Effect of Cough on Coronary Perfusion Pressure: Does Coughing Help Clear the Coronary Arteries of Angiographic Contrast Medium?

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SUMMARY To evaluate if coughing after coronary angiography improves the pressure gradient to clear contrast medium from the coronary circulation, we studied the effect of a single forceful cough on the coronary perfusion pressure (CPP), calculated as diastolic aortic minus right atrial pressure. During coughing before angiography in 12 normotensive subjects, right atrial pressure increased more than aortic pressure increased, causing CPP to decrease by 17 ± 12 mm Hg (mean ± SD, p < 0.0001). Immediately after the cough, aortic pressure was less than before, and CPP was decreased by 9 ± 4 mm Hg (p < 0.0001). Increased central venous pressure during coughing was not transmitted beyond the thoracic and abdominal exits. The effects of coughing in 23 patients after coronary angiography, when aortic pressures were as low as 28 mm Hg (mean 64 ± 20 mm Hg), were similar to those in normotensive subjects: the CPP decreased by 21 ± 14 mm Hg (p < 0.0001) during coughing, and was decreased by 7 ± 6 mm Hg (p < 0.0001) after coughing.

To study the cause of these effects, 200 forceful coughs in nine normal subjects were studied with simultaneous transesophageal M-mode echocardiography and Doppler brachial artery pulse velocity recordings. Coughing during diastole did not open the aortic valve but produced a peak of diastolic brachial arterial flow velocity. Flow velocity in the beat after coughing was less than control.

We conclude that in normal subjects, coughing displaces aortic volume peripherally, without producing cardiac output in diastole, and prevents venous outflow, causing the CPP to be decreased during and after the cough. Coughing produces similar decreases in CPP in patients with moderate hypotension after coronary angiography. If coughing helps to clear the coronary arteries of contrast medium in such patients, it does not do so by increasing the CPP.

SERIAL COUGHING can maintain cardiac output and consciousness during sustained ventricular fibrillation or asystole. 1 2 In a canine model of ventricular fibrillation, the acute increase in intrathoracic pressure during coughing causes blood to move initially from the ascending aorta toward the brachiocephalic vessels. 3 The aortic valve then opens and blood is propelled from the pulmonary vasculature through the left heart into the arterial circulation. After the cough, the aortic valve closes, maintaining sufficient aortic pressure to support coronary perfusion. Increased intrathoracic pressure due to thoracic compression, as used in cardiopulmonary resuscitation, produces similar effects in severely hypotensive experimental animals. 4 5

Coughing has been recommended as a means of interrupting bradycardia or arterial hypotension after selective coronary angiography. 6 8 Because aortic pressure increases markedly during a cough, the apparent beneficial effect of coughing after coronary angiography has been attributed to a clearing of the angiographic contrast medium from the coronary arteries. 6 8 These observations of the effect of coughing during severe hypotension caused by sustained ventricular fibrillation or asystole suggest that after a cough the aortic and coronary perfusion pressures increase. 1 8

We observed in a patient who underwent a transesophageal echocardiographic examination that vigorous coughs in diastole did not open the aortic valve. This finding suggested that the effect of a sudden increase in intrathoracic pressure may depend on the level of arterial pressure, and that in normotensive patients, coughing may not produce the same beneficial effects on aortic pressure and coronary perfusion as it appears to do during severe hypotension. Thus, we undertook this investigation of the effect of coughing on aortic and coronary perfusion pressures in normotensive subjects and in patients with varying degrees of hypotension after coronary angiography.

Methods

This study was performed in three parts: catheterization measurement of the effect of coughing in normotensive subjects, noninvasive evaluation of the effect of coughing in normal subjects and determination of the effect of coughing on the coronary perfusion pressure after selective coronary angiography.

Catheterization Studies Of Normotensive Subjects

The effect of a single forceful cough on the aortic, right atrial and coronary perfusion pressures were determined before angiography in nine patients undergoing diagnostic catheterization for evaluation of chest pain. There were eight males and one female, ages 39–56 years. Three patients were normal and six
had coronary artery disease. All had left ventricular ejection fractions greater than 40% and no valvular dysfunction. The central aortic pressure was monitored with a #8F catheter and the right atrial pressure was simultaneously measured with a #7F catheter. Both catheters were connected to Statham P23Db strain gauges and the pressures were recorded using an Electronics for Medicine VR12 recorder at paper speeds of 25-100 mm/sec. The coronary perfusion pressure was calculated as diastolic aortic minus right atrial pressure. Control diastolic aortic, right atrial and coronary perfusion pressures were determined at end-diastole in the beat before the cough (fig. 1). In some instances, subjects inspired forcibly just before coughing. When this occurred, control measurements were made in the preceding beat. Only coughs that increased diastolic right atrial pressure to more than 50 mm Hg were analyzed. The pressures during the cough were measured at peak diastolic right atrial pressure; diastole was defined as the time from the aortic incisura (if recognizable) or the end of the ECG T wave until the onset of the QRS. The end-diastolic pressures immediately after cough were measured in the first cardiac cycle after the cough. Systolic pressures were measured at peak systolic aortic pressure before, during and immediately after coughing.

The extent of venous peripheral transmission of the increased right atrial pressure during cough was evaluated with a #7F triple-lumen Swan-Ganz catheter inserted from an antecubital cutdown (right arm in three patients, left arm in five patients) or percutaneously from the femoral vein below the level of the inguinal ligament (right leg in nine patients, left leg in two patients). The catheter tip was placed in the right atrium and pressure simultaneously recorded from the tip and from the lumen opening 30 cm proximal to the tip. The patients coughed forcibly at 5–10-second intervals while the catheter was slowly withdrawn in 1-cm increments after each cough. The location of the proximal lumen was determined by manually injecting a small amount of contrast medium through the proximal lumen during fluoroscopic visualization.

Noninvasive Studies Of Normal Subjects
Nine normal subjects (seven males and two females), ages 23–48 years, were studied with simultaneous ECG, echocardiographic visualization of the aortic valve, brachial artery flow velocity recording, and intrathoracic pressure monitoring during single forceful coughs. The M-mode echocardiogram was obtained transesophageally using a KB-Aerotech 3.5-MHz TET transducer and a SKI Echoline 20 with a sampling rate of 1000 per second. Intrathoracic pressure changes during the cough were estimated using an esophageal balloon. The diastolic arterial pressure was determined by sphygmomanometry before the study and only coughs that increased esophageal balloon pressure by more than this amount were analyzed. The brachial artery flow velocity measured with a transcutaneous pulsed Doppler transducer fixed over the brachial artery. All measurements were recorded on a Honeywell model 1856-A recorder at a paper speed of 50–200 mm/sec. An index of relative brachial artery flow was derived by expressing the area under the flow-velocity curve during coughing, and in the systole after coughing, as a percentage of the mean area of the two beats before the cough. The zero level was defined as the flow velocity at end-diastole, which correlated well with a zero determined by cuff occlusion of brachial flow. This brachial artery flow index was determined in 20 diastolic coughs and in 20 systolic coughs.

Studies After Coronary Angiography
The effect of coughing on right atrial, aortic and coronary perfusion pressures was determined in 23 patients undergoing diagnostic coronary angiography by the standard Judkins technique. There were 19 males and four females, ages 39–74 years. Five patients had normal coronary anatomy, three had one-vessel disease, four had two-vessel disease, and 11 had three-vessel disease. All patients were premedicated with 0.6 mg of atropine and 50 mg of diphenhydramine 45 minutes before the procedure. Right atrial pressure was measured through a #7F catheter and central aor-

![Figure 1. Simultaneous recording of central aortic (Ao) and right atrial (RA) pressures in a normal patient before angiography. The thin arrows indicate where diastolic aortic and right atrial pressure were measured before coughing, during coughing at peak diastolic right atrial pressure and immediately after the cough. The magnitude of the coronary perfusion pressure (CPP) is indicated by the length of the vertical arrows. During cough (large arrow), aortic pressure increased less than right atrial pressure, causing the coronary perfusion pressure to decrease. After the cough aortic pressure was slightly lower than control and the coronary perfusion pressure was decreased. Aortic pressure returned to control during the next few beats.](http://circ.ahajournals.org/content/605/4/1777/F1.large.jpg)
tic pressure through the coronary catheter. Immedi-
diately after each coronary injection of 4–8 ml of meglumine diatrizoate (Renografin-76), the catheter was returned to pressure monitoring. If any evidence of pressure damping was observed, the catheter was immediately withdrawn from the coronary ostium. Two to 5 seconds after the coronary injection was completed, the patient was asked to perform a single forceful cough. The aortic, right atrial, and coronary perfusion pressure were determined before, during and immediately after the cough as described above. Coughs that increased diastolic right atrial pressure to more than 50 mm Hg and in which aortic diastolic pressure did not vary by more than 4 mm Hg in the three beats before the cough were analyzed. The two instances in which asystole occurred were included.

Measurements obtained during and after coughing were compared with the values before the cough using one-way analysis of variance for repeated measures over time. All results are expressed as mean ± SD.

**Results**

**Catheterization Studies of Normotensive Subjects**

Twenty-four coughs met the criteria and were included. Before the cough, the diastolic aortic pressure was 82 ± 11 mm Hg. A typical record of the effect of coughing on right atrial and aortic pressure in a normal is shown in figure 1. During coughing, diastolic right atrial pressure increased by more than the increase in aortic pressure so that the coronary perfusion pressure decreased by 17 ± 12 mm Hg (p < 0.0001) (fig. 2, table 1). Immediately after the cough, the aortic diastolic pressure was less than the pre-cough value, while right atrial pressure was slightly but not significantly increased (p = 0.15), causing the coronary perfusion pressure to be 9 ± 4 mm Hg less than before the cough (p < 0.0001). Aortic pressure returned to the pre-cough value over the next several seconds. Similarly, aortic systolic pressure increased less than right atrial pressure during the cough and was slightly reduced from control after the cough.

Recordings of venous pressure during slow withdrawal of the catheter from the right atrium during serial coughing (fig. 3) showed that while coughing produced a marked increase in right atrial, intrathoracic and abdominal venous pressures, the increased pressure was not transmitted beyond the venous exits from the thorax and abdomen.

**Noninvasive Evaluation of Normal Subjects**

Simultaneous recordings of transesophageal M-mode echocardiograms of aortic valve motion and transcutaneous Doppler brachial flow velocities during 200 coughs in nine normal subjects showed that coughs in diastole consistently produce a peak of flow velocity in the brachial artery without opening the aortic valve in diastole (fig. 4). We have not observed a cough that opened the aortic valve during diastole in a normal subject. Brachial artery flow index during a diastolic cough was 158 ± 79% of the control (p < 0.001) and the brachial artery flow index in the systole after the cough was reduced to 50 ± 32% of the control value (p < 0.001) (fig. 5). Similarly, the systolic brachial artery flow index was markedly increased during coughs limited to systole and slightly decreased during the following systole (fig. 5).

**Table 1. Effect of Coughing on Aortic, Right Atrial and Coronary Perfusion Pressure**

<table>
<thead>
<tr>
<th></th>
<th>Normotensive subjects before angiography (n = 24)</th>
<th>Immediately after selective coronary artery contrast injection (n = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aortic diastolic pressure (mm Hg)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>82 ± 11</td>
<td>64 ± 20</td>
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<tr>
<td>During coughing</td>
<td>151 ± 25*</td>
<td>120 ± 32*</td>
</tr>
<tr>
<td>Change from control</td>
<td>69 ± 25</td>
<td>56 ± 23</td>
</tr>
<tr>
<td>After coughing</td>
<td>77 ± 10*</td>
<td>58 ± 19*</td>
</tr>
<tr>
<td>Change from control</td>
<td>−5 ± 3</td>
<td>−6 ± 7</td>
</tr>
<tr>
<td><strong>Right atrial pressure (mm Hg)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>7 ± 4</td>
<td>7 ± 5</td>
</tr>
<tr>
<td>During coughing</td>
<td>93 ± 23*</td>
<td>84 ± 28*</td>
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<tr>
<td>Change from control</td>
<td>86 ± 24</td>
<td>77 ± 27</td>
</tr>
<tr>
<td>After coughing</td>
<td>11 ± 4†</td>
<td>8 ± 5†</td>
</tr>
<tr>
<td>Change from control</td>
<td>4 ± 3</td>
<td>1 ± 4</td>
</tr>
<tr>
<td><strong>Coronary perfusion pressure (mm Hg)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>75 ± 12</td>
<td>57 ± 19</td>
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<tr>
<td>During coughing</td>
<td>58 ± 27*</td>
<td>36 ± 24*</td>
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<tr>
<td>Change from control</td>
<td>−17 ± 12</td>
<td>−21 ± 14</td>
</tr>
<tr>
<td>After coughing</td>
<td>66 ± 10*</td>
<td>50 ± 29*</td>
</tr>
<tr>
<td>Change from control</td>
<td>−9 ± 4</td>
<td>−7 ± 6</td>
</tr>
</tbody>
</table>

*p < 0.0001.

†p > 0.05.
Studies After Selective Coronary Angiography

Immediately after selective coronary angiography and just before the cough, the aortic diastolic pressure ranged from 28–110 mm Hg (mean 64 ± 20 mm Hg). Sixty coughs met the criteria and were analyzed (figs. 6 and 7). During coughing, diastolic right atrial pressures increased more than diastolic aortic pressure increased, causing the coronary perfusion pressure to decrease by 21 ± 14 mm Hg (p < 0.0001) during the cough (fig. 8, table 1). After the cough, the aortic diastolic pressure was slightly less than it was before the cough, and right atrial pressure was slightly higher (p = 0.07), which caused the coronary perfusion pressure to be 7 ± 6 mm Hg less after the cough (p < 0.0001) than before the cough. In some instances the patients inspired forcibly before coughing (fig. 7),
In the normotensive subjects, coughing increased right atrial, intrathoracic and abdominal venous pressures. The increased central venous pressure was not transmitted beyond the exits from the thorax and the abdomen. This finding is consistent with the presence of valves or localized collapse of the relatively thin-walled veins inside the exits from the abdomen and thorax. Because venous collapse or valves prevent venous outflow during coughing, right atrial pressure increases by approximately the same amount as intrathoracic pressure. The thick-walled, valveless arteries transmit the increased intrathoracic pressure to the periphery during the cough. This produces a large peripheral arteriovenous gradient, which explains the increased brachial arterial flow during the cough. Because this marked increase in peripheral arterial flow during diastolic coughs occurred without the aortic valve opening, the cough must squeeze blood out of the central aorta toward the periphery, causing a decrease in the aortic volume and the aortic transmural pressure. This causes aortic pressure to increase less than intrathoracic or right atrial pressure, and the coronary perfusion pressure (aortic-right atrial pressure) decreases. Thus, during coughing, there is an increased gradient for peripheral blood flow but a decreased gradient for coronary flow.

The peripheral displacement of blood from the aorta during coughing also provides an explanation for the lower aortic pressure immediately after the cough in the normotensive subjects. As the aorta refills after the cough, peripheral arterial flow is transiently decreased. Simultaneously in the venous circulation, once intrathoracic pressure returns to normal, the blood that was dammed up in the peripheral veins during the cough can then flow into the right atrium. This may partially explain the slightly increased right atrial pressure we frequently observed after the cough. Thus, in normotensive subjects, the aortic and coronary perfusion pressures are reduced immediately after the cough.

Others have demonstrated a somewhat different effect of cough in severely hypotensive animals and patients with sustained ventricular fibrillation. Under these conditions, a sudden increase in intrathoracic pressure produced by coughing or external
thoracic compression first peripherally displaces blood from the central aorta; then the aortic valve opens and blood is squeezed from the pulmonary vasculature through the left heart into the aorta. The left heart serves as a passive conduit and left ventricular volume does not change. After coughing, central aortic volume and pressure may be higher than before and thus the coronary perfusion pressure increases. In contrast, we have not seen the aortic valve open in diastole in 200 vigorous coughs in nine normal subjects. In these subjects, where the aortic diastolic pressure is much higher than the left ventricular pressure, it appears that a single forceful cough does not displace enough blood from the central aorta to reverse the pressure gradient and open the aortic valve.

After coronary angiography, when aortic diastolic pressures were as low as 28 mm Hg, the effect of coughing was similar to that seen in normal subjects. Coughing increased right atrial pressure more than aortic pressure, causing the coronary perfusion pressure to decrease. After the cough, both aortic and coronary perfusion pressures were somewhat lower. In many instances, aortic diastolic pressure was decreasing before the cough and the cough may not have been responsible for the further decrease in aortic pressure. However, immediately after the cough, the aortic and coronary perfusion pressure were not improved. We suspect, especially in the patients with the lower arterial pressures, that more forceful or prolonged coughs than generated by our patients might have initially displaced enough aortic blood to open the aortic valve and produce enough forward flow from the pulmonary vasculature to increase the aortic and coronary perfusion pressures.

When patients forcibly inspired before coughing, the right atrial pressure decreased more the did aortic pressure, slightly increasing the coronary perfusion pressure. It seems unlikely that this transient effect before some coughs could overcome the detrimental effect on the coronary perfusion pressure that occurs during and immediately after coughing.

The coronary perfusion pressure (or aortic diastolic–right atrial pressure) measured in this study is the pressure gradient across the entire coronary vascular bed. It was measured in diastole, when most of the coronary flow to the left ventricle occurs. In the dog, despite maximal coronary vasodilatation,
coronary flow ceases at an aortic pressure about 20–40 mm Hg above right atrial pressure, which has been termed Pzf. \textsuperscript{10, 17, 18} The true pressure gradient for flow in the coronary arteries may not be the coronary perfusion pressure measured in this study, but instead the aortic pressure – Pzf. \textsuperscript{18} Pzf appears to be determined by diastolic left ventricular intramyocardial pressure, coronary vasomotor tone and right atrial pressure. \textsuperscript{18-20} Pzf could not be measured directly in the circumstances of this study, but we can speculate as to cough's probable effect on Pzf. Because left ventricular diastolic volume does not change during coughing, \textsuperscript{8} the transmural left ventricular pressure should be unchanged and intramyocardial pressure should increase by the same amount as intrathoracic pressure. Intramyocardial pressure should increase by a similar amount, as does right atrial pressure. \textsuperscript{14} Similarly, the luminal closing pressure due to coronary vasomotor tone should increase by the same amount as the intrathoracic pressure. Because all the determinants of Pzf should increase by approximately the same amount as the right atrial pressure during coughing, the coronary flow gradient (aortic pressure – Pzf) should change by about the same amount as the coronary perfusion pressure.

The decreased coronary perfusion pressure during and immediately after coughing does not prove that coughing does not help clear the coronary arteries of angiographic contrast medium. First, one could speculate that coughing might increase coronary flow by producing a reflex coronary vasodilatation similar to the pulmonary inflation reflex that has been observed in dogs. \textsuperscript{21} However, any cough-induced coronary vasodilatation would have to overcome cough's detrimental effect on the coronary perfusion pressure. Second, coughing might squeeze contrast medium out of the coronary arteries into the coronary sinus and right atrium without increasing coronary inflow. However, right atrial pressure increases by approximately the same amount as intrathoracic pressure during cough, \textsuperscript{14} and there is no reason to presume that intramyocardial pressure should increase by more than the increase in intrathoracic pressure. Thus, coughing should not produce a pressure gradient to cause flow from the intramyocardial vessels. Alternatively, interruption of bradycardia after coronary angiography by coughing may be related not to clearing of angiographic contrast, but instead to a direct mechanical stimulation of the heart \textsuperscript{22-24} or to a reflex decrease of vagal tone. Because bradycardia and hypotension after selective injections of contrast media are generally transient, \textsuperscript{23} it is also possible that some of the beneficial effects attributed to coughing are due to coincident spontaneous resolution.

Although coughing markedly increases aortic pressure, the coronary perfusion pressure is decreased both during and immediately after coughing in both normotensive and moderately hypotensive patients. In these situations, coughing does not help clear angiographic contrast medium from the coronary arteries by increasing the pressure gradient across the coronary bed. Except as a form of cardiopulmonary resuscitation for severe hypotension, the mechanism and optimal use of coughing to interrupt moderate hypotension or bradycardia after coronary angiography remain unclear.

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