行政院國家科學委員會補助專題研究計畫成果報告

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※ 在前壁心肌梗塞病患以左心室內等體積舒張期血流形※

※ 式來改良杜卜勒超音波心圖預測左心室填充壓的能力※

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計畫編號：NSC90－2314－B-002－340

執行期間：2001 年 08 月 01 日 至　2002 年 07 月 31 日

計畫主持人：吳造中

共同主持人：劉言彬、林隆君

執行單位：國立台灣大學醫學院內科

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中英文摘要，

背景及目的：過去的研究已顯示左心室收縮功能失全亦會影響到其舒張功能。本研究之目的乃探討左心室前壁運動不良如何影響左心室等體積舒張期間心室內血流之分佈形態。

方法：本研究選取 73 位因前壁心肌梗塞造成收縮功能失全之病患，依其左心室等體積舒張期心室內血流之方向，分為往僧帽瓣（B 組）及其他（A 組），比較其各種超音波杜卜勒指標與左心室舒張末期壓力之關係。

結果：B 組病患之左心室收縮分率較低，心尖部收縮失全較厲害，而其僧帽瓣血流行進亦較慢。A 組病患左心室舒張末期壓力之獨立決定因子為僧帽瓣血流行進速率/舒張早期最大流速，早期僧帽瓣舒張血流之減速時間及等體積舒張時間。然而 B 組病患之唯一獨立決定因子為僧帽瓣血流舒張早期與晚期之速度比（E/A 比）。

結論：前壁心肌梗塞病患之左心室內等體積舒張期血流形式可改良杜卜勒超音波心圖預測左心室填充壓之能力。

關鍵字：心肌梗塞、等體積舒張期血流形式、左心室填充壓。

Background and purpose: Previous studies have shown that left ventricular systolic asynchrony affects both the relaxation and filling phases of diastole. The purpose of this study was to delineate how the anterior wall dyssynergy influenced the intraventricular flow redistribution patterns during isovolumic relaxation period.

Methods: Seventy-three patients with anterior wall myocardial infarction and dyssynergy were enrolled. Those who exhibited the whole isovolumic relaxation intraventricular flow redistributing toward the mitral apparatus, which indicated the reverse physiologic intraventricular pressure gradient in early diastole, were classified as group B, otherwise, as group A. The Doppler echocardiographic variables of mitral inflow were correlated with the left ventricular end-diastolic pressures (LVEDP).

Results: With lower ejection fraction rate and more apical dyssynergy, the group B patients had much slower mitral flow propagation. For group A patients, the independent determinants for LVEDP were the ratio of mitral flow propagation rate to peak velocity in early diastole, the early mitral flow deceleration time and the isovolumic relaxation time, all occurring in early diastole. In contrast, the only

independent determinant for LVEDP in group B patients was the ratio of mitral peak flow velocity in early diastole to that in late diastole.
Conclusions: The intraventricular isovolumic relaxation flow patterns could delineate how the left ventricular systolic dyssynergy influenced the diastolic process, and determine which echocardiographic variables were more useful for predicting LVEDP in patients with anterior wall myocardial infarction.
Key words：myocardial infarction, isovolumetric relaxation flow pattern, left ventricular filling pressure

計畫緣由與目的、

The cardiac diastole is a complex sequence of many interrelated events [1, 2]. Inactivation, left ventricular load and nonuniformity constitute the triple control of relaxation for the intact heart [3]. Given the segmental nature of ischemic heart disease, inappropriately increased nonuniformity may induce early relaxation abnormalities or incoordinate relaxation [3-6]. Normally, regional intraventricular pressure gradients exist in the left ventricle during the isovolumic relaxation period, which generates suction and contributes to the ventricular filling [7]. These intraventricular pressure differences create a flow that can be identified by Doppler or color mapping study [8]. As a consequence of regional systolic dysfunction, the physiological early diastolic intraventricular pressure gradient pattern could be attenuated, lost entirely, or even reversed [9]. High left ventricular end-diastolic pressure (LVEDP) is an independent poor prognostic parameter for the patients after myocardial infarction [10]. The ratio of peak mitral early to late diastolic velocities bas been for a long time the most popularly used parameter for the evaluation of left ventricular diastolic function. However, it has also been well known that it is so variable and uncountable in many conditions, for example, pseudonormalized in patients with severe ventricular systolic dysfunction [1, 2]. Recently, color M-mode Doppler echocardiography has been proposed as a method for assessing left ventricular filling because of its high sampling rate and ability to measure flow velocities in both a temporal and spatial distributions [2, 11-15]. Accordingly, we hypothesized that the intraventricular flow pattern during isovolumic relaxation could further help to delineate the LVEDP in patients with anterior wall myocardial infarction. The objectives of this study were to delineate (1) how the anterior wall dyssynergy affected the intraventricular isovolumic relaxation (IVR) flow patterns, and thereby the early mitral flow propagation, and (2) how the IVR flow patterns illustrated the diastolic dysfunction and determined which echocardiographic variables were more useful for predicting LVEDP in patients with anterior wall myocardial infarction.

結果與討論、

Figure 1 shows the patterns of intraventricular flow during isovolumic relaxation period. With the aid of phonocardiogram, the intraventricular isovolumic relaxation (IVR) flow is identified. Left, pattern A. The intraventricular IVR flow is biphasic. Right, pattern B. The intraventricular IVR flow is totally reversed toward mitral orifice (in blue color). Each panel includes the color M-mode Doppler echocardiography (top) and pulsed wave Doppler tracing with sample volume positioned over the mid-ventricle (bottom).

Fig. 1

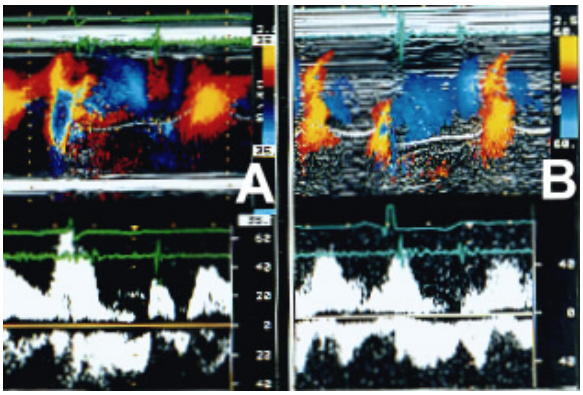

Fig.2

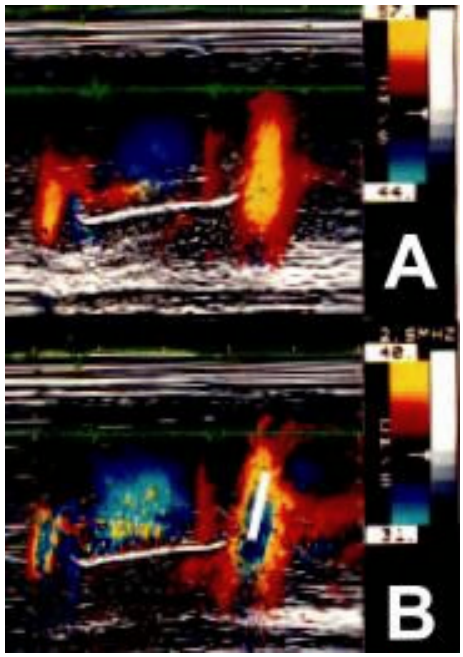

Figure 2 shows color M-mode echocardiographic variables for assessing left ventricular diastolic function. Panel A: The color M-mode Doppler echocardiograms of the left ventricular filling flow at a sweep speed of 100 mm/s. The ultrasound beam is interrogated from the left ventricular apex toward the center of mitral orifice as parallel to the filling flow as possible. The aliasing limit and baseline are adjusted to locate the center of minimized aliasing area around the mitral orifice in early diastole. Panel B: The first aliasing limit is changed to 70% of the maximal velocity in panel A. The aliasing boundary extends. The upward slope (black bar) is defined as the propagation rate of early diastolic filling flow.

According to the intraventricular IVR flow patterns, 52 patients were classified as group A and 21 patients as group B. The group B patients had a higher heart rate, lower LVEF, more prominent apical dyssynergy and lower FPRR. On the other hand, there was no significant difference among the other Doppler mitral inflow variables between these two groups. In group A, the FPRR, DT, IVRT, LVEF and heart rate were correlated with LVEDP, among which FPRR was the most significant one. In contrast, in group B, the E/A ratio, E wave velocity, A wave velocity, IVRT, DT, blood

pressure and age were correlated with LVEDP, among which E/A ratio was the most significant one.

Table. Multiple Stepwise Linear Regression Model for Left Ventricular End Diastolic Pressure and the Echocardiographic Variables

	r^2	p	SEE
All patients (n = 73)			
LVEDP = –0.06×DT + 26.2	0.28	<0.001	5.15
LVEDP = –0.05×DT –20.6×FPRR + 36.2	0.51	<0.001	4.29
LVEDP = –0.05×DT –20.5×FPRR–0.04×A + 38.7	0.53	<0.001	4.20
Group A (n = 52)			
LVEDP = –26.0×FPRR +28.9	0.41	<0.001	4.54
LVEDP = –20.1×FPRR –0.06×DT + 37.1	0.62	<0.001	3.66
LVEDP = – 18.4×FPRR –0.06×DT +0.09×IVRT + 29.6	0.68	<0.001	3.40
Group B (n = 21)			
LVEDP =10.1×E/A + 5.7	0.80	<0.001	3.02
For patients with LVEF≧ 40% (n = 53)			
LVEDP = –0.05×DT+ 25.1	0.24	<0.001	4.77
LVEDP = –0.05×DT– 17.6×FPRR + 34.1	0.43	<0.001	4.18
For patients with LVEF< 40% (n = 20)			
LVEDP = –0.06×DT + 28.6	0.38	0.002	5.66
LVEDP = –0.05×DT – 28.2×FPRR + 40.1	0.59	<0.001	4.72
LVEDP = –0.06×DT – 26.5×FPRR – 0.1×A + 46.5	0.68	<0.001	4.30

All the significant variables in univariate analyses were put into the multivariate stepwise regression model with forward selection (Table). When analyzing the patients as a whole, the LVEDP was independently determined by DT, FPRR and A wave velocity (r^2 = 0.53, p<0.001, and the standard error of the estimate, SEE= 4.20). In group A, the independent variables were FPRR, DT and IVRT (r^2 = 0.68, p<0.001, and SEE= 3.40). In group B, E/A ratio was the only independent determinant for LVEDP (r^2 = 0.80, p<0.001, and SEE= 3.02). When the patients were classified according to the global systolic function, the DT and FPRR were the independent determinants for LVEDP in patients with preserved systolic function (LVEF≧40%; r^2 = 0.43, p<0.001, and SEE= 4.18). The A wave velocity, in addition to DT and FPRR, enhanced the determination of LVEDP for patients with impaired systolic function (LVEF < 40%; r^2 = 0.68, p<0.001, and SEE = 4.30). It could be shown that grouping patients according to the isovolumic relaxation intraventricular flow patterns provided a better estimation of LVEDP than according to global systolic function.

To validate our observation, another 34 consecutive patients (30 men and 4 women aged 38 to 77 yeas, mean 60 ± 10) fulfilling the inclusion criteria underwent the same examinations. Twenty-one patients were classified as group A and 13 as group B. The estimated LVEDP was derived from the equations listed in table 3 according to the isovolumic relaxation intraventricular flow pattern. The correlation between estimated

and measured LVEDP was good ($r^2 = 0.75$, $p < 0.001$, and SEE = 2.79; Fig. 3). The sensitivity in predicting LVEDP $\geqq$ 14 mmHg was 87% (13/15), and the specificity, 84% (16/19).

Discussion

In this study, it could be shown that the intraventricular flow redistribution during isovolumic relaxation would change in patients with anterior wall dyssynergy. With lower ejection fraction and greater apical dyssynergy, intraventricular flow during isovolumic relaxation would completely reverse. In akinetic or dyskinetic apical segments, some elastic potential energy could be stored during systole and then released during the isovolumic relaxation and early diastolic filling periods. These, in turn, should result in loss, or even reverse, of the early diastolic intraventricular pressure gradient and thereby, change the intraventricular IVR flow pattern. The impaired left ventricular relaxation and suction function would result in decreased or even reversed early diastolic intraventricular pressure gradient, and thereby hamper the mitral inflow. In this study, the group B patients had lower LVEF, greater apical dyssynergy, and lower FPRR. The retarded apical filling should reflect a change in the intraventricular pressure gradient and flow redistribution [9, 12, 13].

Doppler echocardiography has emerged as a noninvasive alternative to cardiac catheterization for the evaluation of hemodynamic variables [16, 17]. However, other than the filling pressure per se, the final mitral flow velocity curve depends on multiple and interrelated factors that together determine the ventricular filling [1]. Comparing the coefficient of determination, we have demonstrated that classifying patients with anterior wall dyssynergy according to the patterns of intraventricular IVR flow could offer a more accurate estimation of LVEDP.

For group B patients, the extensive apical dyssynergy reversed the early diastolic intraventricular pressure gradient and the pattern of intraventricular IVR flow. The suction component of ventricular filling could be entirely lost. The passive driving pressure from the left atrium to ventricle determined the transmitral flow velocity curve. In this case, the E/A ratio was the only independent determinant for LVEDP [18, 19]. It means that the pressure gradient between the left atrium and ventricle would be very high during the early diastolic filling, however, decrease rapidly during the late filling phase because of the sharply increased intraventricular pressure.

It has been well known that the mitral flow velocity curves alone are useful in determining filling pressure in patients with depressed left ventricular function [20, 21]. It is also known that in patients with preserved systolic function, other Doppler indices such as mitral flow propagation rate are required to differentiate normal from “pseudonormal” flow patterns. Comparing the results of multiple regression analyses according to two different classifications (by intraventricular IVR flow pattern or by

global systolic function), it could be shown that the former method provided a better estimation for ventricular filling pressure. It revealed that the left ventricular geometry of systolic dyssynergy, in addition to the global systolic function, would influence the intraventricular flow or pressure gradient and played an important role in the diastolic filling process.

計畫成果自評

In this study, we have demonstrated that the left ventricular systolic dysfunction and apical dyssynergy could influence the early diastolic intraventricular pressure gradient, flow redistribution and, thereby, ventricular diastolic function. The color M-mode Doppler echocardiography, with its high sampling rate and ability to measure flow velocity in both temporal and spatial distributions, could be used to identify the intraventricular IVR flow. The IVR flow patterns could delineate how the left ventricular systolic dyssynergy influenced the diastolic process, and improve the predicting power of Doppler echocardiography for LVEDP in patients with anterior wall myocardial infarction.

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