Electrical activation of ventricles and interventricular septum in hypertrophic obstructive cardiomyopathy¹

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In 10 cases with proven left ventricular outflow obstruction, we studied the time sequence of activation at the epicardial surface, in the left ventricular wall, and in the interventricular septum by means of epicardial exploration and intramural needle electrodes carrying 10 to 20 terminals, during surgical exposure. A variable delay (15-40 msec) was found in subendocardial activation of the anterior paraseptal left ventricular wall, probably caused by a block in the anterior division of the left bundle-branch.

Epicardial excitation is additionally retarded by the increased diameter of the left ventricular wall because of hypertrophy. Conduction velocity in the left ventricular wall and in the interventricular septum was found to be approximately normal: ± 45 cm/sec; activation of the hypertrophic interventricular septum starts at normal times and proceeds mainly from left to right, with a smaller contribution from right to left; both fronts meet to the right of the middle of the interventricular septum; total septal activation time is prolonged because of hypertrophy.

Since the original description by Brock (1959) the condition known as hypertrophic obstructive cardiomyopathy or muscular subaortic stenosis has been studied extensively. The clinical manifestations, often of diagnostic significance, have been elucidated by Braunwald *et al.* (1964), Meerschwan (1968), Goodwin (1970), and many others. Wigle and Baron (1966) and also Coyne (1968), in their extensive studies of the electrocardiographic signs of this condition, advanced the hypothesis that the deep and broad Q waves - mimicking myocardial infarction - that are sometimes present in extremity and praecordial leads, are to be attributed to abnormal vectors resulting from hypertrophy of the interventricular septum.

In order to clarify the genesis of the abnormal electrocardiogram in hypertrophic obstructive cardiomyopathy, we studied the activation process of both ventricles and the interventricular septum on exposed hearts during operation.

The results of this study can be properly

evaluated only by their comparison with the normal pattern of ventricular and septal activation, recently published by Durrer *et al.* (1970).

Subjects

The 10 patients studied were of both sexes (8 male, 2 female) and of an age ranging between 10 and 52 years. They all had typical signs and symptoms of this condition and were selected for operation because of severe outflow obstruction and increasing incapacity. In all, a constant pressure gradient of more than 50 mmHg in the outflow tract of the left ventricle was established during cardiac catheterization, and a typical septal hypertrophy had been demonstrated by cineangiography.

All patients survived the surgical procedure.

The electrocardiogram did show left ventricular hypertrophy in 9 cases, abnormal Q waves in lead I, aVL, or the left praecordial leads in 5 patients; left axis deviation was present in one case, and none had right bundle-branch block.

Methods

Ventricular activation was explored in the exposed hearts, before the resection of a portion of the hypertrophic part of the left side of the interventricular septum. All hearts were in sinus rhythm

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and normothermic. The epicardial surfaces of both ventricles were explored with a hand-held electrode from which unipolar complexes were recorded.

In the left ventricular wall of every heart studied, one or more intramural electrodes were inserted (Durrer, 1968); we recorded unipolar and bipolar complexes from the intramural terminals, situated on these needle electrodes. Electrodes of 4 different designs were used. Since in the first cases our usual electrodes, carrying 10 platinum terminals of 0.1 mm diameter, at 2 mm interelectrode distance, proved to be too short, longer electrodes were developed. Also the design used next, carrying 10 terminals at 3 mm interelectrode distance, failed to reach the left ventricular cavity in some hearts because of the thickness of the left ventricular wall. Ultimately we resorted to electrodes that carried 20 terminals at 2 mm distances; the diameter of this electrode was 1.6 mm. Activation of the interventricular septum was studied by means of the latter type, and by intramural electrodes of 60 mm length provided with 10 terminals at distances of 2 mm, located at the distal part of the needle electrode. These electrodes were inserted into the interventricular septum via the right ventricle, and they were withdrawn stepwise after the activation was recorded in every position.

Electrode positions on the epicardial surface and the insertion sites of the intramural electrode were noted on a map of the heart, drawn after its exposure. A more precise anatomical localization of the intramural electrode position was not possible because all electrodes were withdrawn before the bypass started and also since all patients did survive the surgical procedure. Therefore, all positions of the intramural electrodes indicated in the diagram represent our best estimates. In one case, activation of the left septal surface was explored with a hand-held electrode introduced via the aortic valves during bypass, while the heart was not yet cooled and beating in sinus rhythm.

Recordings were made on 35 mm film from the screen of a specially designed 2- or 4-channel cathode-ray oscilloscope which had a high-frequency response, up to 12 KC, a high common mode rejection ratio, and a high input impedance. As a time reference, the left or right ventricular cavity potential was included in every record. Local activation time was measured from the rapid part of the intrinsic deflection in unipolar complexes and expressed in msec after the onset of left ventricular cavity potential.

Results

A: Left ventricular wall 1) *Subendocardial activation* is variably delayed in comparison with the normal left ventricular activation sequence. Delay in some cases (patient C, Fig. 1 and patient J, Fig. 2) is clearly present; the maximal retardation in the left anterior paraseptal area was about 30 msec (patient G, Fig. 3); normally this area is activated in the

FIG. 1 Patient C: A 10-year-old boy. Schematic representation of activation sequence at the 4 intramural electrodes inserted. For reasons of presentation they are depicted in one section of the heart. Their spatial orientation is given in the inset. Intramural electrode I and II show slight delay in subendocardial excitation time. There is no regular outward movement in the inner half of the wall; activation of the 4 terminals located here occurs in the 10–20 msec time interval. Activation then moves outwards at about normal velocity through the hypertrophic left ventricular wall. Intramural electrode III shows normal onset of excitation at both sides of the slightly hypertrophic interventricular septum. Excitation along the left bundle-branch is on time (Purkinje spike at 10 msec before the onset of left ventricular cavity potential). Intramural electrode IV shows irregular excitation usually seen in the anterior attachment of the interventricular septum.

5–10 msec interval after the onset of left ventricular cavity potential.

Activation of a large part of the inner layers of the anterior left ventricular wall appears to be more or less synchronous, whereas their normal activation pattern indicates radial spread in an endocardial direction, after the rapid distribution of early activation along the endocardial surface by the peripheral conducting system. This combination of delayed arrival of excitation of the subendocardial layer and activation of a relatively large inner part of the left ventricular wall in a

FIG. 2 Patient J, 50-year-old man. (a) Pre-operative electrocardiogram. (b) Epicardial activation; left ventricular epicardial excitation is delayed, particularly in the posterobasal area. (c) (opposite) Schematic representation of insertions of intramural electrodes. Electrodes I and II were inserted into the middle posterior and anterior left ventricular wall and show normal onset of subendocardial excitation, followed by conduction towards the epicardial surface.

FIG. 2a.

FIG. 2b.

restricted time interval, without clear indication of outward movement, was observed in the anterior paraseptal area and also in more lateral parts of the left ventricle in some hearts of this series.

In the few recordings obtained at the endocardial part of the posterior paraseptal left ventricular wall, no significant delay was seen (patient J, Fig. 2).

2) *Radial spread* After the excitation of the inner parts of the left ventricular wall, activation progresses outwards at an approximately normal velocity (about 45 cm/sec). Since the distance over which the activation travels towards the epicardial surface sometimes is large because of the increased diameter of the hypertrophic left ventricular wall, epicardial activation is additionally delayed in some cases (patient G, Fig. 3, and patient, I Fig. 4).

In the area overlying the anterior attachment of the interventricular septum, an irregular pattern of excitation was repeatedly found (patient C, Fig. 1), which could be due to the junction between this part of the ventricular septum and right and left ventricular musculature.

B: Activation of interventricular septum

Sometimes, action potentials of the septal subendocardial conduction tissue were recorded (patients C and G, Fig. 3c, and patient H, Fig. 5d). They indicate a normal excitation time of the main stem of the left bundle-branch and of some of its divisions that supply

FIG. 2c.

FIG. 3 Patient G, 17-year-old girl. (a) Pre-operative electrocardiogram. (b) Epicardial excitation. (c) Schematic representation of location of intramural electrodes. Intramural electrode I was introduced via the right ventricle through the upper part of the hypertrophic interventricular septum, located in the subaortic septal region, its tip just reaching the left ventricular cavity. Excitation time in the left bundle-branch is normal, septal activation starts at normal time for this area at the left endocardial surface and meets the excitation wave proceeding from the right side at 70 msec. Intramural electrode II shows abnormally late activation in the inner third part of the anterior paraseptal left ventricular wall; epicardial arrival is additionally delayed by the increased wall diameter. (d) Unipolar and bipolar complexes from intramural electrode I.

FIG. 3a.

FIG. 3b.

the left side of the interventricular septum. At both sides of the interventricular septum, excitation probably starts at normal time intervals after the onset of left ventricular cavity potential, at the different levels, between apex and base, which were studied in 3 patients; in the fourth patient (G), this conclusion depends on the location of the intramural electrode in the interventricular septum. If the intramural electrode was located in its basal posterior half, this conclusion is valid for this patient too. Due to the increased diameter of the interventricular septum – particularly in its upper part – septal activation may take a relatively long time (patient G, Fig. 3b and c): 70 msec versus 40 msec in normal condition. Also the contribution of the right ventricle to septal excitation is much larger than normal. In two cases, activation of the septal hypertrophic region, just below the aortic valves, started at the normal time (patient G, Fig. 3b and c, and patient I (Fig. 4c). In the case in which the left septal surface was explored, activation in the posteroinferior half did occur on time; a con-

FIG. 3c.

FIG. 3d.

spicuous activation delay was present over the anterosuperior septal part; activation in this area proceeded in an upward and forward direction (patient B, Fig. 6d).

C: Epicardial activation Right ventricular activation was normal with early breakthrough at the trabecular area at about 20 msec and eventually reaching the pulmonary conus at about 70 msec. Left ventricular epicardial activation in some cases was essentially normal, in other cases a conspicuous delay was present (patient A, Fig. 7b, and patient J, Fig. 2b).

In some cases (patient A, Fig. 7b) conspicuous Q waves were present in left ventricular epicardial complexes. Their location, voltage, and duration were variable; there was a conspicuous degree of correspondence to the Q waves observed in precordial leads. The presence, location, and voltage of these epicardial Q waves, however, were not clearly related to the degree of endocardial and intramural activation delay.

Discussion

The delay in endocardial activation, occurring mainly in the anterior left ventricular paraseptal area, can be explained by a failure of propagation in the anterior fasciculus of the left bundle-branch. We cannot yet offer a direct proof for this hypothesis in the form of recorded action potentials of this fasciculus. However, it is difficult to visualize a different mechanism. In addition, the activation sequence at the left septal surface in patient B (Fig. 6) offers strong support for this hypothesis, since in this patient activation occurs late in a high anterior portion of the left septal surface, whereas normally activation starts high anteriorly (even in proximity of the mitral valve), in addition to foci of early activation located midseptally and posteroinferiorly. In contrast, in some cases of valvular aortic stenosis, which we studied with the same technique, we found no such delay in subendocardial excitation in the anterior paraseptal area of the left ventricle.

It is remarkable that in only one case left axis deviation of -40° was present (patient G, Fig. 3a). In this case, the latest epicardial excitation observed in the left paraseptal area was approximately at 75 msec (Fig. 3b), which represents the longest activation delay observed in our series. In the other cases no correlation existed between the epicardial excitation time at the left ventricular paraseptal area and the mean QRS axis. This offers additional support for our hypothesis that in hypertrophic obstructive cardiomyopathy conduction in the anterior fasciculus is delayed in a variable degree. Complete blocking of conduction in this fasciculus, giving rise to clearly developed left axis deviation, represents the end of the scale of retardation of conduction and apparently is not too frequent in this condition.

Little is known about the distribution and functional state of the conduction system in hypertrophic obstructive cardiomyopathy. Failure of the anterior fasciculus of the left bundle to conduct may be due to several factors, such as stretching as it overlies the hyper-

Fig. 4a.

FIG. 4 Patient I, 52-year-old man. (a) Pre-operative electrocardiogram. (b) Epicardial activation, showing retardation at the left ventricular surface. (c) Schematic representation of intramural electrode insertions. Intramural electrode I was introduced into the upper part of the interventricular septum and shows essentially normal onset of septal activation. There is moderate septal hypertrophy. Intramural electrode II shows very late onset of activation in the lateral left ventricular wall with subsequent outward spread of excitation.

Fig. 4b.

Fig. 4c.

FIG. 5a.

trophied myocardium, increased left ventricular systolic and diastolic pressures, and mechanical trauma caused by squeezing of the conducting fibres between the hypertrophied region and the adjacent hypertrophied parts of the left ventricular wall or the anterior leaflet of the mitral valve.

Further, some degeneration of the specialized conduction system may be present in hypertrophic obstructive cardiomyopathy. In this respect it is of more than historical importance that Tawara attributed sudden death to pathological changes in the specific conduction system (1908).

The synchronous activation in a relatively large inner portion of the left ventricular wall can be explained in two different ways which are not mutually exclusive. It may be the result of tangential conduction from adjacent areas of the left ventricular wall or from the interventricular septum. This mechanism can be expected to occur when normal early delivery of excitation in the anterior wall fails and leaves an undepolarized area surrounded by rapidly expanding excitation fronts. A similar tangential excitation is present in the anterior attachment of the interventricular septum at the left ventricular wall during left bundle-branch block, and is caused by the excitatory wave coming from the right side.

In cases of delay or block of the anterior fasciculus, this mechanism may be present to a degree, determined by the conduction delay. From our own experiments on the isolated normal human heart, it may be concluded that this delay is about 20 msec, if block in the anterior fasciculus is present. If extensive areas of the subendocardial Purkinje system, connecting the network supplied by the posterior fascicle with the anterior fascicle network, are damaged, larger delays may be expected. Deep penetration of the subendocardial Purkinje system into the ventricular wall is the other mechanism which may be postulated, but no direct and convincing evidence about its presence has been found in our cases.

The genesis of the praecordial and epicardial Q waves, sometimes present in hypertrophic obstructive cardiomyopathy, has been attributed to the occurrence of an abnormal vector resulting from activation of the hyper-

FIG. 5 Patient H, 38-year-old man. (a) Pre-operative electrocardiogram. (b) Epicardial activation, normal pattern. (c) Schematic representation of location of intramural electrodes. Intramural electrode I was introduced relatively low in the interventricular septum and shows normal septal activation. P-1: subendocardial Purkinje spike at 1 msec before the onset of left ventricular septal activation (see also Fig. 5d). Intramural electrode II shows normal activation sequence at the anterior paraseptal left ventricular wall and in the posterior subendocardium. (d) Essentially normal septal activation along intramural electrode I.

FIG. 5b.

FIG. 5c.

trophied septum (Wigle and Baron, 1966). Our material, of necessity limited and inhomogeneous, does not permit us to draw definite conclusions about these Q waves. Undoubtedly septal activation creates an initial vector directed to the right; this may account for Q waves over the lateral part of the left ventricle that were seen in four of our cases, but only if this vector is abnormally large, resulting either from an abnormally large volume of the area of early depolarization, or from an increase of voltage of the equivalent dipole.

We did not find evidence for the latter possibility, as the voltage in the bipolar leads from the interventricular septum was within normal limits.

It seems improbable that the long duration of excitation in the hypertrophied septum is directly discernible in the epicardial Q waves of the left ventricle since these Q waves have a maximal duration of about 30 msec whereas septal activation takes much longer. The terminal septal vector, however, may reduce the R wave voltage in the lateral part of the left ventricle.

The presence or absence of Q waves over the anterior paraseptal region of the left ventricle is more difficult to explain at present. We suggest that retardation of subendocardial and intramural activation and sometimes cancellation due to intramural Purkinje penetration to some degree, resulting in irregular activation in the inner layers, contribute to these Q waves. One would expect Q waves to occur whenever a conduction delay exists in the subendocardial layer; their absence in some cases can be explained only on the assumption of cancellation by other initial vectors directed to this region, such as the tangential spread of activation directed forwards along the left side of the interventricular septum. Undoubtedly, the irregular hypertrophy which characterizes this condition is responsible for the occurrence of an array of abnormal initial depolarization fronts in the inner layers of the left ventricular wall that create an individually variable degree of cancellation, resulting in the variability of the epicardial and praecordial Q waves in hypertrophic obstructive cardiomyopathy. Another factor contributing to the voltage of Q waves

FIG. 5d.

FIG. 6a.

FIG. 6 Patient B, 33-year-old man. (a) Pre-operative electrocardiogram. (b) Epicardial activation; at sites marked I-IV, 4 intramural electrodes have been inserted. (c) Intramural excitation at the 4 intramural electrodes. (d) and (e) Intramural unipolar and bipolar complexes recorded from intramural electrodes II and IV, showing relatively late onset of subendocardial activation. (f) Activation of the left side of the interventricular septum during total bypass and at normal temperature. Excitation in the left upper anterior part, supplied by the anterior division of the bundle-branch, is delayed, as compared to the normal activation sequence and to activation near the end point of the posterior division.

FIG. 6b.

may be the reduced volume of the left ventricular cavity, associated with hypertrophic obstructive cardiomyopathy, which may cause a significant reduction in the degree of cancellation of the initial vectors, generated by septal and subendocardial depolarization (Nelson, 1957).

In general, unipolar complexes recorded from the epicardial surface correspond well to the praecordial leads of the preoperative electrocardiogram. The difference in Q waves seen in some cases between praecordial and epicardial complexes may be related to the surgical procedure. The conditions of operation and anaesthesia may have caused some change in conduction in the myocardium or in the specialized conduction system or in both of them, resulting in a slightly different activation during our direct recordings as compared to the preoperative electrocardiogram. In addition, the changes in the volume conductor caused by the exposure of the heart may have affected the configuration of the recorded complexes.

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FIG. 6c.

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Fig. 6d to 6f and Fig. 7a, b, and c are on the following pages.

FIG. 6d.

FIG. 6f.

FIG. 6e.

FIG. 7a.

FIG. 7b.

FIG. 7 Patient A, 12-year-old boy. (a) Pre-operative electrocardiogram. (b) Epicardial unipolar complexes and activation times in msec after the onset of left ventricular cavity potential. I and II: sites of insertion of intramural electrodes. (c) Schematic representation of location of the two intramural needle electrodes and activation sequence at the intramural terminals.

FIG. 7c. pat. A