STUDIES ON THE Q-IIp INTERVAL IN CHRONIC OBSTRUCTIVE LUNG DISEASE — A COMPARATIVE STUDY WITH MITRAL STENOSIS —

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IN RECENT years, indirect estimation of cardiac functions with a combined technique of phonocardiography and electrocardiography has been a subject of interest in clinical cardiology. There appeared many contributing study reports, especially concerning to interrelationship between left ventricular functions and Q-I interval or Q-II interval!¹⁻⁷

In this study, the author intended to pursue the relations between cardiopulmonary hemodynamics and Q-IIp interval in cardiopulmonary patients. Simultaneous recordings of phonocardiography and electrocardiography were obtained to compare with pulmonary artery mean pressure or other parameters of cardiopulmonary functions.

SUBJECTS

Chronic obstructive pulmonary disease: 28 patients consisted of 7 with chronic cor pulmonale, 4 with obscure cor pulmonale, 14 with chronic pulmonary emphysema, and 3 with bronchial asthma. Mean age of this group was 58. The youngest was 33 and the eldest was 72 years old.

Cardiac patients as a control: 31 patients were included in this group. Twenty five had established mitral stenosis, 6 was patients with other heart diseases. Mean age of this group was 28.7. Their age was from 15 to 59 years old.

Normal control subjects: Fifty three healthy

subjects collaborated on this study. They were divided into two groups following their age. The one was 23 subjects aging from 16 to 39. Mean age of this younger age group was 22.0. Another group consisted of 30 subjects aging from 40 to 69. Mean age of this elder group was 55.0.

METHODS

1) Q-IIp interval

Simultaneous phonocardiography and electrocardiography was recorded on all the subjects at end-expiratory phase on resting supine position. Q-IIp interval was defined as the interval between the beginning point of Q wave on electrocardiogram and the earliest point of the pulmonary artery component of the second heart sounds (IIp) on phonocardiogram. It was expressed in terms of msec.

Phonocardiogram and electrocardiogram were recorded with FUKUDA AC-31S (FUKUDA electronics Co. Ltd, Tokyo Japan) equipped with photography system, air conduction type dynamic microphone, and 3 screening filters (low, medium, and high tones). Specificities of the filters are shown in Fig. 1. Recording paper speed was set at 100 mm/sec. Phonocardiogram was obtained putting microphone at right costal margin on the second interspace, at left costal margin on the second, third and fourth interspace, and at the apex.

Carotid artery wave and apex cardiogram were obtained simultaneously to differentiate IIp from aortic component of the second heart sound (II_A), opening snap of mitral valve (OS), and the third heart sound (IIIS).

2) Pulmonary artery pressure and pulmonary vascular resistance

Right heart catheterization was performed

Key Words:

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Fig.1. Filter Characteristic of phonocardiograph.

following routine procedure to obtain pulmonary artery wedge pressure (WP), pulmonary artery pressure (PAP) and right ventricular pressure (RVP). Cardiac index was obtained by Fick's

direct method. Pulmonary vascular resistance (PVRI) and total pulmonary vascular resistance (TPRI) were calculated from cardiac index and pressure parameters.

RESULTS

Q-Iip interval showed close relations with heart rate in all study groups. Relations of Q-Iip interval to heart rate (HR) or pulmonary hemodynamics in each group were as follows.

I. Normal control group

In younger age group, Q-Iip interval correlated with HR in such a way as;

$$\begin{aligned} \text{Q-Iip} &= -1.56 \times \text{HR} + 545 \\ (r &= -0.96, p < 0.01) \end{aligned}$$

Q-Iip interval reduced as HR increased. In elder age group, relation between Q-Iip and HR was:

$$\begin{aligned} \text{Q-Iip} &= -1.84 \times \text{HR} + 561 \\ (r &= -0.97, p < 0.01) \end{aligned}$$

Q-Iip interval of this group reduced as HR increased too. However Q-Iip interval of this group was shorter than that of the younger age group as illustrated in Fig. 2.

II. Chronic obstructive pulmonary disease group.

1) Pulmonary artery mean pressure (PAm) and Q-Iip.

Q-Iip interval and HR in 9 subjects whose

Fig.2. Relation between Q-Iip interval and age in healthy group.

Fig. 3. Relation between Q-IIp interval and pulmonary artery mean pressure (PAm) in pulmonary disease group.

PAm was normal (16 mmHg or less) correlated each other as follows;

$$\begin{aligned} \text{Q-IIp} &= -2.46 \times \text{HR} + 591 \\ (r &= -0.95, p < 0.01) \end{aligned}$$

The relation between Q-IIp and HR in 19 patients with PAm higher than 17 mmHg was;

$$\begin{aligned} \text{Q-IIp} &= -2.59 \times \text{HR} + 582 \\ (r &= -0.95, p < 0.01) \end{aligned}$$

Generally speaking, Q-IIp interval of the patients with chronic obstructive pulmonary disease was shorter than that of normal control subjects. It was marked in pulmonary hypertensive patients whose PAm was 17 mmHg or more (Fig. 3).

Relation of Q-IIp interval to HR for all 28 pulmonary patients was;

$$\begin{aligned} \text{Q-IIp} &= -2.49 \times \text{HR} + 580 \\ (r &= -0.90, p < 0.01) \end{aligned}$$

This equation was taken as generalized regression equation to obtain predicted Q-IIp interval at a certain heart rate. Predicted Q-IIp interval of a patient was obtained at patient's HR by the above equation. Q-IIp interval measured on patient's record was divided by predicted Q-IIp interval, thus calculated and multiplied by hun-

dred to be expressed as percent Q-IIp interval (% Q-IIp); i.e.

$$\% \text{ Q-IIp} = \frac{\text{measured Q-IIp interval of a patient}}{\text{predicted Q-IIp interval}}$$

The % Q-IIp interval correlated inversely with PAm in 21 patients whose PAm was lower than 21 mmHg as follow:

$$\begin{aligned} \% \text{ Q-IIp} &= -0.87 \times \text{PAm} + 115 \\ (r &= -0.83, p < 0.01) \end{aligned}$$

However, in 7 patients who had higher PAm, 22 mmHg or more, there observed no statistically significant correlation between % Q-IIp and PAm. In another words, % Q-IIp did not show markable decrease but remained unchanged when PAm was higher than 22 mmHg (Fig. 4.).

2) Pulmonary vascular resistance and Q-IIp interval.

There was observed following relationship between Q-IIp and HR in 9 patients with normal PVRI (below 199 dyne-sec-cm⁻⁵/M²);

$$\begin{aligned} \text{Q-IIp} &= -2.11 \times \text{HR} + 561 \\ (r &= -0.95, p < 0.01) \end{aligned}$$

In 10 patients whose PVRI was larger than 200 dyne-sec-cm⁻⁵/M², the following statistically significant inverse relation was observed;

Fig.4. Relation between %Q-IIp interval and pulmonary artery mean pressure (PAm) in pulmonary disease group (Regression line for the patients with PAm below 21 mmHg).

Fig.5. Relation between Q-IIp interval and pulmonary vascular resistance index (PVRI) in pulmonary disease group.

$$\text{Q-IIp} = -2.35 \times \text{HR} + 562$$

($r = -0.96$, $p < 0.01$)

Shortening of Q-IIp interval was more markable in patients with higher PVRI as compared, at a certain HR, to patients with normal PVRI (Fig. 5).

The relation of % Q-IIp to PVRI was such one as follows;

$$\% \text{Q-IIp} = -0.036 \times \text{PVRI} + 108.85$$

($r = -0.83$, $p < 0.01$)

This correlation was statistically significant in

Fig.6. Relation between %Q-IIp interval and pulmonary vascular resistance index (PVRI) in pulmonary disease group.

Fig.7. Relation between Q-IIp interval and total pulmonary resistance index (TPRI) in pulmonary disease group.

15 patients with PVRI smaller than 249 dyne-sec-cm⁻⁵/M². However, in 5 patients who showed larger PVRI over 250 dyne-sec-cm⁻⁵, decrease in % Q-IIp did not correlate with PVRI but tended to remain unchanged (Fig. 6).

TPRI and Q-IIp interval in patients with TPRI

smaller than 449 dyne-sec-cm⁻⁵/M² (14 patients) correlated each other as follows;

$$Q-IIp = -2.00 \times HR + 566$$

$$(r = -0.95, p < 0.01)$$

Fig.8. Relation between Q-IIp interval and pulmonary artery mean pressure (PAm) in cardiac disease group.

Fig.9. Relation between %Q-IIp interval and pulmonary artery mean pressure (PAm) in cardiac disease group (Regression line for the patients with PAm below 40 mmHg).

In other 14 patients with TPRI larger than 450 dyne-sec-cm⁻⁵/M², statistically significant correlation was also observed between Q-IIp and HR;

$$Q-IIp = -2.32 \times HR + 559$$

$$(r = -0.95, p < 0.01)$$

Q-IIp interval showed a tendency to decrease even in patient with larger TPRI samely as in the

Fig.10. Relation between %Q-IIp interval and pulmonary artery wedge pressure (Wp) in cardiac disease group (Regression line for the patients with Wp below 30 mmHg).

Fig.11. Relation between Q-IIp interval and pulmonary vascular resistance index (PVRI) in cardiac disease group.

patients with smaller TPRI (Fig. 7).

III. Cardiac patients

1) Pulmonary artery mean pressure (PAm) and Q-IIp interval.

In 12 cardiac patients (6 established mitral stenosis and 6 patients of other causes) with PAm below 16 mmHg, Q-IIp interval correlated

with HR as follows;

$$Q-IIp = -1.77 \times HR + 565$$

$$(r = -0.94, p < 0.01)$$

It was a statistically significant correlation, and the regression line was located just between

Fig.12. Relation between Q-II interval and total pulmonary resistance index (TPRI) in cardiac disease group.

the lines of the younger age group and the elder age group of normal control group.

In 19 established mitral stenosis with PAm higher than 17 mmHg, Q-IIp interval was correlated with HR as;

$$\begin{aligned} \text{Q-IIp} &= -1.71 \times \text{HR} + 531 \\ (r &= -0.89, p < 0.01) \end{aligned}$$

Q-IIp interval of these patients was apparently shorter than the interval of normal subjects or cardiac patients without pulmonary hypertension. It was statistically significant at the level of 1.0% (Student's T Test) (Fig. 8).

To obtain % Q-IIp on cardiac patients, regression equation was obtained same way as in pulmonary patients covering all cardiac patients. It was;

$$\begin{aligned} \text{Q-IIp} &= -2.24 \times \text{HR} + 581 \\ (r &= -0.84, p < 0.01) \end{aligned}$$

Percent Q-IIp of cardiac patients correlated with PAm when patients PAm was lower than 39 mmHg (22 cases). It was a inverse relationship as follows;

$$\begin{aligned} \% \text{ Q-IIp} &= -0.454 \times \text{PAm} + 109.4 \\ (r &= -0.88, p < 0.01) \end{aligned}$$

However, for the 9 patients with PAm higher than 40 mmHg, no statistically significant relationship was obtained. Percent Q-IIp of these high PAm patients remained relatively high as shown in Fig. 9.

Pulmonary artery wedge pressure (WP) and % Q-IIp related each other in such 22 patients whose WP was lower than 29 mmHg. The relation was statistically significant.

$$\begin{aligned} \% \text{ Q-IIp} &= -0.40 \times \text{WP} + 105 \\ (r &= -0.72, p < 0.01) \end{aligned}$$

However, in 3 patients with WP higher than 30 mmHg, there was observed no significant relationship between them (Fig. 10).

2. Pulmonary vascular resistance and Q-IIp interval.

In 16 subjects with PVRI smaller than 199 dyne-sec-cm⁻⁵/M², Q-IIp interval and HR correlated as follows;

$$\begin{aligned} \text{Q-IIp} &= -2.00 \times \text{HR} + 564 \\ (r &= -0.72, p < 0.01) \end{aligned}$$

For 12 patients with PVRI larger than 200 dyne-sec-cm⁻⁵/M², following regression equation was obtained;

$$\text{Q-IIp} = -2.62 \times \text{HR} + 608$$

$$(r = -0.92, p < 0.01)$$

As shown in Fig. 11, these two regression lines crossed each other at HR 68 or the near showing that Q-IIp interval of the patients with elevated PVRI did not decrease (Student's T test, $t = 0.36$, freedom 23, statistically not significant).

In 11 patients, with TPRI lower than 449 dyne-sec-cm⁻⁵/M² following relationship was observed;

$$\begin{aligned} \text{Q-IIp} &= -2.52 \times \text{HR} + 612 \\ (r &= -0.94, p < 0.01) \end{aligned}$$

For 18 patients with TPRI higher than 450 dyne-sec-cm⁻⁵/M², following correlation was obtained;

$$\begin{aligned} \text{Q-IIp} &= -2.04 \times \text{HR} + 560 \\ (r &= -0.87, p < 0.01) \end{aligned}$$

Q-IIp interval of the patients with higher TPRI tended to decrease as compared at a certain HR to the subjects with lower TPRI (Fig. 12). However, it was not statistically significant (Student's T test, $t = 0.89$, freedom 25).

DISCUSSION

As to the pathogenesis of cor pulmonale, there are general agreement that organic changes of pulmonary vascular bed and functional deteriorations due to hypoxia or hypercapnea cause elevation of pulmonary vascular resistance resulting in pulmonary hypertension, and further, in cor pulmonale.⁸

In phonocardiography, the second heart sound consists of an early component called aortic component (II_A) and another late component called pulmonary component (II_p). Q-IIp interval, the interval from the beginning point of Q wave of ECG to the beginning point of II_p, correlates with right ventricular ejection time and correlates inversely with pulmonary artery pressure if not ventricular conduction is disordered.⁹

In the following, the author will discuss about Q-IIp interval and its relation to age, heart rate, and pulmonary hemodynamics, on the basis of this study including statistical analysis of the results.

1. Effects of heart rate and aging on Q-IIp interval.

In all study groups, Q-IIp interval correlated

with heart rate. It was a reverse correlationship and showed high statistical significance. In normal subjects aged over 40, shortening of Q-IIp interval at a certain heart rate was more evident as compared to younger group aged 16 to 39.

Shah et al.^{10,11} reported essentially same results as author's. They observed statistically significant relationship between Q-IIp interval and a square root of R-R interval or age.

Pulmonary vascular bed shows variable morphological changes as an aging process with innoticeable disorder of cardiopulmonary functions.¹² Occurrence of such a change in pulmonary vasculature associated with aging is supported by a study in which physical extensibility of pulmonary artery trunks was investigated.¹³ Heath et al. observed increased fibrous elements in muscular arteries, arterioles and venules of the subject aged over 40 by a histological investigation.¹⁴ Sakaguchi et al. reported higher incidence of pulmonary hypertension among the aged.¹⁵ It is conceivable that elevation of pulmonary vascular resistance and resulting pulmonary hypertension due to the vascular change in the aging process of the lung will contribute greatly to shortening of Q-IIp interval.

2. Q-IIp interval in chronic obstructive pulmonary disease.

Q-IIp interval in chronic obstructive pulmonary disease patients showed apparent shortening as compared to normal control subjects. It was more evident in patients with PAm higher than 17 mmHg. Percent Q-IIp interval which was set in this report to eliminate the effect of heart rate change on Q-IIp interval correlated inversely with PAm in patients with PAm below 22 mmHg. However, in patients with PAm higher than 23 mmHg, % Q-IIp interval showed no further decrease from the values for less marked pulmonary hypertensive patients. This finding suggests limited shortening of right ventricular ejection time in response to elevation of PAm. The maximum point of Q-IIp shortening in response to PAm elevation seems to rest at PAm 22 mmHg or the near. Itagaki¹⁶ who elaborated a prognostic study of chronic obstructive pulmonary disease reported definite poor prognosis of in the patients with PAm higher than 22 mmHg. This is quite consistent with the author's observation in this study.

More evident shortening of Q-IIp interval was observed in patients with PVRI higher than 200 dyne-sec-cm⁻⁵/M² comparing to the subjects with lower PVRI. Same was true in TPRI; i.e.

Q-IIp interval of patients with larger TPRI was apparently short as compared to subjects with normal TPRI. Relation between PVRI and % Q-IIp was an inverse relationship as far as patient's PVRI remained below 250 dyne-sec-cm⁻⁵/M². When PVRI was high (from 250 dyne-sec-cm⁻⁵/M² to the observed maximum of 500 dyne-sec-cm⁻⁵/M²), % Q-IIp and PVRI did not correlate each other but % Q-IIp in such cases remained unchanged in spite of elevation of PVRI.

These results suggests that shortening of Q-IIp interval in chronic obstructive pulmonary disease is ascribed to diminished right ventricular ejection time due both to increased pulmonary vascular resistance and pulmonary hypertensive state.

3. Q-IIp interval in cardiac patients with or without pulmonary hypertension.

There was no significant difference in Q-IIp interval between normal subjects and cardiac patients (chiefly consisted of mitral stenosis) when patient's PAm was below 16 mmHg. In pulmonary hypertensive patients (PAm over 17 mmHg), there observed apparent shortening of Q-IIp interval.

Percent Q-IIp interval correlated with PAm and WP in this group as far as PAm or WP remain below 39 mmHg or 29 mmHg, respectively. When PAm elevated exceeding 40 mmHg or WP was higher than 30 mmHg, there was observed no significant shortening in Q-IIp interval. Q-IIp interval of these patients with elevated impedance in pulmonary circulation remained unaffected. These facts may suggest limited shortening of right ventricular ejection time in response to the changes in pulmonary circulation. The critical pressures for Q-IIp response may be approximately 40 mmHg in case of PAm and approximately 30 mmHg in case of WP. It is interesting from clinical view point to compare these results with KOTOKU's report.¹⁷ He pointed out that prognosis of mitral stenosis was largely dependent on PAm and WP. When PAm was higher than 45 mmHg and/or WP was elevated exceeding 30 mmHg, prognosis of mitral stenosis was poor. In patients with mitral stenosis, Q-IIp interval correlated to TPRI with certain limitations; shortening of Q-IIp interval in patients with TPRI over 450 dyne-sec-cm⁻⁵/M² was more markable as compared to Q-IIp change in patients with TPRI below 450 dyne-sec-cm⁻⁵/M². However, there was observed no significant difference in Q-IIp shortening between patients with

elevated PVRI and patients without PVRI elevation.

Exact understanding of the cause of difference between pulmonary disease group and cardiac disease group in Q-IIp interval-PAm-WP interrelationship may not possible. If the rebound factor in generation of IIP is taken into counts as suggested by Luisada,¹⁸ compliance of pulmonary vasculature in chronic pulmonary disease seems to be smaller than in cardiac disease, because the age of chronic pulmonary patient is generally high and morphological deterioration of these patients is more marked comparing to cardiac patient. It may become understandable, therefore, that in pulmonary disease group shortening of Q-IIp interval was more marked than cardiac group and the PAm level above which no increase of % Q-IIp was noted was lower (22 mmHg) as compared with cardiac patient (40 mmHg). In the stage of right ventricular failure, right ventricular ejection time will become prolonged and generation of IIP will be delayed, resulting in absence of shortening of Q-IIp interval or, in some, may cause to substantial prolongation.

It seems reasonable on the basis of this study, determination of Q-IIp interval will serve as a criterion for severity evaluation of chronic obstructive pulmonary disease because its shortening correlates inversely with pulmonary artery pressure and pulmonary vascular resistance as evidenced in this study. In mitral stenosis, determination of Q-IIp interval seems to benefit for prediction of severity of the lesion, partially at least, because Q-IIp showed statistically significant inverse relationship with PAm and WP. The fact that Q-IIp interval does not correlated with pulmonary vascular resistance seems to suggest that shortening of right ventricular ejection time is to be ascribed not only to elevation of pulmonary vascular resistance but also to other factors such as left ventricular function, pulmonary venous pressure, cardiac output and pulmonary vascular compliance.

CONCLUSION

Q-IIp interval was determined in 28 patients with chronic obstructive pulmonary disease, 19 mitral stenosis patients with pulmonary hypertension, 6 mitral stenosis patients with normal pulmonary blood pressure, 6 cardiac patients of other causes with normal pulmonary blood pressure, and 53 healthy control subjects. The Q-IIp interval was compared with cardiac functions and

pulmonary hemodynamics resulting in following conclusion;

1. Q-IIp interval correlated very closely with heart rate in all patients and control subjects.
2. Q-IIp interval showed a tendency to decrease with age.
3. In chronic obstructive pulmonary disease, Q-IIp interval was shorter than that of healthy control subjects as compared at a certain heart rate.
4. In chronic obstructive pulmonary patients, Q-IIp interval showed inverse relationship with pulmonary artery mean pressure (PAm), but it was minimum at the level of PAm approximately 22 mmHg and did not show any further shortening when PAm was higher than this level.
5. Within the group of chronic obstructive pulmonary patients, patients with elevated pulmonary vascular resistance and total pulmonary vascular resistance index showed more apparent shortening of Q-IIp interval than the patients without elevation of these two parameters. Correlation with pulmonary vascular resistance was limited within 250 to 500 dyne-sec-cm⁻⁵/M² showing no further shortening of Q-IIp interval as vascular resistance elevated over the above limit.
6. In mitral stenosis Q-IIp interval showed more apparent shortening as compared at a certain heart rate to healthy control subjects.
7. In mitral stenosis, Q-II interval correlated inversely with PAm and pulmonary artery wedge pressure (WP). However, shortening was maximum at the level of PAm 40 mmHg and WP 30 mmHg and no further shortening was observed when patient's PAm or WP exceeded the above maximum levels.
8. In mitral stenosis, shortening of Q-IIp interval of the subjects with elevated total pulmonary vascular resistance index was more marked than those with lower index as compared at a certain heart rate. However, no statistically significant difference in Q-IIp shortening was observed between patient with elevated pulmonary vascular resistance and without elevation.
9. The mechanism involved in shortening of Q-IIp interval in pulmonary hypertensive patients and cardiogenic pulmonary hypertensive patients seems to be different. The causes of this difference is not fully understood, but the results of this study suggest that the following factors are involved to produce this difference.
 - 1) Pulmonary hypertensive patients are generally older than cardiogenic pulmonary hypertensive patients.
 - 2) Decreased compliance due to morphological deferioration in pulmonary vasculature is thought to be more advanced in pulmonary hypertensive patient than in cardiogenic pulmonary hypertensive patients.
 - 3) In cardiogenic pulmonary hypertension, left ventricular function or cardiac output may be involved to cause the above difference.

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