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Amiodarone in Patients with Heart Failure and AF

ABSTRACT & COMMENTARY

Synopsis: *This study presents a favorable profile of the effects of amiodarone in patients with atrial fibrillation and congestive heart failure.*

Source: Deedwania PC, et al., for the Department of Veterans Affairs CHF-STAT Investigators. *Circulation* 1998;98:2574-2579.

Atrial fibrillation (af) is a common problem in patients with congestive heart failure. In this report, Deedwania and the CHF-STAT investigators examine the effects of amiodarone on established and new onset of AF in patients with heart failure. CHF-STAT was a multicenter Veterans Affairs trial that examined the effects of amiodarone vs. placebo on mortality. Entry criteria included documented left ventricular dysfunction and frequent (> 10/h) premature beats on a 24-hour ambulatory ECG. All patients were on what was believed at that time to be appropriate heart failure regimens at entry, but therapy with beta blockers was not permitted. Amiodarone therapy or matching placebo was prescribed at 800 mg/d for two weeks, 400 mg/d for 50 weeks, and then 300 mg/d for the remainder of the study. Dose reduction for presumed toxicity was permitted. Six hundred sixty-seven patients were enrolled in the study. Deedwania and colleagues have previously reported no effects of amiodarone on mortality.

The effects of amiodarone on AF were not the primary end point in this study, but data concerning persistence of AF were gathered in the 103 patients (15% of those enrolled) who had AF at the time of their baseline evaluation. Fifty-one of the AF patients were randomized to receive amiodarone and 52 were randomized to receive placebo. Baseline data comparing these two groups revealed no significant differences. Amiodarone therapy resulted in lower ventricular rates during AF after two weeks, six months, and 12 months of therapy. No improvement in ventricular rate was seen in the placebo group. Sixteen of 51 patients on amiodarone vs. four of 52 patients on placebo converted to sinus rhythm and remained in sinus rhythm for the duration of the study (P = 0.002). The onset of AF in patients in sinus rhythm was also less common in the amiodarone group,

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developing in 4% of those on amiodarone vs. 8% of those on placebo (P = 0.005).

No significant difference in survival was noted between the two groups of the AF patients, but those on amiodarone who converted demonstrated improved survival. Although the role of a number of baseline characteristics was examined, no predictors of conversion to sinus rhythm were identified.

Deedwania et al conclude that amiodarone has multiple benefits that result in better rate control, conversion, or prevention of AF in patients with congestive heart failure.

COMMENT BY JOHN P. DiMARCO, MD, PhD

This paper presents a favorable profile of the effects of amiodarone in patients with AF and congestive heart failure. However, much of what is presented with these data limits the applicability of the observations.

The CHF-STAT trial was designed to assess the effects of amiodarone on mortality. Observations on AF were incidental to the primary end point of the study and no overall mortality benefit was observed. Since AF was not involved in the primary end point, the use of amiodarone in the study did not follow the protocol one would use if AF prevention or termination had been the primary objective. If that had been the case, elective cardioversion would be part of the treatment plan and the drug would be used principally to maintain sinus rhythm after the conversion. Had this protocol been followed in CHF-STAT, it is possible, but certainly not proven, that more benefit from amiodarone in patients with AF at presentation may have been observed.

Although Deedwania et al describe a beneficial effect of amiodarone on rate control, there are certainly other less toxic and less expensive drugs for this indication. Beta adrenergic blockers were not permitted in CHF-STAT. More recent data have indicated that beta blockers are advantageous in patients with CHF and they should probably be an early choice for ventricular rate control in patients with AF.

Finally, the observation of Deedwania et al that conversion to sinus rhythm was associated with an apparent increase in survival may merely be an example of a "healthy responder" phenomenon. Patients with less severe disease would be both more likely to survive and more likely to convert out of AF. The conversion itself may not be the causal factor leading to the improved survival. ❖

The benefit of amiodarone in heart failure patients is:

a. reduced total mortality.
b. reduced sudden death.
c. reduced need for implantable defibrillators.
d. prevention of atrial fibrillation.

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Therapeutic Angiogenesis: Promising Initial Reports

ABSTRACT & COMMENTARY

Synopsis: *Direct myocardial instillation of vascular endothelial growth factor (VEGF) via thoracotomy shows clinical benefit.*

Source: Losordo DW, et al. *Circulation* 1998;98:2800-2804.

Gene therapy using a variety of vectors and growth factors is a promising new approach to the therapy of myocardial ischemia. Losordo and colleagues at St. Elizabeth's Medical Center in Boston are among the world pioneers and have previously reported on the successful use of an adenoviral vector expressing vascular endothelial growth factor (VEGF) for severe limb ischemia in humans. A new study, the first use of direct intramyocardial instillation of naked plasma DNA that encodes VEGF, is reported in five male subjects with refractory angina, all of whom had had between two and three prior revascularization procedures and were deemed to be inoperable. The results,

while preliminary and short term in a small cohort, are dramatically positive.

The gene therapy was initiated through a small thoracotomy, with injections of a vector encoding the 165-amino acid isoform of the human VEGF gene, using plasmid DNA administered in four aliquots via direct myocardial injection into the LV anterolateral free wall. Mean operative time was less than two hours and all patients were discharged within 3-4 days without complications or evidence of myocardial necrosis. Serial studies, evaluated by blinded investigators, were carried out and included a dobutamine SPECT-sestamibibi perfusion study at baseline and at 30 and 60 days; coronary angiography with explicit attention to collateral status at baseline and 60 days; and assessment of clinical status (angina frequency and severity NTG consumption). The patient population consisted of five men with class IV angina pectoris, age 53-71; two were diabetic. All were on polypharmacy for angina and were severely limited. Approximately three weeks following the VEGF administration in the operating room, all patients began to notice clinical improvement, and by 60 days represented a major decrease in angina rates compared to preoperatively. The ability to perform physical activity increased substantially, and NTG use decreased. Objective evidence for improvement in ischemia and collateralization was obtained in each individual. Perfusion imaging with dobutamine demonstrated an increase in the number of normally perfused segments per patient from 6.0 ± 1.1 to 8.0 ± 0.7 ($p < 0.05$ at 60 days) and a decrease in the number of irreversible defects from 2.4 ± 0.2 to 1.2 ± 0.4 ($p = < 0.05$). This is suggestive of improvement in hibernating myocardium.

Coronary artery angiography performed before and two months after gene transfer indicated improved collateral flow to the ischemic areas in all five patients. New collateral vessels were suggested by improvement in filling of previously identified collaterals as well as new collateral vessel development. Losordo and colleagues conclude that "the present study provides the first evidence for favorable clinical effect of direct myocardial injection of naked plasmid DNA encoded VEGF." They comment that the ideal number of injections is unknown, as is the optimal anatomic site for placement of the DNA. They note that the vectors and formulations incorporating VEGF are subjects for future research. Losordo et al comment that groups have used VEGF protein with preliminary success in the treatment of limb and myocardial ischemia in animals. Some investigators are exploring catheter-based systems, as well as direct myocardial instillation of fibroblast growth factor (FGF) at the time of coronary bypass surgery. FGF variants in gene or protein formulation are the focus of ongoing and future clinical trials.

COMMENT BY JONATHAN ABRAMS, MD

This report is of enormous interest, as it suggests that gene transfer may enhance perfusion in the human heart with coronary atherosclerosis, presumably through the induction of a more robust and extensive collateral system. Losordo et al have previously shown this approach works in the treatment of severe limb ischemia. Several reports presented at the recent American Heart Association meetings in Dallas in November 1998 confirmed that many groups are working on a variety of techniques to provide VEGF, human growth factor, FGF, and other moieties with a variety of delivery systems in animal models. The Germans have previously reported similar but favorable results of FGF in conjunction with bypass surgery (Schumacher B, et al. *Circulation* 1998;97:645). This field is moving rapidly and clinicians are alerted to keep abreast of these developments. Protocols are now available in the United States from a variety of centers to enroll patients with refractory angina in randomized trials incorporating theracotomy for direct myocardial injection of gene products, catheter-based systems, as well as gene therapy in association with concomitant coronary bypass surgery.

Assuming that minimally invasive or noninvasive techniques are effective in enhancing collateral circulation (or in preventing or attenuating restenosis following coronary angioplasty), the future is bright indeed. Many biotech companies are involved in this rapidly expanding field. The *New York Times* published a comprehensive article on this subject (*New York Times*. December 22, 1998). The molecular biology technology is sophisticated and advances are moving rapidly. Losordo et al are to be congratulated for pursuing research that initially seems to be truly revolutionary, but that may result in commonplace therapy within the next decade. While caution is advisable until long-term results in larger groups of patients are obtained, this is an exciting area of investigation. ❖

Therapeutic coronary angiogenesis is based on:

a. endothelial growth factors.
b. adenoviral vectors.
c. direct myocardial injections.
d. All of the above

Intraoperative TEE

ABSTRACT & COMMENTARY

Synopsis: *New segmented wall motion abnormalities detected by TEE during coronary bypass surgery without cardiopulmonary bypass that persist at the end of surgery identify a group with increased postoperative morbidity.*

Source: Moises VA, et al. *J Am Soc Echocardiogr*

1998;11:1139-1144.

The practical value of monitoring left ventricular function during coronary bypass surgery by transesophageal echocardiography (TEE) is uncertain. However, coronary surgery performed without cardiopulmonary bypass may represent a unique opportunity for intraoperative TEE. Thus, Moises and colleagues evaluated their experience with 27 patients undergoing coronary bypass surgery without cardiopulmonary bypass who had intraoperative TEE monitoring. Transthoracic echocardiography was performed one day prior to surgery and on the seventh post-operative day. During 48 coronary artery clampings, new segmented wall motion abnormalities were observed in 31 (64%). Half had recovered by the end of the operation and one-third showed partial recovery of wall motion, but five (17%) did not recover. The latter five segments were still abnormal at seven days, as were two of the 10 with partial recovery. Those with persistent new wall motion abnormalities at seven days had higher enzyme levels, more electrocardiographic abnormalities, and more clinical events than those without new segmental wall motion abnormalities at seven days post-operatively. Moises et al conclude that new segmented wall motion abnormalities detected by TEE during coronary bypass surgery without cardiopulmonary bypass that persist at the end of surgery identify a group with increased post-operative morbidity.

COMMENT BY MICHAEL H. CRAWFORD, MD

In this small study, new persistent segmental wall motion abnormalities detected during coronary surgery without cardiopulmonary bypass seemed to be of clinical significance. Since the heart is beating and not protected by cardioplegia during coronary artery clamping, transient wall motion abnormalities would be expected depending on the duration of occlusion and other factors such as collaterals. The paper gives no details on factors that may predict the development of wall motion abnormalities, but, clearly, their persistence is associated with myocardial ischemia or infarction. Also, the complications noted in patients with persistent wall motion abnormalities, namely heart failure and atrial fibrillation, were related to reduced left ventricular function.

At this point in the development of coronary surgery on the beating heart, it would appear that TEE provides clinically useful information about left ventricular function, canula position, etc., to justify its routine use. Also, it may contribute to new knowledge about mechanisms of myocardial damage during this type of surgery (ischemia, infarction, stunning). Along these lines, Moises et al point out that coronary contrast echo may add information about the integrity of the microvasculature after revascularization. One practical note is that Moises et al believe it is important to use transgastric as well as transesophageal planes to visualize as much of the left ventricle as possible. ❖

Intra-operative TEE monitoring of LV function is most useful for:

a. noncardiac surgery in patients with known CAD.
b. pericardiectomy.
c. coronary revascularization without heart-lung bypass.
d. aneurysmectomy.

Sustained Ventricular Arrhythmias in Acute MI

ABSTRACT & COMMENTARY

Synopsis: *Early and late occurrences of sustained ventricular tachycardia or ventricular fibrillation denote a high-risk group for both short- and long-term mortality.*

Source: Newby KH, et al., for the GUSTO Investigators. *Circulation* 1998;98:2567-2573.

Newby and colleagues review the gusto-i database to determine the incidence, acute outcome, and prognostic significance of sustained ventricular tachycardia (VT) and ventricular fibrillation (VF) in patients with acute myocardial infarction (MI). GUSTO-I enrolled 41,020 patients admitted within six hours of the onset of chest pain. Patients were randomized to receive one of four regimens: streptokinase plus subcutaneous heparin, front-loaded tissue plasminogen activator plus intravenous heparin, streptokinase plus intravenous heparin, or tissue plasminogen activator and streptokinase plus intravenous heparin. Nurse coordinators in each center later reviewed the charts of the patients enrolled in the study for documentation of any sustained ventricular arrhythmias. VF was defined as irregular undulations of variable contour and amplitude on ECG that produced prompt hemodynamic compromise requiring DC shock for termination. Sustained VT was defined as a wide complex tachycardia of probable ventricular origin lasting more than 30 seconds or requiring early electrical cardioversion. No systematic review of the rhythm strips was performed. In particular, we are not provided data about the cycle length or morphology of the episodes of VT. Arrhythmias were classified as

either early if they occurred within two days of admission or late if they were observed more than two days after admission.

Sustained VT, VF, or both were reported in 4188 patients (10.2%). VT and/or VF was associated with older age, previous infarct, hypotension, higher Killip class, and lower ejection fraction. Higher early and late mortality rates were seen in patients with sustained ventricular arrhythmias compared with those without arrhythmias. In-hospital mortality was 18.6% in those with VT only, 24% in those with VF only, and 44% in those with both VT and VF. These values contrasted with a mortality rate of 4.2% among patients who did not have any sustained ventricular arrhythmias. Long-term mortality was also elevated in those with ventricular arrhythmias. Total one-year mortality rates for those with VT only, VF only, and both VT and VF were 24.2%, 26.0%, and 48.4%, respectively. Patients with none of these arrhythmias had a one-year mortality of 7.2%. Both early and late ventricular arrhythmias were associated with higher mortality. For VT, the one-year mortality was 38.9% for those with early VT and 49.0% for those for late VT. For VF, the one-year mortality rates were 22.0% and 39.3% for early and late VF, respectively. For patients with both VT and VF, the one-year mortality rates were 47.0% and 59.6% for patients with early and late presentations, respectively. Catheterization findings that correlated with ventricular arrhythmias included a higher incidence of TIMI grade 0 flow and lower ejection fractions. Newby et al conclude that, despite the use of thrombolytic therapy, early and late occurrences of sustained VT or VF denote a high-risk group for both short- and long-term mortality.

COMMENT BY JOHN P. DiMARCO, MD, PhD

The clinical significance of early ventricular arrhythmias in patients with acute MI remains controversial. This is primarily due to the fact that VT and VF may be produced by a number of electrophysiologic phenomena in the setting of acute ischemia. VF that occurs in the setting of acute ischemia may have little significance if the patient suffers little myocardial damage from the infarction and has no complications from the resuscitation. However, when VF occurs in the setting of acute infarction and the infarction either results in ventricular dysfunction or ventricular dysfunction was present previously, VF may be a marker of continued electrical instability. VT may also be due to different mechanisms. In the first hours to days after acute MI, benign sustained ventricular arrhythmias due to enhanced automaticity in damaged Purkinje fibers may be seen. These accelerated idioventricular rhythms may meet the ECG definition for VT but have limited long-term significance. Sustained monomorphic VT with a stable cycle length of longer than 230 msec is usually not seen in the first hours after MI unless prior infarction had occurred or if antiarrhythmic drugs were used. When this type of sustained VT develops after the first 24-48 hours, it tends to be malignant and is associated with a high mortality. VT that has a short cycle length (< 230 msec) probably does not represent a stable substrate and behaves more like VF. In this paper, we are not provided any information about the cycle length or morphology of the VT. It is, therefore, likely that what is reported as VT really includes accelerated idioventricular rhythms, VTs arising from prior infarctions, VT seen after antiarrhythmic drugs were administered for VF, VT with short cycle lengths, and more stable arrhythmias.

The data from this large study do point out the fact that patients who have ventricular arrhythmias as a group continue to be at risk. However, careful examination of the other clinical factors in the patient's course and the ECG and clinical features of the arrhythmia should be used to judge whether the patient requires aggressive antiarrhythmic intervention after recovery. ❖

The significance of VTs in post-MI in patients treated with thrombolysis is that:

a. early or late appearance increases mortality.
b. only late appearance increases mortality.
c. only early appearance increases mortality.
d. only late VF increases mortality.

LV Dilation in Athletes

ABSTRACT & COMMENTARY

Synopsis: *About 15% of highly trained athletes have left ventricular (LV) cavity dimensions associated with cardiomyopathy, but with normal ventricular performance and a benign course, suggesting that this dilation represents a physiologic adaptation to intensive aerobic training.*

Source: Pelliccia A, et al. *Ann Int Med* 99;130:23-31.

Much has been written about increases in left ventricular (LV) mass and wall thickness in well-trained athletes, but there is little information about increases in cavity dimensions. Thus, Pelliccia and colleagues evaluated echocardiograms done in 1309 Italian Olympic athletes who were judged to be free of structural heart disease. The athletes participated in 38 sports, ranged in age from 13 to 59 years, and were 73% men. All had trained for at least two years, 26% were compet-

itive at the world level, and the remaining were competitive at the national level. The LV diastolic dimension was less than 54 mm in 55% and was greater than 60 mm in 14%. The range was 38-66 mm (95th percentile 56 mm) in women and 43-70 mm (95th percentile 63 mm) in men. Intraventricular septal thickness ranged from 5 to 15 mm in diastole, and was greater than 12 mm in 1%. In general, wall thickness paralleled cavity dimension (r = 0.64), but only three of 185 athletes with a cavity dimension of 60 mm had a wall thickness greater than 13 mm. Multivariate analysis showed that body surface area and type of sport were the most significant variables associated with cavity dimension, followed by heart rate, sex, and age. Sports associated with large LV cavity size were cycling, ice hockey, basketball, rugby, canoeing, and rowing. All the athletes with large cavities had normal LV systolic and diastolic function, and they had no segmented wall motion abnormalities and no significant valvular regurgitation. Follow-up of the athletes with cavity size greater than 60 mm for a mean of five years (2-12 years) was uneventful. Pelliccia et al conclude that about 15% of highly trained athletes have LV cavity dimensions usually associated with cardiomyopathy, but with normal ventricular performance and a benign course, suggesting that this dilation represents a physiologic adaptation to intensive aerobic training.

COMMENT BY MICHAEL H. CRAWFORD, MD

Because of the association between the rare sudden death in an athlete and hypertrophic cardiomyopathy, there has been considerable work on wall thickness in athletes. Cardiomyopathy has played a role in the deaths of some recent well-known athletes, yet less is known about LV cavity enlargement in highly trained athletes. In this report from Italy, most athletes had normal LV cavity sizes, but 15% had strikingly enlarged ventricular size (> 60 mm), almost always with normal wall thickness. By contrast, only 1% had markedly thickened walls (>12 mm). Since cavity dilation can herald the onset of reduced LV systolic function, this raises the concern of cardiomyopathy vs. athlete's heart. The athletes with marked cavity dilation had normal systolic function and remained well for an average follow-up of five years (2-12 years). Thus, there is no reason to suspect cardiomyopathy in these athletes.

Enlarged hearts in athletes have been well recognized for more than 100 years, but modern imaging studies have shown mainly right ventricular dilation and LV hypertrophy. Why do some athletes develop large LV cavities? This study showed that it was largely related to the type of sport and the size of the individual. However, genetic factors cannot be excluded since some athletes may be born, not made. In this regard, the results of this study in a relatively homogeneous Italian athlete population cannot necessarily be extrapolated to other populations, such as Africans or Asians. Also, certain sports popular in the United States, such as football and baseball, were not represented. Finally, the long-term consequences of these extremely large ventricles are unclear. Whether they will regress after cessation of training or remain large is unknown. In fact, the echo assessments were not made at any specific point in the training season in this study. Data from my laboratory on college athletes suggests that LV cavity size is greatest at the peak of training just before competition starts as compared to the off-season. Thus, the extreme cavity enlargement observed in these athletes may represent the peak of training subgroup.

For the clinician faced with deciding whether this is structural heart disease or athlete's heart, several considerations are important: 1) LV systolic and diastolic function are normal in the athlete. Remember, ejection fraction in a large heart at a slow heart rate often will be in the low normal range, 50-55%, which was observed in this study. 2) The athletes will often be male and large. 3) They will be well trained and competitive in sports that combine aerobic endurance and strength (i.e., cycling or rowing). 4) They will have slow heart rates. 5) They will be young. ❖

LV dilatation in well-trained athletes correlates best with:

a. body size.
b. type of sport.
c. heart rate.
d. All of the above

Transcatheter Closure of ASD

ABSTRACT & COMMENTARY

Synopsis: *Centrally located ASDs and PFOs associated with cerebral emboli can be successfully treated with the double-umbrella-style atrial septal defect occluder system with acceptable morbidity.*

Source: Sievert H, et al. *Am J Cardiol* 1998;82: 1405-1413.

The european trial of the double-umbrella-style atrial septal defect (ASD) occluder system has reported the feasibility, safety, and efficacy of this system in 154 patients with ASD and 46 with patent foramen ovale (PFO) who had cerebral embolism pre-

sumed to be paradoxic. The placement of the two umbrellas requires femoral venous and arterial access, a minimal patient weight of 10 kg, heparinization, and a transesophageal echo to guide seating of the umbrellas. The 200 patients ranged in age from 1 to 74 years (mean 32) and 138 were adults. Total procedure time was 2-3 hours, with mean fluoroscopy times of 30-45 minutes, and the average ASD diameter was about 15 mm. The procedure was unsuccessful in 26 patients (13%); in 20 patients, the device could be brought out by the catheter system, but six required surgery for retrieval because of device embolization in two, atrial wall perforation in two, entrapment in the Chiari network in one, and frame fracture in one. Of the 20 patients with unsuccessful deployment and successful retrieval, almost all had ASD greater than 20 mm in diameter and small septal rims to attach the device. Eleven additional patients had surgery for device removal during follow-up because of complications or large residual shunts. The remaining 163 patients (81%) were followed for 6-36 months (mean 17). Total (initial and follow-up) complications included residual shunt in up to one-third of patients, two cerebral embolic episodes despite evidence of thrombus on transesophagael echo at two weeks in 6% of patients, pericardial effusion in six, atrial perforation in five, infectious endocarditis in two, and device fracture in 23 (14%). Sievert and colleagues conclude that centrally located ASDs and PFOs associated with cerebral emboli can be successfully treated with this device with acceptable morbidity.

COMMENT BY MICHAEL H. CRAWFORD, MD

Unfortunately, this report is not sufficiently detailed to ascertain when each complication occurred and what the clinical outcome was. In the discussion, Sievert et al state that the rate of complete defect closure was 63%, but only 8% of the remaining 37% had significant residual shunts. However, we do not know how many of the successfully closed patients were ASD vs. PFO. Regardless, this does not compare well to the surgical results of significant residual shunts in the range of 2-8%. Surgical series have shown some mortality (0-3%) and morbidity (8-15%) but they were mainly attributable to patients with pulmonary hypertension and other cardiac lesions. In those without these conditions, long-term surgical outcomes have been excellent. Further follow-up will be necessary to judge the efficacy of this device, especially with regard to long-term device fracture.

This device seems best suited for patients with PFOs or small ASDs where there is sufficient septal tissue to anchor the umbrellas. Also, anticoagulation may be necessary for three months or so until the device is endothelialized. In addition, more stringent aseptic techniques than are usually used in the catheterization laboratory may be necessary to prevent infection. Finally, the issue of chronic antibiotic prophylaxis is raised by the one patient who developed device endocarditis six months after implantation. Clearly, progress is being made with transcatheter device ASD/PFO closure and we now have an alternative for the patient in whom surgery is not feasible. However, surgery is still the treatment of choice at this time. ❖

Catheter-based closure systems for ASD are best for:

a. small centrally located ASDs.
b. large ASDs without septal rims.
c. patients with hypercoagulable states.
d. children less than 10 kg.

Superior Vena Cava Doppler for Constrictive Pericarditis

ABSTRACT & COMMENTARY

Synopsis: *Despite similar repiratory variations in the mitral E velocity, COPD patients demonstrate greater changes in SVC systolic forward flow velocity, which is not observed in constrictive pericarditis patients.*

Source: Boonyaratavej S, et al. *J Am Coll Cardiol* 1998;32:2043-2048.

Constrictive pericarditis (cp) and chronic obstructive pulmonary disease (COPD) can have the same clinical presentation and diseases such as tuberculosis can be associated with both. Boonyaratavej and associates from the Mayo Clinic hypothesized that since the exaggerated respiratory variation in mitral inflow velocities is due to increased intrathoracic pressure swings in COPD as opposed to a disassociation of intrathoracic and intrapericardial pressures in CP, superior vena cava (SVC) flow velocity would be different in the two conditions. Thus, they studied 20 patients with COPD vs. 20 patients with surgically proven CP by Doppler echocardiography. Respiratory variation in mitral E wave velocity was similar in both groups (41 vs 46%). However, in CP patients, the E/A ratio was higher throughout the respiratory cycle compared to COPD patients, due mainly to a lower A velocity and a somewhat higher E velocity in the CP patients. Also, deceleration of E was lower in the CP patients, as was SVC inspiratory systolic forward flow velocity (36 ± 9 vs 73 ± 22 cm/s; $P < 0.0001$). Consequently, there was much less respiratory variation in SVC systolic forward flow velocity in CP patients (4 ± 3 vs 40 ± 19 cm/s: $P < 0.0001$), with only one COPD patient who overlapped with the values in the CP patients. Boonyaratavej et al conclude that despite similar respiratory variations in the mitral E velocity, CP patients show a more restricted mitral E pattern than do COPD patients, but COPD patients demonstrate much greater changes in SVC systolic forward flow velocity, which is not observed in CP patients.

COMMENT BY MICHAEL H. CRAWFORD, MD

Patients with COPD and CP can both present with dyspnea, Kussmauls sign, signs of right heart failure, and increased respiratory variation in mitral E wave velocities. Other diseases can also augment respiratory mitral Doppler E wave velocity changes, such as cardiac tamponade or acute right ventricular dilation due to infarction or pulmonary embolism. Usually, clinical features and echo findings, such as pericardial effusion and dilated right ventricle, can distinguish the latter conditions, but COPD can be a challenge clinically and on echocardiography. Thus, the observation that SVC systolic forward flow velocity changes with respiration are discriminative is useful. However, SVC recordings require right supradavicular fossa or suprasternal notch windows that may not be used frequently in many adult echo laboratories.

With obstructive airway disease, intrathoracic pressure swings are increased by augmented diaphragmatic action to attempt to move air. These pressure swings are readily transmitted to the SVC and left atrium, markedly altering flow velocities in these areas. In CP, normal intrathoracic inspiratory pressure drops are not transmitted to the heart chambers, resulting in lower pressure gradients from the pulmonary veins to the left heart—exaggerating the swings in mitral flow velocity but not the SVC. In severe COPD, diaphragmatic movement can be reduced due to lung hyperinflation and the change in SVC flow reduced. This was the explanation for the one patient in the study with COPD whose SVC velocity changes with inspiration were similar to the CP group.

Although this appears to be a useful Doppler echocardiographic finding that should be sought in all patients suspected of having CP, a few cautions are in order. As mentioned, severe lung hyperinflation can cause a false positive SVC velocity sign suggesting CP. Also, it is conceivable that severe tricuspid regurgitation could reduce SVC systolic forward flow velocities, giving the false impression of CP. Severe tricuspid regurgitation could be due to unrecognized right ventricular infarction or pulmonary emboli, which could augment the respiratory variation in mitral E velocities as well. Thus, in the final analysis, the diagnosis of CP rests on detecting thickened pericardium and this is best accomplished by MRI. However, SVC flow velocity measures are an important new screening tool that all echocardiography laboratories should gear up to do well. ❖

Constrictive pericarditis is characterized by which Doppler findings?

a. Marked respiratory variation in SVC flow velocity
b. Marked respiratory variation in mitral E wave velocity
c. Increased mitral E wave deceleration
d. Mitral E/A ratio less than 1.0