Effect on Circulation of Conversion of Atrial Fibrillation to Sinus Rhythm

By ROBERT GILBERT, M.D., ROBERT H. EICH, M.D., HAROLD SMULYAN, M.D., JOHN KEIGHLEY, M.B., B.CHIR., and J. HOWLAND AUCHINCLOSS, JR., M.D.

UNTIL recently enthusiasm for conversion of atrial fibrillation to sinus rhythm in patients with rheumatic heart disease has been dampened by the high rate of reversion to atrial fibrillation soon after conversion. Mitral commissurotomy, if followed by a reduction of left atrial pressure and size, offers the theoretical possibility of a reduction in this reversion rate. Successful commissurotomy of itself, however, does not restore sinus rhythm, and many patients previously in sinus rhythm will fibrillate following surgery. Conversion with quinidine is not a benign procedure and sudden death during conversion attempts has been reported. Thus the increasing number of patients presenting as candidates for conversion has increased the need for a better understanding of the alterations in cardiac performance that occur as a result of atrial fibrillation and the changes to be expected upon conversion.

In 1924, Blumgart demonstrated a reduction in heart rate during exercise following conversion to sinus rhythm. Since then, several additional reports have been published comparing various aspects of cardiac performance during exercise before and after conversion from atrial fibrillation to sinus rhythm. Nevertheless, many aspects of the problem are still in doubt for the following reasons: duplicate control studies in subjects receiving quinidine but not converting have been lacking; it is difficult to determine in most cases how adequately digitalized were the patients prior to the first study; no measurements have been made of cardiac output during exercise in the upright position, presumably the most physiologic for man; and no assessment was made of the patient’s ability to perform a standardized exercise test. The present study was designed to give additional information on the results of conversion to sinus rhythm, with an attempt to give specific information concerning these points.

Patient Material

Twelve sets of studies before and after conversion were performed in 11 patients (table 1). Four of the 11 were studied several months following mitral commissurotomy; in three of these the commissurotomy was technically satisfactory, while in the remaining patient (R.C.) the operation was not entirely satisfactory, since subvalvular stenosis was not relieved. Two of the 11 were women who had auscultatory findings of mitral stenosis, but left heart catheterization failed to demonstrate a diastolic pressure gradient across the mitral valve. These two are classified as mitral stenosis with predominantly myocardial disease. Two male subjects had no demonstrable cardiac abnormalities other than atrial fibrillation; they are designated as idiopathic atrial fibrillation. Three subjects had primarily valvar heart disease but had no surgery up to the time of study; one of them (F.K.) had two sets of studies.

Duplicate control studies several days apart without a change in rhythm were performed in seven subjects (table 2). One of these seven (W.M.) had two studies during atrial fibrillation and one following conversion to sinus rhythm; he thus appears in both tables. Subject M.F. had undergone technically successful commissurotomy several years prior to testing, but was experiencing a return of symptoms. Subjects V.S. and G.F. had undergone exploratory thoracotomy several years prior to study, but the anatomy of the mitral valve or left atrium had precluded commissurotomy. D.H. had auscultatory mitral stenosis but no symptoms. One subject had aortic valve disease and one subject had arteriosclerotic heart disease.

From the Department of Medicine, State University of New York Upstate Medical Center, Syracuse, and the Veterans Administration Hospital, Syracuse, New York.

Supported in part by Grant H-2800 from the U.S. Public Health Service.

Circulation, Volume XXVII, June 1963 1079
### Table 1

**Converted Subjects**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>NYHC</th>
<th>Age</th>
<th>Digitalis status</th>
<th>Rhythm</th>
<th>Minutes completed</th>
<th>Test group</th>
<th>Resting supine heart rate</th>
<th>Exercise heart rate</th>
<th>Cardiac output L./min.</th>
<th>Stroke volume ml./beat</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Standing 1 min. ex.</td>
</tr>
<tr>
<td>W.M.</td>
<td>MS PO</td>
<td>II</td>
<td>57</td>
<td>M†</td>
<td>AF</td>
<td>10</td>
<td>2b</td>
<td>70</td>
<td>174</td>
<td>3.37</td>
<td>5.84</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Standing 1 min. ex.</td>
</tr>
<tr>
<td>W.W.</td>
<td>MS PO</td>
<td>I</td>
<td>49</td>
<td>M†N</td>
<td>AF</td>
<td>10</td>
<td>1</td>
<td>100</td>
<td>140</td>
<td>2.93</td>
<td>3.65</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Standing 1 min. ex.</td>
</tr>
<tr>
<td>R.R.</td>
<td>MS MI</td>
<td>III</td>
<td>53</td>
<td>M</td>
<td>AF</td>
<td>6</td>
<td>3</td>
<td>90</td>
<td>140</td>
<td>3.28</td>
<td>3.96</td>
</tr>
<tr>
<td></td>
<td>AI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Standing 1 min. ex.</td>
</tr>
<tr>
<td>O.G.</td>
<td>MS MD</td>
<td>II</td>
<td>47</td>
<td>M†</td>
<td>AF</td>
<td>2</td>
<td>3</td>
<td>75</td>
<td>160</td>
<td>2.96</td>
<td>5.29</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Standing 1 min. ex.</td>
</tr>
<tr>
<td>M.S.</td>
<td>MS MI</td>
<td>III</td>
<td>32</td>
<td>M†</td>
<td>AF</td>
<td>10</td>
<td>2b</td>
<td>83</td>
<td>114</td>
<td>4.71</td>
<td>8.42</td>
</tr>
<tr>
<td></td>
<td>AI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Standing 1 min. ex.</td>
</tr>
<tr>
<td>R.E.</td>
<td>MS MD</td>
<td>II</td>
<td>57</td>
<td>B</td>
<td>AF</td>
<td>5</td>
<td>3</td>
<td>56</td>
<td>180</td>
<td>8.00</td>
<td>8.7</td>
</tr>
<tr>
<td>M.O.</td>
<td>IAF</td>
<td>I</td>
<td>61</td>
<td>M</td>
<td>AF</td>
<td>10</td>
<td>1</td>
<td>90</td>
<td>116</td>
<td>9.50</td>
<td>9.7</td>
</tr>
<tr>
<td>F.K.</td>
<td>MS MI</td>
<td>II</td>
<td>43</td>
<td>M†NB</td>
<td>AF</td>
<td>10</td>
<td>2b</td>
<td>84</td>
<td>119</td>
<td>147</td>
<td>147</td>
</tr>
<tr>
<td>F.K.</td>
<td>MS MI</td>
<td>II</td>
<td>43</td>
<td>M</td>
<td>AF</td>
<td>10</td>
<td>1</td>
<td>88</td>
<td>119</td>
<td>132</td>
<td>132</td>
</tr>
<tr>
<td>R.C.</td>
<td>MS PO</td>
<td>II</td>
<td>47</td>
<td>M</td>
<td>AF</td>
<td>1</td>
<td>3</td>
<td>88</td>
<td>119</td>
<td>132</td>
<td>132</td>
</tr>
<tr>
<td>S.M.</td>
<td>IAF</td>
<td>II</td>
<td>33</td>
<td>M†V</td>
<td>AF</td>
<td>10</td>
<td>1</td>
<td>100</td>
<td>132</td>
<td>88</td>
<td>88</td>
</tr>
<tr>
<td>G.L.</td>
<td>MS PO</td>
<td>II</td>
<td>45</td>
<td>V</td>
<td>AF</td>
<td>2</td>
<td>3</td>
<td>80</td>
<td>124</td>
<td>112</td>
<td>112</td>
</tr>
</tbody>
</table>

*All patients receiving maintenance digitalis.

N, digitalis increased to point of nausea; M†, maintenance digitalis increased; B, resting heart rate below 60; V, ventricular extrasystoles; M, maintenance digitalis, no evidence for degree of digitalization; MS, mitral stenosis; MI, mitral insufficiency; AS, aortic stenosis; AI, aortic insufficiency; PO, postoperative; MD, myocardial disease; IAF, idiopathic atrial fibrillation; NYHC, New York Heart Association functional capacity.
disease. In all subjects but E.B. and D.H., the second study was performed within a few days of an unsuccessful conversion attempt with quinidine. After the attempt, the subjects remained on maintenance quinidine until the second study.

Method

The exercise test consisted of 4 minutes of standing followed by 10 minutes or less of treadmill walking and 5 minutes of recovery in the standing position. The treadmill was set at 1.7 m.p.h. at a 10-per cent grade; the exercise stress produced an approximately threefold rise in oxygen consumption. The details of the analytical gas circuit have been described in a previous publication. The method allows direct measurement or computation of heart rate, minute ventilation, oxygen consumption, respiratory quotient, and alveolar gas partial pressure on a minute-by-minute basis. The subject was told to try to walk for the full 10 minutes if he could do so without severe discomfort. If he found this impossible, he was to remove the mouthpiece and say, “stop.” The treadmill was immediately turned off, the subject replaced the mouthpiece, and 5 minutes of recovery measurements were recorded.

The test was evaluated on the basis of whether or not the patient was able to walk for the full 10 minutes, and, if he did so, on the further basis of five factors. These were steady state heart rate, ventilation and respiratory quotient, the oxygen deficit at the start of exercise, and the physical fitness index of Bruce with slight modification. Standards for these factors have been determined from a group of 35 normal subjects. The test for each patient was then scored as follows:

Group 1: The patient was able to walk for the full 10 minutes and all 5 factors were normal.

Group 2: The patient was able to complete the test but one or more factors were abnormal. This category was subdivided into (2a) a test with only one abnormal factor and (2b) a test with more than one.

Group 3: The patient asked that the treadmill be stopped before 10 minutes.

These three categories were assumed to represent increasing degrees of disability. The score for each patient is shown in the tables under the column labeled “test group.”

In four sets of conversion studies and four sets of control studies cardiac output was determined by the indicator-dilution technique with radioactive iodinated human serum albumin as the indicator. Injection was made through a catheter threaded into an antecubital vein, and samples
were obtained at 2-second intervals from an indwelling needle in the brachial or radial artery of the opposite arm. The details of the indicator-dilution technic as used in this laboratory have been reported elsewhere.\textsuperscript{10} Output determinations were made just prior to the start of exercise with the patient standing, after 1 minute of exercise, and after 8 minutes of exercise where this was possible.

All patients had been in the hospital at least several days before the study. The first test was performed when the patient had achieved what was considered to be optimal condition, and no patient had overt cardiac failure at the time of testing. Conversion with quinidine was started on the same day or the day after the first test. No patient received more than 3 Gm. of quinidine in a 24-hour period. If the patient converted to sinus rhythm, he received quinidine maintenance (0.2 to 0.4 Gm. four times daily) and the second test was performed as soon as possible. Usually this was the day after the conversion and the longest interval between conversion and the second test was 5 days (W.W.).

All subjects but D.H. were receiving digitalis and were considered adequately digitalized at the time of study. The resting supine heart rates are shown in the tables. Seven subjects were given additional doses of digitalis prior to the first study. In two, this was continued until they experienced nausea. This information is shown in the column labeled "digitalis status" in the tables. In the interval between the two studies the subjects received their usual maintenance digitalis with the exception of W.W., in whom digitalis was discontinued after the first test because of persistent nausea. Subject E.B. in the control group was given quinidine 0.4 Gm. four times daily in the interval between the first and second studies.

Exercise heart rates recorded in the tables are average steady-state values if the patient completed the test. If not, the heart rate is the one recorded just prior to the time of stopping the shortest test. For example, in the case of E.B. in table 2, both heart rates refer to the third minute of exercise. Stroke volume was computed from the heart rate during the time the samples were being collected for the indicator-dilution curve.

**Results**

The results of the conversion studies are shown in table 1, those of the control studies in table 2.

**Cardiac Output**

All converted subjects showed an increase in cardiac output at rest and exercise following conversion where this measurement was made. These increases gain added significance when compared with the oxygen consumptions. In figure 1, the cardiac outputs at exercise are plotted against the oxygen consumptions at the time the output was measured. The broken line was determined by the method of least squares from the data of Reeves, Grover, Blount, and Filley\textsuperscript{11} for normal subjects during treadmill walking. In all but one converted subject, the cardiac output rose while the oxygen consumption diminished. In the fourth case, (W.M.), the 8-minute output and oxygen consumption both rose, but the rise in output was far out of proportion to the rise in oxygen consumption. By contrast, in three of the four control subjects, neither cardiac output nor oxygen consumption changed significantly. In P.P., both the 1-minute and the 8-minute values for cardiac output were higher during the second study, but both of these increases were

---

*Figure 1*

Cardiac output at exercise plotted against oxygen consumption. The broken line was determined by the method of least squares from the data of Reeves, Grover, Blount, and Filley\textsuperscript{11} for normal subjects during treadmill walking.
associated with increases in oxygen consumption; in only the 8-minute results was the increase in output out of proportion to the increase in oxygen consumption.

Heart Rate

All converted subjects showed a decrease in exercise heart rate following conversion; in four subjects this decrease was more than 50 beats per minute. No control subject showed this great a reduction, and in five of the seven there was no significant change in rate. Two control subjects (G. F. and P.P.) had reductions in rate at the second test of 44 and 40 beats per minute respectively. Only in P.P. was this reduction in rate accompanied by an increase in cardiac output.

Stroke Volume

All four converted subjects with output determinations had increases in exercise stroke volume upon resumption of sinus rhythm. In two the stroke volume doubled. One control subject showed no change, one a decrease, and two moderate increases in stroke volume at the second test. In none of the control subjects did the stroke volume double.

Exercise Tolerance

The changes in the results of the exercise performance test are shown in figure 2. In the converted group, the greatest improvement at the time of the second test was shown by two subjects who changed from group-2b to group-1 tests, and two who changed from group-3 to group-2a tests. One control subject showed a similar degree of change. All four control subjects with group-3 tests at the time of the first study, had similar tests during the second study.

Discussion

The results indicate improvement in cardiac output, heart rate, stroke volume, and exercise performance following conversion to sinus rhythm. In 10 of the 21 tests during atrial fibrillation, there was an excessive rise in heart rate with exercise, despite what would appear to be adequate or even excessive doses of digitalis. After conversion all subjects showed a decrease in exercise heart rate to the normal range. In fact, these rates in sinus rhythm are surprisingly low for subjects with the degree of cardiac disability these patients exhibit. Many other patients in sinus rhythm with comparable cardiac disability have performed this test in our laboratory and often they show much higher heart rates at exercise, even when adequately digitalized, than the converted subjects in this study. It seems unlikely that the quinidine would be responsible for the low rates, since quinidine usually has either no effect or will speed the heart rate in subjects with sinus rhythm. Slowing of the heart rate at the time of the second study occurred in only two of the seven control subjects. The converted subjects in this study may have shown such unusually low heart rates during exercise in sinus rhythm because they were digitalized or somewhat overdigitalized while fibrillating, then converted to sinus rhythm. This would imply that digitalis requirements are higher in a given individual when in atrial fibrillation as compared to sinus rhythm. Many of the converted subjects showed first-degree heart block after conversion, even if they showed no evidence of digitalis toxicity while fibrillating; this may have been due to the quini-
dine but also might indicate mild digitalis intoxication.

Since heart rates were invariably lower in sinus rhythm, the increased cardiac output following conversion was the result of marked increases in stroke volume. This increase in stroke volume could have been secondary to slowing of the ventricular rate with longer time for filling or to the contractile force of the atrium present in sinus rhythm but absent in atrial fibrillation, or to both. These two cannot be analyzed separately in the present study, since increases in output were invariably accompanied by a decrease in heart rate. In the studies of Hansen et al.\textsuperscript{4} three subjects had increases in cardiac output following conversion without significant changes in heart rate. Certainly in these cases the contractile function of the atria must have been an important factor. Hecht and Lange,\textsuperscript{13} however, have stated on theoretical grounds that atrial contraction in the presence of mitral stenosis augments flow to only a small degree. They believed that in these cases the improvement is due primarily to slowing of the ventricular rate with a longer diastolic filling period, so important in mitral stenosis. In the study of Kory and Meneely\textsuperscript{7} subjects with lesions other than mitral stenosis gained the least benefit from conversion. A previous report from this laboratory\textsuperscript{8} has presented evidence that atrial fibrillation imposes a greater disability in the presence of mitral stenosis than when it accompanies other forms of heart disease, and that subjects with mitral stenosis and atrial fibrillation are the ones most likely to have excessively high heart rates with exercise. These considerations would indicate that, in mitral stenosis, the improvement in cardiac output following conversion is usually the result of primary slowing of the heart rate. There may be considerations other than those of flow, however. Braunwald and Frahm\textsuperscript{14} have shown that left atrial contraction plays an important part in elevating left ventricular end-diastolic pressure without elevating mean left atrial pressure. This might be an important factor in limiting pulmonary hypertension, especially in subjects with mitral stenosis, and might play an important role in improving exercise performance by minimizing dyspnea.

Evaluation of disability by tests of exercise performance is assuming increasing importance with the recent emphasis on rehabilitation of the cardiac patient. The results of this study show that considerable improvement can be achieved in exercise performance in certain subjects in atrial fibrillation if sinus rhythm can be restored and maintained. Not all subjects showed this improvement in performance; those who did not were the ones who were most disabled on the basis of the first test. The fact that some subjects showed slower heart rates without appreciable change in exercise tolerance casts considerable doubt on the validity of performance tests gauged by heart rate as the sole measure, especially in the cardiac subject.

Although the present series is too small for a definite answer to the question of the likelihood of maintenance of sinus rhythm in converted subjects, the follow-up results in these patients are of interest. Of the 11 converted subjects, three (O.G., R.E., and F.K. both times) reverted back to fibrillation within a few weeks. Two of these had continued taking quinidine, one had discontinued it because of gastrointestinal irritation. One subject (R.R.) died at home a few weeks following conversion. No postmortem examination was obtained and no information is available concerning the heart rhythm just prior to death. None of these patients had cardiac surgery. One subject (M.S.) with valvular heart disease has as yet had no surgery and has remained in sinus rhythm for the follow-up period, which is only 8 months. One subject (M.O.) with idiopathic atrial fibrillation reverted promptly to atrial fibrillation, then converted spontaneously to sinus rhythm. He remained in sinus rhythm for 2 years, then reverted again to atrial fibrillation. The other subject (S.M.) with idiopathic fibrillation had remained in sinus rhythm for 18 months. The other four patients all had mitral com-
CONVERSION OF ATRIAL FIBRILLATION

missurotomies prior to conversion. One subject (G.L.) has left the area and is lost to follow-up, but was in sinus rhythm when last seen 6 months following conversion. The other three have remained in sinus rhythm for periods of 32 months, 20 months, and 18 months. These results suggest that subjects with successful mitral commissurotomies have an excellent chance of remaining in sinus rhythm following conversion, whereas in subjects in other categories the long-term results are uncertain.

Summary

Treadmill exercise tests were performed in cardiac subjects before and after conversion from atrial fibrillation to sinus rhythm. The most striking changes following conversion were a marked reduction in exercise heart rate and increase in stroke volume and cardiac output. Exercise performance as judged by a standardized exercise test improved significantly in some but not all subjects following conversion. Duplicate control studies in nonconverting subjects failed in general to show these improvements. The results indicate that conversion from atrial fibrillation to sinus rhythm is worthwhile from a functional standpoint in patients with valvular heart disease, and is especially indicated after successful mitral commissurotomy.

Acknowledgment

The authors gratefully acknowledge the technical assistance of Mrs. Mary Rensen, Miss Faye Donderwitz, Mrs. Mary Brooks, Mr. Donald Yorkey, Miss Carol Roberts, Mrs. Sherry Lubanski, and Mrs. Inez Heywood.

References

2. BLUMGART, H. L.: The reaction to exercise of the heart affected by auricular fibrillation. Heart 11: 49, 1924.

Circulation, Volume XXVII, June 1963
Effect on Circulation of Conversion of Atrial Fibrillation to Sinus Rhythm
ROBERT GILBERT, ROBERT H. EICH, HAROLD SMULYAN, JOHN KEICHELEY
and J. HOWLAND AUCHINCLOSS, JR.

Circulation. 1963;27:1079-1085
doi: 10.1161/01.CIR.27.6.1079

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/27/6/1079

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/