EVALUATION OF MYOCARDIAL CONTRACTILITY
BY THE NON-INVASIVE METHOD

RYUICHI KIKAWADA, CHUJI NORO, TERUO TSUYUSAKI,
JUN MURAMATSU, YUJI KAKUBARI, FUMIAKI MARUMO,
HIROKO NAGAI, AND YUKIO YABATA

In evaluation of cardiac function by the non-invasive method, the possibility
of separation of cardiac muscle performance from cardiac pump performance
was studied. Among the non-invasive values, SV/ET, SV/(AO/EO), Pd/ICT,
Pd/PEP, 1/ICT², ET/PEP, and ET/ICT were considered as parameters for
myocardial contractility. This research especially focused on Pd/ICT and
ET/PEP.

In auricular fibrillation it was possible to draw Starling-like curves and 3
dimensional coordinates to estimate a Vmax-like value. However this method
could not be used in sinus rhythm. Whereas, in hypertension with abnormal
afterload and uremia with abnormal preload, myocardial contractility was
expressed by Pd/ICT under the influence of almost pure preload and ET/PEP
under the influence of both preload and afterload. Therefore Pd/ICT was
corrected with preload (AO/EO) and (Pd/ICT)/(AO/EO) may be used as the
index for myocardial contractility.

IN RECENT years, problems of myocardial
contractility have drawn much attention.
The main factors which determine cardiac function are i) preload or end-diastolic volume and
passive stress based on this ii) afterload or resis-
tance to ventricular ejection and myocardial
tension in the systolic phase as the result iii)
contractility of the myocardium itself and iv)
synergy during contraction which modifies the
cardiac pump performance synthesized from the
factors of i) to iii) 17 The analysis of cardiac
function which was carried out until now is based
mainly on the cardiac pump performance, and
cannot be a direct expression of myocardial
contractility. In the standard hemodynamical
analysis 30 it is not always possible to conduct a
direct and detailed analysis on the cardiac muscle
performance or myocardial inotropic action.

[Graph: N.F. 68y.f. Coronary Sclerosis, etc]

Fig. 1. A starling-like ventricular function curve in the
case of auricular fibrillation. The relationship
between the preceding cycle length and 1/ICT²
or 1/PEP² was close to the starling curve. With
digitalization, the curve shifted upwards with
steepling of the slope.

Key Words:
Myocardial contractility
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Department of Internal Medicine, Kitasato University School of Medicine, Asamizodai, Sagamihara, Japan

Fig. 2. The curves equivalent to the force-velocity-length relations according to Sonnenblick, Braunwald et al. in a case of auricular fibrillation. ICT was used instead of force and ET/PEP instead of velocity. A Vmax-like point was estimated based on the crossing point with ET/PEP axis. In drugs with a positive inotropic effect such as digitalis, isoproterenol and norepinephrine, a Vmax-like value rose and upon administration of propranolol with negative inotropic action it fell.

Fig. 3. The relationship between the degree of severity in hypertensive heart and vascular dynamics. In cases of congestive heart failure (4'), decrease of cardiac pump performance was evident. Even in some cases with 1' - 3' severity, decrease of stroke volume and cardiac output, and increase of total peripheral resistance was evident. Hypertensive heart may have a latent tendency towards cardiac failure even in the initial stage.

Among various parameters requiring accurate analysis, contractility of intact cardiac muscle is the most difficult to evaluate. Sonnenblick and Braunwald et al. stated that the cardiac muscle performance can be quantitatively evaluated by force-velocity-length relations in 3 dimensional coordinates. However, its clinical evaluation is difficult to obtain as long as patients are studied, because restrictions are always present and the extent of actual clinical application is decided under these restrictions. In daily clinical practice, routine measurement of Vmax is almost impossible. The possibility of obtaining the parameter for myocardial contractility by the noninvasive method was studied in this paper, because this method can be easily and repeatedly used.

**Materials and Methods**

As the representative disease of afterload, 225 cases of essential hypertension were selected, while 60 cases of uremia were selected as the representative disease of preload.

Essential hypertension was classified according to severity using the modified method of Roland. The relationship between this classification of severity and the cardiovascular dynamics constituting hypertension has already been reported. This method essentially consist of evaluating the degree of severity of systolic pressure (Ps), diastolic pressure (Pd), funduscopic findings, renal status, cardiac status, and cerebral status. After making the score of severity for Pd and funduscopic findings double to calculate, the total index is obtained by adding the scores to the other factors. The score of severity for cardiac status is evaluated as follows:

1°: Appearance of Ekg pattern indicating left ventricular hypertrophy
2°: Addition of dyspnea
3°: Cardiac decompensation favorably influenced by treatment

Fig. 4. The degree in severity of hypertensive heart and systolic time intervals. In the heart of 4° failure, Q1 and PEP were prolonged, and ET showed a stepwise fall along with the increase in severity of the cardiac status. Consequently, especially ET/PEP was decreased in 4° heart.

4°: Congestive cardiac failure, not clearing
Such severity is modified by ischemic changes of the heart.

Most cases of essential hypertension had remarkable afterload but some cases, especially, those with severe cardiac status also had abnormal preload. These were considered to be the representative diseases of abnormal afterload. Uremic cases, on the other hand, were sustained with the help of artificial dialysis, so that they exhibited various degrees of and occasionally extreme preload. These were, therefore, considered to be the representative diseases of abnormal preload. However, some cases of uremia had also various degrees of afterload. Moreover, both essential hypertension and uremia may have various degrees of disturbance in myocardial contractility.

In the cases of essential hypertension and uremia, Ekg (L-II), phonocardiogram, carotid and femoral arterial pulse wave, jugular venous pulse wave, and apexcardiogram were simultaneously recorded on minography 81 (Elena-Schoenander). At the same time, the blood pressure was measured by the auscultatory method. Using Blumberger-Holldack's method2,10 cardiac dynamics or systolic time intervals were analyzed by calculating the Q1 time of the left ventricle (“UFZ” or Q1), isovolumetric contraction time (“DAZ” or ICT), pre-ejection period (“AZ” or PEP = Q1 + ICT) and ejection time (“ATZ” or ET). By the use of Wessal’s method28 vascular dynamics were analyzed to measure the stroke volume (SV), cardiac output (CO), total peripheral resistance (TPR) and volume elasticity coefficient of the “Windkessel” system (E’). From the apexcardiogram, AO/EO and A/E0 ratios were obtained. For measurements of vascular dynamics in the cases of uremia, the dye-dilution method was also employed, even
Fig. 6. The relationship between the degree of severity in the hypertensive heart and the relative amplitude of A-wave, and the between the severity of hypertensive heart and Pd/ICT corrected with relative amplitude of A-wave. The relative amplitude of A-wave indicated the amount of preload, increased along with the degree of severity. Pd/ICT corrected with relative amplitude of A-wave probably indicated cardiac contractility, with a definite fall in 4° heart.

after formation of an a-v shunt. No significant difference of cardiac output was observed between the dye-dilution method and Wezler’s method. From the values obtained, SV/ET, SV/(AO/EO), ET/PEP (or ET/ICT), 1/ICT^2 (or 1/PEP^2) and Pd/ICT (or Pd/PEP) were selected, since they were in part expressing myocardial contractility. In order to express the afterload, TPR was chosen, while AO/EO (or A/EO) was taken up for preload. Therefore, under the influence of these two loads, the possibility of evaluation of myocardial contractility based on these parameters was studied.

At the beginning, other attempts were made in evaluating cardiac contractility in special situations. In auricular fibrillation, the preceding cycle length is inconstant, so that cardiac contractions take place under various preloads. For each cardiac contraction, cardiac dynamics (or systolic time intervals) were analyzed. For these cardiac dynamical values, i) a Starling-like ventricular function curve and ii) a curve equivalent to force-velocity-length relations according to Sonnenblick, Braunwald et al. were drawn. The changes in myocardial contractility or the Vmax-like point were evaluated from the later in response to loading with digitalis, isoproterenol, norepinephrine and propranolol. Included in this category were 5 cases with hypertensive or ischemic cardiac disease.

RESULTS

(1) Attempts in evaluating myocardial contractility in cases with aurricular fibrillation.

Fig. 1 shows the relationship between 1/ICT^2 or 1/PEP^2 and preceding cycle length in cases with auricular fibrillation. After digitalization, the curve moved upward and the slope steepened. This tendency was especially pronounced in 1/ICT^2. A similar relationship was noted between ET/PEP, ET/ICT, Pd/ICT or Pd/PEP and preceding cycle length. These curves are probably equivalent to a Starling’s curve and each shows the relationship between preload and cardiac pump performance. In other words, these

Japanese Circulation Journal Vol. 39, July 1975
parameters are influenced by changes in preload. The position and slope of each curve is related to myocardial contractility.

In force-velocity-length relations (Sonnenblick, Braunwald et al.) the force was replaced by ICT and velocity by ET/PEP in order to study the changes in curves upon the use of digitalis, isoproterenol, norepinephrine and propranolol (Fig. 2). Digitalis, isoproterenol and norepinephrine with positive inotropic action steepened the slope of the curve, causing an upward shift at the crossing of the curve with the ET/PEP axis. With the use of propranolol, having negative inotropic action, the slope of the curve became less at the crossing of the curve with the ET/PEP axis. A similar phenomenon was seen when force was replaced by Pd and velocity by Pd/ICT. Consequently, the point on the Y axis (velocity) may be considered equivalent to Vmax.

(2) Cardiac pump performance and cardiac muscle performance in sinus rhythm.

(a) Cardiac pump performance in essential hypertension

Fig. 3 shows the relationship between the degree of severity in hypertensive heart disease and vascular dynamics. Mean values of CO and SV revealed on significant difference in the heart with 1–3° degree severity. In 4°, despite a marked cardiac enlargement, these values were noticeably decreased, indicating a decrease in cardiac pump performance. However, the point were scattered to a large extent, because many hypertensive cases in the initial stage have high output (M) type, and depending upon the stage of hypertension, the vascular pattern of hypertension changes to high TPR (W) type with the lowering of the CO. Moreover, a few individual scattered points revealed a remarkable decrease in SV % CO even under a compensated status at 0–3°. This as 1° degree since Roland's classification includes the subjective complaints, and that hypertension as one of the heart diseases may be already associated with latent cardiac insufficiency at the initial stage. The abnormally high TPR value constituting hypertension is causatively related to cardiac decompensation. In fact, the mean TPR value in cases with 4° heart disease exceeded 3,000 dyne sec/cm². In groups with 0–3° heart, a few cases revealed a markedly high TPR in the initial stage. The incidence of increased E' type in the group of high severity of cardiac status is not only due to the age of the subjects but it also suggests a causative relationship between hypertension and arteriosclerosis.
as vascular diseases.

Fig. 4 shows the relationship between the degree of severity in hypertension and systolic time intervals. The points are also scattered. This shows that these values were influenced by cardiac pump performance including afterload and preload. Abnormally high values of Q1, ICT and PEP were frequently seen in each group. In the group with 4° heart, a prolongation of the Q1 and PEP was more pronounced probably due to the decrease in contractility. ET showed a stepwise decrease along with the increase in the severity of the heart. Consequently, especially in 4° heart, ET/PEP was decreased, along with a marked fall in SV, CO and SV/ET. In 4° heart, afterload or TPR probably rose in response to low output, while preload was definitely increased, and consequently the changes in 1/ICT² and 1/PEP² were indistinct; the mean value of 1/PEP² was somewhat decreased, while that of 1/ICT² was slightly increased; whereas Pd/ICT definitely increased.

(b) Cardiac muscle performance in essential hypertension

Attempts to estimate Vmax in the cases with atrial fibrillation were already described. In the cases of sinus rhythm, however, it is difficult to estimate, unless pacing is used. Under the conditions created to make afterload and preload constant, max dp/dt has been compared to express myocardial contractility. As a parameter corresponding to max dp/dt measured by the non-invasive method, Pd/ICT may be chosen. Unlike max dp/dt, however, Pd/ICT is not influenced by afterload because ICT itself is a factor fluctuating under correlation with Pd or afterload.

The relationship between vascular dynamics constituting hypertension and the non-invasive parameters expressing myocardial contractility was studied. Abbreviations in the lower part of Fig. 5 indicate the types of vascular dynamics in hypertension according to Wezler-Boeger: N means normal type, M high output type, w and W high TPR type (w shows TPR<3,000 dyne sec/cm², W shows TPR>3,000 dyne sec/cm²), and E high E type.

SV/ET represents mean ejection velocity, and was evidently influenced by vascular dynamics. ET/PEP, and 1/ICT² or 1/PEP² tended to be low along with type W. At least in hypertension, these parameters are not sensitive indices which can express the decrease of myocardial contractility before the fall of cardiac pump performance. Mean Pd/ICT values appeared to be relatively independent from vascular dynamics, especially, afterload. As described in the cases of uremia, however, Pd/ICT was definitely influenced by preload and became higher as preload was increased. Therefore, as long as cardiac contractility is in question, Pd/ICT should be corrected with preload. As the parameter indicating preload by the non-invasive method, the relative height of the A-wave to the whole amplitude of apexcardiogram has been suggested and this might be used for correction of Pd/ICT.

As the A-wave height ratio, A/EO and AO/EO were calculated. (Pd/ICT)/(A/EO) and (Pd/ICT)/(AO/EO) were calculated respectively from these. The correlation between these factors and the degree of severity in hypertensive heart is demonstrated in Fig. 6. In the hypertensive heart, as the severity increases, abnormally high A/EO and AO/EO values were frequently encountered. In cases with definite 4° congestive heart failure, A/EO exceeded 10 and AO/EO was above 25% in most cases. Accordingly, (Pd/ICT)/(A/EO) and (Pd/ICT)/(AO/EO) were decreased as the severity of the hypertensive heart was increased; especially in 4° (Pd/ICT)/(AO/EO) became less than 10 mmHg/msec.

(c) Cardiac muscle performance in uremia

Japanese Circulation Journal Vol. 30, July 1975
Noninvasive Evaluation of Myocardial Contractility

![Diagram](image)

**Fig. 11.** The relationship between SV/ET and preload, afterload and contractility in cases of uremia. SV/ET is also called ejection rate, representing mean contraction velocity. The relationship between SV/ET and preload was not evident, and this was definitely controlled by afterload. When (Pd/ICT)/(AO/EO) was decreased below 10mmHg/msec, this was also decreased under correlation with this.

In uremia in which preload changes seriously, the influence of preload and afterload on Pd/ICT and ET/PEP was discussed. (Pd/ICT)/(AO/EO) was used to express myocardial contractility. The group with this value below 5 mmHg/msec, the group between 5 and 10, and the group exceeding 10 were differentiated. Fig. 7 shows the relationship between Pd/ICT and preload in these group, suggesting a Starling’s curve. In the group with (Pd/ICT)/(AO/EO) below 5 mmHg/msec the regression equation of the ascending limb was $y = 2.33x + 0.54$ ($r = 0.64$), in the group between 5 and 10 $y = 8.47x - 0.46$ ($r = 0.87$), and in the group exceeding 10 $y = 26.43x - 2.12$ ($r = 0.97$). In general, Pd/ICT was increased as the preload was increased, and in each group divided with (Pd/ICT)/(AO/EO) Pd/ICT revealed very good correlation with preload. The position shifted upward and the slope of the ascending limb became greater as the myocardial contractility increased. In the group with the (Pd/ICT)/(AO/EO) below 5, the descending limb appeared along with a marked increase of preload.

Although afterload was weakened by the influence of high output in the uremia cases, Pd/ICT was apparently not influenced by TPR or afterload as seen in Fig. 8. In this Figure, 3 groups were also distinguished according to the difference in myocardial contractility. In each of these groups, 2 groups were further divided depending on the presence or absence of abnormal preload. The presence or absence of abnormal preload also resulted in changes of Pd/ICT. Thus Pd/ICT appeared to be influenced exclusively by preload. These data serve to confirm the validity of a parameter obtained by correcting Pd/ICT with AO/EO as the index of myocardial contractility.

As shown in Fig. 9 and 10, the relationship ET/PEP and two loads revealed that ET/PEP was increased with the increase of preload, and was decreased with the increase of afterload or vice versa. A similar tendency was noted in 1/ICT or 1/PEP. These values consequently may be used only in the absence of a significant change in preload and afterload as the index of myocardial contractility. SV/ET, as shown in Fig. 11, was markedly influenced even in the cases of uremia especially by afterload, and showed some correlation with (Pd/ICT)/(AO/EO) only when myocardial contractility was definitely weakened, but was by no means a sensitive index expressing myocardial contractility. SV/(AO/EO) which might be called the ejection fraction obtained by the non-invasive method was affected more profoundly by preload and correlated with (Pd/ICT)/(AO/EO) to some extent only when myocardial contractility was definitely weakened.

**DISCUSSION**

Along with the progress made in studies on the contraction of skeletal muscles beginning with Hill’s attention has been focused on the contractility of the myocardium and several attempts have been made to separate cardiac muscle performance from cardiac pump performance. So far, cardiac pump performance has been mainly discussed by the parameters of cardiac function curves based on Frank-Starling’s principle and it is relatively easy to obtain this clinically either by the invasive or by noninvasive method. However, there is some difficulty in obtaining cardiac muscle performance clinically, because it is evaluated quantitatively according to the 3 dimensional coordinates based on force-velocity-length relations by Sonnenblick and Braunwald et al. under the influences of preload and afterload. Clinical estimation of
Vmax is made by 3 approaches, that of Mason et al.\textsuperscript{17,18} Hungenho1tz et al.\textsuperscript{11} and Dodge et al.\textsuperscript{8} with obvious restrictions as long as patients are involved, and problems are to be solved for practical use. Even if Vmax is measured, it is still far from being introduced in the daily routine examination. Vmax thus obtained is still subjected to criticism such as "fact or fancy?". In a search for a practical value, the non-invasive method is a useful approach in estimating cardiac muscle performance, since it can be easily and repeatedly employed.

Until now, the 3 dimensional coordinates of Sonnenblick and Braunwald have been used for intact heart with aortic pressure instead of force of myocardial contraction, SV instead of change in fiber length, and speed of myocardial contraction (including Vmax). Among the present authors, Muramatsu and Kakubari were mainly responsible for modifying the method of the 3 dimensional coordinates analysis in atrial fibrillation. Vmax may thus be estimated to some extent by the non-invasive method, but it is generally impossible to apply it in cases with sinus rhythm.

In more general cases of sinus rhythm, an attempt to obtain the non-invasive index of myocardial contractility was made. The intact heart contracts generally under the influence of variable grades of preload and afterload. However, there were some conditions with predominant preload or afterload. In these trials, essential hypertension was selected as the representative disease of afterload, while uremia was selected as the representative disease of preload. As mentioned in Materials and Methods, however, hypertensive cases may also have abnormal preload and uremia may have abnormal afterload. Although hypertensive cases, especially in juvenile or early labile stage, often have high output (M) type (20 in 225 cases), increased TPR in the high output type was revealed in comparison with normal cases with same CO. According to the age or stage of hypertension in the advanced disease, abnormal high TPR became remarkable (165 in 225 cases). Therefore, hypertension was selected as the representative disease of afterload. As shown in Fig. 6 however, preload (AO/EO) was increased along with the degree of severity, showing that preload was present in addition to afterload.

All cases of uremia in this paper were under dialysis with a tendency to water retention, and presents variable preload according to the condition of the water control. Depending upon the severity of uremia or interval after dialysis, 44 out of 60 cases had abnormal preload [AO/EO K 0.25] and a few cases exhibited extreme preload. Therefore, uremia was selected as the representative disease of preload. However, uremia could not be the pure preload disease; because 5 cases had abnormal afterload (TPR > 2300 dyne-sec-cm\textsuperscript{-5}).

Under conditions of constant afterload and preload, max dp/dt was used in an attempt to estimate the myocardial contractility. According to the review of Mason et al.\textsuperscript{12} dp/dt by common isovolumetric ventricular pressure serves for evaluation of myocardial contractility with considerable accuracy when afterload stay relatively constant. When preload changes without being related to afterload, max dp/dt by left ventricular end-diastolic pressure, integrated isovolumetric tension, max isovolumetric tension, isovolumetric force etc. may be used. In the non-invasive method, Pd/ICT may be used as an equivalent parameter to max dp/dt.\textsuperscript{16} Since the error of measurement is small, PEP may be used instead of ICT to calculate Pd/PEP. Under such circumstances, QI the component of PEP readily changes due to heart rate, so that the correlation of Pd/PEP with max dp/dt becomes lower.\textsuperscript{15} Since ICT does not depend on heart rate, correlation of Pd/ICT with max dp/dt is high.\textsuperscript{16}

The aortic valve opens when the left ventricular pressure equals the aortic diastolic pressure. Consequently, ICT changes in correlation with Pd.\textsuperscript{1} Pd/ICT, unlike max dp/dt, is therefore said to be scarcely influenced by afterload or TPR.\textsuperscript{21} In our results, Pd/ICT was almost purely influenced by preload, and not by afterload. This was found in hypertension especially with abnormal afterload and in uremia especially with abnormal preload. Correction of Pd/ICT with preload would therefore provide a useful index for myocardial contractility.

In the non-invasive method, the relative height of the A-wave to the whole amplitude of apexcardiogram (A/EO & AO/EO) expresses the end-diastolic volume or pressure.\textsuperscript{2,19} Rios and Massumi\textsuperscript{19} obtained A/EO = 8 b 2.5 and AO/EO = 23 b 4.3% in normal man, while the corresponding values were above 10 and 25% respectively in cases with congestive heart failure. We obtained similar results in decompensated hypertensive cardiac disease. AO/EO almost purely reflects preload, while A/EO expresses preload.

\textit{Japanese Circulation Journal} Vol. 39, July 1975
as well as myocardial fibrosis or changes in cardiac compliance to a considerable degree. Use of AO/EO as the index of preload therefore appears to be most reasonable. As the index of myocardial contractility, (Pd/ICT)/(AO/EO) was therefore taken into account first, and studied under marked preload and afterload; thus the clinical usefulness of this index was demonstrated.

On the other hand, systolic time intervals or ET/PEP were recently considered as the non-invasive index for myocardial contractility by Weissler et al. Systolic time intervals have been studied since the 1950's by Blumberger, and Hollack as cardiac dynamics. Blumberger used the expression of "Volumenreaktion" (volume reaction) and "Druckreaktion" (pressure reaction) in the equivalent state of the heart under preload and afterload. In the volume reaction, ET/PEP is increased while ET/PEP is decreased in the pressure reaction. ET/PEP, in other words, was considered to be the index for studying volume reaction and pressure reaction in the pathologic heart. Use of ET/PEP as the expression for myocardial contractility certainly represents a step forward. For example, Jezeck supported ET/PEP as the best non-invasive factor expressing myocardial contractility. However, the relationship between ET/PEP and preload or afterload has been suggested for a long time and this was confirmed in the present investigations. The absolute value cannot be used as the index for myocardial contractility if preload or afterload is variable. Only when the background factors such as these loads do not change significantly, than ET/PEP may be used as the index for myocardial contractility. The same may be concluded for other non-invasive parameters. Since both ET and PEP are dependent on the heart rate unlike ICT and a difference is found between their dependence on the heart beat, a more careful examination is necessary in evaluating ET/PEP (or ET/ICT). When ICT or PEP is used, the isovolumetric contraction has to be performed normally, and this cannot be used in the presence of regurgitant flow and intracardiac shunt. When cardiac function is studied from each value of the systolic time interval, QI, ICT, PEP and ET, the above-mentioned considerations are necessary. Consequently, a similar care has to be taken when myocardial contractility is evaluated using 1/ICT and 1/PEP.

Other parameters such as VS/ET, and VS/AO/EO were studied to analyze cardiac contractility, but the results were no better than those obtained by (Pd/ICT)/(AO/EO). VS/ET (ejection rate) was considered to express mean ejection velocity, and it was markedly influenced by vascular dynamics in the cases of hypertension. The influence of TPR or afterload was especially pronounced. In a state with extremely low myocardial contractility, however, this was probably parallel with the fall of myocardial contractility. While SV/(AO/EO) was expected to be the ejection fraction obtained by the non-invasive method, this parameter was not directly correlated with myocardial contractility.

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