JACC Vol. 6, No. 2
August 1985:290–5

Significance of the Pericardium in Human Subjects: Effects on Left Ventricular Volume, Pressure and Ejection

DENNIS T. MANGANO, MD, PhD, DONALD C. VAN DYKE, MD, ROBERT F. HICKEY, MD, ROBERT J. ELLIS, MD, FACC

San Francisco, California

To assess the effect of the pericardium, left ventricular systolic function and diastolic compliance were studied in 15 patients before and after pericardiotomy during coronary artery surgery. Using first pass radionuclide angiography, curves for left ventricular systolic function (stroke work versus end-diastolic volume) and a measure of diastolic compliance (pulmonary capillary wedge pressure versus end-diastolic volume) were generated by changing body position to alter venous return. Left ventricular end-diastolic volume ranged from 41 to 111 ml/m^2 and pulmonary capillary wedge pressure from 0 to 24 mm Hg.

No significant changes were found in blood pressure (150/83 to 148/82 mm Hg), heart rate (66.7 to 67.1 beats/min), cardiac index (2.38 to 2.41 liters/min per m^2), ejection fraction (0.56 to 0.54), end-systolic volume index (31.4 to 32.2 ml/m^2), end-diastolic volume index (65.9 to 69.5 ml/m^2) or pulmonary capillary wedge pressure (7.5 to 7.3 mm Hg). The pericardium did not affect the curves relating stroke work and end-diastolic volume or those relating pulmonary capillary wedge pressure and end-diastolic volume. Thus, when filling pressure and volume are normal or only moderately elevated, the pericardium does not appear to affect left ventricular systolic function or diastolic compliance in patients.

(J Am Coll Cardiol 1985;6:290–5)

Controversy exists regarding the effect of the pericardium on left ventricular systolic function and diastolic compliance. When the pericardium is left intact in animals, left ventricular diastolic pressure-volume and pressure-segment length relations can be altered by acute volume loading (1–8), infusion of nitroprusside (1) or obstruction of right and left ventricular outflow (9,10). However, when the pericardium is removed, diastolic compliance is not significantly affected by drug infusion or hemodynamic intervention (1–5,7–9,11). Therefore, in animals, the pericardium affects left ventricular function significantly when filling pressures are very high, but its effect on ventricular function when filling pressures are normal or moderately elevated is uncertain. In a recent study in dogs (12), the effect of the pericardium on the end-systolic pressure-segment length relation was assessed with and without acute volume overload. Pericardiotomy had an effect only with acute volume overload, that is, when the end-diastolic pressure was elevated from 8 to 19 mm Hg. Thus, the pericardium may have little effect when intraventricular pressures and volumes are normal.

In patients, the effect of the pericardium on ventricular function is difficult to measure. The effect on diastolic compliance is unknown; we have only indirect evidence suggesting a possible role (13–21). We earlier investigated (22) the effects of the pericardium on systolic function by studying patients undergoing pericardiotomy during coronary artery surgery. This appears to be the only direct method of measuring the effects of the pericardium in human beings. The pericardium had no effect on the relation between ventricular stroke work and filling pressures when the latter were normal or moderately elevated. However, the effects of the pericardium on diastolic compliance or on the more sensitive measures of systolic function (ejection fraction, end-systolic volume and stroke work versus end-diastolic volume curves) in human beings were not studied.

This study addresses these questions. Using radionuclide angiography to measure ejection fraction, we generated curves for a measure of left ventricular diastolic compliance (pulmonary capillary wedge pressure versus end-diastolic volume) and systolic function (stroke work versus end-diastolic volume) before and after pericardiotomy in 15 patients.

From the Departments of Anesthesia, Nuclear Medicine and Surgery, University of California, San Francisco and the Veterans Administration Medical Center, San Francisco, California. This study was supported in part by the Medical Research Service of the Veterans Administration, San Francisco. Manuscript received January 23, 1985; revised manuscript received March 12, 1985, accepted March 29, 1985.

Address for reprints: Dennis T. Mangano, MD, Department of Anesthesia (129), Veterans Administration Medical Center, Room 3C-14, Building 203, 4150 Clement Street, San Francisco, California 94121.

0735-1097/85/$3.30

Methods

Patients. This study was approved by the Committee on Human Research of the University of California, San Francisco; informed consent was obtained from all patients. We studied 15 men, 39 to 64 years of age, who were admitted for coronary artery surgery. Thirteen patients had had one or more myocardial infarction before admission. No patient had valvular disease, a history of heart failure or evidence of ventricular hypertrophy or dilation. Cardiac catheterization revealed 90% stenosis of luminal diameter of two or more coronary arteries, left ventricular ejection fraction from 0.39 to 0.82 (normal = 0.66 ± 0.06), end-diastolic volume index from 44 to 107 ml/m^2 (normal = 70 ± 20), pulmonary capillary wedge pressure from 1 to 14 mm Hg and central venous pressure from 0 to 9 mm Hg. All patients received isosorbide dinitrate and nitroglycerin, and 13 received propranolol (40 to 160 mg orally four times a day). Medications were continued until surgery.

Selection of anesthetic agents and hemodynamic monitoring. All patients were premedicated with morphine sulfate (10 mg intramuscularly) and diazepam (10 mg orally). Anesthesia consisted of morphine sulfate (1.5 to 3 mg/kg intravenously) and diazepam (0.25 to 0.50 mg/kg intravenously). Pancuronium (0.1 mg/kg intravenously) provided muscle relaxation, and ventilation (with 100% oxygen) was controlled. Hemodynamic variables were monitored using radial artery and triple lumen thermodilution pulmonary artery catheters. All pressure measurements were recorded on a Gilson polygraph from equisensitive Bell and Howell transducers calibrated with a mercury manometer. Before each set of measurements was made, the zero reference point was located 5 cm posterior to the sternal angle in a direction perpendicular to the frontal plane of the chest.

Radionuclide angiography. Ejection fraction was measured from radiocardiograms obtained with a coaxial cardiac scintillation probe (23,24). The radiocardiogram is a recording of the amount of radionuclide, carried by the blood, in the chambers of the heart as a function of time and is generated from the first pass of the bolus through the central circulation (25,26).

We positioned the probe over the left ventricle to record the passage of 1.5 mCi of technetium-99m-sodium pertechnetate, which was injected into the right atrial orifice of the thermodilution catheter. The probe consists of a central collimated detector that accepts gamma photons primarily from the left ventricle and an anular detector collimated to monitor background activity around the left ventricle (23–26). High frequency recording of the count rate from within the left ventricle, when corrected for counts from surrounding structures, provides an accurate measure of left ventricular ejection fraction (26–28).

The radionuclide was flushed through the catheter with the cold solution so that thermodilution cardiac output and radiocardiogram were recorded simultaneously for all measurements. In addition, we did not change the position of the probe throughout the measurement periods. All measurements were made at end-expiration.

End-diastolic volume calculations. Given stroke volume from the thermodilution measurements (cardiac output divided by heart rate) and ejection fraction from the radiocardiograms, end-diastolic volume (that is, stroke volume divided by ejection fraction) can be calculated. Because this calculation is not accurate if valvular regurgitation occurs, no patient with valvular incompetence was studied. In patients with coronary artery disease in whom valvular regurgitation did not occur, the correlation of end-diastolic volume, as determined from cineangiographic measures, versus that determined by radioisotope measures, is 0.88 (27).

Measurements before and after pericardiotomy. After median sternotomy, the pericardium was exposed. The pericardium remained fully intact, and its mediastinal tethering was not disturbed. Immediately before pericardiotomy, the sternum was temporarily reapproximated, surgery was stopped and the probe was placed over the left ventricle. A 2 minute period of hemodynamic stability was established (systolic blood pressure varying <10 mm Hg and heart rate <5 beats/min). With the patient in the supine position (control), we recorded these variables at end-expiration: radial arterial systolic and diastolic pressures, heart rate, pulmonary artery systolic and diastolic pressures, central venous pressure, pulmonary capillary wedge pressure, radionuclide ejection fraction and two thermodilution measurements of cardiac output (within 10%). Next, the legs were elevated 45° relative to the chest. After another 2 minute period of stability, the previous measurements were recorded at end-expiration. The legs were elevated to 90° and the measurements were repeated. The legs were then lowered to the initial position (0°) and, after 2 minutes of stability, measurements were repeated.

The anterior pericardium was then incised from apex to base and sutured laterally to expose the heart fully. The sternum was temporarily reapproximated, surgery was stopped, the probe was positioned and hemodynamic stability was established. Recordings were made in the 0, 45, 90 and 0° leg positions, as previously described. No drug or intravenous volume transfusion was given, and no respiratory adjustment was made for 15 minutes before or during the measurement period.

Results

Control values before and after pericardiotomy (Table 1). Data for hemodynamic variables and curves for diastolic compliance (pulmonary capillary wedge pressure versus end-diastolic volume) and systolic function (stroke work versus end-diastolic volume) were generated before

JACC Vol. 6, No. 2
August 1985:290–5

Table 1. Control Hemodynamic Variables Before and After Pericardiotomy

	Before Pericardiotomy*	After Pericardiotomy*	Average Difference†
Heart rate (beats/min)	66.7 ± 2.1	67.1 ± 1.9	2.4 ± 0.6
Systemic blood pressure (mm Hg)			
Systolic	149.9 ± 4.6	147.6 ± 4.5	3.1 ± 0.4
Diastolic	83.1 ± 2.2	81.7 ± 2.3	2.1 ± 0.3
Systemic vascular resistance (dynes·s·cm^{-5})	1,898 ± 96	1,784 ± 123	121 ± 14
Cardiac index (liters/min per m^2)	2.38 ± 0.12	2.41 ± 0.11	0.31 ± 0.11
Stroke volume index (ml/m^2)	36.4 ± 1.7	37.2 ± 1.8	2.1 ± 0.7
Left ventricular stroke work index (g·m/m^2)	48.28 ± 2.90	49.10 ± 2.72	3.06 ± 0.92
Left ventricular end-systolic volume index (ml/m^2)	31.4 ± 3.3	32.2 ± 3.5	1.4 ± 0.04
Left ventricular end-diastolic volume index (ml/m^2)	65.9 ± 4.6	69.5 ± 5.4	5.2 ± 1.2
Pulmonary capillary wedge pressure (mm Hg)	7.5 ± 1.3	7.3 ± 1.5	0.4 ± 0.17

*Values averaged for 15 patients. †For each patient the difference between the values before and after pericardiotomy was calculated. Average difference is the mean value (for 15 patients) of the individual differences. All values are mean ± SEM.

and after pericardiotomy and were compared for each patient. Using paired sample *t* tests, we found no significant difference between the control values before and after pericardiotomy for the following hemodynamic variables: heart rate ($p > 0.10$), systemic vascular resistance ($p > 0.05$), cardiac index ($p > 0.10$), stroke work ($p > 0.05$), ejection fraction ($p > 0.10$), end-systolic volume ($p > 0.05$), ventricular end-diastolic volume ($p > 0.05$) and pulmonary capillary wedge pressure ($p > 0.10$).

Compliance and systolic function curves before and after pericardiotomy (Fig. 1 and 2). The diastolic compliance curves and systolic function curves before and after pericardiotomy for five randomly selected patients are shown in Figures 1 and 2. For each patient, four data points were obtained before and after pericardiotomy. The four points were derived from the measurements made in the 0 (control), 45, 90 and 0° (control) leg positions. Only the first three of these four points are shown in the figures. Pericardiotomy did not significantly change stroke work ($p > 0.10$), end-diastolic volume ($p > 0.05$) or pulmonary capillary wedge pressure ($p > 0.10$) at any of the four leg positions. When

Figure 1. Left ventricular compliance curves before and after pericardiotomy for five patients. LVEDVI = left ventricular end-diastolic volume index; PCWP = pulmonary capillary wedge pressure. Numbers in parentheses indicate case number.

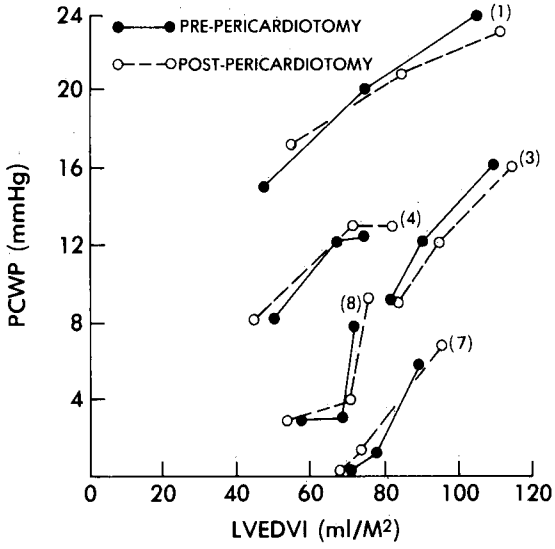
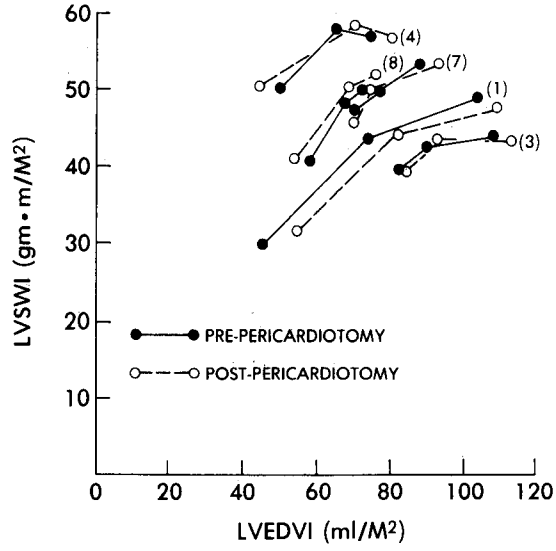


Figure 2. Left ventricular systolic function curves before and after pericardiotomy in the same five patients as in Figure 1. LVEDVI = left ventricular end-diastolic volume index; LVSWI = left ventricular stroke work index.



data for all patients were combined, analysis of variance revealed no difference in the slope ($p > 0.01$) or intercept ($p > 0.05$) of the regression of pulmonary capillary wedge pressure on end-diastolic volume and of stroke work on end-diastolic volume before and after pericardiotomy. Finally, there was no significant difference ($p > 0.05$) between the initial 0° and final 0° measurements for all of the previous variables.

These results were found when filling pressures and volumes were normal or moderately elevated (pulmonary capillary wedge pressure <24 mm Hg and end-diastolic volume <111 ml/m^2).

Discussion

In patients with normal or moderately elevated left ventricular filling pressure and volume, the pericardium does not appear to affect left ventricular function. Neither systolic function (as assessed by function curves, ejection fraction and end-systolic volume) nor diastolic compliance (as assessed by the relation between pulmonary capillary wedge pressure and end-diastolic volume) was affected by pericardiotomy.

General comments and study limitations. In this study, diastolic compliance was assessed using the relation between pulmonary capillary wedge pressure and end-diastolic volume. This relation does not truly reflect ventricular elastance (or compliance), because pulmonary capillary wedge pressure may underestimate the left ventricular end-diastolic pressure as a result of the contribution of left atrial systole (29). Our results do demonstrate, however, that over a range of similar end-diastolic volumes the pulmonary capillary wedge pressures are unchanged with pericardiotomy.

In addition to left atrial systole, other factors, such as changes in preload (1–8,14), afterload (9,10,13,14) and heart rate (18,30), can affect the relation between pulmonary capillary wedge pressure and end-diastolic volume (21). In our study, we found no statistically significant difference between our control values before and after pericardiotomy for our measures of preload (pulmonary capillary wedge pressure and end-diastolic volume), afterload (systemic vascular resistance and blood pressure) or heart rate. This was not surprising; during the measurements, no drug or volume transfusion was made, surgical stimulation was absent, the anesthetic agent was unchanged and all measurements were made at end-expiration. Thus, comparison of the curves before and after pericardiotomy reflects the direct effects of the pericardium and not the indirect effects of these other factors. Finally, the possible differences between the results of this study and those for intact unanesthetized human beings have been minimized. The anesthetic agent used, morphine sulfate with oxygen, does not depress ventricular contractility at the doses used in this study (31). In addition, all measurements were made at end-expiration, at which time the difference between pleural pressures (open versus closed chest) is minimal.

Diastolic compliance studies in animals. In dogs, the pericardium exerts little measurable effect when filling pressures are normal (that is, <10 mm Hg) (1–8,11,13). Hefner et al. (3) demonstrated that the pericardium increased the slope of the left ventricular end-diastolic pressure-circumference relation only when the pressure was greater than 10 mm Hg. Shirato et al. (1) found that the pericardium exerted little restrictive influence on the left ventricle when diastolic pressure ranged from 5 to 10 mm Hg. When the pericardium was intact, volume loading to pressures of 25 to 30 mm Hg displaced the diastolic pressure-segment length curve upward and nitroprusside displaced it downward. After pericardiotomy, control values and data for volume loading and nitroprusside infusion fell on the same curve. Holt et al. (2) also found that the pericardium significantly influenced transmural ventricular diastolic pressure in dogs only when end-diastolic pressure was greater than 10 mm Hg. Spotnitz and Kaiser (5), studying the pressure-volume relation in the excised canine heart, noted that the elastic limits of the pericardium appeared not to be reached when diastolic pressures were normal or moderately elevated (0 to 20 cm H_2O). Glantz et al. (7) found that the coupling relation between right and left ventricular diastolic pressures was tighter when the pericardium was closed, particularly at high end-diastolic pressures. Mirsky and Rankin (8) found that shifts in intraventricular pressure-volume relations in dogs were due to changes in pericardial pressure. However, transmural pressure-volume relations were not markedly altered by action of the pericardium, implying that no alteration in the intrinsic ventricular compliance occurred with pericardiotomy.

Diastolic compliance studies in human subjects. Several studies have examined the effects of hemodynamic and pharmacologic interventions on the pressure-volume relation in the presence of an intact pericardium (13–20). Although these studies suggest several possible effects of the pericardium, none of the studies assessed these effects directly. In our previous study in patients, we found that the relation between pulmonary capillary wedge pressure and central venous pressure was unaffected by the pericardium when central venous pressure (0 to 14 mm Hg) and pulmonary capillary wedge pressure (1 to 25 mm Hg) were normal or moderately elevated (22). Our study not only extends many of the results on diastolic compliance in dogs to human beings, but also extends our previous results. Using the relation between pulmonary capillary wedge pressure and end-diastolic volume, we found that the effects of the pericardium were minimal when filling pressures (0 to 24 mm Hg) and volumes (41 to 111 ml/m^2) were normal to moderately elevated. Over this range, the ventricular muscle itself, and not the stiffer pericardium, appears to be the major determinant of the relation between pulmonary capillary wedge pressure and end-diastolic volume.

Systolic function studies in animals. Berglund et al. (9) found in dogs that when the left ventricle was differentially stressed by increasing outflow resistance, expansion of the right ventricle was limited by the pericardium, resulting in decreased right ventricular stroke work, particularly at high filling pressures. Similarly, Moulopoulos et al. (11) found that when the pericardium was open, distension of the right ventricle impaired left ventricular function only when right ventricular end-diastolic pressure was high. Kenner and Wood (10) produced acute right and left ventricular obstruction by inflating a balloon in the pulmonary artery and aorta. Despite marked elevation of ventricular pressures, intrapericardial pressures did not increase significantly.

Most recently, Kanazawa et al. (12) found that the pericardium exerted an effect on the end-systolic pressure-segment length relation only when the end-diastolic pressure was acutely elevated (8 to 19 mm Hg) by blood transfusion. At normal end-diastolic pressures (8 mm Hg), the pericardium had no significant effect on this relation or on left ventricular segment length, stroke volume or end-diastolic pressure. These results support the hypothesis that the pericardium has little effect when filling pressures are normal.

Systolic function studies in human subjects. The effects of the pericardium have been studied indirectly by Bartle and Hermann (20) using ventricular pressure contours obtained 5 days after the appearance of acute mitral regurgitation. These contours resembled those occurring in constrictive pericarditis. Wayne et al. (32) and Spodick et al. (33) studied the respiratory effects on ventricular function in patients with pericardial effusion without tamponade. They found inspiratory reductions in echocardiographic diastolic diameter together with exaggerated respiratory changes in systolic time intervals. Thus, the pericardium appears to have an effect in patients with effusion or tamponade. However, the data for normal patients are scarce. In our previous study in patients, we examined the effect of pericardiotomy on left and right ventricular function curves (left ventricular stroke work versus pulmonary capillary wedge pressure and right ventricular stroke work versus central venous pressure) (22). When patients had normal or moderately elevated filling pressures, the pericardium did not alter these curves. Our present study extends these results by considering the more descriptive function curves relating stroke work to end-diastolic volume instead of pulmonary capillary wedge pressure. Because pulmonary capillary wedge pressure may not be a reliable and reproducible estimate of end-diastolic volume in these patients (34), as demonstrated in Figure 1, function curves having end-diastolic volume as the independent variable may be more informative. In addition to this measure of systolic function, the present study also examined changes in ejection fraction and end-systolic volume. Our results are consistent and extend those of our prior study, in that the pericardium did not have a significant effect on systolic function curves (stroke work versus end-diastolic volume), ejection fraction or end-systolic volume at any body position studied (0, 45, 90 or 0°). Furthermore, these results applied to both filling pressures (pulmonary capillary wedge pressure) and volumes (end-diastolic volume) that were normal and moderately elevated.

Conclusion. Thus, our studies in human subjects have provided results that continue to support the hypothesis that the pericardium does not have a significant effect on left ventricular systolic function or diastolic compliance in patients having normal to moderately elevated filling pressures and volumes.

We express our appreciation to Kanu Chatterjee, MB, FRCP, John Tyberg, MD and David Bristow, MD for their helpful suggestions throughout this study. In addition, we thank Pat Chu and John Morrison for their technical assistance.

References

1. Shirato K, Shabetai R, Bhargava V, Franklin D, Ross J Jr. Alteration of the left ventricular diastolic pressure-segment length relation produced by the pericardium: effects of cardiac distension and afterload reduction in conscious dogs. Circulation 1978;57:1191–8.
2. Holt JP, Rhode EA, Kines H. Pericardial and ventricular pressure. Circ Res 1960;8:1171–81.
3. Hefner LL, Coghlan HC, Jones WB, Reeves TJ. Distensibility of the dog left ventricle. Am J Physiol 1961;201:97–101.
4. Bartle SH, Herman HJ, Cavo JW, Moore RA, Costenbader JM. Effect of the pericardium on left ventricular volume and function in acute hypervolemia. Cardiovasc Res 1968;2:284–9.
5. Spotnitz HM, Kaiser GA. The effect of the pericardium on pressure-volume relations in the canine left ventricle. J Surg Res 1971;11:375–80.
6. Bemis CE, Serur JR, Borkenhagen D, Sonnenblick EH, Urschel CW. Influence of right ventricular filling pressure on left ventricular pressure and dimension. Circ Res 1974;34:498–504.
7. Glantz SA, Misbach GA, Moores WY, et al. The pericardium substantially affects the left ventricular diastolic pressure-volume relationship in the dog. Circ Res 1978;42:433–41.
8. Mirsky I, Rankin JS. The effects of geometry, elasticity, and external pressures on the diastolic pressure-volume and stiffness-stress relations. Circ Res 1979;44:601–11.
9. Berglund E, Sarnoff SJ, Isaacs JP. Ventricular function: role of the pericardium in regulation of cardiovascular hemodynamics. Circ Res 1955;3:133–9.
10. Kenner HM, Wood EH. Intrapericardial, intrapleural, and intracardiac pressures during acute heart failure in dogs studies without thoracotomy. Circ Res 1966;19:1071–9.
11. Moulopoulos SD, Sarcas A, Stamatelopoulos S, Arealis E. Left ventricular performance during bypass or distension of the right ventricle. Circ Res 1965;17:484–91.
12. Kanazawa M, Shirato K, Ishikawa K, Nakajima T, Haneda T, Takishima T. The effect of pericardium on the end-systolic pressure-segment length relationship in canine left ventricle in acute volume overload. Circulation 1983;68:1290–8.
13. Alderman EL, Glantz SA. Acute hemodynamic interventions shift the diastolic pressure-volume curve in man. Circulation 1976;54:662–71.
14. Brodie BR, Grossman W, Mann T, McLaurin L. Effects of sodium nitroprusside on left ventricular diastolic pressure-volume relations. J Clin Invest 1977;59:59–68.
15. Ludbrook PA, Byrne JD, Kurnik PB, McKnight RC. Influence of reduction of preload and afterload by nitroglycerin on left ventricular

diastolic pressure-volume relations and relaxation in man. Circulation 1977;56:937–43.

16. Ludbrook PA, Byrne JD, McKnight RC. Influence of right ventricular hemodynamics on left ventricular diastolic pressure-volume relations in man. Circulation 1979;59:21–31.
17. Barry WH, Brooker JZ, Alderman EL, Harrison DC. Changes in diastolic stiffness and tone of the left ventricle during angina pectoris. Circulation 1974;49:255–63.
18. Mann T, Brodie BR, Grossman W, McLaurin LP. Effect of angina on the left ventricular diastolic pressure-volume relationship. Circulation 1976;55:761–6.
19. Mann T, Goldberg S, Mudge GH Jr, Grossman W. Factors contributing to altered left ventricular diastolic properties during angina pectoris. Circulation 1979;59:14–20.
20. Bartle SH, Hermann HJ. Acute mitral regurgitation in man: hemodynamic evidence and observations indicating an early role for the pericardium. Circulation 1967;36:839–51.
21. Ross J Jr. Acute displacement of the diastolic pressure-volume curve of the left ventricle: role of the pericardium and the right ventricle (editorial). Circulation 1979;59:32–7.
22. Mangano DT. The effect of the pericardium on ventricular systolic function in man. Circulation 1980;61:352–7.
23. Mangano DT, Van Dyke DC, Ellis RJ. The effect of increasing preload on ventricular output and ejection in man: limitations of the Frank-Starling mechanism. Circulation 1980;62:535–41.
24. Wexler JP, Blaufox MD. Radionuclide evaluation of left ventricular function with nonimaging probes. Semin Nucl Med 1979;9:310–9.
25. Van Dyke D, Anger HO, Sullivan RW, Vetter WR, Yano Y, Parker HG. Cardiac evaluation from radioisotopic dynamics. J Nucl Med 1972;13:585–92.
26. Steel PP, Van Dyke D, Trow RS, Anger HO, Davies H. Simple and safe bedside method for serial measurement of left ventricular ejection fraction, cardiac output, and pulmonary blood volume. Br Heart J 1974;36:122–31.
27. Berndt T, Alderman EL, Wasnich R, Hsieh SC, Van Dyke D, Harrison DC. Evaluation of portable radionuclide method for measurement of left ventricular ejection fraction and cardiac output. J Nucl Med 1975;16:289–92.
28. Parker H, Weber P, Van Dyke D, Davies H, Steele P, Sullivan R. Evaluation of central circulatory dynamics with the radionuclide angiocardiogram. In: Strauss HW, Pitt B, James AE Jr, eds. Cardiovascular Nuclear Medicine. St. Louis: CV Mosby, 1974:67–100.
29. Rahimtoola SH, Loeb HS, Ehsani A, et al. Relationship of pulmonary artery to left ventricular diastolic pressures in acute myocardial infarction. Circulation 1972;46:283–90.
30. Mitchell JH, Linden RJ, Sarnoff SJ. Influence of cardiac sympathetic and vagal nerve stimulation on the relation between left ventricular diastolic pressure and myocardial segment length. Circ Res 1960;8:1100–7.
31. Lowenstein E, Hallowell P, Levine FH, Daggett WM, Austen WG, Laver MB. Cardiovascular response to large doses of intravenous morphine in man. N Engl J Med 1969;281:1389–93.
32. Wayne VS, Bishop RL, Spodick DH. Dynamic effects of pericardial effusion without tamponade. Respiratory response in the absence of pulsus paradoxus. Br Heart J 1984;51:202–4.
33. Spodick DH, Paladino D, Flessas AP. Respiratory effects on systolic time intervals during pericardial effusion. Am J Cardiol 1983;51:1033–5.
34. Ellis RJ, Mangano DT, Van Dyke DC. Relationship of wedge pressure to end-diastolic volume in patients undergoing myocardial revascularization. J Thorac Cardiovasc Surg 1979;78:605–13.