Right Ventricular Function at Rest and during Exercise in Chronic Obstructive Pulmonary Disease

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Right ventricular ejection fraction (RVEF), a measure of systolic pump performance of the right ventricle, is frequently depressed at rest or during exercise in patients with chronic obstructive pulmonary disease (COPD). The most common cause of reduced RVEF in COPD is augmentation of right ventricular afterload, namely an increase in pulmonary artery pressure and pulmonary vascular resistance. Therapy with agents that decrease the afterload on the right ventricle have the potential to improve the systolic performance of this chamber. Oxygen, vasodilators such as hydralazine and nifedipine, theophylline, and sympathomimetics all may augment RVEF in part by reducing pulmonary vascular resistance and, in some cases, pulmonary artery pressures in patients with COPD and cor pulmonale. However, only oxygen therapy has been shown to improve survival.

For many years, little was known of the function of the right ventricle, which was overwhelmed by its muscular neighbor, the left ventricle.1,4 However, over the past 15 to 20 years, right ventricular function has been shown to be important in such diseases as chronic obstructive pulmonary disease (COPD), pulmonary thromboembolism, and right ventricular ischemia secondary to coronary artery disease.1,4 In this article, an update of previous reviews by our group,1,4 we discuss right ventricular function at rest and during exercise in normal subjects and in patients with COPD. We also discuss the results of studies designed to favorably alter cardiovascular-pulmonary hemodynamics and right ventricular function in COPD through therapeutic intervention.

The Normal Right Ventricle

Interrelationships between the Pulmonary Vasculature and the Right Ventricle

Bordered by the concave free wall and the convex interventricular septum, the right ventricle is a crescent-shaped chamber with a thin lateral free wall and greater volume and surface area than the left ventricle (Fig 1).3,4 The right ventricle's geometric configuration enables it to eject relatively large volumes of blood with minimal myocardial shortening.4-6 The pulmonary vasculature provides low resistance to right ventricular outflow under normal circumstances, with approximately one tenth of the resistance to flow of the systemic vascular bed.6-7 Because the pulmonary vascular bed reacts to wide variations in blood flow without much change in pressure, the right ventricle is normally not pressure overloaded. Normally, increased output from the right side of the heart isaccommodated by recruitment of previously nonperfused vessels in the suprerior portion of the lung, and by distention of vessels in the more dependent portions of the lung.6,8 In several diseases, the pulmonary vasculature cannot be recruited; therefore, pulmonary artery pressures are elevated (Fig 2) and the right ventricle dilates and hypertrophies; and cor pulmonale and right-sided failure develop.2-3 This effect occurs because the right ventricle cannot accommodate the high intracavitary pressures induced by increases in pulmonary artery pressure and pulmonary vascular resistance.2-3

Right Ventricular Responses to Acute Increases in Afterload

Early studies showed that when the right ventricle becomes nonfunctional, resting hemodynamics and cardiac output remain unchanged.8 These results imply that the right ventricle is a passive conduit with only a minor role in maintaining cardiac output.8 Later studies, however, have shown that right ventricular performance becomes impor-

![Figure 1. The anatomic relationship of the right ventricle (RV) to the left ventricle (LV), showing the globular shape of the left ventricle and the half moon shape of the right ventricle. (Adapted with permission from Guyton AC: The systemic and pulmonary circulations. In: Guyton AC. Human physiology and mechanisms of disease. 4th ed. Philadelphia: WB Saunders, 1987:124.)](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21646/ on 05/29/2017)
To maintain cardiac output, the right ventricle, by the Frank-Starling mechanism, enlarges, thereby increasing its preload.\textsuperscript{5,6,13} Hypertrophy develops, allowing the stress on the right ventricular wall to normalize and improving ejection performance.\textsuperscript{8} Even when myocardial contractility is depressed, normal hemodynamics can be maintained by compensatory dilatation and hypertrophy.\textsuperscript{6,11,13,14}

The right ventricle also may respond in part to increased afterload by augmenting contractility.\textsuperscript{5,6} Like the left ventricle, the right ventricle responds to positive inotropes.\textsuperscript{18} At any preload or afterload, right ventricular stroke volume is enhanced by catecholamine stimulation. Thus, with either acute or chronic elevations of pulmonary artery pressure, reflex activation of the sympathetic nervous system maintains ventricular function.\textsuperscript{18} Moreover, in hypoxemic patients with pulmonary disease, acidosis and other stimuli increase circulating catecholamines.\textsuperscript{18}

**Right Ventricular Performance at Rest and during Exercise in COPD**

In the United States, COPD most commonly culminates in right ventricular dysfunction more than any other pulmonary disease.\textsuperscript{9} Several investigators have studied pulmonary hemodynamics and right ventricular performance in patients with COPD at rest and during exercise.\textsuperscript{18-18} Using the first-pass radionuclide technique, Matthey et al\textsuperscript{18} measured right and left ventricular ejection fractions at rest and during upright bicycle exercise in 30 patients with COPD and in 25 normal control subjects. The normal response to

**Figure 2.** Mean pulmonary artery responses to increasing cardiac output. Note that the normal pulmonary vascular bed can tolerate an increase in cardiac output (pulmonary blood flow) of 250% without an increase in pulmonary artery pressure. In contrast, even a small augmentation in cardiac output causes a large increase in pulmonary artery pressure in patients with a restricted pulmonary vascular bed. (Reproduced with permission from Robin Ed, Gaudio R. Cor pulmonale. Disease-A-Month. May 1970.)

**Figure 3.** Right ventricular (RV) and left ventricular (LV) ejection fraction at rest and exercise in normal control subjects and in patients with chronic obstructive pulmonary disease (COPD). (A, left two): Fourteen normal control subjects exercised using a maximal graded protocol, and 11 subjects exercised using a single-stage submaximal protocol. Both right and left ventricular ejection fractions increased by 5% in each subject, irrespective of the exercise protocol. On the basis of these data, normal exercise ventricular reserve is defined as an absolute increment in ejection fraction of at least 5%. (B, right two): Right ventricular (RV) and left ventricular (LV) ejection fractions at rest and submaximal exercise in 30 patients with COPD. Data in individual patients are shown as closed circles connected by solid lines. The mean values are shown at the sides of each panel. For the overall group, RV ejection fraction was unchanged with exercise, whereas LV ejection fraction increased normally. (Reproduced with permission from Matthey RA, Berger HJ, Davies RA, Loke J, Mahler DA, Gottschalk A, et al. Right and left ventricular exercise performance in chronic obstructive pulmonary disease: radionuclide assessment. Ann Intern Med 1980; 93:234-39.)
exercise was at least a 5% absolute increase in the ejection fraction of each ventricle (Fig 3A). Right ventricular ejection fraction (RVEF) was abnormal at rest in 8 of the 30 patients with COPD; however, 23 patients had abnormal right ventricular response to submaximal exercise (Fig 3B). Airway obstruction and arterial hypoxemia were significantly more severe in patients with abnormal right ventricular exercise reserve than in patients with normal reserve. Left ventricular performance was abnormal at rest in only 4 patients and during exercise in only 6 patients (Fig 3B). A restricted, relatively nonrecruitable pulmonary vascular bed with inordinately high pulmonary artery pressures was considered the most likely mechanism for the failure of RVEF to increase normally with exercise.16

Brent et al17,18 from the same group evaluated the afterload dependence of the right ventricle in patients with COPD. These investigators found that in 20 patients with COPD, RVEF at rest was inversely related to mean pulmonary artery pressure, peak pulmonary artery pressure, and pulmonary vascular resistance (Fig 4). Right ventricular contractility, measured by load independent indices did not correlate with RVEF, which is load dependent and, therefore, likely a poor indicator of intrinsic contractility.17 RVEF may be depressed in the setting of pulmonary artery hypertension, although contractility is normal. If afterload is lowered, ejection fraction normalizes.4

To further test the hypothesis of afterload dependence of the right ventricle, Mahler et al16 exercised 12 patients with COPD and measured pulmonary artery pressures, cardiac output, and right and left ventricular ejection fractions. In this invasive study, augmented afterload (ie, elevations in pulmonary artery pressures) on the right ventricle appeared to be the major factor in the failure of the mean right ventricular ejection fraction to increase. The results established that during exercise, patients had an inordinate rise in mean pulmonary artery pressure plotted against cardiac index (Fig 5). To ascertain whether the increase in pulmonary artery pressures might be related to changes in intrathoracic pressure during exercise, an esophageal balloon was placed in each patient to correct for transthoracic pressures. After correction for transthoracic pressures, there was a persistent, inordinately elevated pulmonary artery pressure. Mahler et al16 also noted that pulmonary vascular resistance rose rather than fell normally with exercise (349 dynes·sec·cm⁻² at rest and 740 dynes·sec·cm⁻² during exercise). These acute elevations in both pulmonary artery pressure and pulmonary vascular resistance led to an adaptive rise in preload as

**Figure 4.** Right ventricular ejection fraction (RVEF [%]) shown on the ordinate is highly dependent on right ventricular afterload. (A, left two): Two measures of afterload, peak pulmonary arterial systolic pressure (PPASP) and pulmonary vascular resistance index (PVR), are plotted on the abscissa against RVEF. For 20 patients (n = 20), there is a significant inverse correlation between RVEF and the measurements of afterload. (Reproduced with permission from Brent BN, Berger HJ, Matthey RA, Mahler DA, Feilik L, Zaret BL. Physiologic correlates of right ventricular ejection fraction in chronic obstructive pulmonary disease; a combined radionuclide and hemodynamic study. Am J Cardiol 1982; 50:235-62.) (B, right): Relation between mean pulmonary artery pressure (PAP) and right ventricular (RV) ejection fraction in 30 patients with chronic obstructive pulmonary disease. (Reproduced with permission from Brent BN, Mahler DA, Matthey RA, Berger HJ, Zaret BL. Noninvasive diagnosis of pulmonary arterial hypertension in chronic obstructive pulmonary disease: right ventricular ejection fraction at rest. Am J Cardiol 1984; 53:1349-53.)

**Figure 5.** Relationship between resting (circles) and exercise (X) cardiac index and mean pulmonary artery pressure (Ppa) in patients with chronic obstructive pulmonary disease. Note that 7 of 10 patients had a normal resting Ppa (=20 mm Hg), but 9 of 10 developed an elevated Ppa with exercise contrasted with the expected rise (ie, the normal range plotted in the figure). Reproduced with permission from Mahler DA, Brent BN, Loke J, Zaret BL, Matthey RA. Right ventricular performance and central circulatory hemodynamics during upright exercise in patients with chronic obstructive pulmonary disease. Am Rev Respir Dis 1984; 130:722-29.)
measured by an increase in right ventricular end-diastolic volume. Thus, to sustain cardiac output, the right ventricle dilated according to the Frank-Starling mechanism.

Although the cause of augmented afterload in patients with COPD has not been established clearly, by its potent pulmonary vasoconstrictor effect, hypoxemia appears to be a major factor leading to pulmonary hypertension. Pulmonary vascular destruction may be an additional factor in patients with COPD. Ultimately, chronic remodeling of the pulmonary vascular bed leads to reduced recruitability of the pulmonary blood vessels and hence to pulmonary hypertension first at exercise and eventually at rest (Fig 2).

**Right Ventricular and Pulmonary Vascular Responses to Therapeutic Intervention in COPD**

**Oxygen**

*Results of Trials:* Two main goals of oxygen therapy are to relieve tissue hypoxia and to improve survival. The studies from both the National Institutes of Health (NIH) in the United States and the Medical Research Council (MRC) of the United Kingdom showed that long-term oxygen therapy improves the survival rate of hypoxemic patients with COPD. The mechanisms for the improved survival remain unclear and are the subject of controversy. The hypoxic vasoconstriction-pulmonary hypertension hypothesis of mortality in patients with COPD and cor pulmonale implies that oxygen therapy would decrease mortality by retarding the progression of pulmonary hypertension. Yet, after 6 months of therapy, pulmonary vascular resistance decreased only slightly in patients receiving continuous oxygen in the NIH trial and remained unchanged in the MRC trial in patients receiving half-day oxygen. Recently, Weitznbaum et al reported decreases in mean pulmonary artery pressure of 2.15 mm Hg/yr in 12 of 16 severely hypoxemic patients with COPD undergoing oxygen therapy for 1 to 6 years, a longer follow-up period than the NIH and British studies. Before oxygen therapy was started, mean pulmonary artery pressure had been increasing by 1.47 mm Hg yearly in these patients. Thus, oxygen therapy clearly retards the progression of pulmonary hypertension in previously untreated patients with COPD. Whether this hemodynamic improvement contributes to the survival effect of oxygen therapy remains to be established.

Two recent studies suggest that hemodynamic changes account at least in part for improved survival in patients with COPD. Follow-up statistical analysis of the data from the NIH trial by Timms et al indicates that decreases in mean pulmonary artery pressure within the first 6 months of therapy were related to subsequent survival. Also, improvement in pulmonary vascular resistance was associated with improved cardiac function as shown by increased stroke volume index in patients treated with continuous oxygen in the NIH trial. A study by Ashutosh et al provides further support to the concept that oxygen-related hemodynamic changes are associated with and are predictive of outcome. These investigators divided 28 patients with stable COPD and cor pulmonale into 2 groups on the basis of response of the mean pulmonary artery pressure to breathing 28% oxygen for 1 day. Patients whose mean pulmonary artery pressure decreased at 5 mm Hg after short-term oxygen breathing were considered “responders.” All patients received long-term continuous oxygen therapy (2 L/min) subsequently. At 2 years, 88% of the responders were alive, whereas only 11% of the nonresponders survived. These data suggest that the acute effects of supplemental oxygen on pulmonary hemodynamics in hypoxic COPD can predict a subset of patients who are likely to benefit from long-term continuous oxygen therapy.

A study by Olvey and colleagues showed that low-flow oxygen therapy can improve the RVEF response to exercise in some patients with COPD, although maximum exercise performance did not improve.

Of practical importance for the consideration of supplemental oxygen therapy for exercise, the weight of portable oxygen systems apparently does not significantly increase the metabolic demand of exercise (6.7% increase in carbon dioxide production), nor does the added weight negate the improved arterial oxygen saturation provided by oxygen breathing during exercise.

**Recommendations for Oxygen Therapy:** The NIH and MRC clinical trials clearly established that long-term oxygen therapy improves both neuropsychologic function and survival in hypoxemic patients with COPD, although the physiologic mechanisms for these benefits are as yet unclear. Accordingly, based on these studies, patients with COPD should be started on a regimen of long-term “continuous” nasal oxygen therapy if the resting PaO remains less than 55 mm Hg after a 3-week stabilization with maximal medical therapy (eg, bronchodilating agents, angiotensin-converting enzyme inhibitors, and diuretics). Moreover, patients with a PaO above 55 mm Hg should be considered for oxygen therapy if they have polycythemia or clinical evidence of pulmonary hypertension and cor pulmonale; however, persistent hypoxemia after a stabilization period must be documented in these patients. In the NIH trial, 45% of hypoxemic patients initially selected for the study improved enough during 3 to 4 weeks of observation to suspend plans for long-term oxygen therapy.

In fact, a more recent study suggests that an even longer period of 2 to 3 months may be necessary to exclude patients who eventually achieve acceptable PaO values with medical therapy alone. This strategy, however, risks inappropriate or harmful delay in starting oxygen therapy in some patients. Finally, oxygen therapy may be important in patients with an arterial Po2 of 55 mm Hg or less only during exertion or during sleep associated with a disturbed sleep pattern, cardiac arrhythmias, or pulmonary hypertension. Both groups of patients should receive supplemental oxygen therapy, although its long-term benefits remain unproven.

**Digitals**

Digitalis therapy has not been found to improve right ventricular function at rest or during exercise in patients with COPD except where there is coexisting left ventricular failure. The cardiac glycosides augment contractility of the right ventricular myocardium; however, they also produce pulmonary vasoconstriction. As a result, the effect of digitals on right ventricular performance is complex and depends partially on the influences of increased ventricular contractility opposed by a possible increase in right ventricular afterload. Moreover, digitalis therapy in patients with
COPD and cor pulmonale is associated with an increased frequency of untoward side effects such as cardiac arrhythmias. Although the reason for this is unclear, hypoxemia appears to have a significant effect. Although hypoxia alters digitalis disposition, it does not increase myocardial digitalis concentration in dogs. Thus, changes other than heart tissue concentration may account for decreased digitalis tolerance during hypoxemia.

In summary, except in patients with concurrent left ventricular dysfunction, digitalis therapy apparently does not enhance cardiac function or exercise performance in patients with COPD and cor pulmonale. Whether digitalis may have favorable effects when used in combination with other medications, including theophylline, vasodilators, selective β-adrenergic agents, and oxygen, has not been assessed fully.

Vasodilators

General Considerations: Because systemic vasodilating agents are efficacious in the management of left ventricular failure, their potential role in treating disorders characterized by pulmonary artery hypertension and chronic cor pulmonale has been widely studied. The early enthusiasm for using these agents in patients with primary pulmonary hypertension has lessened as it has become clear that only a small fraction of affected patients have long-term beneficial hemodynamic responses. Pulmonary hypertension secondary to COPD differs from primary pulmonary hypertension in many respects, including the fact that active hypoxic vasoconstriction is an established causal factor in COPD. Thus, the current pessimism about the efficacy of vasodilator therapy for primary pulmonary hypertension has not prevented continued, active investigation into such therapy in patients with COPD.

Rubin, Packer, and Klinger and Hill have elucidated the major potential adverse effects of vasodilators in pulmonary hypertensive disorders. These effects include systemic hypotension, decreased arterial oxygen saturation, and decreased cardiac output. Assessing the studies of vasodilator therapy in patients with COPD is difficult because of the complex hemodynamic changes that occur and the uncertainty about which changes are beneficial and which are not. Thus, although reduction in pulmonary hypertension is a frequently stated goal of vasodilator therapy, a decrease in pulmonary vascular resistance with therapy may be offset by a rise in cardiac output, leaving pulmonary artery pressure unchanged. This effect may be beneficial (e.g., increased oxygen transport) despite the unrelieved pulmonary hypertension. In contrast, nitroglycerin therapy, which reduces venous return, or nifedipine therapy, which depresses right ventricular function, may decrease pulmonary artery pressures by lowering cardiac output. This effect may not be beneficial even though pulmonary artery pressures are reduced. Long-term studies to determine what constitutes a beneficial hemodynamic response to vasodilators are needed.

Regardless of the hemodynamic response, vasodilator therapy has not been shown to improve survival in patients with pulmonary hypertension secondary to COPD.

Hydralazine, Nitrates, Nifedipine: Most studies of vasodilator therapy in patients with COPD have utilized hydralazine, a nitrate (e.g., nitroprusside, nitroglycerin), or a calcium channel blocker such as nifedipine.

Figure 6. Effect of aminophylline on right and left ventricular performance in 15 patients with COPD. Data obtained during the control state and at conclusion of aminophylline infusion (solid circles connected by solid lines). Patients with cor pulmonale are noted by dashed lines. (Reproduced with permission from Matthay RA, Berger HJ, Lake J, Gottschalk A, Zaret BL. Effects of aminophylline on right and left ventricular performance in chronic obstructive pulmonary disease: noninvasive assessment by radionuclide angiocardiography. Am J Med 1978; 65:903-10.)

Figure 7A. Short-term cardiovascular and oxygenation effects of subcutaneous terbutaline in patients with COPD. (Left): Right ventricular (RV) and (right) left ventricular (LV) ejection fraction in 8 patients with chronic obstructive pulmonary disease before and after administration of terbutaline. The ejection fraction of each ventricle increased significantly with terbutaline. C: control state; T, 30 min after terbutaline administration.
Results of studies of hydralazine have been mixed. Some studies claim to show a beneficial hemodynamic effect; others indicate that the effect is limited or even detrimental. Brent et al reported that oral hydralazine therapy reduced pulmonary vascular resistance and augmented both cardiac output and RVEF while pulmonary artery pressure and arterial oxygen tension were unchanged in patients at rest with pulmonary hypertension secondary to COPD. Rubin and Peter found that in patients with COPD and cor pulmonale, oral hydralazine therapy increased resting and exercise cardiac output, narrowed the arteriogenous oxygen difference, and reduced both mean pulmonary artery pressure and pulmonary vascular resistance. Lupi-Herrera and co-workers reported that this therapy improved cardiac output and mixed venous oxygen saturation, but did not change pulmonary artery pressure or pulmonary vascular resistance. Finally, DalNogare and Rubin reported that hydralazine therapy lowered both mean pulmonary artery pressure and pulmonary vascular resistance during exercise and augmented maximum cardiac output and mixed venous oxygen tension. Of interest, though, maximum oxygen consumption did not change because patients were apparently limited by ventilatory factors.

In general, the hemodynamic effects of hydralazine in patients with COPD appear to be superior to those of both nitroprusside and nitroglycerin. Brent and co-workers showed that nitroglycerin and nitroprusside reduced preload, cardiac index, and arterial oxygen tension and content and hence systemic oxygen delivery. In contrast, hydralazine reduced pulmonary vascular resistance and increased right ventricular ejection fraction, cardiac index, and systemic oxygen delivery.

The effect of nifedipine therapy in patients with COPD continues to receive considerable interest. This agent often produces an acute drop in pulmonary vascular resistance and an increase in cardiac output. In many instances, pulmonary artery pressure decreases; however, this effect is inconsistent and usually slight. Studies using an exercise protocol showed that nifedipine therapy generally reduces pulmonary vascular resistance and pulmonary artery pressure while improving cardiac output and oxygen delivery. Yet, exercise capacity, itself, may not improve perhaps because exercise is limited in patients with COPD more by ventilatory factors than by cardiovascular dysfunction. Moreover, the favorable resting and exercise vasodilatory effects of nifedipine may not be sustained long term. Agostoni and colleagues showed that nifedipine therapy in patients with COPD acutely reduced pulmonary pressure and vascular tone, but the effects were not sustained after 8 weeks of therapy, and treatment with the medication was not well tolerated. Moreover, although hemodynamics returned to baseline, oxygen therapy no longer reduced pulmonary artery pressure to the degree seen at baseline prior to nifedipine therapy. Also, evidence suggests that the major pulmonary action of nifedipine, inhibition of hypoxic vasoconstriction, may not be sustained long term.

Recommendations for Use and Selection of Vasodilators in COPD: Only when conventional therapy and oxygen have failed to alleviate signs of right ventricular failure or pulmonary hypertension in patients with COPD should vasodilator medications be considered. Because of the potential adverse consequences of these agents, their effects on hemodynamics and oxygenation must be assessed in individual patients; this assessment usually requires invasive right heart catheterization.

As stated above, Rubin has suggested the following preliminary guidelines as to what constitutes a beneficial hemodynamic response to vasodilator therapy: (1) pulmonary vascular resistance is lowered by at least 20%, and (2) cardiac output is increased or unchanged, (3) pulmonary artery pressure is decreased or unchanged, and (4) systemic blood pressure is not significantly reduced (eg, no side effects). After these benefits are established and the patient has begun on a therapeutic regimen of a particular medica-
tion, right ventricular catheterization should be repeated after 4 to 6 months of continued therapy to ascertain whether the hemodynamic benefits persist.

**Theophylline**

Theophylline therapy has been shown to have favorable cardiovascular effects in patients with COPD, with or without cor pulmonale. In early studies by Parker and colleagues of intravenous aminophylline in 9 patients with cor pulmonale secondary to COPD, mean pulmonary artery pressure decreased significantly from 39 to 25 mm Hg with a concomitant reduction in right and left ventricular stroke work; cardiac index, arterial oxygen saturation, and oxygen consumption were unchanged. In 1978, Matthay et al reported the acute effects of intravenous aminophylline on biventricular ejection fraction in 15 patients with COPD, of whom had cor pulmonale (Fig 6). In 6 of 8 patients with initially depressed right ventricular performance, RVEF normalized; left ventricular ejection fraction (LVEF) also improved. This improvement in biventricular function was accompanied by only minimal improvement in forced expiratory volume in 1 s (FEV), and arterial oxygen tension remained unchanged. Moreover, in a control group of normal subjects, both RVEF and LVEF improved significantly with no change in flow rates. These results suggest that aminophylline therapy can improve biventricular performance without improvement in flow rates.

A subsequent study by Matthay and colleagues evaluated the long-term consequences of oral theophylline therapy on right and left ventricular function in patients with COPD. In 11 patients treated for an average of 4 months, RVEF persistently improved and LVEF increased modestly as well.

Postulated mechanisms for this apparent improvement in systolic ventricular pump performance following theophylline administration include reduced right ventricular afterload (lowered pulmonary and systemic vascular resistance) and enhanced myocardial contractility.

**Sympathomimetic Agents**

β-receptor agonists dilate the pulmonary vasculature as well as the systemic vasculature; these agents, therefore, might reduce ventricular afterload and improve cardiovascular function. Brent et al examined 8 patients with severe COPD without reversible bronchospasm to determine the short-term hemodynamic effects of 0.25 mg of subcutaneous terbutaline. All patients had mild to moderate pulmonary artery hypertension and abnormal baseline right ventricular function. After treatment, pulmonary vascular resistance fell in all patients, whereas right ventricular end-diastolic volume index and mean pulmonary artery pressure remained the same. Both right and left ventricular ejection fractions rose significantly with terbutaline therapy (Fig 7A). Cardiac index also significantly improved without change in arterial oxygen tension or content. As a result, systemic oxygen delivery and mixed venous oxygen tension increased (Fig 7B). Two other studies reported similar findings. In these studies, intravenous terbutaline therapy increased cardiac output, while reducing pulmonary vascular resistance at rest. In one of these studies, these favorable changes also occurred with exercise. In a recent double-blind, crossover study, Chan and colleagues administered 5 mg of terbutaline orally to patients with COPD and found that the biventricular ejection fractions of treated patients improved slightly.

MacNee et al showed that another β-agonist, pirbuterol, also produced similar favorable hemodynamic changes. The drug was administered orally and the salutary effects were noted during 6 weeks of treatment.

These salutary cardiovascular effects of β-agonists most likely result from pulmonary vasodilation after stimulation of β-adrenergic receptors. Also, improved myocardial performance through direct inotropic action may play a role.

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