Coupled pacing improves cardiac efficiency during acute atrial fibrillation with or without cardiac dysfunction

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Coupled pacing improves cardiac efficiency during acute atrial fibrillation with or without cardiac dysfunction. Am J Physiol Heart Circ Physiol 287: H2016–H2022, 2004. First published July 29, 2004; doi:10.1152/ajpheart.00347.2004.—Coupled pacing (CP), a method for controlling ventricular rate during atrial fibrillation (AF), performs similarly during concurrent atrial fibrillation and heart failure; rate control; external cardiac work; oxygen consumption

Atrial fibrillation (AF) is the most common sustained cardiac rhythm disturbance and is increasing in prevalence in the United States (13). For many years, the general belief was that it is better to return to sinus rhythm (SR) than to solely maintain ventricular rate control. However, the recent Atrial Fibrillation (AF) Follow-up Investigation of Rhythm Management (AFFIRM) trial has shown that a rate control strategy was similar to a rhythm control strategy in patients with symptomatic AF and stroke risk factors (23). In addition, despite many advances in the treatment of cardiovascular diseases, heart failure is also increasing in prevalence. Heart failure can cause AF, whereas in other cases AF and the subsequent rapid ventricular rate can cause heart failure (12). When these two diseases occur concurrently, the rapid ventricular rate caused by AF clearly accelerates the progression of heart failure (14).

When it is not possible to maintain SR, ventricular rate control during chronic AF is the only remaining option. We have recently begun to reevaluate an alternative method for ventricular rate control, “coupled pacing” (CP) during AF (24).

CP consists of electrical stimulations applied to the heart after the effective refractory period of the each spontaneous ventricular activation. The somewhat similar concept of “paired stimulation” was proposed several decades ago as a therapy for heart failure (3, 8, 17). Paired stimulation paces the ventricles at a basic interval that is slightly less than the prevailing one during SR. Then, a second closely coupled electrical stimulus is applied. The second stimulus of each pair for both paired stimulation and CP is premature enough to result in no mechanical contraction. However, the second stimulus enhances contractility postextrasystolic potentiation (6). Paired stimulation does not decrease the rate of mechanical contraction and necessitates artificial pacing of every beat, making it potentially harmful in the setting of high heart rate and normal ventricular conduction. In contrast, CP uses the intrinsic activation of the ventricles as the first of the paired ventricular “beats.” In the case of CP, the paced beat (second of the paired activity) prevents the subsequent intrinsic activation. Thus the intrinsic activation of the ventricles occurs about half the prior rate. In both cases (paired stimulation and CP), the contractile state is enhanced (6). Paired stimulation resulted in the ventricular rate of mechanical contraction (VRMC) remaining the same, whereas CP resulted in VRMC decreasing to approximately half its original rate. Although paired stimulation (17) effectively increased systolic function, it increased markedly myocardial oxygen consumption (MV\(\dot{O}_2\)). A recent study (18) showed a new positive inotropic agent did not increase MV\(\dot{O}_2\) in heart failure because it resulted in a reflexly induced bradycardia. However, when this bradycardia was prevented, the MV\(\dot{O}_2\) increased. The purpose of this present study is to show that CP can reduce the rate of ventricular mechanical contractions and improve cardiac function during acute AF while not dramatically increasing MV\(\dot{O}_2\). We previously showed that CP dramatically increases the external work of the heart during AF (24). Thus, without a comparable increase in MV\(\dot{O}_2\), as occurs for external work during CP, the myocardial efficiency should improve.

The primary hypothesis of the present study is that CP improves cardiac function during acute AF (24) without a comparable increase of MV\(\dot{O}_2\). A secondary hypothesis of the study is that the presence of cardiac dysfunction (CD) enhances the effect of CP in AF.
COUPLED PACING AND MYOCARDIAL EFFICIENCY

METHODS

This investigation was approved by the Institutional Animal Research Committee at Cleveland Clinic Foundation, and it conforms to the Guide for the Care and Use of Laboratory Animals published by the National Institute of Health (NIH Pub. No. 85-23, Revised 1996).

Experimental protocol. We used adult mongrel dogs (22–29 kg) in an experimental design that consisted of two phases. In phase 1 (n = 4 dogs), the aim was to establish and validate the method of external work per MVO₂ measurement under varying heart rhythm conditions. The experiments consisted of two stages: SR (stage 1) and AF (stage 2). Each stage lasted at least 10 min and was divided into two 5-min periods: before and after the application of CP. In each period, we collected data during the last 60 s. In phase 2 (n = 7 dogs), to study how concurrent CD alters the effects of CP on cardiac energetics during AF, we added two additional stages: CD and CD + AF (i.e., AF in the presence of CD). That is, we first reestablished SR. We then induced CD by administering 3–5% isoflurane in addition to the α-chloralose anesthesia (stage 2). We chose this method of CD induction because we could titrate the extent of CD to a prescribed level of ~50% cardiac output that was found during SR (11). See Table 1 for the changes in hemodynamics resulting from this CD. After obtaining a stable but reduced cardiac output, we collected data before and during CP in the same manner as the first two stages. Finally, we induced AF during the acute CD and again obtained data before and during CP (stage 4).

Experimental preparations. Dogs were anesthetized with morphine (2 mg/kg im) and α-chloralose (80 mg/kg iv). Supplemental anesthesia was given hourly. We started positive pressure ventilation. Normal arterial blood gas values and pH were maintained by appropriate adjustments throughout the experiment. We used micromanometer-tipped catheters (Millar: Houston, TX) to measure mean arterial pressure (mAoP) and left ventricular (LV) pressure (LVP). After a right thoracotomy, a third pressure catheter was inserted and advanced into a right pulmonary vein branch to measure left atrial pressure. We isolated the ascending aorta and placed a flow probe (Transonic Systems; Ithaca, NY) on the vessel.

A quadrupolar catheter was placed in the right atrium via a femoral vein to induce AF by constant rapid pacing. A second quadrupolar catheter was placed in the right ventricular apex via the left jugular vein to sense the electrical activation of the ventricles and then to apply CP. We used a computer-controlled program (custom program by K. A. Mowrey) to apply CP via an analog-to-digital board (Microstar Lab; Bellevue, WA). The stimulation output was controlled from a Microsoft Excel program via a Microsoft Visual Basic interface with the analog-to-digital board. All the stimulation parameters and measurements of cardiac cycle lengths were controlled in real time. We determined the optimal parameters as described earlier (24).

Because not all electrical activations of the left ventricle results in its mechanical contraction and this contraction does not always result in ejection of blood into the aorta, we measured the ventricular rate of electrical activations (VREA), VRMC, and ventricular rate of ejections (VREJ). We define the VREA as the rate of electrical activations (including both intrinsic activations and paced beats), VRMC as the rate of LV mechanical contractions that reach at least a developed pressure of 10 mmHg, and VREJ as the rate of measurable ejections from the left ventricle.

The azygos vein was isolated to insert our coronary sinus catheter. After the completion of this surgery, we heparinized the animal (500 U/kg). Via this vein, the tip of the coronary sinus catheter was inserted into the ostium of the coronary sinus, and the cuff at its distal end was inflated to divert all of the coronary sinus blood into the catheter. The proximal end of the catheter was connected to silicone tubing that was used to return the blood to the animal via the right jugular vein. An in-line flow probe (Transonic 4N) was connected to this tubing. With this extracorporeal system, we could continuously measure coronary blood flow and obtain periodic blood samples.

Data acquisition. All hemodynamic and electrogram measurements were continually monitored and periodically recorded at the times described above (Cardio Lab, GE Marquette Medical Systems). The above measurements were digitized and analyzed off-line with our custom data analysis software (K. A. Mowrey).

Measurement of stroke work. Single-beat stroke work was calculated as stroke work (in joules) = stroke volume (in ml, an integral of aortic flow rate) × (mean LVP during ejection in mmHg) × 1.33 × 10⁻⁶ (14). In four experiments, we validated this calculation with the calculation based on the area of individual pressure-volume loops obtained by a pressure-conductance catheter (Millar Instruments) (24).

Measurement of MVO₂. From the coronary sinus-cervical venous circuit, we sampled the coronary sinus blood while simultaneously obtaining an arterial blood sample. From these two blood samples, we calculated the O₂ extraction by the heart at each stage of the experiment. Next, we multiplied these O₂ extractions by coronary blood flow rate to obtain MVO₂ rate (in ml/min) for each stage.

Because we did not observe dramatic increases in coronary blood flow during CP as reported during paired stimulation (17), we performed the following two tests. First, we would temporarily occlude the silicone tubing distal to the flow probe. This occlusion would build up pressure and caused increases in coronary blood flow following this occlusion that were much greater than any of the increases occurred during our experimental protocol. Thus the extracorporeal circuit did not provide resistance that would limit a potential increase in coronary flow. Second, no marked increases in the extraction of oxygen or release of lactic acid was detected during AF, CD, or the application of CP, which would have indicated that the coronary vasculature could not increase its flow in a manner needed to match increased metabolic demands. Thus the coronary vasculature reserve was adequate in this present study.

Calculation of myocardial efficiency. We defined external cardiac work (ECW) as the sum of stroke work over a 1-min period at the same time blood samples were taken to determine MVO₂. Stroke work from each ejection was calculated as the product of stroke volume times the mean LV ejection pressure. Prior work showed that hearts produce 20.2 J of energy for each milliliter of O₂ consumed (1). Thus

<table>
<thead>
<tr>
<th>Table 1. Effects of cardiac dysfunction induction on baseline hemodynamics</th>
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<tr>
<td>SR</td>
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<tr>
<td>VRMC, beats/min</td>
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<tr>
<td>Peak systolic AoP, mmHg</td>
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<tr>
<td>Peak diastolic AoP, mmHg</td>
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<td>Pulse pressure, mmHg</td>
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<td>Mean AoP, mmHg</td>
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<td>Peak systolic LVP, mmHg</td>
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<td>Peak dP/dt, mmHg/s</td>
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<td>LVEDP, mmHg</td>
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<td>Mean LAP, mmHg</td>
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<td>LVEDV*, ml</td>
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<tr>
<td>Ejection fraction*, %</td>
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<tr>
<td>Peak AoF, ml/s</td>
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<tr>
<td>Stroke volume, ml</td>
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<tr>
<td>Cardiac output, l/min</td>
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<tr>
<td>Mean coronary flow, ml/min</td>
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<tr>
<td>ECW, J/min</td>
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<tr>
<td>O₂ extract, ml/100 ml</td>
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<td>MVO₂, ml/min</td>
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Values are means ± SE. VRMC, ventricular rate of mechanical contraction; AoP, aortic pressure; LVP, left ventricular (LV) pressure; dP/dt, first derivative of LVP; LVEDP, LV end-diastolic pressure; LAP, left atrial pressure; LVEDV, LV end-diastolic volume; ECW, external cardiac work; MVO₂, myocardial O₂ consumption; SR, sinus rhythm; CD, cardiac dysfunction; NS, not significant. *Obtained from 3 animals, whereas the rest are from 7 animals.
the myocardial efficiency of the heart was calculated as myocardial efficiency (ECW = MV / MV \times 20.2) × 100.

Statistical analysis. Data are present in our graphs as means ± SE. We used the paired t-test to separately examine the effects of CP on various ventricular function parameters (ventricular rate of mechanical contraction, mAoP, cardiac output, coronary blood flow, total stroke, or ECW per minute, MV \times 20.2) × 100. We also examined the overall effects of AF, CD, and CD + AF on the change in the above parameters when CP was applied in the last seven animals. In this later case, we used a two-factor repeated-measures ANOVA design to explore the effects of acute AF and CD: dependent variable (such as VRMC, mAoP, CO, etc.) = C + AF + CD + CD AF = Di + Error where C is a constant, AF and CD denotes the presence or absence AF and CD, respectively, and Di (with i = 1 . . . 7) denotes the individual dog effect. P values < 0.05 were considered significant.

RESULTS

Validation of determination of stroke work via two methods. Figure 1 shows a sample of one such comparison. There was a very strong correlation over a wide range of stroke volumes during AF between these two methods for measuring stroke work. The values of stroke work from our calculation method averaged 2.1 ± 1.5% higher than the calculation from pressure-volume (PV) loops.

Representative responses to CP during SR, AF, CD, and CD + AF stages. Each of the eight panels of Fig. 2 show representative recordings of ECG, right ventricular electrogram, LVP and its derivative (LV dP/dt), and aortic flow (AoF) before (baseline) and during CP. Note that CP decreased the ventricular rate of mechanical contractions but increased the peak rise in LVP and the rate of ejection of blood in all four stages of this representative experiment.

Effect of CP on cardiac energetics. Figure 3 shows changes of cardiac parameters that reflect changes in cardiac energetics as the result of CP. CP dramatically reduced ventricular rate of mechanical contraction in all four stages of this study (Fig. 3, top left). In contrast, CP had only moderate effect on mAoP (middle left). Both AF and CD depressed cardiac output. However, the application of CP significantly increased these depressed outputs (bottom left). Similarly, CP dramatically increased the external cardiac work during AF and CD (top right). In contrast, CP did not significantly alter either cardiac output or ECW during SR. Despite the increase in ECW as the result of CP during AF and/or CD, the MV02 did not increase (middle right) as much as ECW. Therefore, myocardial efficiency increased as a result of CP during all stages except SR (bottom right).

Overall effects of AF and/or CD on cardiac energetics to CP (ANOVA). We also examined how the states of acute AF and CD altered various cardiac parameters when CP was applied. Overall, both AF and application of CP altered VRMC (P = 0.01). CP increased mAoP (P = 0.04) with AF enhancing (P = 0.046) the CP effect. CP increased cardiac output (P = 0.016) with the increase being higher in the presence of either AF or CD (P = 0.001 and P = 0.005). As expected, the absence of both acute AF and CD led to significantly smaller effect of CP on cardiac output (P = 0.03). Overall, CP increased ECW (P = 0.001) with the increase being higher in the presence of AF (P = 0.015). Interestingly, neither the presence of AF nor CD altered the nonsignificant increase in MV02 in response to CP. As a result, myocardial efficiency increased during CP (P = 0.007), with the increase more evident in the presence of CD (P = 0.007).

Effects of CP on electromechanical activation and ejection and the energetics of each contraction. Table 2 is a summary of average VREA, VRMC, and VREJ as well as the MV02 and external work per beat. This application of CP results in approximately half of the intrinsic ventricular depolarizations that would have occurred. Thus the VREA remained virtually constant despite the additional paced stimulation from the CP. With these reductions in VRMC, VREJ equals the VRMC; that is, all contractions result in ejection of blood (100% ejections). In contrast, the percentage of ejections to ventricular contractions was 70% and 77% before the application of CP during AF and CD + AF. Thus the application of critically timed ventricular pacing (CP) reduced the VRMC to half its prior rate during AF and ensured that ejection of blood occurred after every contraction.

The average interval for ventricular contractions during AF was 325 ms (99 SD). The CP pacing increased the mean interval to 566 (SD 71). The percent ratio of the average standard deviation of the intervals between ventricular contractions to mean intervals is a rough measure of variability (inverse of regularity). Thus CP reduced this ratio of SD to mean interval from 29% during AF to 12% during AF + CP. These results show that CP regularized the contractile rate as well as slowed it significantly during AF.

Because changes in heart rate affect cardiac metabolism and there were wide ranges of the contractions and ejections rates in the four stages of this study before and after CP, we also measured MV02 and external work on a per beat basis (see lower portion of Table 2). Note that AF did not dramatically affect MV02 per contraction (0.45 vs. 0.41), whereas CP increased the MV02 by a factor of 2. The induction of CD resulted in a reduction of MV02 to approximately half its prior value. However, CP still increased MV02 by 2. During SR, the external work per beat doubled because the rate contraction decreased by half. In contrast, the external work per beat more than doubled when AF was present.

![Graph](http://ajpheart.physiology.org/DownloadedFrom/10.1152/ajpheart.00707.2004)
DISCUSSION

The major finding of this study is that CP reversed the effects of AF and CD on cardiac output and ECW, whereas MVO₂ increased only moderately. As the ECW increased to a greater degree, the CP significantly increased myocardial efficiency during CD, both in the absence and presence of AF.

Cardiac function and O₂ usage. Paired stimulation was investigated as a potential therapy for heart failure because it directly increased myocardial contractility (3, 17). However, this therapy was abandoned because paired stimulation applied acutely also greatly increases MVO₂. This increase in MVO₂ could compromise an already ischemic heart (8, 17). Whereas the increase in MVO₂ in response to CP was moderate, the CP improved myocardial efficiency. We explain this important difference as follows: Heart rate, contractility, wall tension, and the extent of fiber shortening all influence MVO₂ (4, 17, 19). Because changes in MVO₂ correlate with changes in heart rate (2), the reduction of the rate of contraction by half with CP should decrease MVO₂ by half. In contrast, paired stimulation would result in no reduction in the rate of ventricular contraction. Although CP results in two electrical activations for each mechanical contraction, prior work has shown that electrical activation and repolarization of the heart uses less than 5% of the energy used each cardiac cycle (10). A positive increase in myocardial contractility (second factor) increases MVO₂ (19). Increases in LV wall tension normally elevate MVO₂ (third factor). However, because CP decreases both aortic diastolic pressure and LV end-systolic volume (24), changes in wall tension would have little effect increasing MVO₂ in our experiments. The doubling of stroke work via the doubling of stroke volume (fourth factor) (24) has less influence on MVO₂ than the other three factors (4). Finally, CP permits intrinsic activation of the ventricles, whereas paired stimulation results in an inefficient contraction due to pacing-induced ventricular dysynchrony (22). In conclusion, the reduction in the rate of contraction appears to attenuate, to a large degree, the increases in MVO₂ that normally occur.

Fig. 2. Representative recordings of the hemodynamic responses to coupled pacing (CP) during all four stages of experiments. Left, baseline responses before the application of CP. Right, responses after the application of CP. ECG, lead II electrocardiogram; RVe, right ventricular electrogram; dLVP/dt, rate of LVP development; AoF, aortic flow; SR, sinus rhythm; AF, atrial fibrillation; CD, cardiac dysfunction. See text for more details.
Concept of partitioning O₂ usage. Because of the earlier work of Braunwald and colleagues (3, 5, 8, 10, 16), Suga and associates (20) established a concept of partitioning myocardial oxygen usage for contraction into nonrelated cellular metabolism, electromechanical coupling, contractility level, and generation of PV area (PVA), the last being a sum of external (stroke) work and potential energy.

Suga and co-workers (21) showed that paired pacing doubled contractility-dependent oxygen use per mechanical beat. In this work, contractile efficiency was defined as total contractile work (both potential energy and external work) per total energy expenditure (MVO₂). He and his colleagues demonstrated that paired stimulation resulted in an upward shift in the relationship between the total PVA (both potential and external work) and MV₀₂. Because the inverse slope of this relationship was defined as contractile efficiency, which did not change, Suga concluded that PVA-independent oxygen consumption was augmented without affecting the contractile efficiency.

CP during rapid AF affects oxygen use through several opposing mechanisms. It eliminates the pressure-generating beats with no or little associated ejection, eliminating oxygen used for the development of potential energy of these beats. CP increases the stroke volume of ejecting beats. It reduces the rate of contraction, thus MV₀₂. However, the postextrasystolic potentiation elicited by CP increases contractility-dependent oxygen use. Finally, CP had no effect on electromechanical coupling because the number of depolarization sequences remained constant.

Table 2. Effects of CP on electromechanical activation and ejection and the energetics of each contraction

<table>
<thead>
<tr>
<th></th>
<th>SR</th>
<th>AF</th>
<th>CD</th>
<th>CD + AF</th>
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<tr>
<td>VREA, activations/min</td>
<td>135±7</td>
<td>149±13</td>
<td>226±15</td>
<td>225±12</td>
</tr>
<tr>
<td>VRMC, contractions/min</td>
<td>135±7</td>
<td>80±78</td>
<td>197±15</td>
<td>112±6§</td>
</tr>
<tr>
<td>VREJ, ejections/min</td>
<td>135±7</td>
<td>80±78</td>
<td>136±10</td>
<td>111±6†</td>
</tr>
<tr>
<td>VREJ/VRMC, % eject/contract</td>
<td>100±0</td>
<td>100±0</td>
<td>100±0</td>
<td>100±0</td>
</tr>
<tr>
<td>MV₀₂/VREA, ml activations</td>
<td>0.045±0.004</td>
<td>0.051±0.009</td>
<td>0.035±0.004</td>
<td>0.041±0.004*</td>
</tr>
<tr>
<td>MV₀₂/VRMC, ml/contractions</td>
<td>0.045±0.004</td>
<td>0.089±0.0121</td>
<td>0.041±0.005</td>
<td>0.082±0.008§</td>
</tr>
<tr>
<td>MV₀₂/VREJ, ml/ejections</td>
<td>0.045±0.004</td>
<td>0.089±0.0121</td>
<td>0.060±0.008</td>
<td>0.083±0.008§</td>
</tr>
<tr>
<td>MV₀₂/VREJ, ml/activation</td>
<td>0.157±0.019</td>
<td>0.158±0.017§</td>
<td>0.055±0.007</td>
<td>0.089±0.009§</td>
</tr>
<tr>
<td>MV₀₂/VREJ, ml/contraction</td>
<td>0.157±0.019</td>
<td>0.294±0.035§</td>
<td>0.062±0.006</td>
<td>0.179±0.185§</td>
</tr>
<tr>
<td>MV₀₂/VREJ, ml/ejection</td>
<td>0.157±0.019</td>
<td>0.294±0.035§</td>
<td>0.088±0.007</td>
<td>0.180±0.017§</td>
</tr>
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</table>

Values are means ± SE. VREA, ventricular rate of electrical activations; VREJ, ventricular rate of ejection; ECW, external cardiac work; AF, atrial fibrillation.  §P < 0.0001, †P < 0.001, ††P < 0.01, *P < 0.05 vs. baseline.
In contrast to Suga and colleagues (20, 21) complex analysis of oxygen partitioning, our myocardial efficiency is the simple ratio of only external work ([stroke work/time]/total energy [MV02/time]). Thus the “mechanically bradycardic” effect of CP increases the external work-to-potential energy area ratio by eliminating the aborted beats, thus improving efficiency of the ventricle as we defined it.

With the use of Suga and colleagues (20, 21) concepts of oxygen partitioning by the heart, a more recent study (25) showed that the contractile efficiency was maintained only if the negative chronotropic effect of β-blockade was manifested. Therefore, the bradycardiac effect of β-adrenergic blockade is important in preventing an increase in the energy expenditure for nonmechanical work. Once again, rate reduction is important in either maintaining efficiency or possibly enhancing it.

CP and O2 usage. Only one previous study (9) assessed MV02 during CP somewhat similarly to ours. The study showed that CP increased MV02 by 66% and decreased myocardial efficiency by 50%. All patients had normal heart rates (average heart rate, 79 beats/min). CP induced bradycardia (heart rate, 44 beats/min) and decreased cardiac index by 34%. We found that during SR, our results with CP were similar to this clinical study. Our study differed from this clinical study in that we also assessed the effects of CP during tachycardia. Our experiments showed that CP was most effective as a therapy during tachycardia (acute AF, CD, and CD + AF). In conclusion, the slowing of the rate of contraction below normal levels causes a decrease in efficiency.

Clinical implications. The increasing prevalence of heart failure in patients and the detrimental effect of concurrent AF with concurrent heart failure provide a strong impetus for reexamination of this pacing therapy. We have shown that CP can increase LV pump function without adversely affecting myocardial efficiency in AF and in AF with concurrent LV dysfunction. Thus this therapy could potentially be applied in patients with ischemic heart disease, which accounts for many patients with HF. The improvement in ventricular function as the result of CP may outweigh the potential risk of the induction of ventricular tachycardia. To minimize the risk of this pacing therapy, such therapy could be given through a defibrillator and only during the times of tachycardia. Also, to reduce the risk of proarrhythmia, the coupled beat could be given with a paced output just slightly above the capture threshold. This pacing therapy could be applied via an existing right ventricular lead or a temporary lead, using either a new or threshold. This pacing therapy could be applied via an existing

Limitation. The number of animals was small. Also, because this study was performed in an acute setting, we can only speculate about whether CP may become a viable therapy for chronic AF and/or heart failure. We are aware that our acute CD induced by excessive anesthetia is substantially different from chronic heart failure. Thus the compensatory responses of chronic heart failure with enlarged hearts and chronic AF may alter the heart’s response to CP. However, the limited increases in MV02 in this study as opposed to paired stimulation (large increases in MV02) suggest that CP as pacing therapy should be reexamined during chronic AF and heart failure. The larger increases in external cardiac work compared with MV02 translate into an increase in myocardial efficiency during CP. However, if the MV02 increases moderately as the result of CP during chronic AF and HF, as we have observed in this acute study, some coronary flow reserve would need to be present in these patents to avoid myocardial ischemia and committant-related issues.

The animals in this study have normal intraventricular conduction. However, this study does not answer how regional alterations in the conduction that sometimes occur in patients with heart failure would affect the extrasystolic interval of CP in various portions of the heart and thus the magnitude of regional changes in postextrasystolic potentiation. Further experiments are needed to determine how the coupling intervals of these premature beats affect the efficiency of these diseased hearts.

In conclusion, we clearly showed that CP improves myocardial efficiency in AF, CD, and CD + AF. With the evolution of pacemakers and internal defibrillators, this pacing algorithm may become a novel strategy for treating patients with AF and/or heart failure.

GRANTS

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REFERENCES


