Intraperitoneal and Retropertoneal Carbon Dioxide Insufflation Evoke Different Effects on Caval Vein Pressure Gradients in Humans

Evidence for the Starling Resistor Concept of Abdominal Venous Return

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Background: The authors hypothesized that intraperitoneal and retropertoneal carbon dioxide insufflation during surgical procedures evoke markedly different effects on the venous low-pressure system, induce different inferior caval vein pressure gradients at similar insufflation pressures, and may provide evidence for the Starling resistor concept of abdominal venous return.

Methods: Intra- and extrathoracic caval vein pressures were measured using micromanometers during carbon dioxide insufflation at six cavity pressures (baseline and 10, 15, 20, and 24 mmHg and desufflation) in 20 anesthetized patients undergoing laparoscopic (supine, n = 8) or left (n = 6) or right (n = 6) retropertoneoscopic (prone position) surgery. Intracavitary, esophageal, and gastric pressures also were assessed. Data were analyzed for insufflation pressure-dependent and group effects by one-way and two-way analysis of variance for repeated measurements, respectively, followed by the Newman–Keuls post hoc test (P < 0.05).

Results: Intraperitoneal, unlike retropertoneal, insufflation markedly increased, in an insufflation pressure–dependent fashion, the inferior-to-superior caval vein pressure gradient (P < 0.00001) at the level of the diaphragm. In contrast to what was observed with retropertoneal insufflation, transmural intrathoracic caval vein pressure increased at 10 mmHg insufflation pressure, but the increase flattened with an insufflation pressure of more than 10 mmHg, and pressure decreased with an inflation pressure of 20 mmHg (P = 0.0397). These data are consistent with a zone 2 or 3 abdominal vascular condition during intraperitoneal and a zone 3 abdominal vascular condition during retropertoneal insufflation.

Conclusions: Intraperitoneal but not retropertoneal carbon dioxide insufflation evokes a transition of the abdominal venous compartment from a zone 2 to a zone 2 condition, presumably impairing venous return, supporting the Starling resistor concept of abdominal venous return in humans. (Key words: Laparoscopy; retropertoneoscopy; surgery; vena cava.)

BECAUSE it causes less postoperative pain and pulmonary dysfunction and hence provides quicker recovery with shorter hospital stays,1 endoscopic surgery has been established as an effective alternative for standard surgical procedures such as cholecystectomy, appendectomy, hernia repair, and even adrenalectomy.1–5 Because a retropertoneoscopic approach to the adrenal gland has been described,6 there is controversy about the optimum surgical approach to adrenalectomy.3–5 Laparoscopy and intraperitoneal carbon dioxide insufflation can have detrimental cardiovascular effects.7 Although several studies have addressed the cardiovascular effects of intraperitoneal carbon dioxide insufflation and increased intraabdominal pressure,8–12 the pathophysiology of this intervention is complex, with interaction of many mechanical, chemical, and neurohumoral mechanisms. Reported results differ depending on what population of patients is studied7,10,13 and apparently are affected by blood volume expansion or positioning.14,15 In contrast, retropertoneal carbon dioxide insufflation

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with pressures up to 20 mmHg for posterior retroperitoneoscopic adrenalectomy did not decrease cardiac output.16

We therefore focused our attention on the effects of intraperitoneal and retroperitoneal carbon dioxide insufflation on the body's low-pressure system, i.e., the venous circulation, and hypothesized that much of the controversy may be reconciled by the concept of "abdominal vascular zone conditions."17-19 This concept describes the vena cava as a collapsible tube traversing the abdominal cavity, in which varying pressures can prevail. Flow through such a collapsible tube depends on the relation between upstream extrabdominal vascular pressure, downstream intrathoracic caval vein pressure, and the intraabdominal ("compression chamber") pressure. The concept, therefore, represents a special type of a threshold resistor named after Starling. To our knowledge, a Starling resistor originally was described for explanation of the pressure-flow relation in the pulmonary circulation by Bancroft and Torrance.20 In the abdominal Starling resistor concept,17 inferior caval venous return is thought to decrease if thoracic caval vein pressure decreases below intraabdominal pressure because of development of a vascular waterfall.21 Increased intraabdominal pressure evoked by intraperitoneal carbon dioxide insufflation resulted in an increased pressure gradient between intraabdominal and intrathoracic caval vein pressures in anesthetized pigs.22

According to results of the experimental work of Guyton and Adkins,23 which emphasized the importance of abdominal pressure for inferior caval venous return, we hypothesized that in humans retroperitoneal or intraperitoneal carbon dioxide insufflation evoke an increase in inferior-to-superior caval vein pressure gradient, that this caval pressure gradient differs with retroperitoneal or intraperitoneal insufflation for similar insufflation pressures, and that pressures and gradients measured support the Starling resistor concept of abdominal venous return.

Materials and Methods

Patients

After approval of the local ethics committee, Ethikkommission der Medizinischen Fakultät, Essen, Germany, and with written informed consent, 24 patients were enrolled prospectively. Patients had cholecystolithiasis or disease of the right or left adrenal gland and were scheduled for laparoscopic cholecystectomy or retroperitoneoscopic adrenalectomy, respectively. Four patients were excluded for technical reasons (unsuccessful catheterization within an acceptable time), leaving six patients (three men, three women) undergoing left-sided retroperitoneoscopic adrenalectomy, six patients (three men, three women) undergoing right-sided retroperitoneoscopic adrenalectomy (for pheochromocytoma, hormonally inactive adenoma, and Conn or Cushing adenoma), and eight patients (five women, three men) undergoing laparoscopic cholecystectomy, respectively. Mean patient age was 55 ± 10 yr (mean ± SD), and patients were classified as American Society of Anesthesiologists physical status II or III.

General Procedures

All patients were administered flunitrazepam (1 mg per os) 1 h before surgery. Anesthesia was induced and maintained with intravenous propofol (1.5 mg/kg + 5 mg · kg⁻¹ · h⁻¹), alfentanil (50 µg/kg + 125 µg · kg⁻¹ · h⁻¹), and atracurium (0.5 mg/kg + 0.3 mg · kg⁻¹ · h⁻¹). Patients in all groups received Ringer's solution 4 ml · kg⁻¹ · h⁻¹. After tracheal intubation, the lungs were ventilated mechanically with an oxygen-air mixture (inspired oxygen fraction = 0.5) without positive end-expiratory pressure. Respiratory rate and tidal volume at baseline were adjusted to obtain an end-expiratory carbon dioxide tension of 28-35 mmHg and were maintained unchanged during data collection. After gastric aspiration via a conventional nasogastric tube, this tube was removed, and two balloon catheters (New Esophagus Catheter; Jäger GmbH, Höchberg, Germany) were inserted for measurement of esophageal and gastric pressures.

To record arterial pressure, a 20-gauge polyethylene catheter (Viggo-Spectramed, Montigny le Bretonneux, France) was inserted into the left radial artery. For measurement of central venous pressure and fluid replacement, a triple-lumen central venous catheter (Arrow, Reading, PA) was inserted via the right internal jugular vein, and its placement just above the sinus node confirmed by an intravascular electrocardiogram. To measure simultaneously intraabdominal and intrathoracic vena caval pressures and blood-flow velocities, a custom-built 8-French catheter with two integrated micromanometers mounted 30 cm apart and side-by-side to electromagnetic velocity sensors (Millar Instruments, Houston, TX) was inserted into the vena cava inferior via the jugular vein under fluoroscopic guidance using an introducer (Arrow). The distal transducer pair was positioned 15–18 cm below the diaphragma, with the
upper pair located in the superior vena cava. Catheter position was adjusted and documented by radiograph using a radiopaque ruler positioned under the patient's back.

In two additional patients undergoing laparoscopic cholecystectomy inferior caval vein blood velocity was measured using a Doppler flow wire inserted via a femoral vein.

**Retroperitoneal Carbon Dioxide Insufflation**

Patients scheduled for retroperitoneoscopic adrenalectomy were positioned in a prone position with moderately bent hips, laying on mattresses that allowed inclination of the abdomen and eccentric exposure of the surgical area. A distension balloon trocar (PDB 1000 Preperitoneal Distension Balloon; Origin, Gießen, Germany) was inserted ventrally to the lumbodorsal fascia. Subsequently, an artificial cavity 6–8 cm in diameter was created by inflating the balloon under endoscopic control. For endoscopy, two additional trocars were inserted into this cavity, one of them attached to a carbon dioxide insufflator (WISAP; Therme Pneu Electronic, Sauerlach, Germany) adjusted to generate and maintain a predetermined insufflation pressure. During data acquisition the second trocar was used to record intracavitary pressure. After surgery, patients were monitored in the postanesthesia or intensive care unit.

**Intraperitoneal Carbon Dioxide Insufflation**

For laparoscopic cholecystectomy in the supine position, carbon dioxide insufflation was performed using a standard laparoscopic technique. After a small skin incision the first trocar was inserted intraperitoneally in the umbilicus and attached to a carbon dioxide insufflator allowing initial insufflation under endoscopic control. A Veress needle was inserted intraperitoneally under visual control for continuous measurement of intraperitoneal cavity pressure. The Veress needle was changed for another trocar after data acquisition, to complete surgery.

**Measurements**

Heart rate was recorded from an electrocardiogram (Sirecust 1281; Siemens, Erlangen, Germany). Arterial and central venous pressures were measured by electromanometry (DTX Pressure Transducer System; Ohmeda, Madison, WI) relative to barometric pressure and referenced to a midthoracic plane. End-expiratory carbon dioxide tension was measured by infrared radiation, and tidal volume and respiratory rate by a hot wire anemometer (PM 8050; Dräger, Lübeck, Germany). For calibration of carbon dioxide measurements a calibration gas (5% CO₂ in air) was used (QUICK CAL gas cans; Datex Engstrom, Helsinki, Finland).

Intrathoracic and intraabdominal caval vein pressures were measured by catheter mounted micromanometers connected to transducer control units (Mikro-Tip Transducer Control Unit, Model TCB-500; Millar Instruments) for balancing and calibration. These units have an internal calibration circuit to provide an electrical zero and 20- and 100-mmHg voltage calibration signals. To minimize offset and gain errors, electric calibration was verified by exposing the micromanometers to defined pressures in a calibration device (Pressure Calibrator; Hugo Sachs, March-Hugstetten, Germany). After data acquisition, calibration was checked by immersing the micromanometers into warm saline to a defined hydrostatic depth using a stand cylinder.

Intrathoracic and intraabdominal vena caval blood-flow velocities were measured by two catheter-mounted electromagnetic velocity transducers (Millar Instruments; velocity range −200 to 200 cm/s), integrated into the catheter 30 cm apart and side-by-side to the respective micromanometers and connected to synchronized electromagnetic flowmeters (Model 501D; Carolina Medical, King, NC). Velocity sensors were calibrated in vitro using a saline-filled tubing system (cross-sectional area = 1.13 cm²) and a large reservoir, through which various constant flows were collected into a graduated cylinder. Because artifact-poor caval blood velocity measurements were obtained only in two patients undergoing carbon dioxide insufflation, however, as a result of electromagnetic interference, we measured intraabdominal inferior caval vein blood velocity by Doppler ultrasound in two additional patients. For this purpose a Doppler guide wire (FloWire .014"; Cardiometrics, Mountain View, CA) was inserted via a femoral vein and connected to a velocity meter (FloMap, Cardiometrics).

Esophageal and gastric pressures were measured by electromanometry (DTX Pressure Transducer System; Ohmeda) using air-filled multiperforated polyethylene tubes (internal diameter = 1 mm) connected to flexible latex rubber balloons (length = 10 cm, diameter = 1 cm, wall thickness = 0.6 mm, unstressed volume = 4.5 ml, operating volume = 0.4 ml air). These catheters had length markers and were inserted under laryngoscopic vision for 50 and 42 cm from the nostrils to be placed in the stomach and esophagus, respectively. They were thought to be placed appropriately if a pressure increase was obtained by minimal manual abdominal compres-
RETROPERITONEAL VERSUS INTRAPERITONEAL CO₂ INSUFFLATION

sion (gastric balloon), and respiratory and cardiac oscillations were observed (esophageal balloon). Intraperitoneal or retroperitoneal cavity pressures were measured by electromanometry using air-filled systems. Pressures were measured relative to barometric pressure at end-expiration.

Transmural pressures were calculated as the difference of intraluminal venous and surrounding pressures, as appropriate. Transmural inferior caval vein pressure for patients undergoing intraperitoneal carbon dioxide insufflation was calculated as the difference of intraabdominal caval vein and intraperitoneal cavity pressures.

Signals were recorded continuously on a strip chart theroarray recorder (K2G Polygraph System; Astro-Med, West Warwick, RI) and stored on tape (RD 200T PCM Data Recorder; TEAC, Wiesbaden-Erbenheim, Germany).

Experimental Protocol

Baseline values of cardiovascular variables were sampled 15 min after positioning of the anesthetized patients with the insufflation and recording trocars in situ; i.e., after an initial insufflation and desufflation of a small amount of carbon dioxide. Retroperitoneal or intraperitoneal spaces then were insufflated with carbon dioxide using target insufflation pressures of 10, 15, 20, or 24 mmHg. To minimize any time-dependent effects, these target pressures were applied in a randomized fashion. Intracavital pressures were maintained for 3-5 min to achieve steady state conditions before data sampling. Hemodynamic and respiratory variables were measured again 3 min after cavity desufflation. Then intraperitoneal insufflation pressure again was increased to approximately 27 mmHg (n = 3) or 10 mmHg (n = 2), and the micromanometer-tipped catheter was withdrawn slowly toward the right atrium while continuously recording intraabdominal caval vein pressure. Finally, inferior caval vein blood velocity was measured in two additional patients using a Doppler system during carbon dioxide insufflation.

Statistics

Results are reported as the mean ± SD unless indicated otherwise. Values of variables were analyzed by two-way or one-way analysis of variance for repeated measurements followed by the Newman–Keuls post hoc test, as appropriate. The following a priori null hypotheses were tested: There is no significant difference in values of variables during retroperitoneal or intraperitoneal carbon dioxide insufflation with increasing insufflation pressure and between groups for equal insufflation pressures. To assess the relation between intraabdominal cavity pressure and intraabdominal caval vein pressure, we calculated the correlation coefficients and the equation of the regression lines for every single patient undergoing intraperitoneal insufflation. Correlation coefficients, slopes of the regression lines, and intercepts were averaged. To test whether the slopes differed significantly from each other we performed an analysis of covariance. To test whether correlation coefficients were significantly different from 0, we used a Student t test. A null hypothesis was rejected and statistical significance assumed if the α error was smaller than 5%.

Results

Intraperitoneal Insufflation

The pressure gradient between the inferior and superior caval veins increased with insufflation from 1.4 ± 0.7 mmHg at baseline to almost 19 mmHg with an insufflation pressure of 24 mmHg (figs. 1 and 2 and table 1). Intraabdominal caval vein pressure increased as insufflation pressure increased, attaining almost four times baseline pressure (figs. 1 and 2 and table 1). Corresponding transmural intraabdominal caval vein pressure initially decreased with insufflation but did not further change with a further increase in intraabdominal pressure (table 1).

After a significant initial pressure increase with an insufflation pressure of 10 mmHg, intrathoracic caval vein pressure relative to atmosphere remained unchanged with further increases in insufflation pressure (fig. 2 and table 1). Both gastric and esophageal pressure increased with increasing intraperitoneal pressure (fig. 2 and table 2).

Transmural intrathoracic caval vein pressure initially increased slightly but showed no further increase with intraperitoneal insufflation pressures more than 10 mmHg. There was a significant decrease in transmural intrathoracic caval vein pressure with 20- and 24-mmHg insufflation pressures (fig. 2). All pressure changes were reversible, and abdominal desufflation was followed by a significant increase in transmural intrathoracic and intraabdominal caval vein pressures.

Retroperitoneal Insufflation and Comparison between Groups

Both intraabdominal and intrathoracic caval vein pressures increased significantly during both left and right retroperitoneal carbon dioxide insufflation as insufflation pressure increased. In contrast to intraperitoneal insufflation, the gradient between intraabdominal and
Baseline intraperitoneal CO₂ insufflation

<table>
<thead>
<tr>
<th>Target Insufflation Pressure</th>
<th>Baseline</th>
<th>Intraperitoneal CO₂ Insufflation</th>
<th>Desufflation</th>
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</thead>
<tbody>
<tr>
<td>Intraabdominal Cavai Vein Pressure</td>
<td>0 mmHg</td>
<td>10 mmHg</td>
<td>15 mmHg</td>
</tr>
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</table>

Intrathoracic caval vein pressures remained unchanged. Only with inflation pressures more than 20 mmHg and only with right-sided retroperitoneal carbon dioxide insufflation did a significant increase in gradient develop (figs. 3A and B and table 1).

Transmural intrathoracic caval vein pressure increased with retroperitoneal inflation in an insufflation pressure-dependent fashion (figs. 3A and B and table 1). This contrasts with intraperitoneal insufflation, in which after an initial increase transmural intrathoracic caval vein pressure remained unchanged or even decreased with increasing insufflation pressures. Also in contrast to intraperitoneal insufflation, both intraabdominal caval vein pressure and gastric pressure increased to similar extents from baseline with left-sided and right-sided retroperitoneal insufflation.

Esophageal pressure remained unchanged during both left-sided and right-sided retroperitoneal insufflation (table 2).

Mean arterial pressure increased with both intraperitoneal and retroperitoneal carbon dioxide insufflation; heart rate did not change. The arterial pressure increase was not related to insufflation pressure, and comparison between groups yielded no significant differences (table 3).

**Relation of Vascular Pressures and Gradients to Abdominal Pressure**

As shown by the catheter-withdrawal maneuvers, the hydraulic pressure gradient between the extrathoracic, subdiaphragmatic and the intrathoracic, supradiaphragmatic caval vein, which increased with intraperitoneal insufflation, arose at the level of the diaphragm. Figure 4 illustrates local venous pressure during slow catheter withdrawal from the infrarenal to the supradiaphragmatic thoracic caval vein in a patient undergoing intraperitoneal carbon dioxide insufflation.

To illustrate abdominal vascular zone conditions and the back-pressure important for inferior caval venous return with increasing intraperitoneal or retroperitoneal pressure, differences between gastric and corresponding intrathoracic caval vein pressures also are plotted against intraperitoneal pressures (figs. 2 and 3A and B). In contrast to both left-sided and right-sided retroperitoneal insufflation, with intraperitoneal insufflation there was a significant increase from negative values at baseline to clearly positive values at insufflation pressures more than 15 mmHg. With a negative gradient, the intrathoracic caval vein pressure is the effective back-pressure, corresponding to an abdominal vascular zone 3 condition. With a positive gradient, the intraabdominal pressure is the effective back-pressure, corresponding to an abdominal vascular zone 2 condition. At 10 mmHg intraperitoneal pressure, the gradient is approximately 0 at end-expiration, reflecting a transition in which both zone 2 and zone 3 conditions are likely present during a respiratory cycle. Interestingly, no significant changes occurred with retroperitoneal insufflation (figs. 3A and B). This is consistent with an all-zone 3 condition.

The increase in intraabdominal caval vein pressure of all patients was correlated linearly (r = 0.99 ± 0.006) to the increase in intraabdominal cavity pressure (fig. 5).
Fig. 2. Intraabdominal and intrathoracic caval vein pressure and gastric pressure (top) during intraperitoneal carbon dioxide insufflation at baseline (open symbols) and during different insufflation pressures (closed symbols). Corresponding differences between gastric pressure and intrathoracic caval vein pressure (middle) illustrates the transition (arrow) from a zone 3 abdominal condition (shaded zone) to a zone 2 condition with increasing intraperitoneal pressure. Transmural intrathoracic caval vein pressure (bottom) also is shown. The data are the mean ± SD from eight anesthetized, mechanically ventilated patients undergoing intraperitoneal carbon dioxide insufflation. *P < 0.05 versus group baseline; #P < 0.05 versus group desufflation; § P < 0.05 versus 10 mmHg insufflation pressure.

Because the slopes of the patients’ pressure relations did not differ significantly (P = 0.78), a regression equation can be calculated as: intraabdominal caval vein pressure = 0.85 (± 0.09) × intraperitoneal pressure + 7.39 (± 2.7) (P < 0.001). The mean intercept of 7.39 mmHg is only 0.9 mmHg greater than the mean baseline central venous pressure (6.5 ± 3.1 mmHg), indicating that without abdominal pressure there would be almost no caval pressure gradient at the level of the diaphragm or, vice versa, that abdominal pressure is responsible for the gradient.

Caval Vein Blood Velocity

Unfortunately, artifact-poor caval vein blood velocity measurements could not be obtained by electromagnetic methods because of unresolvable electromagnetic interference in the operating room. Inferior caval vein blood flow velocity, however, decreased with insufflation pressures greater than 15 mmHg in the two additional patients undergoing Doppler ultrasound measurements (fig. 6). Under baseline conditions with the abdomen uninflated, phasic caval vein blood velocity toward the heart increased with positive airway pressure; with an insufflation pressure of 15 mmHg, each lung inflation led to a further decrease in phasic blood velocity.

Discussion

This study is the first to assess in humans hydraulic pressure gradients in the low-pressure system during intraperitoneal and retroperitoneal carbon dioxide insufflation. We hypothesized that intraperitoneal and retroperitoneal carbon dioxide insufflation evoke fundamentally different cardiovascular changes, and that measurements of hydraulic venous pressure gradients during laparoscopy would provide an opportunity to assess in humans the Starling resistor concept of abdominal venous return. These hypotheses were confirmed because at similar insufflation and hence cavity pressures intraperitoneal but not retroperitoneal carbon dioxide insufflation evoked an abdominal pressure-dependent increase in the pressure gradient between the intrathoracic and abdominal inferior caval vein at the level of the diaphragm; resulted in a biphasic change of transmural intrathoracic caval vein pressure, suggesting increased initial cardiac filling but decreased cardiac filling with insufflation pressures greater than 10-15 mmHg; and decreased inferior caval vein blood-flow velocity in individuals in whom reliable measurements were obtained. All these changes are consistent with the Starling resistor concept of abdominal venous return.

These results emerged if carbon dioxide was insufflated either retroperitoneally in a modified prone posi-
transmural intraabdominal caval vein pressure

Table 1. Caval Vein Pressures and Related Variables of Patients Undergoing Intraperitoneal or Left or Right Retroperitoneal* CO₂ Insufflation

<table>
<thead>
<tr>
<th>Target Insufflation Pressure (mmHg)</th>
<th>Baseline</th>
<th>10 mmHg</th>
<th>15 mmHg</th>
<th>20 mmHg</th>
<th>24 mmHg</th>
<th>Desufflation</th>
<th>ANOVA</th>
<th>P Value</th>
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<tr>
<td>Intraabdominal caval vein pressure</td>
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<tr>
<td>Intraperitoneal</td>
<td>6.5 ± 3.1</td>
<td>9.4 ± 3.7*</td>
<td>9.3 ± 3.9'</td>
<td>9.2 ± 3.5'</td>
<td>8.9 ± 3.9'</td>
<td>††</td>
<td>7.5 ± 2.4</td>
<td>(P = 0.0397)</td>
</tr>
<tr>
<td>Left retroperitoneal</td>
<td>9.2 ± 2.9</td>
<td>11.9 ± 3.7'</td>
<td>12.2 ± 3.7'</td>
<td>12.8 ± 3.9'</td>
<td>13.6 ± 4.4'</td>
<td>§</td>
<td>11.0 ± 2.6</td>
<td></td>
</tr>
<tr>
<td>Right retroperitoneal</td>
<td>9.4 ± 2.4</td>
<td>12.1 ± 2.1*</td>
<td>13.0 ± 2.5'</td>
<td>14.2 ± 3.3'</td>
<td>15.8 ± 3.1'</td>
<td>††</td>
<td>11.5 ± 1.6</td>
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<tr>
<td>Intraabdominal caval vein pressure</td>
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</tr>
<tr>
<td>Intraperitoneal</td>
<td>7.9 ± 2.9</td>
<td>14.9 ± 1.8'†</td>
<td>19.0 ± 1.6'††</td>
<td>23.8 ± 1.4'††</td>
<td>27.1 ± 2.2'††</td>
<td></td>
<td>9.1 ± 2.7</td>
<td>(P &lt; 0.00001)</td>
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<tr>
<td>Left retroperitoneal</td>
<td>11.8 ± 2.6</td>
<td>14.6 ± 3.1'</td>
<td>15.0 ± 2.9'</td>
<td>16.4 ± 3.0'</td>
<td>16.7 ± 3.1'</td>
<td>††</td>
<td>14.7 ± 3.8</td>
<td></td>
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<tr>
<td>Right retroperitoneal</td>
<td>11.0 ± 1.9</td>
<td>14.3 ± 1.4*</td>
<td>15.8 ± 1.0'</td>
<td>19.7 ± 1.0'</td>
<td>22.8 ± 0.6'</td>
<td>††</td>
<td>14.0 ± 1.4</td>
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<tr>
<td>Intrathoracic caval vein pressure</td>
<td>1.4 ± 0.7</td>
<td>5.5 ± 2.3'†</td>
<td>9.7 ± 2.9'††</td>
<td>13.9 ± 2.6'††</td>
<td>18.3 ± 2.5'††</td>
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<td>1.7 ± 1.3</td>
<td>(P &lt; 0.00001)</td>
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<tr>
<td>Left retroperitoneal</td>
<td>2.2 ± 1.5</td>
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<td>2.8 ± 2.0</td>
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<td>3.7 ± 2.1</td>
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<tr>
<td>Right retroperitoneal</td>
<td>1.6 ± 0.8</td>
<td>2.2 ± 1.5</td>
<td>2.8 ± 2.0</td>
<td>5.4 ± 2.7'</td>
<td>7.1 ± 3.1'</td>
<td>†</td>
<td>2.4 ± 1.1</td>
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<td>Intraabdominal-intrathoracic caval vein pressure gradient</td>
<td>4.4 ± 3.6'</td>
<td>6.3 ± 3.7'†</td>
<td>5.2 ± 3.2'†</td>
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<td>5.4 ± 2.2'†</td>
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<tr>
<td>Left retroperitoneal</td>
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<td>12.6 ± 3.1'</td>
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<td>14.4 ± 3.8'</td>
<td>††</td>
<td>11.7 ± 2.5</td>
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<tr>
<td>Right retroperitoneal</td>
<td>9.1 ± 2.6</td>
<td>11.4 ± 2.5'</td>
<td>12.5 ± 2.4'</td>
<td>13.5 ± 3.1'</td>
<td>14.9 ± 3.1'</td>
<td>††</td>
<td>10.8 ± 2.4</td>
<td></td>
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<tr>
<td>Transmural inraabdominal caval vein pressure</td>
<td>7.2 ± 3.1</td>
<td>5.3 ± 2.1'†</td>
<td>5.3 ± 1.9'†</td>
<td>5.3 ± 1.6'†</td>
<td>4.6 ± 1.8'†</td>
<td></td>
<td>8.1 ± 2.5</td>
<td>(P &lt; 0.0001)</td>
</tr>
</tbody>
</table>

Data are mean ± SD from 20 anesthetized patients undergoing either intraperitoneal (n = 8) or left (n = 6) or right (n = 6) retroperitoneal (prone position) CO₂ insufflation. P values in parenthesis derive from one-way** (insufflation pressure) and two-way (insufflation pressure × group) analysis of variance for repeated measurements within and across groups, respectively, as appropriate.

* P < 0.05 versus group baseline.
† P < 0.05 for comparison between groups at same insufflation pressure.
‡ P < 0.05 versus group desufflation.
§ P < 0.05 versus corresponding left retroperitoneal value.
|| P < 0.05 versus preceding group value.
# P < 0.05 versus 10 mmHg insufflation pressure.
ANOVA = analysis of variance.

tion or intraperitoneally in the supine position in anesthetized, relaxed, mechanically ventilated humans. Although positional changes per se can affect cardiovascular performance, values of cardiovascular variables in groups at baseline after positioning showed no significant differences. During data acquisition body position remained unchanged and no surgical interventions interfered. Interpretation of alterations in the venous low-pressure system depends on meticulous measurements of very small pressure changes. A 1-mmHg pressure change is related to a blood volume change of about 200 ml and may alter systemic venous return by 17%. We used a custom-built double micromanometer, avoiding problems that result from incorrect positioning of a hydrostatic zero reference point or insufficient transducer system frequency response. Changes in venous pressures induced by retroperitoneal or intraperitoneal carbon dioxide insufflation were accurately recorded.

Esophageal pressure as an estimate of intrathoracic pressure was determined according to the technique of Milic-Emili et al. Although esophageal pressure does not always represent intrathoracic pressure accurately, and the weight of the heart may increase esophageal pressure to above intrapleural pressure in the supine position, with the esophageal balloon inserted for at least 32-40 cm from the nares, esophageal pressure is close to atmospheric pressure and is believed to be only slightly above adjacent pleural pressure in supine humans. With esophageal pressure approximately 0.6 mmHg greater in our supine patients compared with the prone patients, our baseline measurements are well within the range reported in the literature. Changes in esophageal pressure likely reflected those of intrathoracic pressure.

Pressure transmission within the abdomen is reported to be nearly homogeneous in humans, especially if sufficient fluid or gas is present to allow hydraulic continuity throughout the abdomen. During active diaphragmatic contraction, however, pressure between the liver and diaphragm may be higher than in other parts of the abdomen. The amount retroperitoneal cavity pressure transmitted to tissues surrounding the caval vein is unknown quantitatively and may not be assessed reliably by gastric pressure measurements. Furthermore, al-

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Table 2. Intracavitral, Gastric, and Esophageal Pressures of Patients Undergoing Intraperitoneal or Left or Right Retroperitoneal CO₂ Insufflation

<table>
<thead>
<tr>
<th>Target Insufflation Pressure (mmHg)</th>
<th>Baseline</th>
<th>10 mmHg</th>
<th>15 mmHg</th>
<th>20 mmHg</th>
<th>24 mmHg</th>
<th>Desufflation</th>
<th>ANOVA P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracavitral pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraperitoneal</td>
<td>0.8 ± 0.5</td>
<td>9.6 ± 0.7*</td>
<td>13.9 ± 0.5*</td>
<td>18.6 ± 1.0*</td>
<td>22.9 ± 0.7*</td>
<td>1.2 ± 0.7</td>
<td>(NS)</td>
</tr>
<tr>
<td>Left retroperitoneal</td>
<td>0.6 ± 0.4</td>
<td>9.7 ± 0.8*</td>
<td>13.9 ± 0.7*</td>
<td>19.0 ± 0.8*</td>
<td>22.7 ± 0.7*</td>
<td>0.7 ± 0.6</td>
<td></td>
</tr>
<tr>
<td>Right retroperitoneal</td>
<td>0.8 ± 0.5</td>
<td>9.7 ± 0.7*</td>
<td>13.5 ± 0.8*</td>
<td>19.2 ± 1.1*</td>
<td>23.2 ± 0.3*</td>
<td>0.8 ± 0.8</td>
<td></td>
</tr>
<tr>
<td>Gastric pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraperitoneal</td>
<td>3.4 ± 1.6</td>
<td>9.4 ± 0.8*</td>
<td>12.9 ± 1.6†</td>
<td>17.1 ± 2.7†‡</td>
<td>20.4 ± 3.4†‡§</td>
<td>3.6 ± 1.2</td>
<td>(P &lt; 0.0001)</td>
</tr>
<tr>
<td>Left retroperitoneal</td>
<td>5.3 ± 3.6</td>
<td>6.3 ± 3.8</td>
<td>6.6 ± 4.2</td>
<td>7.6 ± 4.3</td>
<td>8.5 ± 4.5†</td>
<td>5.5 ± 3.8</td>
<td></td>
</tr>
<tr>
<td>Right retroperitoneal</td>
<td>8.2 ± 3.4</td>
<td>9.9 ± 3.9</td>
<td>10.8 ± 4.3</td>
<td>11.1 ± 5.1†</td>
<td>12.9 ± 5.8†‡</td>
<td>9.6 ± 3.7</td>
<td></td>
</tr>
<tr>
<td>Esophageal pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraperitoneal</td>
<td>2.1 ± 1.9</td>
<td>3.1 ± 2.6</td>
<td>4.1 ± 3.2†</td>
<td>4.9 ± 3.8†‡</td>
<td>5.4 ± 4.1†‡</td>
<td>2.1 ± 2.0</td>
<td>(P &lt; 0.0001)</td>
</tr>
<tr>
<td>Left retroperitoneal</td>
<td>-0.8 ± 1.5</td>
<td>-0.8 ± 1.5</td>
<td>-0.8 ± 1.5</td>
<td>-0.8 ± 1.5</td>
<td>-0.8 ± 1.5</td>
<td>-0.8 ± 1.5</td>
<td>-0.7 ± 1.5</td>
</tr>
<tr>
<td>Right retroperitoneal</td>
<td>0.3 ± 1.6</td>
<td>0.8 ± 2.4</td>
<td>0.8 ± 2.5</td>
<td>0.8 ± 2.4</td>
<td>0.8 ± 2.4</td>
<td>0.8 ± 2.2</td>
<td></td>
</tr>
</tbody>
</table>

Data are mean ± SD from 20 anesthetized patients undergoing either intraperitoneal (n = 8) or left (n = 6) or right (n = 6) retroperitoneal (prone position) CO₂ insufflation. P values in parenthesis derive from two-way (insufflation pressure × group) analysis of variance for repeated measurements within and across groups, respectively, as appropriate.

* P < 0.05 versus group desufflation.
† P < 0.05 versus group baseline.
‡ P < 0.05 versus preceding group value.
§ P < 0.05 for comparison between groups at same insufflation pressure.
ANOVA = analysis of variance; NS = not significant.

though gastric pressure reflects intraabdominal pressure in supine patients if measured with air-filled balloons, baseline values may have been increased by pressure on the epigastric area in the prone position, by the weight of abdominal organs, or by eccentric positioning on the operating table in our patients. This may explain the slightly higher gastric pressures in patients undergoing right-sided compared with left-sided adrenalectomy. Our baseline values, however, are in line with measurements in supine awake or anesthetized subjects.

To avoid iatrogenic injuries, placement of cannulae for intracavitral pressure measurements was performed under visual control after initial insufflation of a small amount of gas. To prevent the cavity from collapsing on the measuring cannula, some gas probably is necessary. We cannot exclude that some gas remained within the cavity during baseline and desufflation. Although baseline intraperitoneal cavity pressure recorded via the Veress needle is about 0.8 mmHg higher than reported by others, however, these issues do not affect measurements during further insufflation.

The baseline intraabdominal-to-intrathoracic caval vein pressure gradient observed in our study is within the range reported in a single subject by Gauer and Thron. Based on our experiments in pigs, we expected that increased abdominal pressure would increase this pressure gradient along the inferior caval vein in humans as insufflation (intraperitoneal) pressure increased. This is exactly what we observed: The pressure gradient increased from 1.4 mmHg at baseline intraperitoneal pressure to almost 19 mmHg. Furthermore, intraperitoneal but not retroperitoneal carbon dioxide insufflation appeared to impair cardiac filling with inflation pressures greater than 15 mmHg. This process was fully reversible because abdominal desufflation was accompanied by a significant increase in transmural intrathoracic caval vein pressure.

Our findings in humans are consistent with the Starling resistor concept of abdominal venous return, in which, analogous to pulmonary vascular zones, flow through the inferior vena cava is a function of the pressure difference between either upstream venous and abdominal pressure or downstream intrathoracic caval vein pressure. With intraabdominal pressure greater than intrathoracic caval vein pressure, the abdominal venous compartment acts as a collapsible Starling resistor (zone 2 abdominal condition), resulting in a decrease in inferior caval venous return and a decrease in transmural intrathoracic caval vein pressure. Intra-and extrathoracic venous systems under these conditions are separated hydraulically like a waterfall, in which downstream intrathoracic caval vein pressure has no impact on flow. With intrathoracic caval vein pressure greater than intraabdominal pressure (zone 3 abdominal

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condition) at baseline and desufflation, the inferior caval vein and surrounding abdominal chamber function as a capacitor. Here flow is a function of the pressure difference between upstream venous pressure (reflected by intraabdominal caval vein pressure) and downstream intrathoracic caval vein pressure. The initial increase in abdominal pressure to 10 mmHg enhanced intrathoracic filling, transmural intrathoracic caval vein pressure increased, and transmural intraabdominal caval vein pressure decreased. With intraperitoneal pressures between 10 and 15 mmHg, there is a transition zone without significant net changes.

Intraperitoneal fluid infusion or gas insufflation increased abdominal pressure also in dead dogs and anesthetized pigs, respectively, and increased the pressure difference between central venous and iliac venous pressures. This has not been investigated in humans, and the potential relevance in the clinical setting is unclear. An increase in femoral vein and an initial increase in left ventricular cardiac suggested by transesophageal echocardiography was observed in patients undergoing laparoscopic cholecystectomy. Because maximum inflation pressures of only 15 mmHg were applied in the latter study, alterations in end-diastolic left ventricular area at higher inflation pressures have not been reported.

Our finding that the hydraulic gradient between the extrathoracic, subdiaphragmatic and intrathoracic, su-
Table 3. Cardiovascular and Respiratory Variables of Patients Undergoing Intraperitoneal or Left or Right Retroperitoneal CO₂ Insufflation

<table>
<thead>
<tr>
<th>Target Insufflation Pressure (mmHg)</th>
<th>Baseline</th>
<th>10 mmHg</th>
<th>15 mmHg</th>
<th>20 mmHg</th>
<th>24 mmHg</th>
<th>Desufflation</th>
<th>ANOVA P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Intraperitoneal</td>
<td>83 ± 18</td>
<td>102 ± 19*</td>
<td>101 ± 18*</td>
<td>98 ± 18*</td>
<td>101 ± 21*</td>
<td>85 ± 20</td>
<td>(NS)</td>
</tr>
<tr>
<td>Left retroperitoneal</td>
<td>81 ± 20</td>
<td>85 ± 18*</td>
<td>90 ± 18*</td>
<td>91 ± 21*</td>
<td>89 ± 18*</td>
<td>90 ± 17</td>
<td></td>
</tr>
<tr>
<td>Right retroperitoneal</td>
<td>88 ± 18</td>
<td>108 ± 19*</td>
<td>107 ± 19*</td>
<td>111 ± 18*</td>
<td>112 ± 17*</td>
<td>98 ± 18</td>
<td></td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraperitoneal</td>
<td>65 ± 12</td>
<td>71 ± 10</td>
<td>68 ± 10</td>
<td>68 ± 8</td>
<td>67 ± 5</td>
<td>63 ± 9</td>
<td>(NS)</td>
</tr>
<tr>
<td>Left retroperitoneal</td>
<td>62 ± 10</td>
<td>68 ± 12</td>
<td>68 ± 10</td>
<td>68 ± 10</td>
<td>65 ± 8</td>
<td>63 ± 5</td>
<td></td>
</tr>
<tr>
<td>Right retroperitoneal</td>
<td>60 ± 12</td>
<td>64 ± 15</td>
<td>65 ± 15</td>
<td>65 ± 16</td>
<td>66 ± 14</td>
<td>64 ± 10</td>
<td></td>
</tr>
<tr>
<td>Endexpiratory CO₂ tension (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraperitoneal</td>
<td>27 ± 2</td>
<td>28 ± 2*</td>
<td>29 ± 2*</td>
<td>29 ± 2*</td>
<td>29 ± 2*</td>
<td>30 ± 2*</td>
<td>(NS)</td>
</tr>
<tr>
<td>Left retroperitoneal</td>
<td>27 ± 2</td>
<td>29 ± 2*</td>
<td>30 ± 2*</td>
<td>30 ± 2*</td>
<td>31 ± 2*</td>
<td>29 ± 2*</td>
<td></td>
</tr>
<tr>
<td>Right retroperitoneal</td>
<td>26 ± 2</td>
<td>30 ± 2*</td>
<td>29 ± 2*</td>
<td>29 ± 2*</td>
<td>30 ± 2*</td>
<td>30 ± 2*</td>
<td></td>
</tr>
</tbody>
</table>

Data are means ± SD from 20 anesthetized patients undergoing either intraperitoneal (n = 8) or left (n = 6) or right (n = 6) retroperitoneal (prone position) CO₂ insufflation. P values in parenthesis derive from two-way (insufflation pressure × group) analysis of variance for repeated measurements within and across groups, respectively, as appropriate.

* P < 0.05 versus group baseline.
† P < 0.05 for comparison between groups at same insufflation pressure.
ANOVA = analysis of variance; NS = not significant.

pradiaphragmatic inferior vena cava arose at the diaphragmatic level is also consistent with physical models of the inferior caval vein. With increasing surrounding pressure a collapsible tube with flow, i.e., the vena cava or a Penrose drain, narrows and finally collapses at the exit point of the traversed chamber (abdominal cavity). That is what likely happened in our patients during intraperitoneal insufflation.

The abdominal vascular zone concept also is supported by interpretation of blood velocity changes. Analogous to pulmonary vein flow with lung inflation under different vascular zone conditions, phased velocity increased under baseline (zone 3) conditions with mechanical inspiration and an increase in abdominal pressure but decreased with inspiration in a zone 2 condition. We could not measure volumetric inferior caval vein blood flow and therefore did not assess abdominal venous return. With a decrease in transmural intrabdominal caval vein pressure (and thus inferior caval vein diameter), however during intraperitoneal insufflation and decreased inferior caval vein blood velocity, inferior caval vein blood flow in all likelihood decreased. The systolic peak velocities of 40 cm/s assessed by Doppler ultrasound are in the range reported in conscious volunteers. A decrease in femoral venous blood velocity also was shown by periodically performed duplex scanning during laparo-
Relation between intraperitoneal pressure and intraabdominal caval vein pressure

**Fig. 5.** Relation of intraabdominal caval vein pressure to intraabdominal cavity pressure. Data from eight patients undergoing intraperitoneal carbon dioxide insufflation showing a linear association between both variables ($r = 0.99 \pm 0.006$) with the regression equation: intraabdominal caval vein pressure = $0.85 \pm 0.09 \times$ intraperitoneal pressure + $7.39 \pm 2.7$ ($P < 0.001$).

With retroperitoneal insufflation, intrathoracic caval vein pressure always is greater than intraperitoneal, respectively gastric, pressure. This is consistent with an all-zone 3 condition, resulting in a continuous increase in intrathoracic caval vein pressure with increasing retroperitoneal insufflation pressures. Because we did not observe a prominent increase in gastric or esophageal pressures even up to retroperitoneal insufflation pressures of 24 mmHg, a much smaller pressure transmission can be assumed from the inflated retroperitoneal cavity to adjacent tissues and the peritoneal cavity than with intraperitoneal inflation. Possibly, carbon dioxide either is propagated in other tissue planes or acts on the caval vein only over a short length. The latter hypothesis is supported by the assumption that the artificial cavity created by retroperitoneal insufflation is much smaller than with intraperitoneal insufflation.

In conclusion, our data show in humans that intraperitoneal carbon dioxide insufflation evokes a transition of the abdominal venous compartment from a zone 3 condition at baseline to a zone 2 condition, likely impairing cardiac filling at higher insufflation pressures. This effect is not observed during left or right retroperitoneal carbon dioxide insufflation. These findings are consistent with a Starling resistor concept of abdominal venous return in humans.

The authors thank Dr. med. D. Baumgart, Department of Cardiology, University-GH Essen, for Doppler ultrasound blood-flow velocity measurements; and S. Birnbrich, R. Gutt, R. Martin, and C. Ochterbeck for skilful technical help and assistance in the operating room.

**References**


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