The singular function of the right ventricle, left ventricle, and the lungs will be discussed elsewhere. Nonetheless, particularly in the field of congenital heart disease, we are becoming increasingly aware of the importance of the interactions between them. There is continual cross talk between the two sides of the heart, and in turn, the ventricles are continually responding to subtle changes occurring within the thorax as a whole. In this chapter, these interactions, and their modification by congenital heart disease and its surgical repair, will be discussed.

### COMPARISON OF RIGHT AND LEFT HEART HEMODYNAMICS

The average cardiac output from the right ventricle must, of course, essentially equal the cardiac output from the left heart. Nonetheless, the mechanism by which this is achieved is very different. The right ventricle performs approximately one quarter of the external mechanical work compared with its left ventricular counterpart. External mechanical work is a function of stroke volume and developed ventricular pressure, and is more accurately described as the area enclosed by the ventricular pressure–volume curve. Figure 22.1 shows a schematic comparison of left and right ventricular pressure–volume curves. Not only is the developed pressure substantially lower in the right ventricle, but its trapezoidal shape still further reduces the amount of work performed on the circulation to generate the cardiac output. The left ventricle essentially works as a square wave pump, its stroke work being reasonably well represented as a direct product of its stroke volume and developed pressure (stroke work = stroke volume \times peak left ventricular pressure – minimum left ventricular pressure). Because of its ability to eject blood into the pulmonary circulation during both pressure rise and pressure fall (1), the external work performed by the right ventricle cannot be described using such a simple derivation. Furthermore, it can be seen that small changes in hemodynamics might impose a major change to global workload of the right ventricle. Indeed, small changes in right ventricular afterload can lead to major changes in workload and the shape of the pressure–volume characteristics to mirror the left ventricle (2).

The trapezoidal shape of the right ventricular pressure–volume relationship is exquisitely matched to the low hydraulic impedance imposed by the pulmonary vascular bed. Unlike the systemic vascular resistance, which reflects a dynamic balance between vasodilatory and vasoconstrictor influences, the pulmonary vascular bed appears to be maximally vasodilated. The low pulmonary vascular resistance requires a healthy endothelium and normal lung function for its integrity. In health, additional inhaled nitric oxide, for example, fails to lower the pulmonary vascular resistance, suggesting pulmonary endothelial vasodilatory capacity is at its maximum (3). This is a markedly different mechanism to that of the systemic vascular bed where a wide portfolio of vasodilatory substances can lower its resistance. The pulmonary vascular bed is also uniquely affected by external factors. The status of lung inflation, even the normal circulation, has major effects on the pulmonary vascular resistance and hemodynamic function. Normal respiration, ventilating around functional residual capacity, minimizes the pulmonary vascular resistance. Underinflation of the lungs leads to an increased pulmonary vascular resistance, as a result of atelectasis and secondary alveolar hypoxemia, and overinflation of the lungs leads to an increase, secondary to alveolar stretch and direct vascular compression (Fig. 22.2) (4). Both should be avoided whenever right ventricular afterload needs to be minimized.

### CARDIOPULMONARY INTERACTIONS IN THE NORMAL CIRCULATION

Descent of the diaphragm during normal inspiration leads to a modest fall in pleural pressure (3 to 5 cm of water) (5) and a concomitant rise in intra-abdominal pressure. These two changes lead to increased venous return and an increased right ventricular stroke volume, in accord with the Frank Starling mechanism. There is thus a waxing and waning of cardiac output of approximately 10% to 15% during the cardiac cycle (6).
The classic experiments of Courmand in the 1940s (7) were interpreted as confirmation that right heart filling and cardiac output were related to intrathoracic pressure. Positive-pressure ventilation via a mask in conscious volunteers led to a fall in cardiac output of approximately 10% to 15%. This was initially thought to be entirely due to changes in systemic venous return (and reduced ventricular preload) imposed by a raised mean intrathoracic pressure. It has subsequently become clear that reduced preload, as a result of increased airway pressure, is not the whole story. In an elegant series of experiments in dogs, Henning (8) showed that restoration of preload during positive-pressure ventilation failed to restore cardiac output to its baseline levels. The persistent reduction in right ventricular stroke volume, despite normalized preload, suggested an adverse effect on intrinsic right ventricular performance. It was hypothesized that the right ventricle shows signs of reduced systolic function, even under the circumstances of a modest hemodynamic burden imposed by lung hyperinflation, as a result of increased afterload occurring via the mechanism described in Figure 22.2. No matter what the mechanism, however, the functional implications of these changes are not simply theoretic. In a study of children undergoing cardiac catheterization performed by Shekerdemian et al. (9), a negative-pressure cuirass device was used to mimic normal ventilation to compare the effects of positive-pressure and negative-pressure ventilation on cardiac output. In essentially normal children having undergone closure of a small arterial duct, for example, there is an approximate 16% fall in cardiac output, simply as a result of a modest rise in mean airway pressure (to approximately 8 cm of water) secondary to positive-pressure ventilation. These adverse hemodynamic effects of increased right ventricular afterload (negative cardiopulmonary interactions) become even more important when the right heart circulation is affected by congenital heart disease.

Cardiopulmonary Interactions in Congenital Heart Disease

Given that normal right heart function is dependent on a low right ventricular afterload, normal ventricular preload, and maintained right ventricular systolic function, it would be surprising if congenital heart diseases did not have major effects on its performance. This is indeed the case.

Reduced Right Ventricular Contractile Performance

It has long been known that right ventricular ischemia, in the setting of atherosclerotic coronary disease, is an extremely poorly tolerated hemodynamic burden (10). This, in part, is related to adverse right-left heart interactions (see below), but illustrates the importance of right ventricular contractile performance, even in the presence of a relatively normal pulmonary vascular bed. A more common scenario in congenital heart disease is the adverse effect of cardiopulmonary bypass on right heart function. Brookes et al. (11) showed that even a brief period of cardiopulmonary bypass and cardioplegic arrest, during coronary bypass surgery, leads to a significant decline in right ventricular systolic performance, as assessed by end-systolic elastance. This translates to an even greater dependence on cardiopulmonary interactions in children undergoing congenital heart surgery. Shekerdemian (9), in the study described above, showed that positive-pressure ventilation had an even greater adverse effect in such patients. Compared with negative-pressure ventilation, there was on average a 25% fall in cardiac output with positive-pressure ventilation in children on the intensive care unit after simple right heart surgery (ventricular septal defect [VSD], atrial septal defect [ASD], etc.).

CARDIOPULMONARY INTERACTIONS AND THE ABNORMAL RIGHT HEART

The potential for beneficial and adverse cardiopulmonary interactions is greater when the right heart is intrinsically abnormal because of congenital anomalies or is primarily affected by surgery. There are two circumstances in which these concepts are exemplified, those patients with abnormal right ventricular diastolic function and those with...
exclusion of the right ventricle from the venopulmonary circulation.

Abnormal Right Ventricular Diastolic Function

It is now known that restrictive right ventricular physiology is a common sequel of surgery for hypoplasia of the right heart, e.g., pulmonary atresia with intact ventricular septum (12), and after repair of tetralogy of Fallot, for example. The characteristic physiology of these patients is the presence of antegrade diastolic pulmonary blood flow during atrial systole. This occurs when the resistance to right ventricular filling exceeds the pulmonary vascular resistance. Atrial contraction ejects blood through the tricuspid valve, but there is little or no right ventricular filling as the blood passes through the right ventricle (which acts as a passive conduit) to the pulmonary artery. Consequently, up to one third of the antegrade pulmonary blood flow, and therefore cardiac output, is dependent on atrial systole. Furthermore, this flow is generated by only modest pressure transients (1 or 2 mm Hg) between the right atrium and the pulmonary artery in diastole. Clearly a low pulmonary vascular resistance is crucial for this source of cardiac output to be maintained. An important element of the total pulmonary resistance, as discussed above, is the mean airway pressure. Indeed, antegrade diastolic flow is often entirely abrogated during positive-pressure inspiration. Conversely, negative-pressure ventilation may have a major beneficial effect on cardiac output. In postoperative tetralogy patients, positive-pressure ventilation reduces cardiac output by >30% compared with that achieved during negative-pressure ventilation with a cuirass device (13).

The influence of cardiopulmonary interaction is even more impressive when one considers right heart bypass procedures. Here, resting and exercise pulmonary blood flow is markedly dependent on the work of breathing. In our earlier Doppler studies, the phase relationship between ventilation and pulmonary blood flow was shown clearly in both the venopulmonary and atriopulmonary Fontan's circulations (14,15). Subsequently, MRI studies have suggested that well over one third of the cardiac output occurs as a direct result of the work of breathing (16). This may be even more important during exercise (17), particularly in those with total cavopulmonary anastomosis. Positive-pressure ventilation in the Fontan circulation has long been known to adversely affect cardiac output. In early studies of the use of positive end-expiratory pressure, a linear relationship between positive end-expiratory pressure and cardiac output was demonstrated (18). Unsurprisingly, negative-pressure ventilation under these circumstances can lead to a marked increase in cardiac output compared with positive-pressure ventilation. In a separate series of studies, Shekedemian et al. (19) showed the profound effects of positive and negative pressure ventilation on the pattern of pulmonary blood flow in the Fontan circuit (Fig. 22.3) as well as on total cardiac output measured by respiratory mass spectrometry.

These studies and others have reinforced the desirability of normal ventilation in such circulations, and this, wherever possible, should be established as early as possible after surgery. In those requiring positive-pressure ventilation, efforts to reduce the mean airway pressure will reap benefits in terms of changes in cardiac output. Thus, minimizing positive end-expiratory pressure, shortening the inspiratory time, and reducing the airway pressure plateau time will all help to reduce the hemodynamic burden on the right heart. Clearly this must not be at the expense of alveolar ventilation (to avoid hypercapnic pulmonary vasoconstriction) or alveolar inflation (to avoid hypoxemic vasoconstriction).

Exclusion of the Right Ventricle

Because of the very marked changes in right ventricular hemodynamics imposed by progressive pulmonary hypertension or right ventricular outflow tract obstruction, the effects of subtle changes in airway pressure on right ventricular intrinsic contractile performance are much less marked. Indeed, one can consider the pressure–volume relationships of the hypertensive right ventricle to be similar to those of the normal left ventricle (2). Consequently, while changes in preload will continue to occur, the effects of afterload are much less marked. Also, it should not be forgotten that the adverse effects of positive-pressure ventilation on the right heart are in contradiction to those on the left heart, particularly the failing left ventricle.

CARDIOPULMONARY INTERACTIONS AND THE LEFT HEART

Although the manifestations are different, the left ventricle is also subject to cardiopulmonary interactions and the effect of mean airway pressure on its function. Although in general the effects of increased mean airway pressure are largely adverse on the right heart, they are largely beneficial on the left heart. This is because the total afterload of the left ventricle (transmural pressure) is reduced by increased mean airway pressure (20). Although essentially insignificant to the normal left ventricle, such changes can provide beneficial effects, for example, in dilated cardiomyopathy. Indeed, continuous positive airway pressure (CPAP) has a multitude of beneficial effects on the failing left heart (21). By increasing alveolar pressure, the transalveolar gradient for edema formation is reduced. Furthermore, the afterload of the left ventricle is also reduced, improving its ejection fraction and stroke volume. Although relatively infrequently used in pediatric practice, CPAP masks have proven to be particularly useful in the dilated cardiomyopathy of ischemic and acquired heart disease in adults (22), and such therapy merits further investigation in children.
RIGHT-LEFT HEART INTERACTIONS

It has been traditional to examine left and right ventricular function as separate entities. Nonetheless, the last two decades have seen an explosion in our understanding of the ways in which the two sides of the heart interrelate and contribute to each other. Not only is this a manifestation of its shared cavity, the pericardium, but also the recognition of shared myofibers that can neither be defined as exclusively left or right ventricular (23). Thus, the function of the left ventricle has profound effects on the function of the right ventricle, and vice versa, both in health and disease.

The Effects of the Left Ventricle on the Right Ventricle

The classic experiment of Damiano et al. in 1991 (24) confirmed the presence of substantial cross talk between the ventricles in health. Albeit in an experimental model, the effects of left ventricular performance on right ventricular force generation were clearly demonstrated. In their exquisite study, the electrically isolated but mechanically contiguous ventricles were examined during individual chamber pacing (Fig. 22.4). Under these circumstances, pacing the right ventricle led to virtually no mechanical effects on the left side of the heart. Pacing the electrically isolated left ventricle, however, led to almost normal right ventricular pressure development. It appears, therefore, that the geometric change, consequent on left ventricular shortening, imposes a major mechanical effect on the right ventricle. The crescent-shaped free wall, wrapped around the ventricular septum and contiguous with the left ventricular free wall, is presumably deformed to generate a right ventricular pressure. This effect appears to be largely independent of the right ventricular free wall function. In another set of experiments, Hoffman et al. (25) showed that replacement of the right ventricular free wall with a noncontractile patch was still associated with significant right ventricular pressure generation during left ventricular contraction. Overall, it has been estimated that over one third of the work performed by the right ventricle is a direct consequence of left ventricular shortening. It might be possible to harness this ventricular-ventricular cross talk to improve biventricular function. In animal experiments, aortic constriction, leading to an increase in left ventricular afterload and work, was shown to increase right ventricular stroke volume, again as a result of the cross talk phenomenon (26).

The Effects of the Right Ventricle on the Left Ventricle

In the experiments by Hoffman et al. (25) described above, the effect of left ventricular shortening on right ventricular (RV) pressure development in a model of RV free wall replacement was described. This experiment also showed that as the size of the artificial right ventricle was increased, there appeared to be an adverse effect on left ventricular mechanical function. As the right ventricle dilated, left ventricular pressure development fell. Whether this was a parallel effect (reflecting adverse ventricular cross talk) or a series effect (reflecting reduced cardiac output from the right ventricle and therefore reduced preload to the left ventricle).
ventricle) could not be determined in these experiments. In the mid-1990s, Brooks et al. (27) aimed to dissect out these influences in a porcine model. Isolated right ventricular ischemia was used to induce acute right heart dilation, during which right and left ventricular contractile performance was measured using end-systolic elastance derived from pressure-volume analysis. It was shown that right ventricular dilation imposes adverse effects on left ventricular mechanical performance directly, presumably owing to geometric changes influencing left ventricular contractile efficiency. These effects were more manifest when the pericardium was intact, supporting this hypothesis.

It would be naive to assume that all of these effects are manifestations purely of systolic interactions. Independent of major changes in contractile performance, adverse diastolic ventricular-ventricular interaction is frequently encountered. Primarily a manifestation of septal shift toward the left ventricle in early diastole, pulmonary hypertension, for example, leads to reduced left ventricular early diastolic filling velocities and increased dependence on atrial systole (28).

The superimposition of congenital heart disease and the effects of surgical correction further amplify these ventricular-ventricular effects and will be discussed below.

### Right-Left Heart Interactions in Congenital Heart Disease

It is likely that all congenital heart diseases have more or less subtle abnormalities of ventricular-ventricular interaction. However there are some major, clinically significant interactions that bear more detailed analysis. These can loosely be described as functional and geometric and will be discussed in detail below.

#### Functional Interactions

Surgery to the right ventricular outflow tract almost invariably leads to some degree of residual pulmonary regurgitation, and it is now well known that this ventricular volume load leads to right ventricular dilation in most patients. The effects of pulmonary regurgitation after repair of tetralogy of Fallot are probably the best described example of this phenomenon. Although our understanding of the effects of right heart dilation under these circumstances have evolved over the last 15 years, it is only in the last 5 years that the biventricular effects of this problem have become apparent. Several studies have now shown a loose but linear relationship between right ventricular ejection fraction and left ventricular ejection fraction late after repair of tetralogy of Fallot (29,30). Furthermore, those with overt biventricular dysfunction have a worse outcome compared with those without (30). Not only are ventricular-ventricular interactions important in terms of global function, but abnormalities of ventricular-ventricular timing may also have significant adverse effects. D’Andrea et al. (31) have explored this phenomenon in a recent study analyzing the dysynchrony between the ventricles. They studied the onset of right and left ventricular contraction in patients after repair of tetralogy of Fallot, showing a worse exercise tolerance and an increased frequency of arrhythmia in those with significant ventricular-ventricular delay.

It is likely that subtle regional abnormalities will also have significant biventricular effects. Regional wall motion abnormalities have been described in virtually all congenital heart diseases (32,33). They are also almost always associated with decreased global performance and therefore likely biventricular effects. It remains to be seen whether this intraventricular and interventricular incoordination will be responsive to interventions such as biventricular pacing, but early data appear promising (34).

#### Geometric Interactions

Unlike the more directly functional interaction described above, acute changes in geometry can modify functional performance of both sides of the heart, particularly in congenital heart disease. Acute right heart dilation not only affects right ventricular performance, but also induces left ventricular dysfunction via systolic and diastolic interactions (see above).

More chronic geometric changes can lead to unique abnormalities in the setting of congenital heart disease. The systemic right ventricle is particularly susceptible to such changes. Here, the morphologic tricuspid valve is the systemic atrioventricular valve and is characterized by its septal papillary muscle and chordal attachments. It is now well recognized both under the circumstances of surgical repair of simple transposition and in the setting of congenitally corrected transposition that septal shift makes a significant contribution to the development of tricuspid regurgitation in these hearts. Conversely, efforts to modify this septal shift can produce profound improvements in the degree of tricuspid incompetence. Figure 22.5 shows just such a change. The right-hand panel from this

![BEFORE PA BANDING](image1)

![AFTER PA BANDING](image2)

**FIGURE 22.5** The acute effects of pulmonary artery (PA) banding on tricuspid valve regurgitation in congenitally corrected transposition. Left ventricular (LV) hypertension induces septal shift toward the systemic right ventricle (RV), leading to restoration of tricuspid leaflet apposition by its effect on its septal attachments. As a result, the left atrial (LA) size is markedly reduced. RA, right atrium.
patient with congenitally corrected transposition shows a dilated right atrium and hugely dilated morphologic left atrium as a result of severe tricuspid valve incompetence. The left-hand panel shows minimal tricuspid incompetence in the same heart, just 20 seconds later. The reduction in tricuspid regurgitation and the remarkable change in left atrial size have occurred as a consequence of pulmonary artery banding. Elevation of left ventricular pressure to modify septal geometry has been demonstrated in patients after the Mustard procedure (35) as well as in patients undergoing left ventricular retraining in the setting of congenitally corrected transpositions. It is beyond the scope of this chapter to discuss the advisability, prerequisites, and methods for evaluation of left ventricular retraining under such circumstances, but by its effects on tricuspid incompetence, pulmonary artery banding alone may be destination therapy for some of these patients.

## CONCLUSIONS

Important cardiopulmonary and ventricular-ventricular interactions are intrinsic to normal cardiovascular physiology. The consequences of these effects are amplified by disease in the structural normal heart and may be profound when the heart is modified by congenital anomalies. Our understanding of the effects of congenital heart disease on cardiopulmonary and ventricular-ventricular interactions continues to evolve, but we have learned that description of functional performance in any patient is incomplete without their consideration.

### References

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