Effects of lung volume changes on cardiac output in man

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Small swings in intrathoracic pressure during quiet breathing are recognizable on pressure tracings derived from the right heart and pulmonary circulation (Lauson, Bloomfield, and Cournand, 1946). In patients with chronic lung diseases, such as chronic bronchitis and emphysema, these respiratory swings are much increased, and pulmonary artery pressure is highest during expiration (Fishman, 1963). During inspiration, systemic venous return and pulmonary blood flow increase (Brecher, 1956) whereas pulmonary vascular outflow probably decreases (Shuler, Ensor, Gunning, Moss, and Johnson, 1942) and pulmonary blood volume rises (Lauson et al., 1946). The effect of inspiration on pulmonary artery pressure is that of a fall in the intravascular and a rise in the transmural pressure, whereas pulmonary vascular resistance changes appear to depend on the degrees of lung distension (Quincke and Pfeiffer, 1871; Burton and Patel, 1958; and Roos, Thomas, Nagel, and Prommas, 1961).

Previous investigations in man have shown reductions in cardiac output with rises in intrathoracic pressure (Werkö, 1947; Cournand, Motley, Werkö, and Richards, 1948; Kilburn and Sieker, 1960), and cough syncope represents the extreme clinical example of the effects on cardiac output of sustained positive intrathoracic pressure (Stucki, 1958). In man this decline in cardiac output is almost linear with progressive rises in intrathoracic pressure. A less clear-cut relationship obtains in respect of increases in cardiac output and stepwise decreases in intrathoracic pressure (O'Neill, Vallet, and Cudkowicz, 1963). The methods for varying intra-oesophageal pressure in the latter investigation were those of the Valsalva and Mueller manoeuvres conducted at approximately the mid-tidal level of lung inflation. The range of the intra-oesophageal pressure changes was from +40.0 to -15.0 mm. Hg.

In the current investigation an attempt has been made to measure simultaneously right (Qr, v) and left (Ql, v) ventricular outputs and the corresponding total pulmonary vascular resistances (T.P.V.R.1 and T.P.V.R.2) at three different levels of lung inflation, namely the functional residual capacity (F.R.C.), total lung capacity (T.L.C.), and residual volume (R.V.). These levels were maintained voluntarily for the short duration required for the inscription of dye-dilution curves. The range of change in intra-oesophageal pressure (IOP) in this investigation is therefore more restricted than in the aforementioned study (O'Neill et al., 1963), and the biventricular flows and their corresponding pulmonary vascular resistances can be more clearly related to the actual levels of lung inflation.

MATERIAL AND METHODS

The present investigation is derived from 10 patients with unilateral lung disease who, before surgery, underwent right heart catheterization. The diagnoses were pulmonary tuberculosis (3), bronchial carcinoma (4), bronchiectasis (2), and pectus excavatum (1). All studies were carried out in the unanaesthetized, fasting state and in recumbency.

For the simultaneous determination of the biventricular outputs the method of Fritts, Harris, Chidsey, Claussen, and Cournand (1957) was used.

A No. 9 double lumen right heart catheter was placed with its tip in the main pulmonary artery and the distal end attached to an Atlas densitometer, and this in turn was connected to a withdrawal system delivering 0.75 ml of blood per second.

A second polyethylene p60 catheter was placed percutaneously into an antecubital vein in the opposite arm and threaded towards the thoracic inlet. Of a 2% solution of Coomassie Blue, 3 to 3.5 ml was flushed as a bolus through this catheter followed by five times its volume of normal saline into the superior vena cava at the signal of injection. The total time needed for this injection was less than 2 seconds.

1 This study was supported by Grant No. 9310-96, Defence Research Board, Canada

2 Atlas-Werke, Bremen, West Germany


A No. 17 Courmand needle was placed under local anaesthesia into the right femoral artery, and this was attached by polyethylene tubing to another densitometer through which identical quantities of blood were withdrawn.

The outputs of the cuvettes were fed through the Atlas double oximeter amplifier system, and dye curves were inscribed on two Honeywell strip-chart recorders.

With a single injection of Coomassie Blue into the superior vena cava, dye dilution curves were obtained simultaneously from the pulmonary artery, representing \( Q_{RV} \), and the femoral artery, representing \( Q_{LV} \).

Pressures from the pulmonary and femoral arteries as well as from a saline-filled polyethylene oesophageal catheter, having its tip 35 cm. from the nostril in the mid-oesophagus, were monitored continuously via Sanborn pressure transducers on a direct writing recorder. All pressures were referred to zero levels at 10 cm. above table top.

For the purpose of determining levels of lung inflation all patients had their residual volume determined before the catheterization study by the nitrogen washout technique of Darling, Courmand, and Richards (1946). Spirograms, during the cardiac output determinations, were inscribed on a 9 L Collins spirometer, and the patients were instructed to maintain lung inflation at the levels of F.R.C., T.L.C., and R.V. respectively for approximately 25 seconds. At these constantly monitored levels of lung inflation the dye was injected and the dye curves were recorded during blood withdrawal through the densitometers. Collection of blood commenced at the signal of injection, and simultaneously with this pulmonary artery and intra-oesophageal pressures were also monitored on a slow speed. Withdrawal of blood ceased with an inscription of the down-slope of the curves before the onset of recirculation.

The computation of cardiac output was carried out by the analysis of the integrated plasma samples for Coomassie Blue concentrations in a Beckman DU spectrophotometer at a wavelength of 585 \( \mu \) and by reploting of the dye curves on semi-logarithmic paper to within 1% of peak concentration. The final calculation followed the outline of McNeely and Gravallese (1954).

Each patient was studied after a basal state cardiac output determination by the Fick method. Intra-oesophageal pressure (Iop) in this study has been expressed as the mean Iop obtained from the continuous tracing during breath-holding and dye curve inscription.

Total pulmonary vascular resistances were calculated separately for each ventricular output. In T.P.V.R.\(^{1}\), \( Q_{RV} \) has been used in the denominator of the resistance formula, while \( Q_{LV} \) is used in T.P.V.R.\(^{2} \), i.e., T.P.V.R.\(^{2} \)

Mean pulm. art. pressure—mean pulm. wedge pressure

\[
\frac{Q_{LV}}{l./min.} = \frac{Q_{RV}}{l./min.}
\]

**RESULTS**

The results in summary are shown throughout as the means of 10 sets of observations at the three levels of lung inflation.

Table I shows the findings at the level of the F.R.C. The mean lung volume was 3-75 litres. The mean Iop was 1.72 mm. Hg. The mean \( Q_{RV} \) was 5.47 l./min. and the mean \( Q_{LV} \) 6.14 l./min. The mean resting cardiac output as determined by the Fick method was 4.94 l./min. The difference between \( Q_{LV} \) and \( Q_{RV} \) was 0.67 l./min. or 11.0%. The results concerning total pulmonary vascular resistance show that the mean pulmonary artery pressure (P.A.P.) was 18.72 mm. Hg and the mean pulmonary wedge pressure (P.C.P.) 9.5 mm. Hg, while the mean T.P.V.R.\(^{1} \) was 134 dynes sec. cm.\(^{-5} \), and the mean T.P.V.R.\(^{2} \), using \( Q_{LV} \) in the calculation, 121 dynes sec. cm.\(^{-5} \) (see Fig. 1).

**TABLE I**

| CARDIAC OUTPUT AND PULMONARY VASCULAR RESISTANCES AT FUNCTIONAL RESIDUAL CAPACITY |
|---------------------------------|---------------|----------------|----------------|---------------|----------------|----------------|----------------|----------------|
|                                | F.R.C. (l. B.T.P.S.) | Iop (mm. Hg) | \( Q \) Fick (l./min.) | \( Q \) RV (l./min.) | \( Q \) LV (l./min.) | P.A.P. (mean mm. Hg) | P.C.P. (mean mm. Hg) | T.P.V.R.\(^{1} \) (dynes sec. cm.\(^{-5} \)) | T.P.V.R.\(^{2} \) (dynes sec. cm.\(^{-5} \)) |
| N = 10                         | 3.57           | -1.72         | 4.94                   | 5.47                   | 6.14                   | 18.72                   | 9.5                        | 134                        | 121                        |
| Mean                           | 3.57           | -1.72         | 4.94                   | 5.47                   | 6.14                   | 18.72                   | 9.5                        | 134                        | 121                        |
| S.D. ±                         | 2.32           | 2.28          | 0.54                   | 1.45                   | 3.74                   | 4.09                     | 4.73                       | 96                         | 81                         |

**FIG. 1.** The mean values concerning: lung volume (FRC); intra-oesophageal pressure (Iop); right (QLV) and left cardiac output (QLV); mean pulmonary artery pressure (MPAP); mean pulmonary wedge pressure (MPCP); and total pulmonary vascular resistance (TPVR\(^{1} \)) are shown at the level of the functional residual capacity against an arbitrary scale on the ordinate.
Table II provides the same information at the level of the T.L.C. Here the mean lung volume was 5-25 litres, the mean Iop = 6-9 mm. Hg, mean $Q_{RV}$ 10-96 l./min. and $Q_{LV}$ 8-49 l./min. The difference between $Q_{RV}$ and $Q_{LV}$ is -2-47 l./min. or 29% of $Q_{LV}$. The changes from the levels at the F.R.C. are +5-49 l./min. or 100% for $Q_{RV}$ and +2-35 l./min. or 38% for $Q_{LV}$. The mean P.A.P. of 16-2 mm. Hg has decreased from a mean of 18-72 mm. Hg and the mean P.C.P. of 6-2 mm. Hg has declined from the mean of 9-5 mm. Hg at the F.R.C. level. Mean T.P.V.R. has dropped by 55% to 73 dynes sec. cm.$^{-5}$ and T.P.V.R. by 22% to 94 dynes sec. cm.$^{-5}$ (see Fig. 2).

Table III depicts the results at the level of residual volume (R.V.). In this series of patients there were six with some obstructive lung disease, and this is responsible for the high mean R.V. of 2-96 litres. The mean Iop was +4-6 mm. Hg. The mean $Q_{RV}$ declined to 4-27 l./min. and mean $Q_{LV}$ to 3-87 l./min., thus providing a difference between $Q_{RV}$ and $Q_{LV}$ at this level of -0-4 l./min. or 10% of $Q_{LV}$. The change in means from that at the F.R.C. was therefore -1-21 l./min. or 22% for $Q_{RV}$ and -2-3 l./min. or 37% for $Q_{LV}$. Both the mean P.A.P. of 21-0 mm. Hg and the mean P.C.P. of 12-2 mm. Hg have risen from the means extant at the F.R.C. level.

The mean T.P.V.R.$^1$ of 151 dynes sec. cm.$^{-5}$ has risen from a mean of 134 at the F.R.C. level by 13% and T.P.V.R.$^2$ by 49% (see Fig. 3). Only the latter change is statistically significant.

Figure 4 illustrates in summary the results at the three levels of lung inflation.

Table III

**CARDIAC OUTPUT AND PULMONARY VASCULAR RESISTANCES AT TOTAL LUNG CAPACITY**

<table>
<thead>
<tr>
<th>T.L.C. (L. B.T.P.S.)</th>
<th>Iop (mm. Hg)</th>
<th>$Q_{RV}$ (l./min.)</th>
<th>$Q_{LV}$ (l./min.)</th>
<th>P.A.P. (mean) (mm. Hg)</th>
<th>P.C.P. (mean) (mm. Hg)</th>
<th>T.P.V.R.$^1$ (dyynes sec. cm.$^{-5}$)</th>
<th>T.P.V.R.$^2$ (dyynes sec. cm.$^{-5}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 10 Mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>5-25</td>
<td>-6-9</td>
<td>10-96</td>
<td>8-49</td>
<td>16-2</td>
<td>6-2</td>
<td>72</td>
</tr>
<tr>
<td>S.D. ±</td>
<td>1-4</td>
<td>2-2</td>
<td>6-88</td>
<td>4-93</td>
<td>10-8</td>
<td>3-4</td>
<td>61</td>
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<tr>
<td>P (comparison with F.R.C.)</td>
<td></td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.03</td>
<td>&lt;0.05</td>
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</table>

**CARDIAC OUTPUT AND PULMONARY VASCULAR RESISTANCES AT RESIDUAL VOLUME**

<table>
<thead>
<tr>
<th>R.V. (L. B.T.P.S.)</th>
<th>Iop (mm. Hg)</th>
<th>$Q_{RV}$ (l./min.)</th>
<th>$Q_{LV}$ (l./min.)</th>
<th>P.A.P. (mean) (mm. Hg)</th>
<th>P.C.P. (mean) (mm. Hg)</th>
<th>T.P.V.R.$^1$ (dyynes sec. cm.$^{-5}$)</th>
<th>T.P.V.R.$^2$ (dyynes sec. cm.$^{-5}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>2-96</td>
<td>+4-6</td>
<td>4-27</td>
<td>3-87</td>
<td>21-0</td>
<td>12-2</td>
<td>151</td>
</tr>
<tr>
<td>S.D. ±</td>
<td>1-78</td>
<td>3-83</td>
<td>3-4</td>
<td>3-1</td>
<td>10-0</td>
<td>5-6</td>
<td>67</td>
</tr>
<tr>
<td>P (comparison with F.R.C.)</td>
<td></td>
<td>&lt;0.01</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>0.1</td>
</tr>
</tbody>
</table>

The mean values concerning: lung volume (T.L.C.): intra-oesophageal pressure (Iop); right ($Q_{RV}$) and left ($Q_{LV}$) ventricular output; mean pulmonary artery pressure (MPAP); mean pulmonary wedge pressure (MPCP); and total pulmonary vascular resistance (T.P.V.R.$^1$) are shown at the level of the total lung capacity against an arbitrary scale on the ordinate.
It shows that at full lung inflation Iop decreases by a mean of $-5$ mm. Hg. The mean flow through the main pulmonary artery ($Q_{RV}$) is twice that at the F.R.C. The mean fall in P.A.P. is about $2.5$ mm. Hg, while the mean P.C.P. declined by $3.3$ mm. Hg. Associated with this is a fall in T.P.V.R. $Q_{LV}$, while rising by approximately $38\%$ above that at the F.R.C., is well below that of the $Q_{RV}$, suggesting a temporary decrease in pulmonary vascular outflow.

At temporary lung deflation to the level of the residual volume, the mean intra-oesophageal pressure rises by more than $5$ mm. Hg above that at the F.R.C. The minute flows of both ventricles decline from the level extant at the F.R.C., that through the pulmonary artery by $22\%$ and the flow through the aorta by $37\%$. The mean pulmonary artery pressure rises by $2.1$ mm. Hg and the mean pulmonary wedge pressure by $2.7$ mm. Hg. The mean total pulmonary vascular resistance rises, no matter if right or left ventricular output is utilized in the resistance calculation. Nevertheless, a somewhat greater pulmonary artery flow would appear to obtain during that state than that through the aorta, resembling to a lesser extent the temporary flow disequilibrium at the total lung capacity state of inflation.

**Discussion**

Experimental evidence in open-chested animals indicates that lung inflation from the collapsed position initially leads to a fall in pulmonary vascular resistance, followed by an increase in resistance as the lung is further distended (Burton and Patel, 1958). Such a U-shaped resistance curve has been explained on the basis of initial unkinking and dilatation of pulmonary arterioles and subsequent mechanical distortion of these resistance vessels as alveolar pressure increases (Howell, Permutt, Proctor, and Riley, 1961). In the close-chested animal, positive pressure breathing is analogous to positive pressure breathing in man and impedes systemic venous return (Werkö, 1947), reduces cardiac output (Lauson et al., 1946), and increases pulmonary vascular resistance (Brecher, 1956). The reduction in cardiac output is almost linear with step-wise elevations in positive pressure and affects the outputs of both ventricles (O’Neill et al., 1963). During a normal expiration, and particularly in patients with chronic chest disease, right heart filling is diminished as intrathoracic pressure gradients are almost abolished. The expiratory elevations in right heart and pulmonary vascular pressures are well recognized, but stroke volume determinations in man during that phase are not available.
The current observations indicate that in full expiration to the level of the residual volume the decline in cardiac output is proportional to the rise in intrathoracic pressure, and that this effect is somewhat greater on left than right ventricular output. Total pulmonary vascular resistance increases significantly only if left ventricular output is utilized in the resistance calculation. It seems relevant therefore in pulmonary vascular resistance measurements, particularly during temporary reductions in lung volume, to define the respective ventricular minute flows used in the calculation. The largest changes in cardiac output in the course of the present investigation were observed during full lung inflation. This doubled right ventricular output while that of the left ventricle increased by 38%, suggesting a temporary distension of the pulmonary capacitance vasculature. The corresponding mean change in intra-oesophageal pressure of -5 mm Hg remained within the range known to be associated with significant increases in cardiac output (Thomas, Roos, and Griffo, 1961; O'Neill et al., 1963). The pulmonary vascular resistance fell significantly when either right or left ventricular output was used in the resistance calculation. These observations are in accord with the experimental findings of Shuler et al. (1942), but appear to differ from those of Roos and others (1961). The latter investigators have shown that during quiet breathing changes in pulmonary vascular resistance are small and that maximum decreases in total pulmonary vascular resistance occur at half maximal inflation and at intra-pleural pressures of -5 to -10 cm H2O. Resistance finally increases again with lung volumes in excess of half inflation and at intra-pleural pressures of -10 to -25 cm H2O. Mechanical distortion by stretching the resistance vessels is thought to be responsible for the rising pulmonary vascular resistance during high degrees of distension rather than an increase in transmural pressure. These observations by Roos and others support the concept of a U-shaped pulmonary vascular resistance curve elaborated by Burton and Patel (1958) from observations concerning the effects of inflation of the rabbit lung.

The excessive number of dye dilution curves needed for the estimate of biventricular flows during successive steps of lung inflation precludes at present the establishment of a similar distribution curve in man. Measurements of stroke volume from the two ventricular outflow-paths throughout the phases of respiration are ideally required for a more precise elucidation of the human pattern of the normal pulmonary vascular resistance curve.

**SUMMARY**

Breath holding at the level of the F.R.C. in 10 patients with lung disease shows that left ventricular output (QLV) exceeded that of the right (QRV) by a mean of 0.67 l/min or 11% of QLV. Mean pulmonary artery pressure (P.A.P.) was 18.7 mm Hg and mean pulmonary wedge pressure (P.C.P.) 9.5 mm Hg. Total pulmonary vascular resistance, utilizing Qav (T.P.V.R.), was 134 units, and 121 units if QLV is used instead.

At full lung inflation, leading to a decrease of approximately -5 mm Hg in intra-oesophageal pressure (IOP), flow through the main pulmonary artery is doubled and the P.A.P. falls by a mean of 2.5 mm Hg, while the mean P.C.P. declines by 3.3 mm Hg. Associated with this is a fall in T.P.V.R. and T.P.V.R. QLV rises by approximately 38% above that at the F.R.C. A temporary disequilibrium in the minute flows of the two ventricles has to be postulated.

At temporary lung deflation to the level of the residual volume, mean IOP rises by about 5 mm Hg above that of the F.R.C. QRV and QLV both decrease by 22% and 37% respectively. Mean P.A.P. and P.C.P. rise by about 2.5 mm Hg. The mean T.P.V.R. increases significantly only if QLV is used in the resistance calculation. Again a somewhat greater pulmonary artery flow than that through the aorta seems temporarily to be evident at these extremes of lung volume.

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**REFERENCES**


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