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Ventricular Contractile Interaction Following Coronary Ligation in Dogs

Ying-Tsung Chen[1,2,3,4], Chun-Jou Lin[1], Andrew Ying-Siu Lee[1]

[1]Department of Internal Medicine, Taichung Veterans General Hospital, Taichung; [2]National Yang-Ming University School of Medicine, Taipei; [3]Chung-Shan Medical and Dental College; and [4]Chinese Medical College, Taichung, Taiwan, R.O.C.

Abstract

Background. Ventricular interdependence has already been reported. Diastolic ventricular interaction is well studied, but information is rare regarding systolic ventricular interaction and has shown only that maximal acceleration is a sensitive indicator of left ventricular performance. Hence, this study was conducted.

Methods. Eighteen mongrel dogs were anesthetized and two Millar catheters were advanced from the femoral artery and vein to the left ventricle and pulmonary artery for measurement of pressure, flow and velocity in each. Before and after ligation of the left anterior descending or right coronary artery, both ventricles, dP/dt max, maximum acceleration (MA), time to maximal acceleration (TTMA) were measured simultaneously and the percentage of area change and ventricular wall motion were recorded by two-dimensional echocardiography.

Results. The percentage of fraction area change decreased significantly when associated with decrease in dP/dt, maximal acceleration and TTMA in both ventricles. The parameters of contractility dP/dt and MA were marked and occurred earlier, after ischemia. In the ligation of LAD, infarct area involved the anteroseptal and apical region and both ventricular dysfunctions were noted. In the ligation of RCA when the interventricular septum motion was preserved, the RV hemodynamic had significant changes including dP/dt and MA, but there was insignificant change in LV.

Conclusions. Ventricular interaction is less important than the direct effects of coronary occlusion on the myocardium, and the interventricular septum plays a relatively important part in ventricular interaction.
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Keywords: maximum acceleration, ventricular function

Introduction

Changes in right ventricular function are well known to influence left ventricular function through ventricular interaction and vice versa [1-5]. Diastolic ventricular interaction is well understood, but relatively little information is available about the importance of systolic ventricular interaction in ventricular contractility. Recently, maximum acceleration of blood from the ascending aorta has been a subject of interest. Studies performed during left sided heart catheterization in animals and humans have demonstrated that aortic blood flow velocity and acceleration are sensitive indicators of left ventricular performance [6-10]. Hence, the purpose of this study was to directly measure the changes of contractilities of both ventricles in acute cardiac ischemia, using large artery flow velocity.

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Address reprint requests to: Ying-Tsung Chen, M.D., Taichung Veterans General Hospital, 160, Section 3, Taichung-Kang Road, Taichung, Taiwan, R.O.C.

Materials and Methods

Twenty mongrel dogs of either sex, weighing between 12-18 kgs, were anesthetized with pentobarbitone sodium

(60 mg/Kg); tracheal intubation and artificial ventilation (16-18 strokes/min, 300 ml/kg, min) was performed, under fluoroscopic guidance; two Millar catheters were advanced from the femoral artery and vein to the left ventricle (LV) and pulmonary artery for measurement of pressure flow and velocity. After putting a suture around the artery, each dog was allowed to equilibrate for 20 minutes when the preligation hemodynamics were stabilized normally. Before and after occlusion of either the left anterior descending or the right coronary artery, all parameters of both ventricles were recorded. Maximal velocity in ms^{-1} represents the highest velocity achieved during systole. Maximum acceleration (MA) which is the first differential of velocity is measured in ms^{-2}, and time-to-maximum-acceleration (TTMA) is measured from the beginning of the upstroke of both great arteries blood velocity to the greatest rate of rise of velocity, and the time derivative of the left ventricular pressure (dP/dt max) were obtained by electronic differentiation.

Ventricular Wall Motion

A two-dimensional Doppler Echocardiography Hewlett-Packard 1000 imaging system was used. The ultrasound transducer frequency was 3.5 MHz, and the transducer was placed directly on the dog's heart. Cross-sectional echocardiography images at the level of papillary muscles were recorded and the epicardial and endocardium margins were traced at each cycle. The percentage of area change was calculated from LV end diastolic area - LV end systolic area / LV end diastolic area.

The above measurements of cardiac function and wall motion were then repeated at 5, 10, 20 and 30 minutes following ligation of the coronary artery.

Statistics

Repeated-measure analysis of variance followed by multiple comparisons were used to compare left or right ventricular function as a function of time in control and after ligation and between the two chambers. A p-value of less than 0.05 was considered as statistically significant. Values are given as mean ± SEM.

Results

Eighteen of the 20 dogs' hearts where the left anterior descending artery (LAD) perfused the anterior apical area of the left ventricle and the right coronary artery (RCA) was dominant in supplying the major portion of the right ventricle (RV) were included in this study.

Biventricular Hemodynamic Changes

Within one to two minutes after ligation of the coronary artery, the supply area of the myocardium became hypokinetic, and within three to five minutes the area further deteriorated to dyskinesia. Fractional area change was markedly decreased from 54% to 32.3% within five minutes after ligation of LAD . There was no significant LV area change after ligation of RCA.

The data defining the time courses of hemodynamic alternation in both ventricles are summarized in Tables 1 and 2. There are related changes between the maximum acceleration and dP/dt (Figure 1), and maximum acceleration and fractional area change in the left ventricle (Figure 2) . It is evident that the longer the myocardial ischemia, the more the left ventricular contractility decreased. There was no significant change in systemic pulmonary vascular resistance during ligation of coronary artery.

Ligation of Left Anterior Descending Artery

Significant hemodynamic changes were more pronounced and became statistically significant within five minutes after ligation of LAD. The parameters, especially LV diastolic pressure, maximum acceleration and time to maximum acceleration, appeared more sensitive to the infarction process, and these marked changes occurred earlier. At the right ventricle, the hemodynamic developed statistically significant changes up to ten minutes.

Ligation of Right Coronary Artery

With right ventricular infarction, the contractile parameter dP/dt, MA had significant alternation within 5 and 10 minutes, but was less pronounced compared to LV infarction. At the left ventricle, there were no distinct change of hemodynamic parameters after ligation of the right coronary artery.

Discussion

This study documented the systolic ventricular interdependence which was the change of contractility after acute myocardial ischemia; the contractile index of dP/dt and MA was more sensitive and appeared earlier than other parameters of ventricular function such as stroke volume or aortic velocity.

Contractility is independent of load, and several studies have shown that MA is sensitive to an inotropic state and relatively insensitive to a loading condition. MA was noted with infusion of an inotropic agent - dobutamine or phenylephrine infusion which caused a significant increase in MA with minimal increase in stroke volume [1, 6, 9]. However, an increase in diastolic volume by infusion of dextran or by the application of body positive pressure could systemically alter the preload [6], where there was relatively little increase in MA. Although some studies have shown that a very high systemic vascular resistance (afterload) MA falls, these was no manipulation to raise the afterload or alter the preload during the

Table 1. Time course of hemodynamic change in both ventricles after ligation of left anterior descending coronary artery

Parameters	Control	5 min	10 min	20 min	30 min
Mean Ao (mmHg)	92±3.1	82±3.6	83±4.1	80±5.1	81±4.3
HR (beats/min)	128±4.3	126±3.4	124±3.6	128±3.7	126±3.7
SV (ml/min)	28±1.5	22±1.4[a]	22±1.5[a]	21±1.3[a]	20±1.2[a]
SVR (dyne-sec-cm^{-5})	2600±30	2429±48	2705±54	2380±28	2571±30
Left ventricular					
LVEDP (mmHg)	4.3±0.6	9.3±1.3[a]	10±1.2[a]	11±1.2[a]	11±1.4[a]
dP/dt (mmHg/sec)	1870±80	1281±70[a]	1184±50[a]	1048±60[a]	1142±60[a]
Maximal aortic velocity (cm/sec)	183.2±1.8	183.2±1.9	176.5±3.2	180.4±1.5	159.4±1.8
Maximal acceleration (cm/sec)	1974±80	1140±50[a]	1084±64[a]	1180±30[a]	1024±30[a]
Time to MA (msec)	44.4±1.2	77.4±3.6[a]	78±2.1[a]	80.5±2.1[a]	78.3±2.0[a]
Fractional area change (%)	54.4	32.3[a]	30.2[a]	31.4[a]	31.7[a]
Right ventricular					
MPA (mmHg)	9±1.2	9±1.4	9±1.7	10±1.8	10±1.1
PVR (dyne-sec-cm^{-5})	205±28	266±24	266±34	307±22	320±24
RVEDP (mmHg)	3.2±0.4	4.2±0.2	4.3±0.1	4.5±0.3	5.1±0.2[a]
dP/dt (mmHg/sec)	218±17	204±18	170±18[b]	182±17[b]	184±14[b]
Maximal pul. velocity (cm/sec)	137.4±1.6	126.5±1.8	130.4±1.5	132.3±4.3	131±4.5
Maximal acceleration (cm/sec)	312.1±6.8	304±6.4	284±5.8[b]	283±5.6[b]	285±6.4[b]
Time to MA (msec)	45.1±1.3	48±4.2	47.7±5.2	45.3±1.6	44.2±1.8

a: $p<0.01$; b: $p<0.05$; HR: heart rate; MPA: mean pulmonary artery pressure; RV: right ventricle; LVEDP: left ventricular end diastolic pressure; RVEDP: right ventricular end diastolic pressure; SVP: systemic vascular resistance; PVR: pulmonary vascular resistant; MA: maximal acceleration; pul.: pulmonary.

Table 2. Time course of hemodynamic change in both ventricles after ligation of right coronary artery

Parameters	Control	5 min	10 min	20 min	30 min
Mean Ao (mmHg)	94±4.1	90±4.2	89±5.1	90±4.1	89±4.2
HR (beats/min)	127±4.2	125±3.1	128±2.1	126±3.4	126±3.2
SV (ml/min)	27±1.4	26±1.6	27±1.5	26±1.3	26±1.4[a]
SVR (dyne-sec-cm^{-5})	2211±60	2250±76	2094±74	2250±68	2225±80
Left ventricular					
LVEDP (mmHg)	4.3±0.6	4.5±0.8	4.8±0.4	5.2±0.6	6.4±0.4
dP/dt (mmHg/sec)	1864±45	1820±80	1808±78	1845±60	1802±70
Maximal aortic velocity (cm/sec)	196.4±3.5	200.5±1.3	197.8±1.4	187.5±3.2	198.7±4.2
Maximal acceleration (cm/sec)	1894±80	1878±70	1940±60	1860±40	1786±60
Time to MA (msec)	48.4±1.3	46.4±1.2	50.3±1.8	49.4±1.2	48.1±1.4
Fractional area change (%)	52.4	50.4	51.2	51.8	50.6
Right ventricular					
MPA (mmHg)	9±1.2	9±1.4	9±1.1	10±1.6	10±1.3
PVR (dyne-sec-cm^{-5})	211±14	225±20	211±19	225±18	250±13
RVEDP (mmHg)	2.8±1.4	3.5±0.4	6.8±1.2[a]	7.7±1.5[a]	7.9±1.0[a]
dP/dt (mmHg/sec)	238±16	142±16	140±17	139±15	140±14
Maximal pul. velocity (cm/sec)	142.8±1.4	130.4±1.2	128.5±1.8	120.5±1.4	126.7±1.6
Maximal acceleration (cm/sec)	269±6.7	184±4.2[a]	183±3.5[a]	179±3.8[a]	196±4.2[a]
Time to MA (msec)	46.7±1.2	70.2±1.4[a]	76.4±1.5[a]	80±3.2[a]	77.3±4.1[a]

a: $p<0.01$; HR: heart rate; MPA: mean pulmonary artery pressure; RV: right ventricle; LVEDP: left ventricular end diastolic pressure; RVEDP: right ventricular end diastolic pressure; SVP: systemic vascular resistance; PVR: pulmonary vascular resistant; MA: maximal acceleration; pul.: pulmonary.

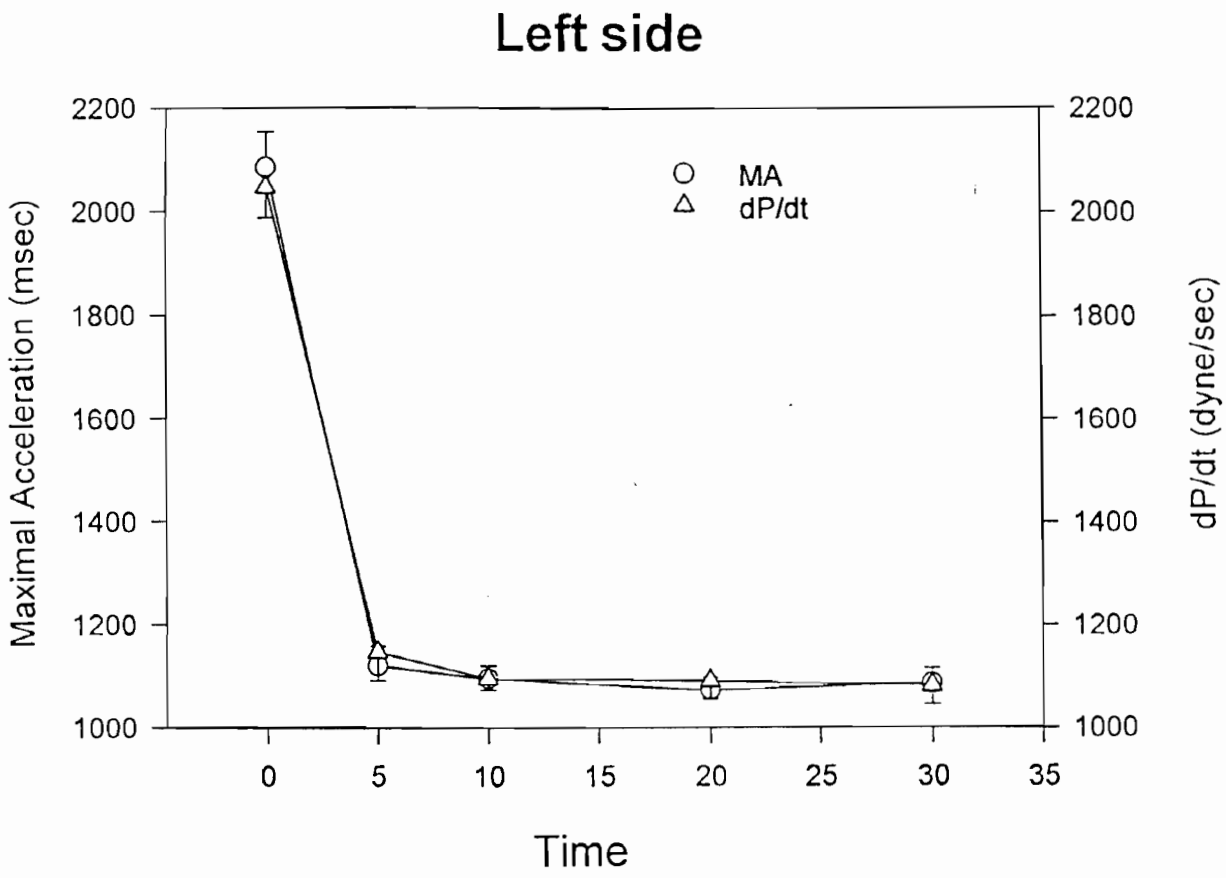

Figure 1. The maximum acceleration and dP/dt were proportionally decreased after ligation of left anterior descending artery.

procedure; the systemic and pulmonary vascular resistance underwent insignificant change after ligation of coronary artery, so the decreased MA was not related to load condition, rather directly related to ischemic area of the myocardium.

DP/dt has been used widely by invasive methods but is an inconvenient process. Recently MA could be measured by Doppler flow from the ascending aorta [9]. This study shows that MA is a sensitive index as dP/dt, and that there was a good linear relationship between these two indices. Although this study was not designed to compare MA by Doppler flow velocity, it is still suggested that MA is a simple index for clinical evaluation of ventricular contractility by a non-invasive method.

The myocardium is composed of muscle fibers tethered within a supportive network of collagen; because the right and left ventricles are aligned in series and mechanically coupled, a perturbation in the mechanical events of one ventricle will influence the behavior of the other ventricle. Previous studies have shown that increased distention of either ventricle during diastole has tended to alter the compliance and geometry of the opposite ventricle [1-4, 11-13]. This study showed that left anterior descending artery occlusion produced anteroseptal infarction which involved the interventricular septum, and the anterior LV wall became akinetic and dyskinetic. The left ventricular dP/dt and MA fell within five minutes of coronary artery ligation, while the right ventricular contractile index took ten minutes, indicating that the RV function was indirectly depressed by the left ventricle. With the right ventricular infarction induced by the right coronary ligation, the right ventricular free wall and inferioposterior wall became hypokinetic and, where the interventricular septum was preserved, the right ventricular function was impaired; both dP/dt and MA decreased in a similar way to the left ventricle, but there was no change in the left ventricular function. These data suggest that ventricular interaction is less important than the direct effects of coronary occlusion on the myocardium of the right ventricle.

The relative importance of septal motion to ventricular interaction was also evident in the study. By using two-dimensional echocardiography, change could be observed in the systolic shape of the left ventricle with ligated LAD. The change in configuration was confined mainly to the interventricular septum and apex; on

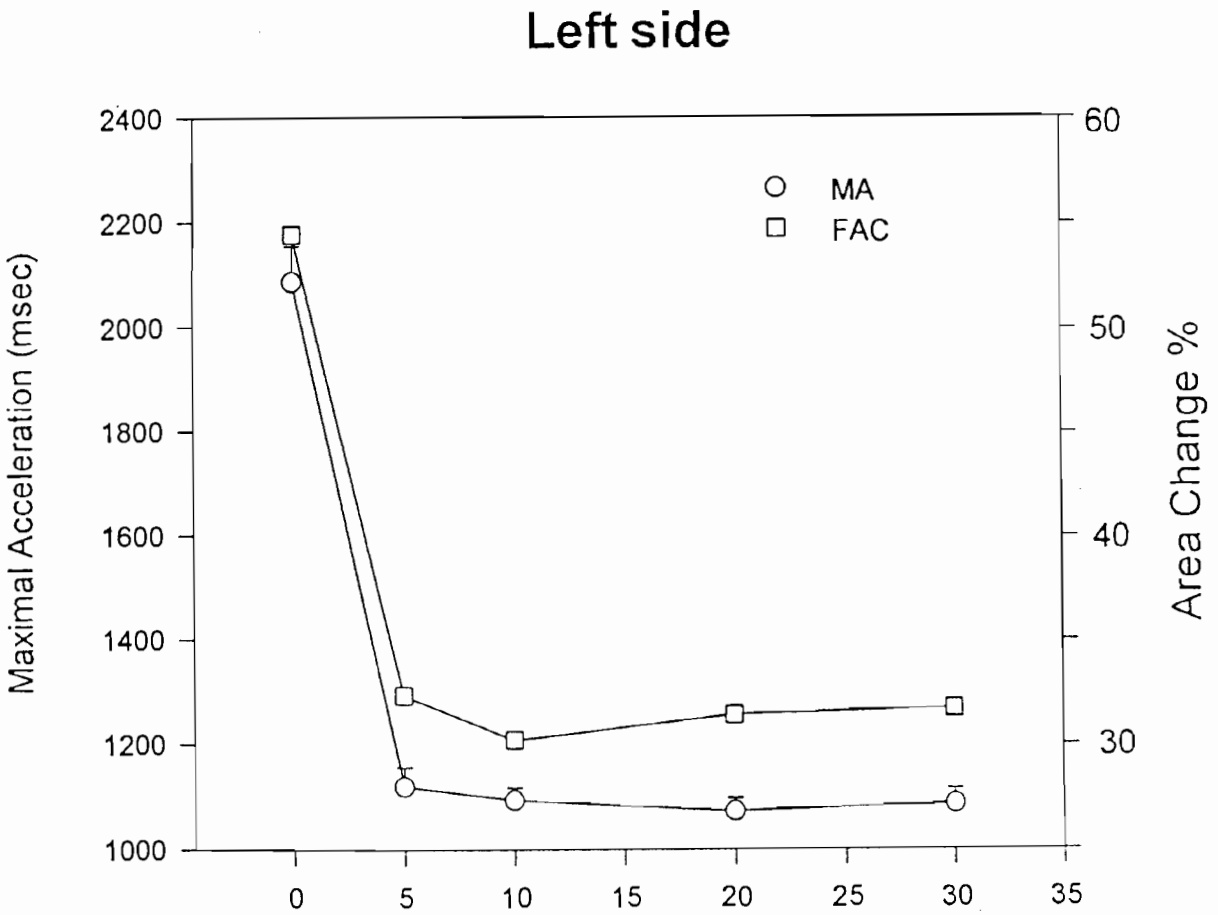

Figure 2. Maximum acceleration was markedly decreased as percentage area change of left ventricle after ligation of left anterior descending artery.

morphological grounds, the septum can be considered part of the left ventricle. With the left ventricular wall becoming abnormal, motion-induced change in the left ventricular pressure-volume relationship would affect the right ventricular function. Brook et al. [14] have shown that right ventricular performance was significantly altered by ischemia of the anteroseptal wall; that result is similiar to that obtained in this study, but with the occlusion high up in the right coronary artery, the left ventricular function was altered while the ischemic area involved the inferoseptal portion. This phenomenon was not demonstrated here. It appears that the reason for this discrepancy is that the hemodynamic alterations appear to be closely related to the anatomical distribution of the occluded artery.

Acknowledgments

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心室之間收縮力關係在狗動物實驗的觀察

陳穎從[1,2,3,4] 林君柔[1] 李應紹[1]

台中榮民總醫院 內科部[1] 國立陽明大學醫學院[2] 中山醫學院[3] 中國醫藥學院[4]

摘 要

背景 左右兩心室之間功能的變化具有互相牽制的作用，改變左心室功能會導致右心室功能變化，反之亦然。然而其影響程度如何？至今仍無完整之文獻報告。本研究的目的是分別結紮左前降枝或右冠狀動脈來評估左右兩心室之間收縮功能的交互關係。

方法 18隻狗分爲兩組各9隻，全身麻醉並使用呼吸器，在主動脈及肺動脈放置電磁力導管（electromagnetic catheter）測量壓力及血流的變化，利用雙面超音波測量心室壁動力（ventricular wall motion）及面積百分率（percentage change of fractional area）。開胸之後分別結紮左前降枝或右冠狀動脈，結紮前後分別測量左、右心室收縮力（dp/dt）、最大加速度（maximal acceleration, MA）、開始收縮至最大加速度的時間（time to maximal acceleration, TTMA）。

結果 發現心肌缺氧後，心室收縮力及最大加速度很快就有變化，而且當面積百分率變化時，dp/dt、MA及TTMA亦隨之明顯下降。結紮左冠狀動脈時，梗塞範圍包括前壁、室中膈及心尖，左右心室功能均有變化。結紮右冠動脈時，室中膈動力不變，右心室的血流動力學明顯改變，但不影響左心室功能。

結論 冠狀動脈梗塞直接對於心肌的影響遠大於對心室之間的交互作用，且室中膈在心室的牽制作用中扮演一個重要的角色。

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關鍵詞：最大加速度，心室功能