Pseudonormalisation of the T wave: old wine?

A fresh look at a 25-year-old observation

A. Simon, L.J.H. Robins, T.E.H. Hooghoudt, B.T.J. Meursing, A.J.M. Oude Ophuis

A 74-year-old woman with documented coronary artery disease presented with symptoms of angina at rest. During these episodes of angina, the initial abnormal terminal negative T waves converted to normal positive T waves. In this article the significance of pseudonormalisation as a sign of ischaemia is reviewed. The underlying electropathological basis of this phenomenon is discussed as well. (*Neth Heart J* 2007;15:257-9.)

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Acute myocardial ischaemia can present with clear-cut ECG abnormalities such as ST-segment depression or elevation, which will enable the physician to institute appropriate treatment. Occasionally, however, patients with pre-existent abnormal negative T waves on the ECG present with complete reversion to positive T waves during anginal symptoms. These ECG changes are subtle and can often only be appreciated through continuous STT-segment monitoring. Frequently, these ECG changes are mistakenly interpreted as an improvement of the ECG, and in consequence, the opportunity to treat these patients adequately for instable angina may be missed.

Case report

A 74-year-old woman presented with symptoms of angina at rest for one day. Her medical history revealed

a transient ischaemic attack three years before presentation. No cardiac disease was reported. The patient was a non-smoker and the family history revealed three siblings with myocardial infarction before the age of 60. The baseline ECG on presentation without symptoms (figure 1A) showed negative T waves in leads aVF, V₅ and V₆. A subsequent ECG recorded during an episode of angina (figure 1B) showed positive T waves in leads V₅ and V₆, isoelectric in aVF and more pronounced positive in I, II and aVL. These changes returned to the baseline ECG after the patient took nitroglycerine sublingually and her symptoms disappeared. Laboratory results included a maximum troponin-T of 0.19 µg/l (normal 0 to 0.03 µg/l), aspartate aminotransferase 45 U/l (0 to 40 U/l), alanine aminotransferase 26 U/l (0 to 40 U/l) and creatine kinase 141 U/L (0 to 170 U/l). On coronary catheterisation a 70% stenosis of the circumflex coronary artery, as well as a 50% proximal left anterior descending artery stenosis and an 80% stenosis of M0 and D1 were observed. The patient was referred for coronary artery bypass grafting.

Discussion

Pseudonormalisation of T waves was first defined in the 1970s, when continuous electrocardiographic recordings became available.¹⁻³ When these recordings were used to monitor patients with frequent acute ischaemic episodes, pseudonormalisation of repolarisation was often observed, not always accompanied by angina.

Evidence for pseudonormalisation as a sign of myocardial ischaemia

Maseri et al. were the first to present evidence that pseudonormalisation of T waves is directly related to transmural myocardial ischaemia.^{4,6} Thallium scintigraphy performed during anginal attacks at rest in patients with pseudonormalisation of T waves showed a massive reduction of ²⁰¹Tl activity in the myocardial region corresponding to the location of T-wave changes.^{4,6} This reduction of ²⁰¹Tl activity was similar to that seen in patients with ST-segment elevations during angina (while scintigrams in patients with ST-segment depression showed a milder reduction).⁶

A. Simon

L.J.H. Robins

T.E.H. Hooghoudt

B.T.J. Meursing

A.J.M. Oude Ophuis

Department of Cardiology, Canisius Wilhelmina Hospital, Nijmegen, the Netherlands

Correspondence to: A.J.M. Oude Ophuis

Department of Cardiology, Canisius Wilhelmina Hospital, PO Box 9015, 6500 GS Nijmegen, the Netherlands

E-mail: ton@oude.ophuis.net

Figure 1. (A) Baseline ECG of patient. (B) ECG during an episode of angina demonstrating pseudonormalisation of T waves, especially in leads V_5 and V_6 .

When coronary angiography was performed during spontaneous episodes of transient myocardial ischaemia with concurrent pseudonormalisation of T waves on the ECG, a severe but reversible occlusive coronary vasospasm was observed similar to that seen at times of ST-segment elevation.⁴ The site of the coronary spasm always corresponded to that of the T-wave changes and perfusion defect on scintigraphy. The sequence of events during angina at rest with pseudonormalisation of T waves and the accompanying haemodynamic signs indicating acute impairment of left ventricular function are indistinguishable from those observed during episodes with ST-segment elevation.⁵

Pseudonormalisation may be the only ECG change seen during acute myocardial ischaemia, but it can also be an early sign, preceding frank ST-segment elevation. It can occur in patients who remain asymptomatic. Chierchia et al. monitored six patients with transient recurrent episodes of angina at rest for a mean of 8.6 hours, and observed 137 ischaemic episodes. Seven out of 21 episodes with ST-segment elevation were accompanied by angina while 14 episodes remained asymptomatic, while only two of 104 episodes of pseudonormalisation of T waves were symptomatic.⁵

The defects on scintigraphy as well as on angiography were always located at the site corresponding to the T-wave normalisation; thus simultaneous ST-segment depressions in other ECG leads, which are often far more obvious, can be interpreted as reciprocal signs of ischaemia.⁶

Electrophysiological basis of T-wave pseudonormalisation

The electropathology behind the pseudonormalisation of the T wave may be explained by a superposition of acute ischaemic effects on the action potential of myocardial cells on top of chronic ischaemic effects. The precise mechanism of these ischaemic effects has not yet been completely elucidated, but the following theory is generally thought to apply (figures 2 and 3).

Under normal conditions, the ST segment is iso-electric because all myocardial cells attain the same

transmembrane potential during repolarisation (figure 2A). Repolarisation starts in subepicardial cells before moving to the endocardium; phase 3 of the transmembrane action potential in the epicardial cells therefore occurs before that of the endocardial cells.⁷ At point X in figure 2A, the action potential (and thus the charge inside the cell) is more positive in subendocardial cells than in subepicardial cells. Thus, subendocardial cells will have a more negative external charge than subepicardial cells. Since currents tend to flow from areas that are negative to those which are (more) positive, the repolarisation current flows from endocardial to epicardial regions. This will result in a positive T wave in leads orientated to the epicardial surface.⁸

Hyperacute ischaemia shortens the duration of the action potential in the ischaemic area, resulting in earlier repolarisation (figure 2B). At point Y, the fully repolarised ischaemic cells will already have a negative internal, and positive external charge. The myocardial cells from the uninjured area will still be negatively charged externally and thus a repolarisation current will flow from the negatively charged uninjured cells to the positively charged ischaemic region, towards a lead at the site of the injury. This will result in an upright T wave, which will be exaggerated in amplitude because it starts earlier and will therefore not be balanced by recovery of other cells in remote healthy areas of the heart: the hyperacute T wave.^{7,8}

In subacute ischaemia, there are further changes of the action potential in myocardial cells. The resting membrane potential is lowered, and the action potential will be of shorter duration and lower amplitude (figure 2C). The different external charges of ischaemic and healthy myocardial cells will result in depression of the T-Q baseline and elevation of the ST segment (which will seem to be more impressive because of the depressed baseline).

Chronic ischaemic injury of a myocardial cell has a different effect on its action potential: it will be of longer duration (figure 3A). At point Z, the uninjured cells will already be fully repolarised and thus positively charged, while the chronic ischaemic cells will have a

Figure 2 and 3. Diagrams illustrating the relationship between the transmembrane action potential of a subendocardial (uninjured) cell (black continuous line) and a subepicardial cell (red dotted line), and the effect on the ECG reading of the epicardial lead. Adapted from Schamroth *et al.*⁸

(2A) Normal endocardial to epicardial depolarisation, resulting in a normal, positive T wave. (2B) Hyperacute ischaemia of the subepicardial cell, resulting in a shorter action potential (dotted line) and a hyperacute positive T wave. (2C) Subacute ischaemia of the subepicardial cell, resulting in lowered resting membrane potential and decreased duration and amplitude of the action potential (dotted line). This is seen on the ECG as ST-segment elevation. Point X and Y: see text.

(3A) Chronic ischaemic injury of the subepicardial cell, which causes a longer duration of the action potential (dotted line), and therefore a negative T wave. (B+C) Pseudonormalisation of T wave: (hyper)acute ischaemic injury in a subepicardial cell with previous chronic ischaemic injury will progressively shorten the duration of the action potential, leading to an iso-electric (B) or positive (C) T wave. Point Z: see text.

negative external charge. This results in a current directed away from the lead at the location of the injury, and therefore a negative T wave.

When a new hyperacute ischaemic event occurs in cells which have chronic ischaemic injury, this will lead to shortening of the duration of the action potential (figures 3B and 3C). Depending on the severity and duration of the acute ischaemia, this will result in an iso-electric T or even a positive T wave: the phenomenon known as pseudonormalisation. If ischaemia persists, this may of course further affect the action potential, resulting in the configuration shown in figures 2B and 2C.

In conclusion, pseudonormalisation of T waves is a sign of acute myocardial ischaemia. Serial recording of ECGs or continuous STT-segment monitoring in patients with transient anginal symptoms is helpful to detect this phenomenon. Although pseudonormalisation has received little attention in the last 25 years, knowledge of the phenomenon and its electrophysiological basis may facilitate cardiologists in clinical decision making in patients with angina. ■

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