Effect of Ventricular Extrasystoles on Closure of Mitral Valve

By Russell A. VandenBerg, M.B., John C. P. Williams, M.B., Ralph E. Sturm, and Earl H. Wood, M.D., Ph.D.

SUMMARY

Mitral valve function was assessed by roentgen videodensitometry. Mitral reflux was rare when single ventricular ectopic systoles were produced by electronic stimulation of the right or left ventricle at various times in the cardiac cycle. It was also rare during the compensatory pause after the ectopic systole or with the following postectopic systole. Recurrent ventricular ectopic systoles interposed once per cycle were associated with minor reflux when introduced in mid-cycle. Such extrasystoles occurred late enough in the cardiac cycle for the ventricle to relax after the primary systole and for the mitral valve to open before the extrasystole. The extrasystolic contractions were, however, weak and incapable of opening the aortic valve. When interposed early in the cardiac cycle, extrasystolic potentiation of the primary ventricular contraction occurred, and no or minimal mitral reflux was observed.

Additional Indexing Words:
Cardiac function
Angiocardiography
Mitral regurgitation
Videodensitometry
Extrasystolic potentiation

It is thought that ventricular extrasystoles occurring during angiocardiography are associated with mitral regurgitation because they are not preceded by, and the mitral valve is not preclosed by, an effective, normally sequenced atrial contraction.\textsuperscript{1-3} However, in previous studies from this laboratory in which isolated ventricular systoles have been produced by driving the atria and ventricles simultaneously or by inducing atrial fibrillation while driving the ventricles at a constant rate, the amount of mitral reflux observed has frequently been no different from the amount seen with normally sequenced atrial and ventricular driving.\textsuperscript{4,5} When reflux has been observed with isolated ventricular systoles, it has been possible to relate the amount of reflux to variations in ventricular function.\textsuperscript{6} Thus, it has seemed probable that any reflux accompanying ventricular extrasystoles might be related to variations in ventricular function in addition to lack of preclosure of the valve. However, spontaneous ventricular extrasystoles differ from the previously studied isolated ventricular systoles in one important respect—they occur irregularly, while the latter occurred regularly. In the present study the effect on mitral valve function of ventricular extrasystoles introduced at various times in the cardiac cycle so that no preceding atrial contraction occurred was studied by means of the videodensitometer previously described by Wood and co-workers.\textsuperscript{7}

From the Section of Physiology and Biophysics, Mayo Clinic and Mayo Foundation, and Mayo Graduate School of Medicine (University of Minnesota), Rochester, Minnesota. Dr. Wood is a Career Investigator, American Heart Association; Dr. VandenBerg is a Fellow of the Minnesota Heart Association and the National Heart Foundation of Australia.

This investigation was supported in part by Research Grants HE-3532 and HE-4664 from the National Institutes of Health, U. S. Public Health Service, NaG-327 from the National Aeronautical and Space Administration, and CI 10 from the American Heart Association.
Methods

The methods used have been described in detail previously.4.6 Twelve dogs anesthetized with morphine (5 mg/kg) and pentobarbital (15 mg/kg) and prepared in most cases with acute heart block, stellate ganglionectomy, and cervical vagotomy were studied without thoracotomy. Atrial and ventricular contractions were controlled electronically, and stimuli to electrode catheters in the right atrium and ventricle could be dropped or added as desired. Left ventricular angiograms made after injections of a contrast medium (0.2 to 0.3 ml/kg of an aqueous solution providing 69% diatrizoate salts [Renovist]) into the body of the ventricular cavity via a 5-F Rodriguez spray-tipped catheter were recorded on videotape. The duration of injections was approximately 1 sec. The dogs were positioned in half-body molded Lucite casts so that the plane of the mitral valve ring was parallel to the x-ray beam, and the left atrial and left ventricular videotdensograms could be recorded from sites immediately upstream and downstream to the mitral valve on replay of the left ventricular angiograms.

Isolated ventricular systoles were introduced at various times in the cardiac cycle by stimulating the right ventricle of six dogs and the left ventricle of three dogs. The next one or two normally sequenced atrial and ventricular contractions sometimes were included and sometimes excluded; stimulation of the free ends of the distal segments of the cut cervical vags was used to inhibit spontaneous atrial contractions when driving was stopped for one or more beats. The effects of regularly recurrent right ventricular

![Figure 1](image)

Figure 1

Competent mitral valve closure with isolated extrasystoles introduced into right ventricle of a 28.5-kg dog (prepared with morphine-pentobarbital anesthesia, heart block, and vagotomy) 210, 310, and 445 msec after previous normally sequenced atrial and ventricular contractions and with two normal beats after each extrasystole excluded. Spontaneous escape of atrial beats during cessation of normally sequenced atrial and ventricular driving was prevented by vagal stimulation. Bottom tracing, which records position of piston of syringe containing Renovist, along with electrocardiogram, shows timing of 4.5-ml injections of solution (containing 69% diatrizoate salts) into left ventricle for each angiogram. Left ventricular and left atrial densograms (upper and middle tracings) represent voltage output of videodensitometer, which is logarithmically related to change in Renovist content under sampling window of videodensitometer, when it is positioned over these two cardiac chambers, respectively, during successive replays of each videotaped angiogram. Control variations in densographic recordings produced by change in depth and position of cardiac chambers associated with extrasystole and subsequent long diastolic pauses are shown at right of each panel. Note close similarity between control changes of left atrial density and changes when high concentrations of Renovist were present in left ventricle, indicating that the mitral valve was competent throughout these disturbances in cardiac rhythm.
VENTRICULAR EXTRASYSTOLES

CONTROL           MULTIPLE EXTRASYSTOLES

Figure 2
Minor mitral regurgitation during multiple ventricular extrasystoles occurring by chance with injection of 4 ml of Renovist into left ventricle of 16-kg dog prepared with vagotomy. Note lack of deflection in left atrial videodensogram in control observation (left panel) while driving with heart rate of 135 beats/min and an A-V stimulus interval of 80 msec and the small deflection during multiple extrasystoles with similar driving (right panel).

Figure 3
Variation of mitral regurgitation with timing of recurrent extrasystoles (17-kg dog with stellate ganglionectomy, vagotomy, and acute heart block). Heart rate 100 beats/min; interval between atrial and ventricular stimuli 100 msec. Calibrations of videodensitometer curves in roentgen density units, which are linearly related to change in content of contrast medium under sampling window, are shown on left. A, V, and V' refer to artifacts in electrocardiogram produced by atrial, primary ventricular, and extrasystolic ventricular stimuli, respectively. With recurrent mid-cycle extrasystoles (middle panel), V' stimulus was timed to occur after 52% of V-V interval had elapsed. In this situation regurgitant index increased to 8% as compared to control level of 2% during normally sequenced atrial and ventricular driving (left panel). Systolic and end-diastolic pressures for normal, non-extrasystolic beats during this mode of driving were similar to control levels, while systolic pressure was lower and end-diastolic pressure higher for each extrasystolic beat. With recurrent early extrasystoles (V-V' interval 36% of V-V interval, right panel) no discrete extrasystolic-pressure wave was discernible despite occurrence of two electrical depolarizations. Primary ventricular systoles were potentiated as evidenced by increase in systolic pressure and decrease in end-diastolic pressure. Regurgitant index decreased to 2%.
extrasystoles were studied in six dogs. The extrasystole was interposed in each cycle at a constant time interval after the R wave. This time interval—that is, the temporal relationship of the extrasystole to other events in the cardiac cycle—could be varied at will.

Intracardiac and vascular pressures were measured from tracings on photokymographic records (150 mm/sec) made immediately before each injection of the contrast medium. The maximal rate of change of left ventricular pressure (dp/dt) was measured with a Philbrick linear differentiator. The areas of videodensograms were computed as described previously, and the area of the left atrial videodensogram, expressed as a percentage of the left ventricular area, was used as an index of mitral regurgitation.

The method of calibration, sensitivity, and analysis of videodensograms has been described previously.

Results

Competent mitral valve closure was found in four of the six dogs in which isolated right ventricular extrasystoles were introduced (fig. 1) and in two of the three dogs in which isolated left ventricular extrasystoles were introduced. This occurred independently of the timing of the extrasystoles and whether the next one or two normally sequenced atrial and ventricular contractions were included or excluded. Some mitral regurgitation was detected in two dogs with isolated right ventricular extrasystoles and in one with left ventricular extrasystoles; it was of minor degree and usually occurred at the time of onset of the extrasystole and not with the postectopic systole, even when one or more

Figure 4

Comparison of mitral regurgitation during early and mid-cycle recurrent ventricular extrasystoles in 18-kg dog with stellate ganglionectomy, vagotomy, and acute heart block. V-V', stimulus interval for mid-cycle extrasystoles, was 49% of V-V interval, and that for early cycle extrasystoles 36% of V-V interval. Videodensograms, upper panels, were recorded at slower paper speed than ventricular pressure records shown below. Note moderate amount of mitral regurgitation in control observation with heart rate of 100 beats/min and A-V stimulus interval of 100 msec, striking increase in mitral regurgitation with recurrent mid-cycle extrasystoles, and equally striking decrease below control levels with recurrent early extrasystoles. Note also striking increase in left ventricular systolic pressures and decrease in end-diastolic pressures associated with extrasystolic potentiation of ventricular contraction produced by recurrent early extrasystoles.

Circulation, Volume XXXIX, February 1969
ventricular beats were dropped after the ectopic beat. When multiple extrasystoles occurred by chance during an injection of contrast medium into the left ventricle, mitral regurgitation was often undetectable or minor (fig. 2). However, occasionally it was definite and obvious.

Such observations prompted study of the effect on mitral valve function of recurrent ventricular extrasystoles interposed once per cycle in the hope that mitral regurgitation might be exaggerated and analysis thereby facilitated. Mitral regurgitation increased when recurrent right ventricular extrasystoles were interposed in the middle of the cardiac cycle and decreased when they were interposed early in the cycle (figs. 3 and 4). These changes were more evident when the degree of mitral regurgitation was significant rather than minimal during control observations—that is, when the recurrent extrasystoles were omitted (figs. 3 and 4). Left atrial videodensograms recorded at high speed and sensitivity showed that regurgitation, noted when extrasystoles were interposed in the middle of the cardiac cycle, were related to the onset of ectopic systole rather than to the normally sequenced atrial and ventricular contractions (fig. 5). The changes in mitral regurgitant indexes and hemodynamic variables in six dogs with regularly recurrent early and mid-cycle extrasystoles are summarized in table 1.

From the left ventricular pressure tracings in figure 4 and the data in table 1, it is evident that recurrent extrasystoles were interposed so early in the cycle that a discrete second ventricular contraction usually did not occur despite a second ventricular depolarization. The second depolarization resulted in extrasystolic potentiation of the primary ventricular contractions. The weak extrasystolic mechanical event occurred during the relaxation phase of the primary systole so that it is unlikely that the mitral valve opened prior to the ectopic systole. It is not surprising, therefore, that mitral regurgitation did not occur or was minimal in association with this type of very early extrasystole (fig. 4, right panel). Recurrent ventricular extrasystoles in the middle of the cardiac cycle, however, occurred late enough to allow

![Figure 5](http://circ.ahajournals.org/)

**Figure 5**

*High-sensitivity recording of left atrial and left ventricular videodensograms shown in middle panel of figure 3. R and R' refer to primary and extrasystolic ventricular depolarizations, respectively. A, V, and V' refer to stimuli as in figure 3. Note phasic mitral regurgitation occurring with each extrasystolic depolarization but not with primary ventricular depolarization.*
the mitral valve to open after each primary ventricular systole (fig. 4, middle panel). Thus, mitral regurgitation is possible at the onset and during each extrasystole of this type.

With recurrent early extrasystoles the primary ventricular contraction was potentiated and mitral regurgitant indexes were decreased from control levels (table 1). With recurrent mid-cycle extrasystoles, end-diastolic pressure prior to each extrasystole tended to be higher than in the control rhythm or for the primary beats associated with the extrasystoles; the systolic pressure of the extrasystolic beats was decreased, and the mitral regurgitant indexes were increased significantly (mean increase 7%, standard error 1.2%, P < 0.01).

**Discussion**

The previously demonstrated linearity and sensitivity of the videodensitometer,\(^4\)\(^-\)\(^7\) coupled with the facility provided for careful choice of sampling site and repeated recording of videodensograms from different sites on the same videotaped angiogram, preclude the possibility that significant mitral regurgitation occurred which was not detected. Thus, our inability to detect reflux with most single extrasystoles indicates that the valve was competent despite the irregularity of ventricular rhythm and the lack of a preceding, normally sequenced atrial systole able to preclose the valve prior to the extrasystolic ventricular contraction. This is consistent with previous observations from this laboratory that reflux is frequently minor or undetectable in the presence of regular ventricular systoles\(^4\)\(^,\)\(^5\) which are not preceded by normally sequenced atrial systoles. It is also consistent with the observations of a number of other workers\(^8\)\(^-\)\(^10\) who have not detected reflux in the presence of isolated irregular ventricular systoles which are dissociated from atrial systoles or occur with atrial fibrillation and an irregular ventricular response.

The lack of reflux during the long diastole or with the ventricular systole terminating...
VENTRICULAR EXTRASYSTOLES

the prolonged diastole which followed each isolated ventricular extrasystole (fig. 1) is of interest. The ventricle is obviously large, the valve ring probably is, and end-diastolic pressure is comparatively high at the termination of such a prolonged diastole. If the occurrence of reflux during the systole which terminates this prolonged diastole depended on the size of the ventricle and the valve ring, reflux would be expected. However, such a postectopic systole usually consists of a strong contraction with a rapid rise in pressure as blood is ejected against a low outflow resistance occasioned by the decrease in aortic pressure associated with the long diastolic pause and decreased stroke volume of the preceding ectopic systole. Mitral regurgitation has been produced consistently in the present study only when regularly recurrent extrasystoles were introduced late enough in the cardiac cycle for the mitral valve to open after each primary normal systole. Such mid-cycle extrasystoles were preceded by very short diastolic-filling periods and were without an atrial-systolic boost to aid ventricular filling and possibly aid closure of the mitral valve. Thus, it is likely that the ventricular volume prior to such extrasystoles was smaller than the volume prior to primary systoles or to the normal systoles in control observations. Despite this, the left ventricular end-diastolic pressure prior to such extrasystoles was similar to, or higher than, the pressure preceding the primary systole or the systole in control observations. The ensuing extrasystolic contraction was too weak in most cases to open the aortic valve, and the maximal rate of pressure rise in the ventricle during systole was less than that for the primary systole or for the systole in the control observations. The occurrence of mitral regurgitation in time with such weak extrasystoles not preceded by a normally timed atrial systole is consistent with previous observations from this laboratory. The amount of reflux occurring with isolated regular ventricular systoles (simultaneous atrial and ventricular driving) before, during, and after extrasystolic potentiation of ventricular contraction was related inversely to the rate of pressure rise in the left ventricle during systole and directly to the level of end-diastolic pressure or the size of the ventricle prior to the onset of systole. Thus, although in this study the size of the ventricle prior to such mid-cycle extrasystoles was probably small, the valve is probably not closed rapidly and tightly enough to prevent reflux because of the slow rise of pressure during systole.

The data suggest that when reflux occurs in association with single isolated ventricular extrasystoles during clinical angiography, mitral valve disease, impairment of ventricular function, or both, should be suspected and that such reflux should not be attributed wholly to the lack of preslosure of the valve by a normally timed atrial systole. Also, as pointed out by Williams and co-workers, if an atrial contraction occurs during angiocardiography and, due to temporary ventricular refractoriness or block of atrioventricular conduction, is not followed by a normally sequenced ventricular contraction, significant diastolic mitral valve reflux would be expected to occur. The occurrence of isolated atrial systoles might also explain the findings of Paul and co-workers who observed mitral reflux in experimental animals during long diastolic pauses.

However, it is also possible that the larger volumes of contrast medium injected in their study and in clinical medicine (0.7 to 1.5 ml/kg) might cause diastolic reflux which was not observed in the present study because of the smaller volumes injected (0.2 to 0.3 ml/kg). In assessing clinical angiograms, one must also take into account the position of the injecting catheter. If the tip is pointing directly toward the mitral valve, reflux is probably more likely to occur than it is if the catheter tip is pointing toward the apex, as it was in these studies.

References

1. Friedman, B., Daily, W. M., and Wilson, R. H.: Studies on mitral valve function: Effect of acute hypervolemia, premature beats


Effect of Ventricular Extrasystoles on Closure of Mitral Valve

RUSSELL A. VANDENBERG, JOHN C.P. WILLIAMS, RALPH E. STURM and EARL H. WOOD

Circulation. 1969;39:197-204
doi: 10.1161/01.CIR.39.2.197

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1969 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/39/2/197

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org///subscriptions/