Annals of Biomedical Engineering, Vol. 15, pp. 297–310, 1987
Printed in the USA.

0090-6964/87 $3.00 + .00

MUELLER MANEUVER AND LV FUNCTION IN CORONARY ARTERY DISEASE

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Decreasing pleural pressure impedes the ejection of blood from the left ventricle (LV), may lead to decreased LV compliance because of interdependence effects and leads to increased transmural LV systolic and diastolic pressure. Previous work from this laboratory has shown that patients with coronary artery disease (CAD) often develop akinetic segments of the LV wall during the Mueller maneuver. In the presence of increased LV transmural pressure regional akinesis could be caused either by the development of regional ischemia or by mechanical inhibition of motion of an area of nonfunctional myocardium as would be caused by previous myocardial infarction (MI). The present study was designed to distinguish between these two mechanisms by determining if the presence of CAD alone is sufficient to lead to regional akinesis or if prior MI is necessary. We used first pass radionuclide ventriculography (RVG) in the 30° LAD supine position to measure LV ejection fraction (EF), end-diastolic (EDV) and end-systolic (ESV) volumes, heart rate and to assess regional wall motion during the Mueller maneuver. This was done in four groups of subjects: (1) 13 normal subjects, (2) 25 patients with CAD but no prior MI, (3) 13 patients with prior nontransmural MI and (4) 36 patients with prior transmural MI. All subjects had angina pectoris and underwent contrast coronary arteriography. Most also underwent routine contrast left ventriculography as well. There were no significant differences among the three patient groups as regards medications, extent and severity of CAD, and response to routine exercise tolerance testing. EF decreased significantly in the three patient groups (4%–9%, $p<0.01$) but not in the normals during the Mueller maneuver. Heart rate increased (5–10 bpm, $p<0.05$) in the normals and in patient groups 2 and 4. EDV decrease in all four subject groups (8%–10%, $p<0.01$), while ESV remained unchanged. Akinesis of the LV wall developed during the Mueller maneuver only in one group-2 patient, but did so in 17/36 patients with prior transmural MI (group 4, $p<0.001$). One-half of the akinetic LV wall segments seen during the Mueller maneuver on RVG were not seen on routine contrast ventriculography. We tested the effects of posture (supine versus upright) on the response to the Mueller maneuver in six normal subjects and found no changes in the response of EDV and

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ESV to the Mueller maneuver. We conclude that (1) the appearance of LV wall akinesis during the Mueller maneuver signifies the presence of prior transmural MI, and not just CAD; (2) the Mueller maneuver can enhance the sensitivity of the RVG for detecting nonfunctional myocardium; (3) regional akinesis develops even when LV volume decreases, suggesting it is due to changes in LV transmural pressure; (4) there are changes in LV function which can lead to a decrease in global EF during the Mueller maneuver; (5) the effects of the Mueller maneuver on LV volume are complex, variable and are subject to multifactorial influences.

INTRODUCTION

Since the mid 1800s (7), it has been recognized that decreasing intrathoracic pressure can impede the ejection of blood from the left ventricle (LV) (7,18,20,23). This effect is analogous to increasing afterload. When afterload is increased by increasing aortic pressure with, for example, a vasoconstrictor, there is an increase in the pressure the LV must generate relative to pleural pressure. That is, there is an increase in LV systolic transmural pressure. When intrathoracic pressure is lowered relative to the aortic pressure, the effect is similar to that of vasoconstriction, i.e. there is an increase in LV systolic transmural pressure, this time by virtue of a decrease in intrathoracic pressure, rather than by increasing arterial pressure. There is one difference between the two maneuvers, however. With administration of a vasoconstrictor, LV diastolic transmural pressure rises, and eventually, because of back transmission through the pulmonary circulation and the effects of interventricular interdependence (1,8,13), right atrial transmural pressure also rises. Since intrathoracic pressure does not change, there is an increase in right atrial pressure measured relative to atmospheric pressure. This leads to a decrease in venous return, which modulates the increase in LV transmural pressure, thus buffering the afterload effects. When pleural pressure decreases, however, right atrial pressure actually decreases relative to atmospheric pressure, although transmural pressure increases (21). This effect tends to maintain or even increase venous return (2,11), forcing the LV to maintain a constant or increased stroke output against increased afterload. Thus it might be expected that for the same increase in LV systolic transmural pressure, decreased pleural pressure might lead to greater cardiac effects than increased arterial pressure (vasoconstriction). Another theoretical effect of decreased pleural pressure is related to increased venous return which leads to right ventricular dilation. By the mechanism of ventricular interdependence, this leads to decreased LV compliance and inhibits LV filling.

The Mueller maneuver, a forced inspiratory effort with no change in lung volume, greatly decreases intrathoracic pressure. Considerations of the afterload effects of the decreased intrathoracic pressure on LV function have led to a number of investigations regarding the effects of the Mueller maneuver on LV dynamics in normal individuals and in patients with coronary artery disease. The afterload effects of the Mueller maneuver may be useful clinically as a stress test. Stress testing (4) is used for detecting and evaluating heart disease. Some theoretical advantages of using respiratory maneuvers, like the Mueller maneuver, for stress testing include short duration and easy reversibility, both of which are potential safety factors. Furthermore, patients unable to exercise on a treadmill because of other medical problems might be able to perform the appropriate respiratory maneuvers. Finally, many patients with coronary artery disease (CAD) also suffer from diseases of the respiratory tract, especially obstructive lung disease, which may lead to profound decreases

in mean intrathoracic pressure during acute exacerbations (9,24). Studies of the effects of decreased intrathoracic pressure in these patients could contribute to the understanding of the way in which mechanical abnormalities of the respiratory system affect cardiac function.

Figure 1 illustrates some of the theoretical relationships between venous return (VR) and cardiac function (CF) during the performance of the Mueller maneuver. VRC is a venous return curve following the ideas of Guyton (11). As pleural pressure decreases, so does right atrial pressure (PRA) by direct transmission. At some point VR reaches its maximum, and flow becomes limited because of collapse of the great veins entering the thorax (FL: flow limiting point). The normal cardiac function curve (CF1) intersects with the VR curve at point *A*. If there were no change in CF during the Mueller maneuver, then the cardiac function curve would shift leftward by an amount equal to the decrease in pleural pressure associated with the Mueller maneuver. Thus for any given cardiac output (CO) transmural PRA (PRA measured relative to pleural pressure) would not change. CF2 represents this cardiac function curve. During a Mueller maneuver leading to a decrease of −20 units in this figure, a new intersection point represented by point *B* is reached. For the purposes of this discussion we have assumed that a steady state is reached during the time it takes to perform the Mueller maneuver. To the extent that the Mueller maneuver produces afterload effects on the heart, the cardiac function curve would shift downward to the right. This is shown as CF3 in the figure. Depending on the degree of shift of the cardiac function curve, PRA transmural would increase. In the figure the intersection of the two curves is again at point *A*. However, since pleural pressure is decreased, PRA transmural increases. In this example we have ignored the effects of

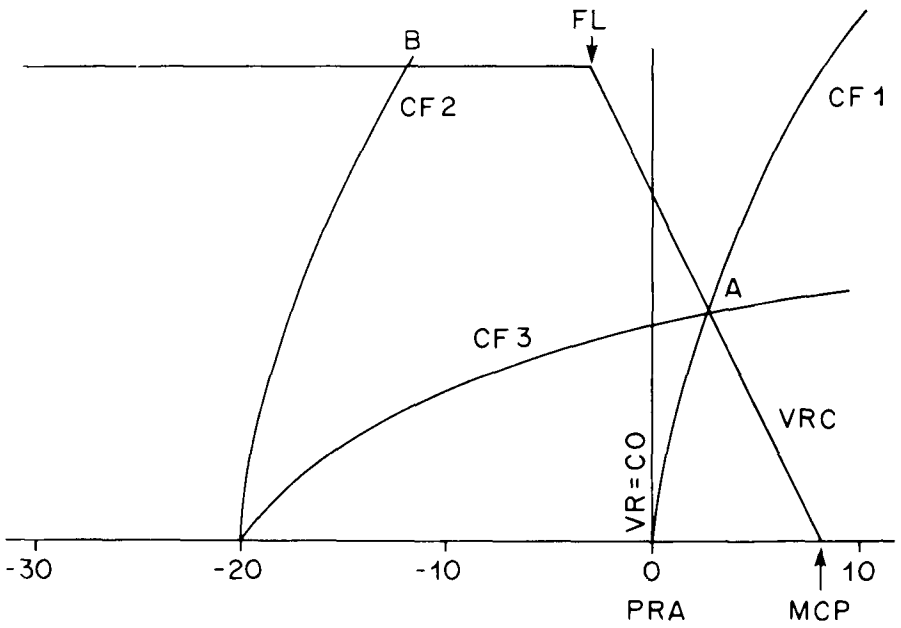

FIGURE 1. Theoretical effects of Mueller maneuver on venous return (VR) and cardiac function (CF). See text for discussion.

pooling of blood in the heart and lungs during the Mueller maneuver which might lead to a decrease in the mean circulatory pressure and, thereby, shift the VRC.

Experimental data have been consistent with the prediction of increased transmural right atrial filling pressure during the Mueller maneuver. When pleural pressure was decreased by approximately 31 Torr during performance of Mueller maneuvers in normal subjects, right atrial pressure decreased only by approximately 21 Torr, leading to increased PRA transmural of around 10 Torr and increased right ventricular (RV) volume (21).

The afterload like effects of decreased pleural pressure on left ventricular dynamics are shown in Fig. 2. The solid lines ("diastolic" and "systolic") refer to diastolic and maximum (isovolumic) volume–pressure curves. During isovolumic contraction from end-diastole (point *B*), pressure increases to the level of aortic diastolic transmural pressure, afterload level 1, point *C*. Shortening then occurs along line CD to point *D* on the maximum volume–pressure curve. We have ignored the fact that aortic pressure also rises during systole and assumed istotonic ventricular shortening. From point *D*, relaxation occurs isovolumically to point *A*, and the ventricle then fills during diastole along line *AB* to start the cycle again. When afterload is increased (level 2), for the first beat ventricular contraction occurs along the path *BHIE*. Stroke volume (the length of *HI*) is reduced. If, however, venous return and heart rate are held constant, ventricular enlargement occurs and in the steady state contraction proceeds along path *FGIE*, in which both end-diastolic and end-systolic volumes are increased. During Mueller maneuvers generating pleural pressures of approximately −31 Torr, arterial

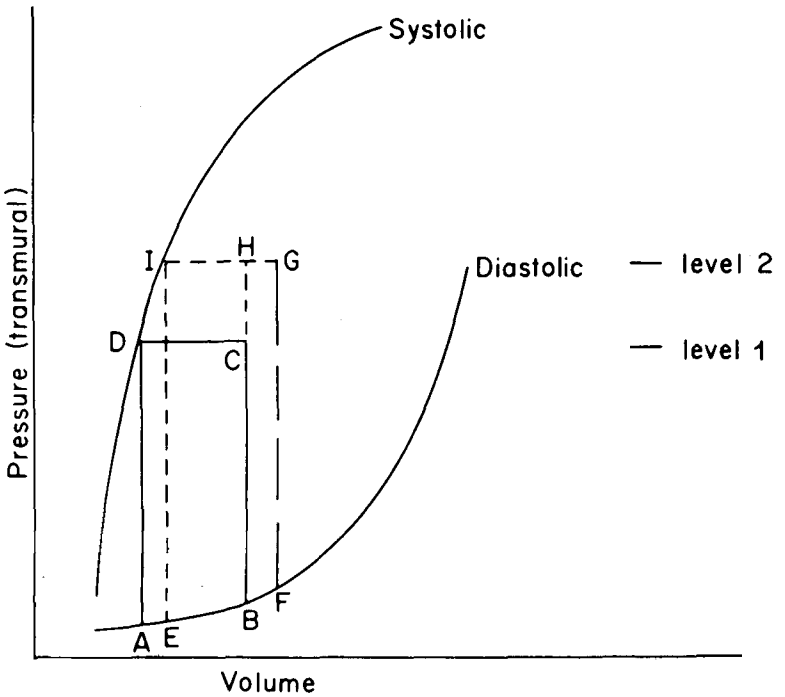

FIGURE 2. Theoretical effects of increased afterload on LV dynamics. See text for discussion.

diastolic pressure decreased by only approximately 4 Torr, thus leading to an increase in aortic transmural pressure of approximately 28 Torr (21). Since cardiac output remains unchanged during the Mueller maneuver (22), it may be assumed that venous return is also not diminished. The net effect of the afterload effects of the Mueller maneuver would be to increase LV end-diastolic transmural pressure and volume (point *F*), as well as end-systolic transmural pressure and volume (point *I*).

Another effect of the Mueller maneuver on LV hemodynamics relates to RV dilation (3,12,21) caused by increased venous return, which, through ventricular interdependence (1,13), decrease LV compliance. The effects of a decrease in compliance on the hemodynamics of the LV are shown in Fig. 3. *D*1 is the normal pressure volume curve. *D*2 is diastolic pressure volume curve following an increase in RV transmural pressure. Normally, LV contraction takes place along path *ABCD* (see explanation of Fig. 2 for details). During the performance of the Mueller maneuver, as the RV dilates, the diastolic volume pressure curve shifts to *D*2. During the first beat following this shift, the cardiac cycle proceeds along path *GHDE*, in which stroke volume is reduced (length of *HD*). If venous return and heart rate are maintained constant, then stroke volume is restored and contraction takes place along line *FCDE*. The prediction here is that end-diastolic transmural pressure would increase while end-diastolic and end-systolic volumes would remain unchanged.

Previous studies (15,16) have confirmed that LV transmural filling pressure (left atrial transmural pressure) increases during the performance of the Mueller maneu-

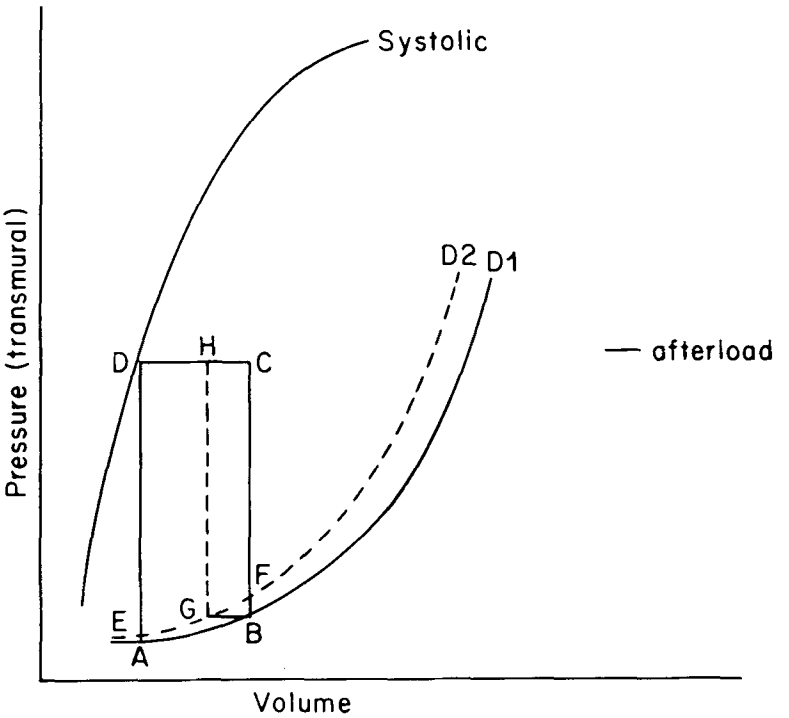

FIGURE 3. Theoretical effects of decreased LV compliance on LV dynamics.

ver in normal humans. To date this has not been measured in patients with CAD. In previous studies on upright normal subjects and patients with CAD LV end-diastolic and end-systolic volume were found to increase (Fig. 4, Refs. 14, 21, 22). In supine subjects, performing comparable degrees of inspiratory effort, others have found these volumes to decrease (3,12). Buda *et al.* (5) found no change in LV volumes with small inspiratory efforts (−30 cm H_2O) and an increase at larger inspiratory efforts (−60 cm H_2O). Thus under different circumstances the relative effects of afterload versus interdependence may vary, as will be discussed below.

Effects of the Mueller Maneuver on Patients with CAD

In a previous study (22) we found that during the Mueller maneuver, ejection fraction fell significantly in patients with CAD but not in normals. Changes in LV end-diastolic and end-systolic volumes were similar in normals and in patients with CAD.

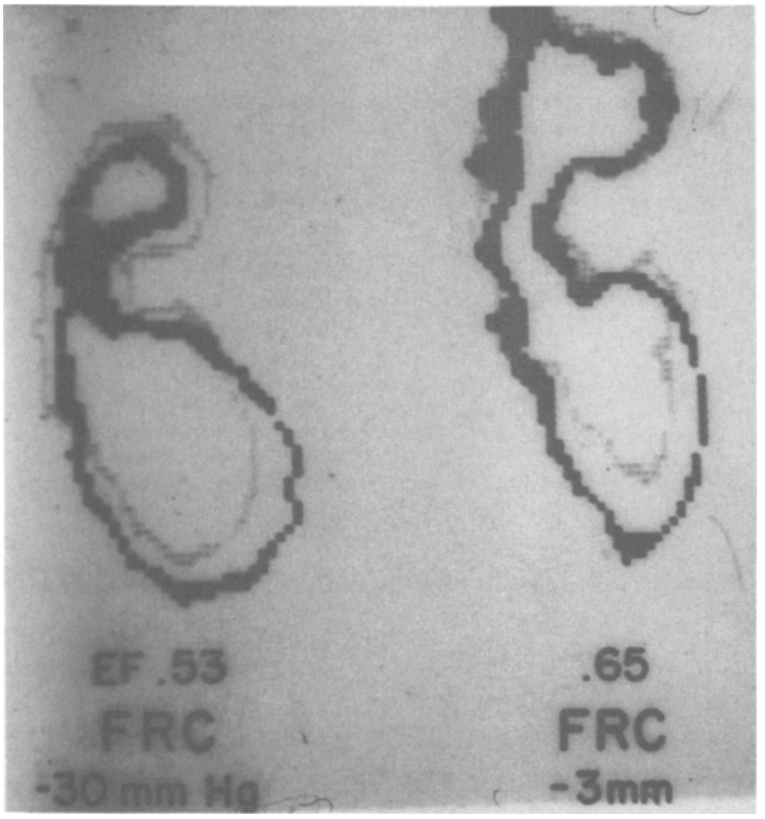

FIGURE 4. Effect of Mueller maneuver on a normal subject in the upright posture. Shown is a radionuclide left ventriculogram performed in the 30° left anterior oblique (LAO) (see METHODS for details). Figure on the right shows a normal radionuclide ventriculogram, dark outline is end-diastolic perimeter and light outline is the end-systolic perimeter. Figure on the left shows the same subject during the performance of a Mueller maneuver generating a pleural pressure of −30 cm H_2O. EF = ejection fraction. During the Mueller maneuver, there is a decrease in EF (not a constant feature in the normals) and an increase in end-diastolic and end-systolic volumes.

The important finding was the appearance of regions of LV wall akinesis in case 9/14 of the CAD patients during the Mueller maneuver. This was not seen in normals or in patients with noncardiac disease (Fig. 5).

Two hypotheses were advanced to explain this finding. These are illustrated in Fig. 6. First, increased wall stress (increased transmural pressure) leads to increased myocardial wall tension, which leads to increased myocardial oxygen demand during the Mueller maneuver. Normally, myocardial blood flow increases in response to this increase in energy demand. In areas supplied by a diseased coronary artery blood supply is marginal, and the normal hyperemic response does not occur. As the ratio of supply to demand decreases myocardial ischemia results. Wall motion (17) diminishes since, in the ischemic area, the ischemic myocardium cannot develop enough tension to overcome transmural LV pressure.

The second hypothesis is that the development of regional wall akinesis is due to the presence of noncontractile tissue in the myocardium, i.e. areas of loss of muscle fibers and fibrous tissue formation due to prior myocardial infarction. Under normal conditions, these areas appear to have normal wall motion because they are mechanically linked to surrounding areas where contraction is normal. During the performance of the Mueller maneuver, as LV end-diastolic transmural pressures increase, this abnormality becomes apparent.

According to the first hypothesis, the presence of CAD is a sufficient condition for the appearance of regional wall akinesis during the Mueller maneuver. According to the second the presence of noncontractile tissue (prior myocardial infarction) is a necessary condition. We therefore designed a series of studies to evaluate these hypotheses.

A clinical study was undertaken to differentiate between these hypotheses. We reasoned that if the first hypothesis were correct, then the presence of ischemic heart disease would be a sufficient condition for the development of LV wall akinesis during the Mueller maneuver. If the second hypothesis were correct, then the presence of prior myocardial infarction (MI) would be a necessary condition for this to occur.

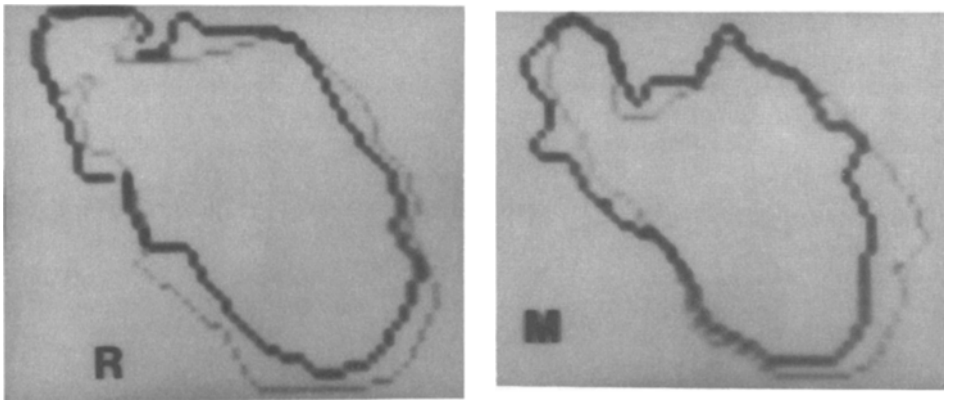

FIGURE 5. Effects of Mueller maneuver in a patient who had suffered an anterior-septal myocardial infarction in the past. Radionuclide left ventriculogram performed in the supine posture, in the 30° LAO position. R = rest, M = Mueller maneuver, performed so as to generate −30 cm H_2O pleural pressure. Note that appearance of akinesis along the septal margin (on the left), as shown by overlap of the end-diastolic and end-systolic perimeter.

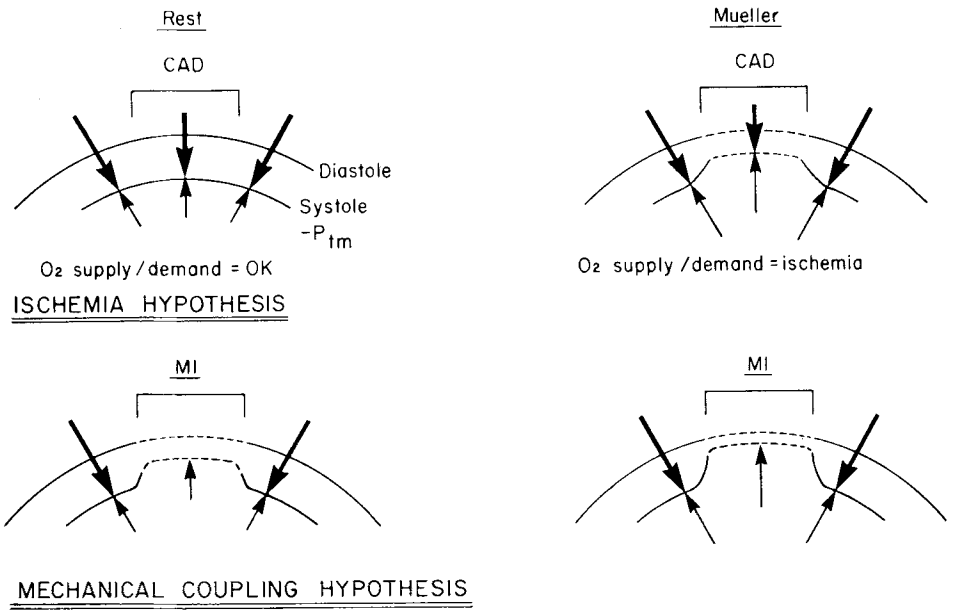

FIGURE 6. Two hypotheses to explain the appearance of regional wall akinesis during the performance of the Mueller maneuver in patients with CAD. During the performance of the Mueller maneuever, increased oxygen consumption of the myocardium engendered by increased wall tension cannot be met by increasing blood flow through an abnormal coronary artery. The resulting loss of contractile function leads to an imbalance of forces and the ventricle is unable to move during systole. Conversely, areas of nonfunctioning tissue appear to contract normally under resting conditions because they are mechanically linked to normally functioning surrounding myocardium. As transmural pressure increases during the Mueller maneuver the area of noncontracting tissue becomes apparent.

MATERIALS AND METHODS

We studied four groups of subjects before and during the performance of the Mueller maneuver. *Group 1*, the normal subjects, consisted of 13 male physicians, with no known cardiopulmonary disease. The records of 74 male patients admitted to our medical center for the evaluation of coronary artery bypass surgery were reviewed. All patients had angina pectoris and had undergone cardiac catheterization. Coronary anatomy was defined by standard contrast coronary angiography, and 60/74 patients also underwent LV wall motion evaluation by standard contrast ventriculograms in the 60° left anterior oblique (LAO) and 30° right anterior oblique (RAO) projections. The patients were grouped according to the history of prior myocardial infarctions (MI) as follows: *Group 2* (no MI): These patients had no history of MI and no residual ECG changes suggestive of prior MI (25 patients). *Group 3:* This group had a history of documented nontransmural MI, i.e. chest pain, cardiac enzyme increases but no evolution of *q* waves on ECG (13 patients). *Group 4* (prior transmural MI): These patients had a documented history of prior transmural myocardial infarction as judged by chest pain, cardiac enzyme rises and evolution of *q* waves on ECG and/or an area of marked hypokinesis on standard contrast ventriculography (36 patients).

First-Pass Radionuclide Ventriculography (RVG)

The details of performing first-pass RVG along with validation of our techniques have been published (21). Briefly, radionuclide ventriculography was performed in the 30° LAO position with the detector at a 30° caudad tilt. In these studies the subjects were almost supine (10° head up). A bolus of 20 Mci of 99 mTc labelled sodium pertechnetate was injected intravenously while at rest or 2–6 sec after the start of the Mueller maneuver. The passage of the radionuclide bolus through the heart and lungs was monitered by a multicrystal gamma scintillation cameral interfaced with a computer. Data were acquired at 40 frames/sec for 20–25-sec post injection. The LV phase of the study was identified by anatomic configuration and the temporal appearance of the radioactivity.

The transit of the bolus was replayed as a series of 1-sec analog images, each representing 40 summed 25-msec frames. The LV region of interest was flagged and marked with a light pen by an experienced observer. Time-activity curves of the LV region of interest were generated and corrected for background activity, and a representative cardiac cycle was derived from 4 to 6 beats. Global ejection fraction (EF) was determined after subtraction of the background counts as the summed end-diastolic minus end-systolic counts divided by the end-diastolic counts. Further computer processing yielded end-diastolic and end-systolic cavitary perimeters. We assume that the data represent cardiac cycles 10–15 sec into the performance of the Mueller maneuver. End-diastolic and end-systolic perimeters were evaluated for the presence of akinesis in three LV regions: septum, apex and lateral walls. Akinesis was defined as failure of the end-diastolic and end-systolic perimeters to separate. Left ventricular end-diastolic volume (EDV) was calculated by standard techniques (19) from the end-diastolic cavitary perimeter. Dimensions were calibrated based on the size of the pixels, assuming no magnification correction for the image as perceived by the detector and a prolate ellipsoid configuration for the LV. End-systolic volume (ESV) was calculated from EDV and EF. Heart rate was determined from the time-activity curve and cardiac output (CO) as calculated as (EDV − ESV) × (heart rate).

Mueller Maneuver

Following a study performed at rest, subjects performed a Mueller maneuver by performing inspiratory efforts from a closed mouthpiece attached to an anaeroid barometer which they could read. A target level was used which had previously been determined by trial and error as that level which they could sustain for 20–25 sec. A small leak allowed detection of the use of buccal muscles to generate the pressure. Since lung volume remained constant (ignoring the leak), pleural pressure decreased as much as mouth pressure. No attempt was made in these subjects to control for time of day, fluid or food intake, or medication use.

Other Assessment

Routine contrast angiography was assessed for the presence of significant CAD defined as a greater than 50% reduction in the vessel diameter. Exercise performance was assessed in 51 patients was standard treadmill exercise tolerance test by a Modified Bruce protocol. Although the patients were receiving a variety of anti-anginal and other cardiac medications, there were no significant differences among the three patient groups with regard to the frequence of a given class of medication.

Finally, since these subjects were studied in the supine position, whereas previous studies from our laboratory were performed in the upright position, we studied the effects of change in posture in five normal male volunteers. Subjects were studied on separate days in both the upright and supine posture, before and during the performance of the Mueller maneuver as described. These five subjects were instructed to abstain from oral intake for 2–3 h prior to the performance of the test.

Data were expressed as mean ±SEM. Statistical significance was assessed using Student's t test for unpaired variates with correction for multiple comparisons (Bonferroni's intervals) or Chi-square test.

RESULTS

Table 1 presents the basic hemodynamic data. Note that heart rate increased and LV EDV decreased in each of the subject groups. Ejection fraction decreased significantly in each of the patient groups, but not in the normals. There were no significant changes in ESV for any of the groups. During the Mueller maneuver cardiac output decreased in groups 3 and 4. There was no significant difference between any of the patient groups regards the location and severity of coronary artery disease (Table 2).

The major differences between the groups was in the appearance of akinetic LV wall segments during the Mueller maneuver. In groups 1, 2 and 3, no patient showed regional wall akinesis at rest. In group 2 one patient developed an area of akinesis during the Mueller maneuver. Among the group-4 patients, four had an akinetic wall segment at rest, while 17 others developed at least one akinetic segment during the Mueller maneuver. The difference between group 4 and the rest of the subject groups was significant ($p<0.001$, chi-square). Table 3 shows the location of the akinetic segments at rest and during the Mueller maneuver in the group-4 patients.

Of the 17 patients in group 4 who developed regional wall akinesis during the Mueller maneuver, 13 had undergone routine contrast left ventriculography. Among these 13 patients, there were a total of 18 akinetic segments noted on RVG during

TABLE 1. Hemodynamic changes.

Group	*N*	Ages	MM	HR_r	Hr_M	EF_r	EF_M	EDV_r	EDV_M	ESV_r	ESV_M	CO_r	CO_M
A	13	25–39	−42.3	61.3	71.9[b]	52.9	51.4	213.1	189.2[b]	100.0	94.6	5.9	±5.5
			±1.3	±3.3	±2.8	±1.7	±1.7	±8.2	±9.4	±3.7	±4.8	±0.6	±0.5
B	25	46–75	−32.0	58.6	64.8[c]	53.4	46.4[b]	209.2	193.8[a]	98.0	99.9	6.2	6.0
			±1.6	±3.2	±2.9	±1.1	±2.2	±8.4	±7.2	±4.6	±4.6	±0.5	±0.5
C	13	50–66	−33.6	64.5	67.0	49.2	40.8[b]	259.1	236.5[a]	135.2	142.9	7.4	6.3[a]
			±1.9	±3.8	±4.3	±2.5	±1.6	±14.9	±14.2	±11.4	±10.9	±0.6	±0.5
D	36	36–73	32.6	63.4	70.6[c]	38.8	34.9[b]	257.8	236.3[a]	155.7	160.3	6.5	5.9[a]
			±1.1	±2.2	±2.2	±1.9	±1.5	±10.6	±10.8	±10.7	±9.3	±0.3	±0.3

Shown is mean ± SEM.

MM = Strength of Mueller Maneuver (cm H_2O change in pleural pressure); HR = heart rate; EF = ejection fraction; EDV = end-diastolic volume; ESV = end-systolic volume; CO = cardiac output; Subscripts r and M are "rest" and "Mueller," respectively.

Significance is for Mueller compared with rest (Student's test for paired variates).

[a] $p < 0.05$; [b] $p < 0.01$; [c] $p < 0.001$.

Group 1 = normal volunteers, group 2 = coronary disease, no MI; group 3 = nontransmural MI; group 4 = transmural MI.

TABLE 2. Extent and location of coronary disease.

Group	1 vessel	2 vessel	3 vessel	LM	RCA	LAD	LCX
2	7 (28%)	9 (36%)	6 (24%)	3 (12%)	14 (56.6%)	18 (72%)	11 (44%)
3	4 (30.8%)	2 (15.3%)	6 (46.2%)	1 (7.7%)	8 (61.5%)	12 (92.3%)	8 (61.5%)
4	6 (16.7%)	15 (41.7%)	14 (38.9%)	4 (11.1%)	24 (16.7%)	29 (80.6%)	21 (58.3%)

LM = left main coronary artery; RCA = right coronary artery; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery.
Group numbers as in Table 1. Numbers in parenthesis represent the percent of each group.

TABLE 3. Akinetic segments, group 4 (transmural MIs).

Septum		Apex		Lateral-posterior wall		Total	
R	M	*R*	M	*R*	M	*R*	M
4 (11.1%)	11 (30.6%)	0	4 (11.1%)	0	11 (30.6%)	4 (11.1%)	21 (58.4%)

R = rest; M = Mueller.
Numbers represent the number of patients with an akinetic segment in the area indicated.
$p < 0.001$ for differences between groups 1, 2, 3 and 4 for frequency of akinetic segments (Chi-square test).

the Mueller maneuver. On routine contrast ventriculography none of these 18 akinetic segments showed marked wall motion abnormality, while the other nine were normal. Thus one-half of the akinetic segments found on RVG during the Mueller maneuver were not demonstrably abnormal by routine left ventricular contrast angiography.

Figures 7 and 8 demonstrate the effects of the Mueller maneuver on ventricular volumes in both supine and upright postures. In these normal subjects, there were no significant changes in heart rate.

DISCUSSION

These data demonstrate that regional LV wall akinesis developed almost exclusively during a Mueller maneuver in those patients with prior transmural myocardial infarction (group 4). Since this group was comparable to the other patient groups with regards to symptoms, the strength of the inspiratory effort, extent and severity of coronary artery disease, response to exercise tolerance test and medication, we conclude that the presence of prior myocardial infarction was necessary for the development of regional akinesis during the Mueller maneuver. Although all the patients suffered from ischemic coronary artery disease, this was not sufficient to lead to regional wall akinesis. In addition, no patient experienced angina during the performance of the Mueller maneuver. Accordingly, regional akinesis is probably related to the effects of increased LV transmural pressure on nonfunctioning myocardium, rather than the development of regional ischemia.

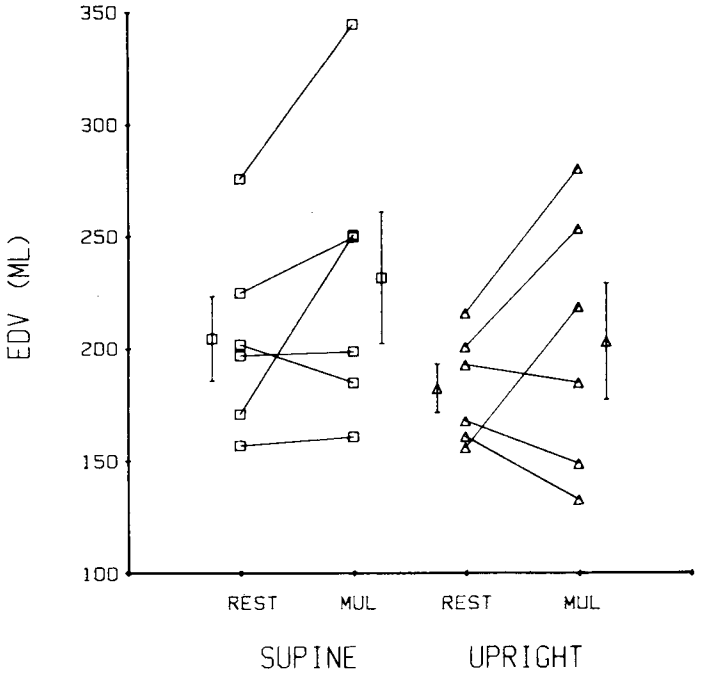

FIGURE 7. Effect of Mueller maneuver on EDV in supine and upright posture. None of the changes was statistically significant.

It was of interest that whether LV volume increased (21,22) or decreased (Table 1), akinesis could be observed. According to our hypothesis, the important factor is the transmural pressure and not the volume *per se*. As discussed above, transmural pressure increase whether LV afterload or RV-LV interdependence is the dominant mechanism at work.

These findings are of clinical importance since the Mueller maneuver increases the sensitivity for detection of CAD by radionuclide ventriculography. Indeed, one-half of all the akinetic segments detected during the Mueller maneuver by the RVG were undetected by standard contrast ventriculograms. We failed to detect the presence of prior myocardial infarction in 19 of the patients. It is possible that the areas involved by prior myocardial infarction were located on the anterior or posterior surfaces of the heart and were not visible in the LAO projection. Additional studies performed in the RAO projection could clarify this matter.

The decrease in LV volume during the Mueller maneuver illustrated in Table 1 is at variance with previous studies from this laboratory showing increases LV volumes during Mueller maneuvers (21,22), although they agree with findings of others (3,12). Although Buda *et al.* (5) found in increase in LV volume during Mueller maneuvers performed at an inspiratory effort of -60 cm H_2O, there was no change in LV volume at a lesser degree of inspiratory effort (-30 cm H_2O). As noted above, the net effect of the Mueller maneuver on LV volume will depend in part on the interaction between the forces of LV afterload and interventricular interdependence. These effects will be modulated, in turn, by changes in contractility and heart rate and the

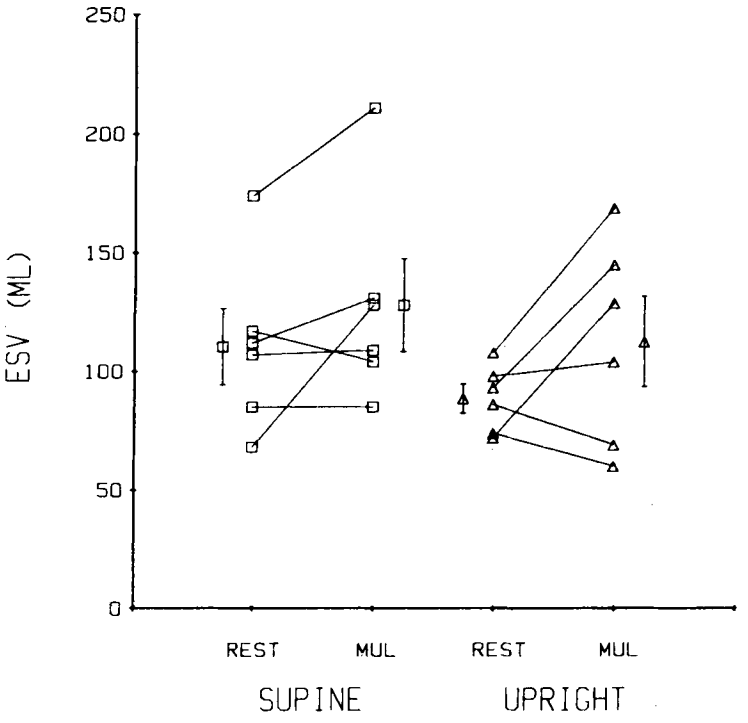

FIGURE 8. Effect of Mueller maneuver on ESV in supine and upright posture.

position of the LV on its diastolic pressure-volume curve. In supine subjects the heart is close to its maximum volume (10). Thus the extent to which an increase in afterload could lead to increases in LV volume would have been expected to be more limited than in upright subjects. However, as illustrated in Figs. 7 and 8, we were unable to demonstrate that LV volumes decreased in supine as opposed to upright subjects, and we cannot invoke this hypothesis to explain the difference in the LV volume response between the studies illustrated in Table 1 and our previous work.

In the studies illustrated in Table 1, heart rate tended to increase. This may, in part, account for the decrease in LV volume during the Mueller maneuver. An increase in heart rate leads to increased contractility. This would tend to decrease EDV and ESV. The fact that ESV does not decrease may reflect the effect of increased afterload. However, changes in heart rate were relatively small, and it is not clear if changes of this magnitude could have increased contractility enough to have decreased EDV against the increase in afterload. Further, in group 3, even though LV EDV did decrease significantly, heart rate did not.

We do not have a satisfactory explanation for the differences in the LV response to the Mueller maneuver between our present study, where LV volume decreased and previous studies where LV volume increased. It is possible that uncontrolled factors, for example, fluid status, medication use and room temperature, determine the response to the Mueller maneuver. The variable nature of the LV volume response suggests multifactorial effects which must be explored further.

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