Diagnostic Value of the First and Second Derivatives of the Arterial Pressure Pulse in Aortic Valve Disease and in Hypertrophic Subaortic Stenosis

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IT HAS been appreciated for many years that characteristic alterations in the configuration of the central and peripheral arterial pressure pulses occur in the presence of abnormalities of the aortic valve, whether they are induced experimentally or occur in patients with aortic valve disease.1 It is also recognized that the arterial pressure pulse is modified in patients with idiopathic hypertrophic subaortic stenosis, although the changes that occur in this disease differ strikingly from those seen in patients with valvular aortic stenosis.6-8 In the past, the characterization of arterial pressure pulses in patients with these lesions has consisted of descriptions of the pulse contour, determination of the presence and position of the anacrotic and dicrotic notches, measurement of the duration of systole and of the systolic upstroke time, and estimation of the slope of the pressure rise. In patients with severe valvular aortic stenosis, there is often prolongation of the total duration of ejection and of the systolic upstroke time.9-13 Although the latter period is shortened in patients with idiopathic hypertrophic subaortic stenosis, there is considerable overlap in these measurements among various groups of patients and normal individuals.9 In order to derive more diagnostic information from the pressure pulse, some investigators have calculated the mean rate of arterial pressure rise by dividing the pulse pressure by the systolic upstroke time, or have estimated the slope of the pressure rise from the recorded tracing.8 It has recently become possible, by electronic means, to compute continuously and instantaneously the rate of change, i.e., the first derivative (dp/dt) of the pressure pulse, from which the second derivative (d²p/dt²) can be determined. A study of the first and second derivatives of the direct arterial pressure pulse in patients with various forms of aortic valve disease and with hypertrophic subaortic stenosis was undertaken, since it was considered that this quantitative analysis of the pulse contour might provide information of greater diagnostic value than that available from the older, more qualitative descriptions.

Clinical Material

A total of 140 subjects were studied. Twenty-three were normal individuals who ranged in age from 18 to 53 years (Av. = 28). The remaining 117 patients had various forms of congenital or acquired heart disease and, in each of them, the diagnosis and severity of the lesion were established by left heart catheterization. Twenty-nine patients had valvular aortic stenosis; this site of obstruction was visualized at open operation in 24 of them and the presence of valvular stenosis was proved by left ventricular angiocardiography or continuously recorded pressure tracings during catheter withdrawal across the valve in the other five. The peak systolic left ventricular-arterial pressure gradients in these patients varied widely and ranged between 22 and 162 mm. Hg (Av. = 83). Six patients had discrete subaortic stenosis with systolic pressure gradients ranging from 55 to 170 mm. Hg (Av. = 112); in each the diagnosis was confirmed at open operation. In 33 patients with idiopathic hypertrophic subaortic stenosis the diagnosis was established by a combination of hemodynamic and angiocardiographic means, as described previously.7 Intraventricular pressure gradients ranging from 18 to 135 mm. Hg (Av. = 71) were

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recorded, in the basal state, in 20 of these patients. The other 13 had severe left ventricular hypertrophy, but no evidence of obstruction at rest and in the basal state. However, a typical subvalvular gradient was provoked in each patient by the administration of isoproterenol or with muscular exercise. In 24 patients free aortic regurgitation was present. This diagnosis was proved at open operation in 19 patients and in 23 of them by aortography as well. A significant degree of associated aortic stenosis was excluded in all 24 of these patients by the findings at left heart catheterization; the peak left ventricular-aortic systolic pressure gradients did not exceed 20 mm Hg in any patient in this group. In 20 of 25 patients the diagnosis of combined aortic stenosis and regurgitation was proved at open operation. At left heart catheterization, the peak systolic gradients in the patients with the combined lesions varied widely and ranged from 30 to 120 mm Hg (Av. = 67); significant aortic regurgitation was demonstrated by means of aortography.

Measurements of dp/dt were carried out both before and after operation in 16 patients. Four of these patients had valvular aortic stenosis and the surgical treatment consisted of open valvulotomy and debridement in two, complete replacement with a Teflon (Muller) valve prosthesis in one patient, and with a caged-ball (Starr-Edwards) prosthesis in another. One patient had discrete subvalvular obstruction and underwent excision of the obstructing membrane. Five patients had pure aortic regurgitation and the operation consisted of the placement of a Teflon valve prosthesis in three patients and a caged-ball valve prosthesis in two. Two patients had combined aortic stenosis and aortic regurgitation; both were treated with the Teflon valve prosthesis. Four patients had idiopathic hypertrophic subaortic stenosis and all of them underwent myotomy and excision of the hypertrophied subvalvular tissue.

Methods

The brachial artery was cannulated with an 18-gage Cournand needle and, in order to insure high-fidelity tracings free from artifacts, the needle was directly connected through a stopcock to a pressure transducer (Statham P23D) without any intervening tubing. When tested in a sine-wave generator, this system was found to provide a uniform response to frequencies of 40 cycles per second. The first derivative of the pressure pulse was continuously determined with an R-C differentiating circuit having a time constant of 9.4 \times 10^{-5} \text{ seconds}, which provided differentiations of linear amplitude having no phase distortion to 50 cycles per second, as described in detail elsewhere. The mean rate of rise of the first derivative, i.e., the second derivative \(d^2p/dt^2\) of the arterial pressure pulse was calculated by dividing the peak first derivative

![Figure 1](https://example.com/figure1.png)

**Figure 1**

BA dp/dt in normal subjects and in patients with abnormalities of the aortic outflow tract. AS, valvular aortic stenosis; AS/Al, combined valvular aortic stenosis and regurgitation; Al, pure aortic regurgitation; DSAS, discrete subvalvular aortic stenosis; IHSS, idiopathic hypertrophic subaortic stenosis. In the group with IHSS, the open circles refer to patients without an intraventricular pressure gradient in the basal state and the closed circles refer to patients with obstruction in the basal state.
0

AORTIC PEAK SYSTOLIC GRADIENT
mm Hg

The relationship between BA dp/dt and the peak aortic systolic gradient in patients with valvular aortic stenosis.

by the time interval between the onset of the pressure pulse and the peak dp/dt. The dp/dt was recorded at a paper speed of 100 or 200 mm./sec. to permit accurate determination of d^2p/dt^2.

Results

In the normal subjects, the peak first derivative of the brachial arterial pressure pulse (BA dp/dt) averaged 811 ± 185 (SD) mm. Hg/sec. (fig. 1A). In the patients with valvular aortic stenosis the BA dp/dt was significantly lower (p < .01) than in the normal subjects, and averaged 358 ± 85 mm. Hg/sec. The BA dp/dt fell within the range observed in the patients with valvular aortic stenosis in only one of the 23 normal subjects, and 21 of the 29 patients with valvular aortic stenosis had levels of the BA dp/dt below 428 mm. Hg/sec., the lowest normal value (fig. 1B).

Figure 2 illustrates the relation between the BA dp/dt and the peak systolic pressure gradient in the patients with valvular aortic stenosis. It is clear that an inverse correlation existed between these two variables, the patients with the lowest gradients having values of the BA dp/dt close to the normal range, and the patients with the most severe obstruction

Figure 3

Representative tracings of the BA pressure pulse and dp/dt obtained from normal subjects and from patients with abnormalities of the aortic outflow tract. Grad., aortic outflow tract peak systolic pressure gradient; CI, cardiac index; OA, aortic outflow orifice. For other abbreviations see figure 1.
tending to have the lowest values \((r = -0.51, p < 0.01)\).

In the patients with combined aortic stenosis and regurgitation the BA dp/dt averaged 724 ± 212 mm. Hg and was, therefore, in the normal range (fig. 1C). There was no overlap between the values noted in these patients and those with pure valvular aortic stenosis. The highest values of the BA dp/dt were observed in the patients with pure aortic regurgitation (Av. = 1,736 ± 530 mm. Hg) (fig. 1D). Only one patient with pure aortic regurgitation had a value of the peak dp/dt that was lower than the highest value observed in the patients with the combined lesions. In the six patients with discrete subvalvular aortic stenosis, the BA dp/dt averaged 547 ± 94 mm. Hg; five of these had BA dp/dt values that were within the normal range, and although the values in the patients with discrete subaortic stenosis overlapped those observed in the patients with valvular obstruction, the mean value in the

![Figure 4](https://circ.ahajournals.org/)

**Figure 4**

The effects of operative correction on the BA dp/dt in patients with abnormalities of the aortic outflow tract. The horizontal broken lines show the range of BA dp/dt in the normal subjects. The solid horizontal bars refer to the average BA dp/dt before and after operation in each group. PREOP., preoperative study; POSTOP., postoperative study. In figure A (upper left) the solid circles represent data from patients with valvular aortic stenosis, while the open circles represent data from a patient with discrete subvalvular obstruction.
patients with discrete subaortic stenosis was significantly ($p < .01$) higher than in the patients with valvular aortic stenosis and significantly ($p < .01$) lower than the mean value observed in the normal subjects.

In the patients with idiopathic hypertrophic subaortic stenosis, the BA dp/dt averaged 1,092 ± 372 mm. Hg, and in each instance exceeded the highest value observed in the patients with valvular aortic stenosis (fig. 1F). Although there was considerable overlap between the findings in the normal subjects and in those with idiopathic hypertrophic subaortic stenosis, the highest normal value was exceeded in 11 or the 33 patients with this lesion, and the mean value in the patients with hypertrophic subaortic stenosis was significantly ($p < .01$) higher than that observed in the

Figure 5

The effects of surgical treatment on the BA dp/dt in a patient with aortic stenosis. Representative tracings are shown of the BA pressure pulse and dp/dt (top) and of the BA and left ventricular (LV) pressure pulses recorded at the time of cardiac catheterization (bottom), before surgery (left) and following operative correction (right). Note the elevation of the BA dp/dt.
normal subjects and in the patients with discrete subvalvular obstruction \((p < .01)\). Only two patients in the latter group had a \(\text{dp/dt}\) that exceeded the lowest value observed among the patients with hypertrophic subaortic stenosis (figs. 1E and F). There was no consistent difference in the values observed in the patients with idiopathic hypertrophic subaortic stenosis who had obstruction in the resting state and those who did not (fig. 1F). A positive correlation \((r = .57, p < .02)\) existed between the BA \(\text{dp/dt}\) and the effective orifice size in the patients with idiopathic hypertrophic subaortic stenosis who had obstruction at rest, i.e., the smaller the orifice size, the lower was the BA \(\text{dp/dt}\). Tracings representative of the BA pressure pulse and of the BA \(\text{dp/dt}\) observed in the six groups of patients are shown in figure 3.

The effects of operative correction on the BA \(\text{dp/dt}\) of 16 patients are shown in figure 4. In four patients with valvular aortic stenosis, and in one patient with discrete subaortic obstruction, the peak \(\text{dp/dt}\) rose substantially after relief of the stenosis (figs. 4A and 5). Conversely, in the five patients with aortic regurgitation the peak \(\text{dp/dt}\) fell to within the normal range (fig. 4B). Essentially no changes in the BA \(\text{dp/dt}\) occurred in the two patients with combined aortic stenosis and regurgitation (fig. 4C). The BA \(\text{dp/dt}\) fell in three of the four patients with idiopathic hypertrophic subaortic stenosis in whom myotomy and resection of the hypertrophied muscle was performed and showed little change in the fourth patient (fig. 4D).

When the peak value of the BA \(\text{dp/dt}\) was divided by the time interval between the onset of the arterial pressure rise and the peak \(\text{dp/dt}\), i.e., when the mean second derivative \((d^2p/dt^2)\) was calculated, a number of additional findings became apparent (fig. 6). In the patients with valvular aortic stenosis, not only were the peak \(\text{dp/dt}\) values low, but the time intervals from the onset to the peak \(\text{dp/dt}\) were prolonged, compared to the nor-

![Figure 6](Image)

**Figure 6**

The relationship between the BA \(\text{dp/dt}\) and the time interval from onset to peak \(\text{dp/dt}\). The isopleth lines represent values for the second derivative of the BA pressure pulse. The graph on the left illustrates data obtained from each individual patient in each group. ●, normal subjects; ○, AS; □, AS/AI; △, AI; ■, DSAS; ◆, IHSS with obstruction at rest; ▲, IHSS without obstruction at rest. The graph on the right shows the range of values in each group of patients.
mal, resulting in extremely low values of the second derivative. In patients with valvular aortic stenosis the $d^2p/dt^2$ ranged between 1,700 and 20,277, with an average value of 9,046 mm. Hg/sec.$^2$, whereas in the normal subjects the range was between 15,010 and 44,000, with an average value of 31,335 mm. Hg/sec.$^2$. In the patients with discrete sub-aortic stenosis the values of the $d^2p/dt^2$ were intermediate between the normal subjects and the patients with aortic stenosis, and ranged between 6,471 and 28,000 and averaged 16,717 mm. Hg/sec.$^2$. Although the range of values for the first derivative in the patients with combined aortic stenosis and regurgitation was essentially identical with that in the normal individuals (fig. 1), the onset to peak dp/dt intervals in many of the patients with combined lesions exceeded the normal range, and therefore their second derivatives were substantially lower than those observed in the normal group and ranged between 5,950 and 54,250 (Av. = 19,787 mm. Hg/sec.$^2$). Finally, since in many of the patients with idiopathic hypertrophic subaortic stenosis and pure aortic regurgitation the onset to BA dp/dt intervals were shorter than normal (i.e., under 20 msec.), their second derivatives were extremely high, ranging between 23,333 and 110,556 and averaging 51,844 mm. Hg/sec.$^2$ in the patients with hypertrophic subaortic stenosis, and ranging between 29,474 and 204,167 and averaging 78,565 mm. Hg/sec.$^2$ in the patients with aortic regurgitation.

**Discussion**

The contour of the pressure pulse in the ascending aorta is determined in large measure by the instantaneous velocity of ejection from the left ventricle, by the distensibility of the systemic arterial bed and by the mass of blood that is accelerated. Normally, as the pulse wave travels to the periphery, it undergoes a series of characteristic transformations which result in part from friction of the blood with the vessel walls, hysteresis of the vessel walls, and the superimposition of pressure waves reflected from the smaller arteries and arterioles.$^5, ^10, ^21$ In normal human subjects the brachial arterial pressure pulse usually does not exhibit the anacrotic shoulder seen in the central aorta, but rises smoothly and rapidly to a peak that generally exceeds the maximum pressure in the ascending aorta.$^{22}$ When obstruction to left ventricular ejection occurs, the central aortic pressure rises more gradually than normal.$^2, ^3$ and does not undergo its usual transformation as it travels to the periphery; as a consequence, the contour of the peripheral pressure pulse resembles that of the central aortic pulse.$^3$

Clinicians have appreciated the importance of a small and weak arterial pulse on palpation in patients with aortic stenosis since Hope’s description of this sign in 1835.$^{23}$ The characteristics of the brachial artery pressure pulse in aortic stenosis are now well known and include a prolongation of the build-up time and a narrow pulse pressure.$^1, ^9, ^10, ^12, ^13, ^24, ^28$ Similarly, in patients with aortic regurgitation, the sharp arterial pulse and wide pulse pressure have been clinical hallmarks of the disease since Corrigan’s description in 1832.$^{29}$ It has been shown that when this lesion is produced experimentally, the wide peripheral arterial pulse pressure is a consequence of the large central aortic pressure and the normal augmentation of the pulse pressure that occurs as the pulse wave travels peripherally.$^4$ The rapid upstroke in the central and peripheral pressure pulses results primarily from an increased velocity of left ventricular ejection.

The measurement of the rate of rise of the arterial pressure represents a further refinement of the analysis of the pressure pulse; in patients with aortic valve disease and related lesions, this variable is more sensitive and provides more information than do the standard measurements of upstroke time and pulse pressure, since in normal individuals and in patients with aortic valve disease the values for the latter two variables frequently overlap, limiting their diagnostic value.$^9$ However, in the present study, measurement of the BA dp/dt permitted almost complete separation of the normal subjects from those with valvular aortic stenosis (fig. 1). Although there was a distinct tendency for the dp/dt to vary reciprocally with the severity of obstruction, as re-
DERIVATIVES OF THE ARTERIAL PRESSURE PULSE

The development of secondary hypertrophic subaortic stenosis in a patient with valvular aortic stenosis. Panel A illustrates tracings obtained before operation; panel B shows the tracings obtained in the operating room following surgical placement of a Teflon valve prosthesis; panel C shows the tracings obtained 3 weeks after operation, and panel D shows the tracings obtained 4 months after operation. AV area, effective aortic orifice size.

Figure 7

The development of secondary hypertrophic subaortic stenosis in a patient with valvular aortic stenosis. Panel A illustrates tracings obtained before operation; panel B shows the tracings obtained in the operating room following surgical placement of a Teflon valve prosthesis; panel C shows the tracings obtained 3 weeks after operation, and panel D shows the tracings obtained 4 months after operation. AV area, effective aortic orifice size.

One of the characteristic physical findings in patients with hypertrophic subaortic stenosis is the rapid rise of the peripheral arterial pulse, and measurement of the dp/dt has made it possible to quantify this physical finding. In the present investigation it was observed that the dp/dt was always greater in the patients with idiopathic hypertrophic subaortic stenosis than in those with valvular aortic stenosis (fig. 1). Indeed, the pressure pulse in the patients with idiopathic hypertrophic subaortic stenosis was frequently found to rise more rapidly than in the normal subjects. It appears likely that the obstruction in patients with hypertrophic subaortic stenosis does not remain fixed throughout systole, as in patients with valvular or discrete subvalvular stenosis, and the left ventricle ejects a disproportionately large fraction of its stroke volume in early systole, resulting in a supranormal velocity of ejection in early systole, a rapid rise of the arterial pressure pulse, and a relatively high BA dp/dt. The finding that the patients with idiopathic left ventricular hypertrophy without obstruction in the basal state exhibited values for dp/dt in the same range as those observed in the patients with idiopathic hypertrophic subaortic stenosis with obstruction suggests that, even in the absence of obstruction, the hypertrophied left ventricle may eject blood more rapidly than normal. Measurement of the BA dp/dt would thus appear to be a simple technic that is of considerable value in the differential diagnosis of valvular aortic stenosis and idiopathic hypertrophic subaortic stenosis.

In two patients with calcific aortic stenosis a particularly interesting sequence of measurements was obtained (fig. 7). Preoperatively, both patients had the typical low values of the BA dp/dt characteristic of severe valvular obstruction (fig. 7A). At operation their aortic valves were completely replaced, and measurements at the operating table revealed essentially no residual obstruction (fig. 7B). Three
weeks after operation repeat left heart catheterization revealed a return of severe obstruction, associated now with striking elevations of the BA dp/dt above the preoperative levels (fig. 7C). When these measurements were repeated 4 months after operation, the gradient had almost disappeared, and the peak dp/dt had fallen to the normal range (fig. 7D). It is likely that 3 weeks after operation the marked obstruction and associated high value for the BA dp/dt were related to hypertrophic subaortic stenosis, which was secondary to the prolonged valvular obstruction, and which had been unmasked by the surgical treatment of the primary lesion. The absence of a pressure gradient at the operating table can be explained by the depression of myocardial contractility at the end of the operation, a situation that has been found to abolish the obstruction in patients with idiopathic hypertrophic subaortic stenosis as well. Finally, the regression of the obstruction, and the decline of the BA dp/dt to the normal range is compatible with the regression of secondary hypertrophic stenosis after complete relief of the primary obstruction. It is not always feasible and, indeed, it may not be desirable, to subject patients to frequent measurement of left heart pressures and selective angiocardiography after operation. However, on the basis of the findings of this investigation it is suggested that high levels of the BA dp/dt in the postoperative period in the presence of obstruction to left ventricular outflow and in the absence of valvular regurgitation suggest that secondary hypertrophic subaortic obstruction is present.

From a clinical point of view the marked differences in the values of BA dp/dt noted among the patients with pure aortic stenosis, combined lesions, and pure aortic regurgitation should prove helpful. When severe aortic regurgitation is present, a loud systolic ejection murmur and a systolic thrill are generally present in the second right intercostal space and along the carotid vessels. These findings may be due to associated aortic stenosis, but may also occur in patients with isolated aortic regurgitation. Measurement of the BA dp/dt permits differentiation of these two groups of patients (fig. 1C and D). Similarly, when a significant degree of aortic regurgitation accompanies aortic stenosis, the dp/dt is higher than in patients with pure stenosis (fig. 1B and C).

The relative differences among the values for d²p/dt² were greater than those for dp/dt in the various groups of patients studied, and the overlap of the values for d²p/dt² in the various groups of patients was less than for the dp/dt. Thus, the values of dp/dt in the patients with combined aortic stenosis and regurgitation were within the range noted in normal subjects (fig. 1), but in nine of the 25 patients with this lesion the d²p/dt² was below the lowest normal value. Similarly, the values of dp/dt in the six patients with discrete subaortic stenosis were all within the normal range, but in three of them the d²p/dt² was abnormally low. Eight of the 29 patients with valvular aortic stenosis had values of dp/dt that exceeded 428 mm. Hg/sec., the lowest normal value. However, in four of these patients the d²p/dt² was below the lowest normal value. The dp/dt exceeded the highest normal value in 11 of the 33 patients with idiopathic hypertrophic subaortic stenosis. However, the d²p/dt² exceeded 44,000 mm. Hg/sec., the highest normal value of this variable in five additional patients with this disease.

The recording of the dp/dt and the calculation of the d²p/dt² are relatively simple and safe technics potentially capable of providing information of considerable diagnostic value in patients suspected of having aortic valve disease or the various forms of subaortic stenosis. A number of limitations of the methods must be appreciated. The rate of arterial pressure rise can be augmented by a number of influences such as peripheral vasodilatation, tachycardia, fever, excitement, circulating catecholamines, and the decrease in arterial distensibility that occurs in arteriosclerosis. Conversely, arteriolar constriction, bradycardia, myocardial depression, and a low stroke volume are among the influences that tend to lower the BA.
Thus, it is be able, basal state and in the absence of overt cardiac decompensation. Since the BA dp/dt can be influenced by factors other than the anatomic state of the left ventricular outflow tract, the range of dp/dt in normal subjects is necessarily wide and this limits the value of the measurement of the dp/dt in the detection of patients with relatively minor anatomic abnormalities.

Summary
The brachial arterial dp/dt was continuously computed by means of an electronic differentiating circuit in 117 patients and 23 normal subjects. The peak dp/dt averaged 1092 ± 372 (S.D.) mm. Hg/sec. in 32 patients with idiopathic hypertrophic subaortic stenosis, 547 ± 94 mm. Hg/sec. in six patients with discrete subvalvular subaortic stenosis, 811 ± 185 mm. Hg/sec. in 23 normal subjects, 358 ± 85 mm. Hg/sec. in 28 patients with valvular aortic stenosis, 724 ± 212 mm. Hg/sec. in 25 patients with combined aortic stenosis and regurgitation, and 1736 ± 530 mm. Hg/sec. in 24 patients with pure aortic regurgitation. It is suggested that the elevated peak dp/dt seen in patients with hypertrophic stenosis is due to the absence of obstruction to ejection early in systole. In contrast, patients with valvular and discrete subvalvular stenosis, who exhibit fixed obstruction to outflow throughout ventricular systole, had a peak dp/dt that tended to be lower than normal. Calculation of the second derivative (d²p/dt²) of the arterial pressure pulse provided even better separation of the various groups of patients studied. The analyses of the dp/dt and of the d²p/dt² of the brachial artery pressure pulse afford a simple and reliable assessment of the nature and location of left ventricular outflow obstruction and are helpful in the differentiation of valvular aortic stenosis, combined stenosis and regurgitation, and pure aortic regurgitation.

References
Aortic Stenosis

This lesion was first noted in 1646 by Riverius (Lazare Vivière, 1589-1655) and then by Vieuussens, but its clinical features were not recognized till after the advent of auscultation in the nineteenth century, and then largely due to Hope's clear account of the physical signs in 1832. Usually a disease of advanced life, cases in rare instances occur in early life; it may be a congenital abnormality due, as Keith pointed out, to arrested development of the bulbus cordis, and analogous to the much commoner lesion on the right side of the heart. Cases of this subaortic stenosis, consisting in an annular thickening of the endocardium below the aortic valves, have been ascribed to failure of the bulbus cordis to atrophy.—Sir Humphry Davy Rolleston. The Harveian Oration. Great Britain, Cambridge University Press, 1928, p. 47.
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