Relationship of Anginal Symptoms to Lung Mechanics during Myocardial Ischemia

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SUMMARY
The anginal syndrome (AP) typically includes sensations of chest tightness or difficulty in breathing. Left ventricular (LV) dysfunction during myocardial ischemia incident with AP is now well documented. Since secondary alterations in lung mechanics could relate to these symptoms, we examined airway resistance (Raw), lung volume (TGV), lung compliance (CL), and LV pressure-volume relations during pacing-induced AP.

LV end-diastolic pressure (EDP) increased suddenly with AP, (mean + 41%, $P < 0.01$), without change in end-diastolic volume (EDV). LV distensibility (EDV/EDP) decreased abruptly, ($-37\%, P < 0.01$), with reduction in airway conductance (1/Raw/TGV), ($-40\%, P < 0.05$), and CL ($-27\%, P < 0.05$). When AP was relieved, these changes returned toward preangina levels.

Ischemia-induced LV dysfunction abruptly increases LVEDP. The resulting increased pulmonary capillary pressure effects an alteration of lung mechanics consisting of increasing Raw and reduced CL. The changes in ventilatory effort which ensue may be interpreted as chest tightness, heaviness, or constriction by the AP patient.

Additional Indexing Words:
Ventricular function  Coronary artery disease  Atrial pacing
Left ventricular end-diastolic pressure  Nitroglycerin  Respiratory mechanics
Airway resistance  Lung compliance

THE SYNDROME of angina pectoris commonly includes sensations of chest tightness, choking, dyspnea, or even wheezing. Although the mechanism responsible for the occurrence of these symptoms remains obscure, cardiac dysfunction, consisting of increased left ventricular end-diastolic pressure occurring during myocardial ischemia incident with angina, is well documented. In other disorders, a similar hemodynamic abnormality (i.e. increased left heart filling pressure) is acknowledged to effect changes in lung function. Specifically in mitral stenosis or congestive heart failure, secondary lung alterations may result in abnormal pulmonary function or even manifest respiratory physical disability. Consequently, this study was designed to examine the possibility that sudden ischemic-induced changes in left ventricular filling pressure may alter pulmonary mechanics, thus accounting for some of the symptoms of the anginal syndrome.

Controlled atrial tachycardia enabled anginal symptoms to be studied while eliminating confusing effects evoked by exercise or drug action. Likewise, airway conductance (1/airway resistance) per unit lung volume and lung compliance (CL) were used to estimate changes in respiratory mechanics in order to minimize patient effort during angina. By relating these measurements to left ventricular
hemodynamic changes, the effect of sudden ischemia-induced hemodynamic alterations on lung mechanics during angina was assessed.

Methods and Materials

Twenty-four male patients (mean age 46.3 years) who underwent diagnostic cardiac catheterization studies in order to evaluate the extent of left ventricular dysfunction and coronary pathology comprise the study group. In addition to typical angina pectoris, each patient showed 50% narrowing of at least one major coronary artery during selective coronary arteriography. In order to assess the functional significance of the coronary artery disease, a myocardial metabolic study was performed on the day following coronary angiography. Concurrently, a respiratory function examination was performed. The investigative nature of the study was explained in detail.

All patients were judged to have angina pectoris by a referring physician and by us. The anginal syndrome conformed to the broad criteria as outlined by Hurst and Logue. Patients with bronchopulmonary disease, other forms of cardiac disease, or heart failure were specifically excluded.

Hemodynamic Studies

Left ventricular (LV) pressure and volume measurements and electrocardiographic signals were recorded in the unmedicated, post-absorptive state during retrograde LV catheterization performed with a specially designed, no. 8, 100 cm double-lumen Courmand catheter. LV pressures were measured with a Statham p 23 Db transducer through the distal opening. A thermistor bead (Victory Engineering Corporation, response time = 0.12 sec), embedded in the proximal opening, was positioned in the ascending aorta. Measurements of LV end-diastolic volume (EDV) were determined from a thermal washout curve obtained by bolus injection of indocyanine green solution at room temperature into the LV. Simultaneously, cardiac output (CO) was determined by the dye-dilution method. Blood was withdrawn from the left brachial artery through a Gilford cuvette densitometer at a constant flow rate by a Harvard withdrawal-perfusion pump. Thermal washout and dye curves, as well as pressures, were recorded by an oscilloscopic photographic recorder. The area under the dye curve was measured by planimetry and CO was calculated by the standard Hamilton formula. From the step-function of the thermal washout curve, the ratio of end-systolic volume (ESV) to EDV was calculated. Stroke volume (SV) calculated from CO was used to determine LVEDV according to: LVEDV = SV/1-ESV/EDV. Stable atrial pacing was achieved with a variable rate-pulse generator following percutaneous introduction of a bipolar pacing catheter into the midcoronary sinus.

After control measurements, including LV end-diastolic pressure (EDP) and volume, heart rate, CO, and ECG, atrial pacing was initiated. The heart rate was increased at 10 beats/min—increments until angina pectoris occurred (16 episodes) or a maximum heart rate of 160 beats/min was achieved. The above hemodynamic measurements were repeated during angina and following relief of angina with cessation of pacing (six patients), or after sublingual nitroglycerin (0.6 mg) while pacing was continued at the angular rate (10 patients).

Respiratory Studies

Under the same conditions, thoracic gas volume (TGV) and airway resistance (Raw) were measured according to DuBois' technic using the constant volume body plethysmograph modified to permit atrial pacing and continuous electrocardiographic monitoring. Raw estimates were made at spontaneous lung volumes (inspiratory flow rate = 0.5 liters/sec) in the sitting position and represent the average of three to five determinations. Intraesophageal pressure was measured according to the method of Sharp et al., utilizing a water-filled catheter positioned in the midesophagus by fluoroscopy. A wedge spirometer (Med Science Electronics model 470) was used to measure tidal volume.

To evaluate the effect of nonspecific precordial pain on airway mechanics, 10 normal volunteers were also studied in the body plethysmograph. Two silver patch ECG electrodes were attached to the skin over the left precordium and connected to a low voltage DC stimulator. The output was adjusted to 1v above their pain threshold avoiding intercostal muscle stimulation. Raw and TGV were then measured before and during a 1-min period of electrically induced chest discomfort.

In this study, changes in myocardial compliance were estimated by a distensibility index expressed as a ratio of EDV:EDP. For statistical purposes, airway resistance values are expressed as the ratio of airway conductance (Gaw) to TGV (Gaw/TGV = liter/sec/cm H2O/liter). C[p]p was obtained by dividing tidal volume by the change in esophageal pressure between points of zero flow. Transient, substernal discomfort described by the patient as chest tightness, pressure, or constriction occurred during periods of myocardial ischemia, documented by significant

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Table 1

Results of Hemodynamic and Respiratory Studies*

<table>
<thead>
<tr>
<th>Period</th>
<th>N</th>
<th>HR</th>
<th>CI</th>
<th>LVEDP</th>
<th>LVEDV</th>
<th>EDV/EDP</th>
<th>Gw (liters/sec · cm H2O⁻¹)</th>
<th>TGV (liters)</th>
<th>Gw/TGV (liters/cm H2O⁻¹)</th>
<th>CL (liters/cm H2O)</th>
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</thead>
<tbody>
<tr>
<td>Control</td>
<td>24</td>
<td>72.4</td>
<td>2.8</td>
<td>12.4</td>
<td>152</td>
<td>11.8</td>
<td>1.03</td>
<td>3210</td>
<td>0.307</td>
<td>0.184</td>
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<td>Pacing: Preangina</td>
<td>16</td>
<td>125.4</td>
<td>3.0</td>
<td>10.3</td>
<td>102</td>
<td>8.3</td>
<td>1.67</td>
<td>3500</td>
<td>0.490</td>
<td>0.172</td>
</tr>
<tr>
<td>Pacing: Angina</td>
<td>16</td>
<td>132.4</td>
<td>2.7</td>
<td>17.5</td>
<td>102</td>
<td>7.2</td>
<td>0.683</td>
<td>3520</td>
<td>0.195</td>
<td>0.130</td>
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<tr>
<td>Pacing: Nonangina</td>
<td>8</td>
<td>144</td>
<td>3.1</td>
<td>7.2</td>
<td>98</td>
<td>13.6</td>
<td>1.21</td>
<td>3100</td>
<td>0.398</td>
<td>—</td>
</tr>
<tr>
<td>Pacing: NTG, postangina</td>
<td>10</td>
<td>132.4</td>
<td>2.6</td>
<td>9.6</td>
<td>96</td>
<td>10.0</td>
<td>1.46</td>
<td>3740</td>
<td>0.406</td>
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<td>6</td>
<td>70.4</td>
<td>3.1</td>
<td>10.7</td>
<td>141</td>
<td>12.2</td>
<td>1.10</td>
<td>3100</td>
<td>0.350</td>
<td>0.176</td>
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<tr>
<td>Normals: Control</td>
<td></td>
<td></td>
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<tr>
<td>Normals: Chest pain‡</td>
<td>10</td>
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</table>

Abbreviations: N = number of patients; HR = heart rate; CI = cardiac index; LVEDP = left ventricular end-diastolic pressure; LVEDV = left ventricular end-diastolic volume; EDV/EDP = left ventricular distensibility index; Gw = airway conductance; TGV = thoracic gas volume; Gw/TGV = specific airway conductance; CL = lung compliance; NTG = nitroglycerin.

*Values represent mean measurements.
†Parentheses ± 1, SEM.
‡Electrically induced (see text).
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EDV was associated was increased during this preanginal period but the change was not significant. These changes occurred at a mean heart rate of 132.4 beats/min. LVEDP suddenly increased during angina (+41%, P < 0.05) while EDV remained reduced without change in cardiac index. With angina, Gaw and Gaw/TGV decreased abruptly (mean −40%, P < 0.05) from control values and was markedly diminished (P < 0.001) from preangina values (fig. 1). CL declined 27% from control (P < 0.05).

Relief of Angina. When angina was relieved by termination of pacing (fig. 1) or by nitroglycerin, despite persistent pacing at the angina rate, lung mechanics returned toward normal as did the hemodynamic alterations (table 1).

Pacing, Nonangina. In eight patients angina was not experienced as the heart rate was increased. In three patients second degree atrioventricular block limited the tachycardia stress. No significant change in LV pressure or Gaw/TGV occurred in those patients achieving heart rates greater than the anginal group (table 1).

Nonspecific Chest Pain. Electrically-induced chest discomfort resulted in small increases in TGV (control pain = 3285 ± 204 → 3917 ± 222 liters) (P < 0.05). During chest pain, Gaw increased appropriately with the change in level of lung inflation as Gaw/TGV increased only minimally (0.303 ± 0.037 → 0.310 ± 0.050).

Discussion

The respiratory features of angina were summarized in Osler’s Lumleian Lectures as early as 1910, yet the clinical significance of these symptoms has not been fully appreciated. He observed “four special features”: (1) distension of the lungs (“acute emphysema”) with limited “inspiratory excursions and prolonged expirations”; (2) at times, actual wheezing and other “physical signs like those of an acute attack of bronchial asthma”; (3) occasionally, transient acute pulmonary edema; and (4) rarely, hemoptysis. These attacks “yielded promptly to amyl nitrate.” In the French literature, Gallavardin recognized a respiratory anginal component described as a feeling of “respiration boucheée” (blocked respiration) which forces the patient to stop his activity. This sensation, which he later termed “blocpneum,” subsided spontaneously with rest or promptly with nitroglycerin. The resemblance of these symptoms to those of patients with obstructive respiratory disorders is apparent. Moreover, others have commented on the difficult diagnostic challenge that results when similar stress-related symptoms (i.e. chest tightness, agonizing...
SYMPTOMS & LUNG MECHANICS IN ISCHEMIA

respirations, or suffocation) occur in emphysematous patients with coexisting coronary heart disease.

Increased left ventricular filling pressure, a consistent accompaniment of angina pectoris, generally precedes the appearance of chest discomfort. Thus, a gap between initiation of ischemic myocardial dysfunction and recognition of symptoms by the patient has been recognized. The rise in LVEDP progresses without significant changes of ventricular volume, effecting reduction of EDV/EDP, and probably reflects impaired myocardial distensibility. Sudden limitation to diastolic filling presumably results in an increased pressure transmitted across the open mitral valve and left atrium directly to pulmonary veins and capillaries. Transient elevation of pulmonary distending pressure may result in the development of pulmonary congestion. Lung mechanical changes secondary to vascular congestion have long been recognized. More recently, acute pulmonary vascular congestion (i.e. left ventricular failure) has been associated with reversible reduction in lung compliance and resistance. Our data imply that similar changes in lung mechanics can occur during transient ischemia-induced left ventricular dysfunction. These mechanical alterations occur in the absence of clinical heart failure or pulmonary edema. Since these pulmonary changes coincide with the experience of some angina-rated symptoms, particularly chest tightness, our observations suggest that increased airway resistance (\( \downarrow \text{Gaw/TGV} \)) and decreased lung compliance may be one of the mechanisms responsible for chest discomfort in angina patients.

Airway conductance is normally directly related to lung volume, and the reduced Gaw/TGV ratio occurring during angina suggests that the airways become less extensible than the alveoli. Reduced airway caliber (bronchoconstriction, edema, secretion, compression, or changes in extensibility of the airway wall) could account for some further decrease of lung compliance. Because individual alveoli become less distensible as they over distend, they are operating over less compliant portions of their pressure-volume curves.

The suddenness of the conductance response and its rapid reversal with relief of angina (fig. 1) favor a disproportionate alteration of airway mechanical properties. The pathophysiology of this change is not known but may be consistent with the earliest sequences of acute pulmonary vascular congestion. Widening of loose connective tissue, surrounding extraalveolar airways, out of proportion to changes in alveolar wall thickness has been well documented in the so-called interstitial phase of pulmonary edema. In addition, increasing intravascular pressure causes dilatation of pulmonary arteries and veins. Subsequent competition for the space between vessels and airways within the bronchovascular sheaths could compress the airways, increasing their resistance. Finally, vagally-induced changes in bronchomotor tone may also be involved. Such effects, acting separately or in combination, would also cause reduction in Gaw and alter the airway resistance-lung volume relationship.

Chest tightness during myocardial ischemia occurred in all patients demonstrating reduced conductance responses. By contrast, the patients with no change in conductance experienced no chest symptoms. Duplicate studies in three patients showed that the conductance response was characteristic and always associated with symptoms (fig. 2). In the patients studied after nitroglycerin was used to relieve their symptoms while pacing was continued, airway conductance returned toward control values (table 1). Utilizing nitroglycerin to relieve anginal symptoms while tachycardia stress is maintained has been shown to effect a decrease in LVEDP while myocardial ischemia (as evidenced by S-T segment depression or abnormal lactate metabolism) persists. Accordingly, our evidence supports this view and suggests that respiratory symptoms occurring during myocardial ischemia can result from sudden alterations in lung mechanics secondary to changes in left ventricular filling pressure.
CORONARY HEART DISEASE

PEPINE, WIENER

ANGINA

manifested by angina pectoris.

In summary (fig. 3), this study indicates that during periods of increased myocardial oxygen requirements, ischemia-induced left ventricular dysfunction effects an abrupt increase in left heart filling pressure. These changes occur coincident with varying degrees of lung mechanical alterations consisting of increased airway resistance and reduced lung

Minimal increases in thoracic gas volume were observed during electrically-induced precordial pain while specific airway conductance increased appropriately with the change in level of lung inflation. These changes may relate to increased catecholamine release during pain. Nonetheless, these subjects maintain the normal direct relationship between airway conductance and lung volume. While tegmental pain is not meant to be equated with the visceral-type discomfort of angina, the possibility that perception of chest pain, of sudden onset and brief duration, may have reflex accompaniments, such as bronchoconstriction, which alter normal respiratory mechanics is unlikely.

Although we have not studied respiratory mechanics in other disorders, these data may be useful in understanding some components of the anginal syndrome in patients without ischemic heart disease (i.e. mitral stenosis, aortic stenosis, and myocardiopathies). In these settings, precipitous changes in left heart filling pressure in the presence of already congested (stiff) lungs could result in abrupt airway changes analogous to those observed in coronary heart disease manifested by angina pectoris.

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In summary (fig. 3), this study indicates that during periods of increased myocardial oxygen requirements, ischemia-induced left ventricular dysfunction effects an abrupt increase in left heart filling pressure. These changes occur coincident with varying degrees of lung mechanical alterations consisting of increased airway resistance and reduced lung
compliance. An ensuing change in ventilatory effort may be recognized by the anginal patient as chest tightness, choking, heaviness, constriction, or difficult breathing.

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