after sympathectomy2 and, as reported by Surawicz, Kemp, and Bellet,3 following the lowering of arterial pressure presumably with one of the antihypertensive agents, administration of nitroglycerin, and incidental slowing of the heart rate.

These observations suggest that inverted U waves in electrocardiograms of hypertensive patients might bear some relationship to the arterial pressure but do not make clear whether the level of the arterial pressure is the critical factor in determining their polarity.

The present study was undertaken to determine the possible relationship between arterial pressure and degree of negativity of U waves in electrocardiograms of hypertensive patients and to evaluate their clinical significance.

Methods and Material

The active files of the Research Division of the Cleveland Clinic were reviewed. Records of hypertensive patients who have had negative U waves in one or more of the left precordial leads of the electrocardiogram and who, following antihypertensive treatment, had repeat electrocardiographic tracings constitute material for this study. A total of 45 records was selected. Funduscopic examinations performed during each visit and arterial pressure measurements at least four times daily in supine and standing positions were available in all. Since arterial pressure measurements were not performed simultaneously each electrocardiographic tracing, for purposes of comparison, the average supine arterial pressure of that day was used.

In addition, in 12 hypertensive patients, who on their recent admission to the Research Ward of the Cleveland Clinic Hospital had negative U waves in one or more of the left precordial leads, the arterial pressure was lowered with intravenous sodium nitroprusside as previously described,4 and simultaneous electrocardiograms were taken serially. In each patient the arterial pressure, measured sphygmomanometrically every half minute, was kept, with the use of sodium nitroprusside, at various desired levels for as long as it was necessary to obtain electrocardiographic tracings. Only the leads showing the negative U waves were taken. In three of these 12 patients, electrocardiograms were also taken during and after intravenous infusion of guanethidine, in both supine and head-up tilt positions.

Results

Review of the Records of 45 Hypertensive Patients with Negative U Waves

Negative U waves in one or more of the left precordial leads of the electrocardiogram were present in all. In nine, negative U waves constituted the only electrocardiographic abnormality. Severe hypertensive retinopathy with exudates, hemorrhages, and papilledema were present in 15, history or physical findings of cerebrovascular complications in nine, angina pectoris in five, and old myocardial infarction in two. Twenty had essential hypertension; 15, the malignant syndrome; and in 10 the hypertension was associated with renal arterial lesions, as demonstrated by renal arteriography. During the follow-up period, which ranged from 4 months to 7 years subsequent to the initial electrocardiogram showing a negative U wave, seven of the 45 patients died. The

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cause of death was severe nephrosclerosis in three, cerebrovascular thrombosis in one, acute myocardial infarction in one, and unknown in the remaining two.

Following institution of antihypertensive treatment and lowering of arterial pressure, previously inverted U waves became upright (fig. 1) or isoelectric in 31 of the 45 patients, less inverted or diphasic in five, and remained unchanged in four. In the remaining five, average arterial pressure fall was insignificant; the negative U waves remained unchanged in all. A direct correlation between arterial pressure levels and negativity of U waves existed in 41 patients and this correlation persisted during the long period of study. In nine of them, elevation of arterial pressure on a few occasions during the follow-up period resulted in re-inversion of the U waves which, with further treatment and control of arterial pressure, disappeared again.

Average supine arterial pressure in the 31 patients in whom conversion of negative U waves took place was 208/126 before antihypertensive treatment and 159/97 after treatment. All four patients in whom conversion of negative U waves did not take place despite a satisfactory fall of arterial pressure, had a history of stroke, with angina pectoris (in two) and old myocardial infarction (in one). The nine patients with isolated negative U waves had no history or clinical evidence of coronary or cerebral arterial disease; lowering of arterial pressure resulted in conversion of the negative U waves in all. In the seven patients who died, the last available electrocardiogram taken 4 days to 6 months prior to death showed upright U waves and the arterial pressure was well controlled in all.

**Effect of Intravenous Sodium Nitroprusside and Guanethidine**

In all 12 patients, lowering of arterial pressure with intravenous sodium nitroprusside (100 to 400 \( \mu \text{g} \) per minute) resulted in conversion of negative U waves to positive ones, which lasted as long as the arterial pressure was maintained at normal levels. When the sodium nitroprusside was discontinued, arterial pressure rose to the preinjection levels and the U waves became negative again (fig. 2).

Study of degree of negativity of U waves...
NEGATIVE U WAVES

Effect of lowering of arterial pressure by intravenous sodium nitroprusside in a 60-year-old hypertensive man. The negative U waves became upright with lowering of arterial pressure and the voltage of R waves decreased. After discontinuation of the drug, the arterial pressure and electrocardiogram returned to control conditions.

At various levels of arterial pressure showed a gradual decrease in negativity proportional to arterial pressure fall. For each patient there was an arterial pressure level below which U waves became upright or isoelectric. In all, the polarity of U waves was related directly to the arterial pressure and was not primarily influenced by changes of the heart rate.

In one patient with atrial premature beats during a control period with direct arterial pressure recording, it was noted that negative U waves became upright with premature contractions during which the arterial pressure fell to normal. The beat following the premature contraction showed higher direct arterial pressure and more sharply inverted U wave than during periods when the rhythm was regular (fig, 3).

In the three patients in whom intravenous guanethidine was given, the initial pressor effect produced by this drug was associated with an increase of the negativity of U waves, whereas during the following period of the depressor effect, the U waves became upright. Tilting of the three patients prior to intravenous infusion of guanethidine did not result in change of the arterial pressure or the polarity of U waves. Tilting of the same patients after the infusion of intravenous guanethidine resulted in lowering of the arterial pressure and upright conversion of the U waves.

Changes in the polarity of the negative U waves were associated in six of the 12 patients with T-wave changes (diphasic T waves and of less amplitude than before). In eight patients lowering of the arterial pressure also resulted in a decrease of the amplitude of the R waves in the left precordial leads (fig. 2).

Discussion

The results indicate a direct correlation between arterial pressure levels and negativity

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of U waves in electrocardiograms of hypertensive patients, regardless of the severity and type of hypertension. This correlation was not only observed during periods ranging from 4 months to 7 years, but also in acute experiments in which it was shown that there is a level of arterial pressure below which a negative U wave becomes upright.

Since negativity of U waves in hypertensive patients increases with increase in arterial pressure and remains unchanged with unsatisfactory control of hypertension, the prognostic significance of persistent negative U waves in the electrocardiograms might reflect inadequate antihypertensive treatment without necessarily representing an additional grave prognostic sign. Change in the polarity of negative U waves following control of hypertension may indicate that these waves are not manifestations of organic changes in the myocardium, as suggested by Palmer, but rather are related to high arterial pressure levels.

Lepeschkin has observed that in many pa-

**Figure 3**

Direct brachial arterial pressure recorded with strain-gage manometer and lead V₅ in a hypertensive patient having atrial premature contractions. The U waves vary in relation to arterial pressure.
tients with angina pectoris the U waves become inverted during the second through the fourth minute after exercise. We have observed this in one hypertensive patient with coronary arterial disease in whom simultaneous arterial pressure measurements were made; the negative U waves were associated with marked pressor response to exercise and disappeared 3 minutes thereafter, at the time when arterial pressure returned to pre-exercise levels. In subsequent exercise, when the pressor response to exercise was eliminated with sodium nitroprusside, negative U waves did not appear. It is possible that in patients with coronary disease, negative U waves following exercise are also a manifestation of the pressor effect of exercise and not of the associated coronary arterial disease.

Surawicz et al. have noted, without reporting simultaneous arterial pressure measurements, that in some cases the faster heart rate was accompanied by a negative, and a slower rate by a positive U wave. In our study the polarity of the U waves was not influenced by the heart rate; in all patients in whom sodium nitroprusside was given, conversion of negative U waves occurred as a result of the arterial pressure fall and in spite of the slight increase in heart rate (fig. 2). Also in patients in whom spontaneous variations in the heart rate occurred, slowing resulted in change of the polarity of a negative U wave only when associated with a fall in arterial pressure. Similarly, positional changes did not influence the polarity of U waves unless the arterial pressure changed.

The four patients in whom negative U waves remained unchanged, despite lowering of arterial pressure, had serious cerebral and coronary arterial disease. Since it is well known that negative U waves also occur in normotensive patients with coronary arterial disease, it may be that vascular disease is an additional factor responsible for negative U-wave persistence in occasional hypertensive patients with well-controlled arterial pressure.

Lepeschkin believed that the best explanation of the U wave is that it corresponds to potential differences produced during the descending limb of a negative afterpotential. Ferrero and Gay suggested that a mechanical factor and an electrical one contribute to the genesis of the U wave. Furbera et al. concluded that U and T-U changes might be present in all cardiovascular diseases in which a hemodynamic abnormality places strain on the structures of papillary muscle. Although the mechanism by which negative U waves are produced is not clear, it is apparent from the results of our study that in hypertensive patients elevated arterial pressure is a contributing factor.

Summary

Direct correlation exists between arterial pressure levels and negativity of U waves in electrocardiograms of hypertensive patients; lowering of arterial pressure results in conversion of negative to positive U waves in the majority of hypertensive patients. Presence of negative U waves does not necessarily indicate organic myocardial changes or a grave prognosis; when their polarity remains unchanged following antihypertensive treatment, it may indicate unsatisfactory control of arterial pressure.

References

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Water

Of all the terrestrial agents by which the surface of the earth is geologically modified, by far the most important is water. We have already seen, when following hypogene changes, how large a share is taken by water in the phenomena of volcanoes and in other subterranean processes. Returning to the surface of the earth and watching the operations of the atmosphere, we soon learn how important a part of these is sustained by the aqueous vapor that pervades the atmosphere.

The substance which we term water exists on the earth in three well-known forms: (1) gaseous, as invisible vapor; (2) liquid, as water; and (3) solid, as ice. The gaseous form has already been noticed as one of the characteristic ingredients of the atmosphere. Vast quantities of vapor are continually rising from the surface of the seas, rivers, lakes, snow fields, and glaciers of the world. This vapor remains invisible until the air containing it is cooled down below its dewpoint, or point of saturation,—a result which follows upon the union or collision of two aerial currents of different temperatures, or the rise of the air into the upper cold regions of the atmosphere, where it is chilled by expansion, by radiation, or by contact with cold mountains. As the vapor is largely raised from the ocean surface, so in great measure it falls back again directly into the ocean. A considerable proportion, however, descends upon the land, and it is this part of the condensed vapor which we have now to follow. Upon the higher elevations it falls as snow, and gathers there into snow fields, which by means of glaciers, send their drainage towards the valleys and plains. Elsewhere it fall chiefly as rain, some of which sinks underground to gush forth again in springs, while the rest pours down the slopes of the land, swelling the brooks and torrents which, fed both by springs and rains, gather into broader and yet broader rivers that bear the accumulated drainage of the land out to sea. Thence once more the vapor rises, condensing into clouds and rain to feed the innumerable water channels by which the land is furrowed from mountain top to seashore.

In this vast system of circulation, ceaselessly renewed, there is not a drop of water that is not busy with its allotted task of changing the face of the earth.—Geikie, *Textbook of Geology*. London, 1903. 4th ed., Vol. I, p. 447.

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