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REVIEW ARTICLE

Cardiopulmonary interactions during mechanical ventilation in critically ill patients

T. G. V. Cherpanath · W. K. Lagrand · M. J. Schultz · A. B. J. Groeneveld

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Abstract Cardiopulmonary interactions induced by mechanical ventilation are complex and only partly understood. Applied tidal volumes and/or airway pressures largely mediate changes in right ventricular preload and afterload. Effects on left ventricular function are mostly secondary to changes in right ventricular loading conditions. It is imperative to dissect the several causes of haemodynamic compromise during mechanical ventilation as undiagnosed ventricular dysfunction may contribute to morbidity and mortality.

Keywords Mechanical ventilation · Preload · Afterload · Positive pressure ventilation · Cardiopulmonary interaction

Introduction

Intubation and mechanical ventilation is often mandatory in critically ill patients to protect the airways and to secure adequate gas exchange. Mechanical ventilation–induced haemodynamic compromise is a common finding in critically ill patients, which may contribute to mortality in the intensive care unit [1, 2]. Appreciating cardiopulmonary interactions is imperative for physicians to understand and treat critically ill patients with deleterious haemodynamic effects induced by mechanical ventilation. This review discusses the physiology of cardiopulmonary interactions in the critically ill during mechanical ventilation. Particular focus will be placed on the use of lower tidal volumes and the open lung concept as these may ameliorate mechanical ventilation–induced haemodynamic compromise.

T. G. V. Cherpanath (✉) · W. K. Lagrand
Department of Intensive Care Medicine, Academic Medical Centre, University of Amsterdam, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands
e-mail: T.G.Cherpanath@amc.uva.nl

M. J. Schultz
Department of Intensive Care Medicine, Laboratory of Experimental Intensive Care and Anesthesiology (L·E·I·C·A), Academic Medical Centre, University of Amsterdam, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands

A. B. J. Groeneveld
Department of Intensive Care Medicine, Erasmus Medical Centre, 's-Gravendijkwal 230, 3015 CE Rotterdam, the Netherlands

Historical perspective

Cardiopulmonary interactions during spontaneous breathing

A well-known cardiopulmonary interaction is pulsus paradoxus [3]. First described by Kussmaul in 1873, it refers to a decline in systolic blood pressure of more than 10 mmHg with inhalation. Since normal variation in systolic blood pressure accounts for a decrease upon inhalation of up to 10 mmHg, the term 'paradox' is somewhat misleading. It probably originates from the description of the phenomenon in patients with severe tuberculous constrictive pericarditis, in whom the radial pulse could not be palpated during inhalation despite heart sounds on auscultation. Therefore, pulsus paradoxus is best described as an *exaggeration* of normal cardiopulmonary interactions, which will be explained later on.

Mechanical ventilation

Humans breathe by 'negative pressure respiration'. With breathing the chest cavity expands by diaphragm contractions and rib cage expansions causing the intra–thoracic pressure to decrease and the lungs to expand to fill the created extra space. The resulting negative pressure of air inside the lungs creates airflow into the lungs via the upper airways, so–called inhalation. When the diaphragm and muscles attached to the rib cage relax the opposite takes

place. The positive pressure of air inside the lungs creates airflow out of the lungs via the upper airways, so–called exhalation.

Negative pressure ventilators or 'iron lungs' were mostly used to assist poliomyelitis patients during the poliomyelitis epidemics in the last century [4]. Iron lungs mimic physiological negative pressure breathing. For iron lung ventilation, patients are encased up to the neck in a cylindrical steel drum. This sealed, air–tight compartment encloses the rest of the body. Pumps periodically decrease the air pressure within the drum, causing the chest cavity to expand resulting in inspiration, followed by expiration upon air pressure increase within the drum. Although sporadically still used, 'negative pressure ventilation' has been largely replaced by 'positive pressure ventilation'.

One of the earliest descriptions of successful positive pressure ventilation was by George Poe, who induced asphyxia in dogs and brought them back to life using an artificial ventilator [5]. Positive pressure ventilation requires intubation of the upper airways using a tube that seals the trachea. The mechanical ventilator periodically pumps air into the airways and the lungs. In between, the ventilator allows air to escape from the lungs and airways. One important difference between negative pressure ventilation and positive pressure ventilation is the pressure inside the airways, existing throughout the whole breath cycle. While airway pressures are mainly negative with negative pressure ventilation, airway pressures are always positive with positive pressure ventilation. With the development of safer endotracheal tubes and easy to use mechanical positive pressure ventilators, positive pressure ventilation has become standard clinical practice and will hereafter be named mechanical ventilation.

Deleterious effects of mechanical ventilation are increasingly recognised. Already in 1974, Webb and Tierney demonstrated macroscopically visible injury to lungs of rats, especially when larger tidal volumes were used [6]. It took until the end of the 20th century till the effects of the size of tidal volumes were examined in clinical trials with shocking results. The ARMA trial showed an absolute reduction in mortality of 10 % when lower tidal volumes were compared with conventional (i.e., large) tidal volumes in patients with acute respiratory distress syndrome while maintaining a maximal airway pressure of no more than 30 cmH_2O [7]. More recent trials suggest that even patients without acute respiratory distress syndrome benefit from the use of lower tidal volumes [8–11]. Mechanical ventilation has the potential to cause lung injury through overdistension as well as repetitive opening and closing of the alveoli [12]. Lung recruitment manoeuvres are used to open up collapsed alveoli followed by application of positive end–expiratory pressure (PEEP) to keep the alveoli open: the so–called open lung concept [13]. A mechanical ventilation strategy called lung–protective ventilation combining low tidal volumes while applying the open lung concept can obviate the need for high inspiratory airway pressures. The aim of lung–protective ventilation is to prevent alveolar overdistension in open lung parts while avoiding repetitive opening and closing of alveoli in closed lung parts [14]. Lung–protective ventilation can theoretically mitigate deleterious haemodynamic effects as well, which will be discussed below.

Cardiopulmonary interactions during mechanical ventilation

The interest in the effects of mechanical ventilation really *took off* during the Second World War, when it was discovered that fighter pilots in unpressurised cockpits receiving 100 % oxygen could reach even higher altitudes when positive pressure was added to the face mask. Research at that time demonstrated a drop in right ventricular (RV) transmural filling pressure (i.e., RV preload) caused by positive pressure mechanical inflation with a simultaneous reduction in cardiac output [15]. In 1990 an inspiratory decrease in RV function, primarily caused by an increase in RV afterload, was demonstrated during mechanical ventilation [16]. A few years later, the inspiratory increase in RV impedance, a major contributor to RV afterload, was shown to correlate with the size of tidal volume used with mechanical inflation [17]. Since the incidence of RV failure is strongly related to airway pressures used during inspiration, with a significant impact on mortality, one could argue that the survival benefit seen in the aforementioned ARMA trial can be explained by a reduction in lung injury, but also by a decrease in haemodynamic compromise [18, 19].

Mechanisms

Cardiopulmonary interactions during spontaneous breathing

The heart and lungs are anatomically coupled as both are situated in the chest cavity, which results in interaction through mechanical compression as well as through changes in intra–thoracic pressure upon respiration. During inhalation, the expending lungs compress the heart in the cardiac fossa compromising preload. Upon inhalation RV preload increases since venous return, mainly determined by the pressure gradient between mean systemic filling pressure (MSFP) and right atrial pressure (RAP), is enhanced and therefore called the respiratory pump. MSFP refers to the volume in the capacitance vessels creating pressure, the so–called stressed volume. More than 70 % of total blood volume resides in the highly compliant capacitance vessels with a large portion not generating pressure, the so–called unstressed volume. Upon inhalation, negative intra–thoracic pressure is created lowering RAP as the right atrium is

highly compliant while the diaphragmatic descent increases abdominal pressure and subsequently MSFP resulting in a raised MSFP–RAP pressure gradient. The inspiration–induced rise in venous return increases RV preload and dilatation. Since the left ventricle (LV) and RV share the same pericardial space and common interventricular septum, LV compliance and filling is decreased upon inspiration through this *parallel* ventricular interdependence. Although RV stroke volume increases upon inhalation while LV stroke volume decreases, explaining the physiological inspiratory decrease in systolic arterial pressure, cardiac output has to be equivalent to venous return within a couple of heartbeats since the two ventricles pump in series: *serial* ventricular interdependence. Guyton superimposed the venous return curve on the Frank Starling curve as both are a function of RAP, and cardiac output can be estimated by the intersection of the two curves [20].

Cardiopulmonary interactions during mechanical ventilation

During inspiration, the mechanical ventilator applies positive pressure to the upper airways, which is higher than that in the alveoli, generating a flow of air into the lungs. During expiration a drop of pressure in the upper airways generates a flow of air out of the lungs. The applied positive pressure to the alveoli, also known as transpulmonary pressure, is determined by intra–alveolar pressure minus extra–alveolar pressure, the latter being equivalent to intra–thoracic pressure. The amount of air upon the present transpulmonary pressure is largely dependent on pulmonary and chest wall compliance. As depicted in the pressure–volume loop in Fig. 1, the highest pulmonary compliance is reached within the normal functional residual capacity (FRC). Noteworthy, mechanically ventilated patients can have both atelectatic and overdistended alveoli since atelectasis largely reduces the available lung capacity leading to overdistension of the remaining lung regions. It has been suggested to keep the lung operating near FRC by regularly opening the lung through lung recruitment manoeuvres and maintaining an open lung with PEEP. The opponents of this open lung concept argue that both lung recruitment manoeuvres and PEEP can cause cardiovascular compromise [21, 22]. Although true during the short term, the benefits of an open lung could benefit the circulation in the long term by optimising the RV loading conditions explained below.

Mechanical ventilation causes an inspiratory rise in positive intra–thoracic pressure opposite to negative pressure breathing during a normal human breath. Given the subsequent increase in RAP, the MSFP–RAP pressure gradient drops resulting in a decrease in venous return, which can be attenuated by a simultaneous increase in MSFP by diaphragmatic descent and venoconstriction through neurohormonal catecholamine release. The amount of rise in intra–thoracic

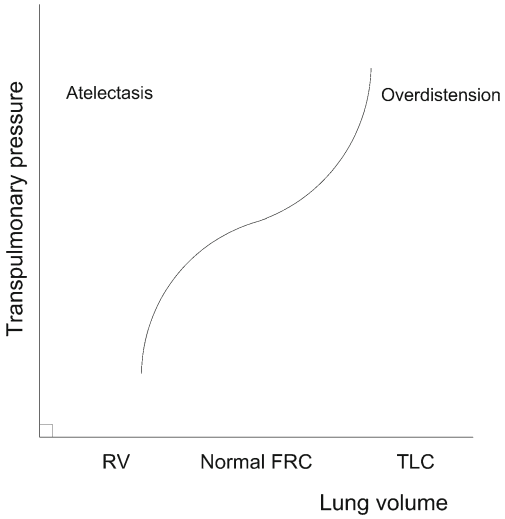

Fig. 1 Schematic representation of lung compliance shown by the pressure–volume relation in mechanically ventilated patients. In atelectatic and overdistended lung regions, more transpulmonary pressure is needed to obtain similar tidal volume compared with normal functional residual capacity (FRC). Hence, lung compliance is highest near FRC. Lung–protective ventilation aims to prevent repetitive opening and closing of alveoli in closed lung parts and alveolar overdistension in open lung parts. RV: residual volume; TLC: total lung capacity

pressure and subsequent drop in venous return and stroke volume is in part dependent on total lung volume, as depicted in Fig. 2 [23, 24]. Although RV preload is determined for the most part by intra–thoracic pressure and thus lung volume, RV afterload changes largely depend on the place on the curve shown in Fig. 3 [25, 26]. Pulmonary vascular resistance (PVR), the major determinant of RV afterload, is minimal near FRC and related to lung volume in a bimodal fashion. Atelectatic alveoli compress extra–alveolar vessels while alveolar overdistension compresses intra–alveolar vessels, both resulting in an increase in PVR.

Transpulmonary pressure is the main determinant of PVR and thus RV afterload [17]. Furthermore, atelectasis gives rise to shunting, perfused but non–ventilated lung regions, and subsequent hypoxia. Overdistension on the other hand causes dead space ventilation, ventilated but non–perfused lung regions, leading to hypercapnia. Both hypercapnia and hypoxia augment RV afterload [22, 27], which is strongly related to RV dysfunction and mortality [28]. Therefore, despite the reported short–term cardiovascular compromise, it can be well argued that maintaining an open lung is not only beneficial for preventing lung injury but also in averting RV dysfunction (Fig. 4). Moreover, it has been demonstrated that elevation of PEEP does not increase RV outflow impedance if applied according to the open lung concept with the potential of decreasing inspiratory RV outflow impedance [29]. The aim is to titrate PEEP to its lowest value while maintaining an open lung [30].

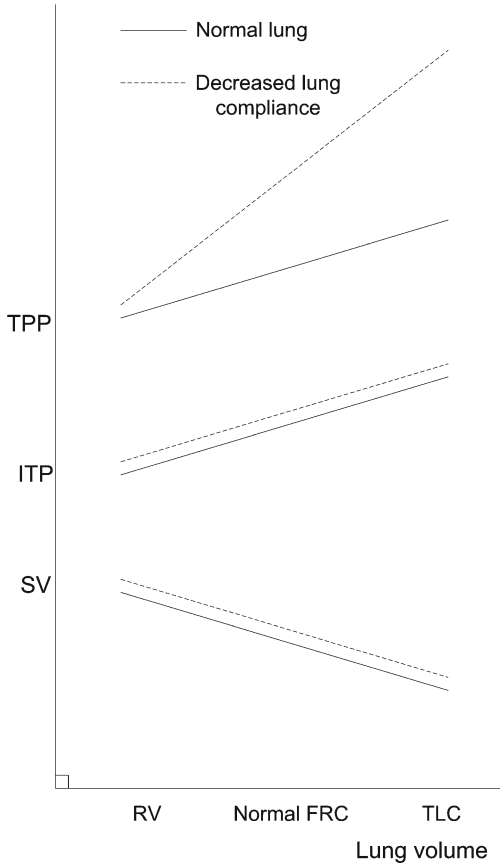

Fig. 2 A normal lung and a less compliant lung are shown with transpulmonary pressure (TPP), intra–thoracic pressure (ITP) and stroke volume (SV) displayed on the vertical axis. In the lung with decreased compliance a higher transpulmonary pressure is necessary to obtain the same lung volume compared with a normal lung. However, intra–thoracic pressures increase similarly in a normal lung as in a lung with decreased compliance as intra–thoracic pressures particularly increase linearly with lung volume despite higher transpulmonary pressures. Subsequently, decreased stroke volume occurs with increasing lung volume as a result of decreased venous return upon increased positive ITP. RV: residual volume; FRC: functional residual capacity; TLC: total lung capacity

Clinical cardiovascular effects during mechanical ventilation

The right ventricle

As RV preload and RV afterload are the main determinants of decreased cardiac output during mechanical ventilation (Fig. 5), it is crucial to decipher which component of RV loading is the primary cause of the haemodynamic compromise [31]. Preload, defined as the end–diastolic tension applied to the ventricular myocardium, is determined by transmural pressure, i.e. intramural minus extramural pressure. It is therefore possible that in the situation of increased central venous pressure during mechanical ventilation, transmural pressures and hence preload remain low in the

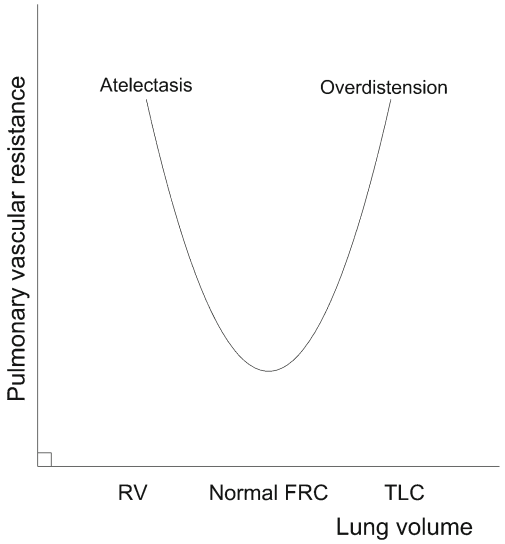

Fig. 3 Pulmonary vascular resistance (PVR), the major determinant of right ventricular afterload, is related to lung volume in a bimodal fashion. Atelectatic alveoli compress extra–alveolar vessels resulting in an increase in PVR. Overdistension of alveoli compresses intra–alveolar vessels resulting in an increase in PVR as well. Therefore the nadir of PVR is near normal functional residual capacity (FRC). RV: residual volume; TLC: total lung capacity

setting of enhanced extramural pressure and volume expansion could still be warranted. Furthermore, determining volume status using pressure recordings is hampered by the fact that the pressure–volume relationship is determined by ventricular compliance. PEEP predominantly decreases cardiac output through a decrease in preload in mechanically ventilated patients, but these effects can be minimised by

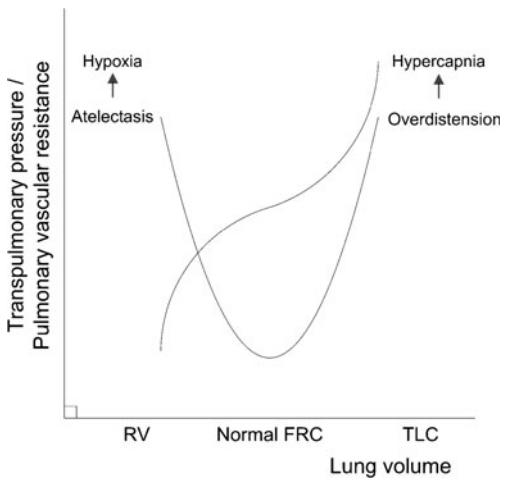

Fig. 4 As the lung is most compliant at normal functional residual capacity (FRC) as shown in Fig. 1 while the pulmonary vascular resistance (PVR) is at its nadir depicted in Fig. 3, these figures can be superimposed. Both hypoxia and hypercapnia, which are provoked by atelectasis and overdistension respectively, increase PVR. Mechanical ventilation near FRC using lung–protective ventilation is potentially able to protect against lung injury while reducing PVR and thus right ventricular afterload as well. RV: residual volume; TLC: total lung capacity

using low PEEP or by volume expansion raising MSFP [32–35]. If no effect of volume expansion occurs, RV dysfunction caused by increased RV afterload has to be ruled out. Acute cor pulmonale, defined as an RV to LV diameter ratio of more than 60 % in combination with paradoxical septal motion during systole, can be assessed by echocardiography [28, 36]. Moreover, RV outflow impedance can be measured by the mean acceleration of the pulmonary artery flow with the ultrasound beam parallel to the long axis of the main pulmonary artery [17, 29, 30, 37]. When afterload appears to cause RV dysfunction, immediate adjustments in respiratory management should be undertaken to decrease transpulmonary pressure for instance by lowering the applied airway pressures. A lung recruitment manoeuvre can be deemed necessary to lower PVR as well as improving oxygenation and ventilation. If without effect, mechanical ventilation in the prone position can be applied to improve oxygenation, reduce atelectasis and decrease RV afterload [38, 39]. Although vasodilators as phosphodiesterase inhibitors have shown to decrease pulmonary artery pressures, increased shunting occurs with decreased arterial oxygenation rendering it unsuitable for patients with hypoxia [40].

The left ventricle

During inspiration, the increase in lung volume squeezes blood out of the pulmonary bed if the intra–alveolar vessels are filled at end–expiration, increasing LV preload. Since LV afterload is in part determined by the transmural aortic pressure, positive intra–thoracic pressure, i.e. positive extramural pressure, will decrease LV afterload. The combination of increased LV preload and decreased LV afterload upon inspiration results in an inspiratory rise in LV stroke volume and subsequent systolic artery pressure termed reversed pulsus paradoxus during mechanical ventilation. Normally, throughout an entire ventilatory cycle diminished LV preload occurs following a decrease in RV stroke volume upon increased RV afterload and/or decreased RV preload resulting in a subsequent decrease in LV stroke volume. However, when severe systolic LV dysfunction is present, LV stroke volume can increase primarily mediated by the decrease in LV afterload despite a decrease in LV preload [41].

As described above, LV stroke volume will increase upon inspiration and decrease upon expiration during mechanical ventilation. The amount of change in LV stroke volume, called stroke volume variation, can shed light on the fluid status. Mechanical ventilation–induced haemodynamic changes in LV stroke volume can be very helpful in predicting the effect of volume expansion, termed fluid responsiveness [42–46]. The subject of fluid management is beyond the scope of this review.

Additional factors

Despite mechanical ventilation–mediated changes in RV loading conditions being the main determinants of decreased cardiac output (Fig. 5), many factors come into play that influence the effect of mechanical ventilation on the circulation. For instance during sepsis, when altered cardiac function, blood flow redistribution and decreased vascular resistance can occur potentiating the deleterious haemodynamic effects of mechanical ventilation [47]. Furthermore, a high respiratory minute volume is often necessary in septic patients to maintain adequate gas exchange with the potential to trap air at end–expiration called intrinsic PEEP. This is often overlooked as a possible mechanism of haemodynamic compromise during mechanical ventilation. Moreover, not only lung compliance but also chest wall compliance can affect the amount of positive airway pressure transmitted to the intra–thoracic cavity, differing hugely between patients. Decreased lung compliance often necessitates higher applied airway

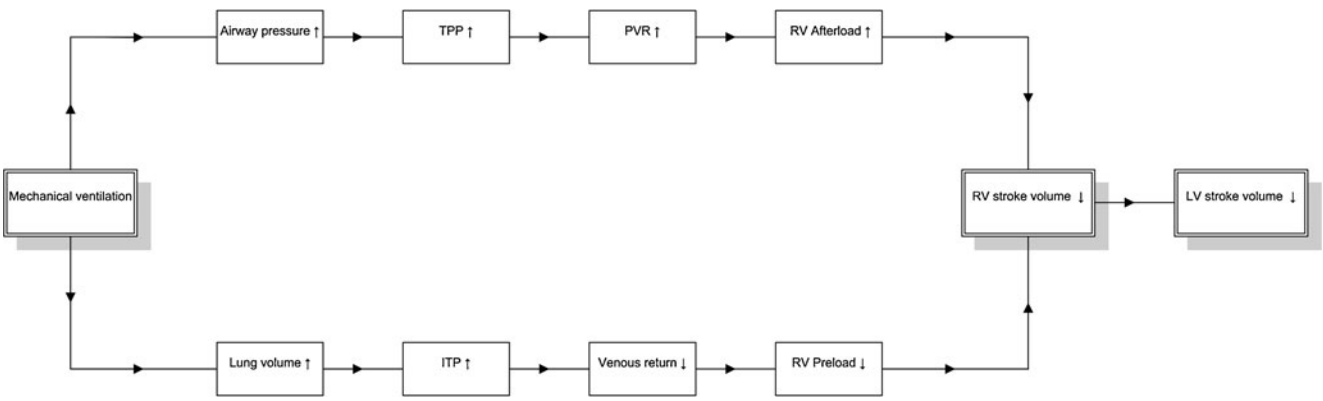

Fig. 5 Global cardiovascular effects of mechanical ventilation. Mechanical ventilation primarily affects the right ventricle (RV) and secondarily the left ventricle (LV) as the ventricles pump in series. When lung–protective ventilation is applied, RV loading conditions can ameliorate the effects on stroke volumes. TPP: transpulmonary pressure; PVR: pulmonary vascular resistance; ITP: intra–thoracic pressure

pressures likely increasing RV afterload while impaired chest wall compliance has the potential to increase intra–thoracic pressures at unchanged tidal volumes likely decreasing RV preload. Furthermore, impaired baseline cardiac function or fluid status can aggravate the haemodynamic effects of mechanical ventilation [48]. This can all lead to a vicious circle of hypotension and hypoxia with a decrease in coronary perfusion pressure and subsequent myocardial ischaemia, resulting in a further reduction in cardiac output.

Conclusions

During mechanical ventilation changes in heart and lung physiology take place. The cardiopulmonary interactions in mechanical ventilation are different with respect to normal breathing conditions. In critical care medicine it is crucial to understand the basic concepts of cardiopulmonary interactions to optimise treatment. Optimal critical care anticipates the changes in loading conditions of the heart as well as in pulmonary function during mechanical ventilation. Lung–protective ventilation, using lower tidal volumes, combining lower airway pressures with the open lung concept, aims to minimise lung injury by mechanical ventilation. Effects of mechanical ventilation on right ventricular loading have declined by lung–protective ventilation but remain unpredictable. In unexplained haemodynamic compromise during mechanical ventilation, echocardiography is advocated providing important information about loading conditions of the heart, in particular of the right ventricle.

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