

## Diaphragmatic Shortening after Thoracic Surgery in Humans

### Effects of Mechanical Ventilation and Thoracic Epidural Anesthesia

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**Background:** Diaphragmatic function is believed to be inhibited after thoracic surgery and may be improved by thoracic epidural anesthesia.

**Methods:** Diaphragmatic function after a thoracotomy was monitored by implanting one pair of sonomicrometry crystals and two electromyogram (EMG) electrodes on the costal diaphragm of six patients undergoing an elective pulmonary resection. Crystals and EMG electrodes remained in place for 12–24 h.

**Results:** During mechanical ventilation, costal diaphragmatic length (as a percent of rest length; %L<sub>FRC</sub>) decreased passively as tidal volume (V<sub>T</sub>) increased (%L<sub>FRC</sub> = 2.81 + 1.12 × 10<sup>-2</sup> V<sub>T</sub> (ml), r = 0.99). During spontaneous ventilation, the costal shortening (2.1 ± 2.3 %L<sub>FRC</sub>) was less than during mechanical ventilation (7.9 ± 3.0 %L<sub>FRC</sub>, P < 0.05) at the same V<sub>T</sub>. Comparing spontaneous ventilation before and 30 min after thoracic epidural anesthesia, there were increases of V<sub>T</sub> (390 ± 78 to 555 ± 75 ml), vital capacity (1.37 ± 0.16 to 1.68 ± 0.21 l), and esophageal (-8.5 ± 1.5 to -10.6 ± 1.7 cmH<sub>2</sub>O), gastric (-0.7 ± 0.8 to +0.8 ± 0.8 cmH<sub>2</sub>O), and transdiaphragmatic (7.7 ± 1.5 to 11.5 ± 1.9 cmH<sub>2</sub>O) pressures, but diaphragmatic EMG and shortening fraction remained constant. In three of six patients,

epidural anesthesia produced paradoxical segment lengthening upon inspiration.

**Conclusions:** Thoracotomy and pulmonary resection produce a marked reduction of active diaphragmatic shortening, which is not reversed by thoracic epidural anesthesia despite improvement of other indices of respiratory function. (Key words: Anesthetic technique: epidural. Instrument techniques: electromyography; sonomicrometry. Lung, ventilation: mechanical ventilation; spontaneous ventilation. Muscle, diaphragm: costal diaphragmatic contraction; postoperative function. Surgery: thoracic pulmonary resection.)

IMPAIRED ventilatory function as reflected by reduced vital capacity occurs after both upper abdominal and thoracic surgery.<sup>1-4</sup> Marked inhibition of diaphragmatic function may contribute to postoperative ventilatory dysfunction and, in animal models and patients, requires several weeks for stable recovery.<sup>4,5</sup> Proposed mechanisms producing diaphragmatic dysfunction include alterations of the contractile properties of the diaphragm related to surgical trauma and/or reflexogenic inhibition of phrenic nerve activation. A reduction of intrinsic diaphragmatic contractile properties is not the predominant factor, because transdiaphragmatic pressures (P<sub>di</sub>) during bilateral phrenic nerve stimulation are reported to be unchanged after upper abdominal surgery in patients.<sup>6</sup> The most likely mechanism of diaphragmatic impairment is due to surgical stimulation of afferent pathways (vagal, phrenic, or spinal) arising in the abdomen or in the thorax leading to postoperative reflex inhibition of phrenic neural activation.

Previous studies have assessed diaphragmatic function in patients indirectly from P<sub>di</sub> measurements and/or tidal changes in rib cage and abdominal dimensions.<sup>2,7</sup> We have developed an awake sheep model with sonomicrometry crystals and electromyogram

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**Table 1. Clinical Characteristics, Operative Procedures, and Preoperative Pulmonary Function Tests**

Patient	Age (yr)	Sex	Diagnosis, Operation	Forced Vital Capacity (l)	Forced Expiratory Volume after 1 s (l)
1	52	F	Adenocarcinoma, right middle and lower lobectomy	1.79	1.16
2	68	F	Large-cell carcinoma, right upper lobectomy	2.45	1.31
3	57	M	Adenocarcinoma, left upper lobectomy	3.95	2.8
4	48	M	Bronchiectasis, left upper lobectomy	4.00	2.71
5	58	F	Bronchoalveolar carcinoma, right upper lobectomy	2.90	2.33
6	60	M	Adenocarcinoma, right upper lobectomy	3.90	2.72

(EMG) electrodes implanted *via* a thoracotomy onto both costal and crural diaphragmatic regions.<sup>5,8-10</sup> In this study, we have adapted techniques used in our sheep studies to measure diaphragmatic length and shortening in patients following pulmonary resection. We reasoned that, because we have demonstrated in sheep that the pressure ratio  $\delta P_{\text{gas}} / \delta P_{\text{di}}$ , which has been used by previous investigators as an index of diaphragmatic shortening, may not correctly predict diaphragmatic shortening,<sup>5</sup> previous studies that did not simultaneously determine diaphragmatic segmental length, shortening, and activation could not directly assess regional diaphragmatic function.

We designed this study to learn whether diaphragmatic inhibition occurs in patients after thoracic surgery and whether epidural anesthesia can reverse it. First, we wished to determine how mechanical and spontaneous ventilation affect regional diaphragmatic shortening. We anticipated that, if diaphragmatic contraction were reduced postoperatively, its shortening during mechanical ventilation (MV) would be greater than the shortening during spontaneous ventilation, providing tidal volume ( $V_T$ ) was equal for the two modes of ventilation. Second, since postural changes from supine to 30° head-up are common in clinical situations, we wished to learn whether a change in body position of this magnitude would alter diaphragmatic length and neural activation. In normal humans, a change in posture from supine to upright causes an increase in lung volume (and by inference, a decrease in diaphragmatic length) and an increase in diaphragmatic EMG activation.<sup>11</sup> Finally, we wished to determine whether injection of 2% lidocaine into the thoracic epidural space to block spinal inhibitory afferent

fibers would augment diaphragmatic shortening, activation, and respiratory pressure generation.

## Methods

### *Surgical Procedure*

This study was approved by the Subcommittee on Human Studies of the Massachusetts General Hospital. Written informed consent was obtained from each patient. Selected clinical characteristics and operative procedures performed on the patients are summarized in table 1. We studied six patients (mean age 57.2 yr, range 48–68 yr) undergoing a pulmonary resection *via* a lateral thoracotomy through the 6th intercostal space. Before general anesthesia, a catheter was inserted in the thoracic epidural space through the T8–T9 interspace. The anesthetic regimen was chosen and delivered by an anesthesiologist unconnected with the study. Thiopental (3–5 mg/kg, intravenous) was used for induction of anesthesia, followed by vecuronium bromide (0.1 mg/kg). One-lung ventilation using oxygen and enflurane (0.5–1%) with controlled ventilation and a double-lumen endotracheal tube was employed. Fentanyl and vecuronium were given as required.

After completion of the surgical procedure and before chest closure, two sonomicrometry crystals (Dimension 3, Hacienda Heights, CA) and two EMG electrodes were implanted into the costal diaphragmatic region, near the central tendon, along the direction of the muscle fibers, inserting near the 8th intercostal space. We believe this corresponds to a location between the mid-axillary and anterior axillary lines. The crystals were mounted on 1-mm stalks of PE-190 tubing fastened with silicone rubber cement to a 15-mm triangular segment

of woven polypropylene fabric to prevent crystal rotation. A 6-mm section of bare, seven-stranded (44-G) stainless steel wire (Medwire, Mt. Vernon, NY) for recording EMG signals also was attached with silicone rubber cement to the fabric directly adjacent to the sonomicrometer crystals. An O-silk suture was sewn circumferentially around the perimeter of the fabric and tied along the entire length of the EMG and sonomicrometer leads. This suture extended from the fabric patch to the external wire connection (fig. 1). The sonomicrometer crystal and EMG electrode were inserted through small incisions in the diaphragmatic pleural surface and into a small separation between the diaphragmatic fibers created by blunt dissection. The Dacron triangle was secured onto the costal diaphragm with 6-O polypropylene sutures placed at the corners of the Dacron patch. Transducer pairs were inserted approximately 20 mm apart. Transducer alignment was initially checked to confirm that the sides of the Dacron patch faced by the sonomicrometer crystals were parallel to each other and perpendicular to the direction of the muscle fibers. Direct electrical muscle stimulation (Microstim, Neurotechnology, Houston, TX) confirmed correct sonomicrometer placement. The stimulator leads were placed directly against the diaphragm, and then, at the maximal output of the stimulator, single twitches and 100-Hz tetanic stimulation were applied as the costal shortening signal was observed on a two-channel oscilloscope (Tektronix 5100, Beaverton, OR). Monitoring leads were externalized through a separate thoracostomy tube and one arm of a Y-connector; the other arm was connected to an underwater seal. Two other chest tubes provided routine thoracic drainage and lung expansion. After closing the thorax, a double-balloon catheter system was inserted transnasally into the stomach and the esophagus to measure respiratory pressures.

Upon completion of the surgery, the trachea was intubated with a single-lumen endotracheal tube, and the patients were transferred to the respiratory intensive care unit. Small amounts of intravenous midazolam and fentanyl or morphine were given if the patient reported discomfort. Tracheal extubation occurred upon completion of measurements if respiratory function was satisfactory. Crystals and EMG electrodes were removed 12–24 h after surgery by placing firm traction on the leads and silk suture, then by withdrawing them into the chest tube containing the monitoring wires. The chest tube was removed in standard fashion. No patients

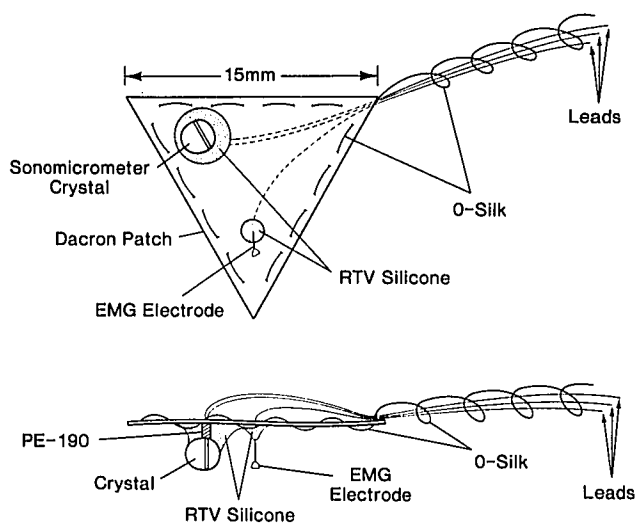


Fig. 1. Schematic diagram of sonomicrometer and electromyogram electrode attached to Dacron fabric patch. RTV silicone bonds the crystal to the Dacron fabric and prevents crystal rotation. The side of the fabric triangle closest to the sonomicrometer is cut parallel to the corresponding face of sonomicrometer. When implanted on the diaphragm, this "active side" of each patch is kept parallel to each other and perpendicular to the muscle fibers, ensuring that the crystals face each other. The O silk suture ensures continuity of the leads and that both the crystal and the leads will be removed.

suffered any injury or complications as a result of the study.

#### Measurements

Measurements were obtained 4–6 h after the thoracotomy. The endotracheal tube was connected to a Fleisch pneumotachograph (model 3700, Hans Rudolph, Kansas City, MO) to measure airflow and a pressure transducer (Valyline MP-45, Northridge, CA) to measure airway pressure.  $V_T$  was obtained by integration of the airflow signal (model 8815A, Hewlett Packard). This signal was calibrated for volume with a 1-liter syringe. We calculated, in addition to  $V_T$ , the mean respiratory frequency ( $R_f$ ) and minute ventilation ( $V_E = V_T \times R_f$ ).

**Diaphragmatic Shortening and EMG.** Dynamic measurements of the distance between the ultrasonic transducers were obtained by sonomicrometry (model 120, Triton, San Diego, CA). The use of sonomicrometry to measure regional diaphragmatic length in dogs was described and validated previously.<sup>12</sup> We measured costal muscle segment length at end-expiration ( $L_{FRC}$ ). Muscle shortening during inspiration was

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expressed as the percentage change of resting length ( $\delta L/L_{FRC} \times 100$ ).

Signals from the costal EMG electrodes were amplified and band-pass-filtered (35 Hz to 2 KHz, model P511, Grass, Quincy, MA). The output signal was averaged using a Paynter filter with a time constant of 100 ms.<sup>13</sup> EMG values were normalized to 100% of the value during quiet breathing in the supine position for each set of measurements.

**Gastric and Esophageal Pressures.** The double-lumen catheter consisted of a nasogastric tube with a 10-cm long esophageal balloon attached (National Catheter, Glen Falls, NY). The catheter was modified with a second balloon, attached with cyanoacrylate cement to the distal 5 cm of the catheter, communicating with the drainage lumen of the catheter. The balloons were filled, respectively, with 2 ml and 1 ml of air. Cardiac contractions were used as a reference to confirm that the esophageal balloon was located in the mid-esophagus.<sup>14</sup> Each lumen of the balloon catheter system was connected to a pressure transducer (Valdine MP-45). Changes in esophageal pressure ( $P_{es}$ ) and  $P_{gas}$  were measured as the difference between peak inspiratory minus peak expiratory pressures. The  $P_{di}$  was computed from the difference between abdominal (gastric) and  $P_{es}$  measured at the same time. Maximal inspiratory pressure (MIP) was measured at residual volume by using a Briggs T-piece containing one-way valves (with inspiratory port occluded) connected to a pressure gauge *via* the airway port. Both MIP and forced vital capacity (FVC) were recorded as the best of three measurements.

**Thoracic and Abdominal Dimensions.** Tidal changes in rib cage and abdominal circumference were measured simultaneously using a respiratory inductive plethysmograph (RIP; Respirace, Ambulatory Monitoring, Ardsley, NY). Technical descriptions and physical properties of the RIP were reported previously.<sup>15</sup> The rib cage band was applied high on the chest, with its upper border just caudad to the axillae. The abdominal band was positioned so that its upper margin was at the level of the umbilicus. Rib cage and abdominal signal gains were set equally. Compartmental volume-motion coefficients were computed by determining the ratio of rib cage signal standard deviation to the abdominal signal standard deviation<sup>16</sup> for five consecutive breaths.

All measurements were recorded simultaneously on an eight-channel recorder (model 7758A, Hewlett

Packard) and an IBM-AT compatible microcomputer (Codas software, Datak, Akron, OH). Sonomicrometric signals were displayed continuously on an oscilloscope. Each value represents the mean of five consecutive breaths, and all results are expressed as mean  $\pm$  SE.

#### *Experimental Procedure*

**Effects of Mechanical Ventilation.** Patients were studied while supine within 2 h after the end of surgery.  $V_{Ts}$  of 200, 400, 600, 800, and 1,000 ml were delivered by a ventilator (Siemens 900C, Danvers, MA) in random order. Then patients were allowed to breathe spontaneously. Measurements obtained in the same position were compared at a similar spontaneous and mechanical  $V_T$ . In addition, measurements of spontaneously breathing patients were repeated in the 30° head-up position. Because body position can influence RIP calibrations,<sup>17</sup> we did not compare RIP measurements between the supine and 30° head-up position.

**Effects of Thoracic Epidural Blockade.** Studies were performed within 6 h after surgery. Baseline respiratory studies during spontaneous ventilation were obtained in the 30° head-up posture. Then patients were placed supine, and a solution of 2% lidocaine was injected through the epidural catheter to provide anesthesia to pinprick between the T1 and T12 dermatomes. This level of sensory blockade was obtained in all patients. The volume injected ranged from 6 to 8 ml. Arterial blood pressure was monitored continuously during the study *via* a radial arterial catheter inserted preoperatively for standard anesthesia management. Phenylephrine was infused when needed to maintain blood pressure at preoperative levels. After 10 min with stable anesthetic and blood pressure levels, spontaneous respiratory data were recorded in the 30° head-up posture. Before and after epidural blockade, we measured the MIP produced at the mouth during a maximal inspiratory effort (Mueller maneuver) at residual volume against the occluded inspiratory limb of a Briggs T-piece with one-way valves, as well as the maximal FVC.

During the study, the position of the RIP bands before and after lidocaine injection were maintained as carefully as possible to eliminate band displacement when patients were placed supine for administration of the local anesthetic.

#### *Statistical Analysis*

All values are expressed as mean  $\pm$  SE. Comparisons of measurements between mechanical and spontaneous

**Table 2. Respiratory Measurements during Mechanical and Spontaneous Ventilation and after Epidural Blockade**

	Mechanical Ventilation, Supine	Spontaneous Ventilation		
		Supine	30°, Before 2% Lidocaine	30°, After 2% Lidocaine
Costal segment				
Length (mm)	16.3 ± 2.2	15.9 ± 1.9	15.7 ± 1.8	15.5 ± 1.8
Shortening (% L <sub>FRC</sub> )	7.89 ± 2.96	2.07 ± 2.28*	1.57 ± 1.58	-0.89 ± 2.64
EMG (% supine spontaneous ventilation)	0 ± 0	100 ± 0	88 ± 8	108 ± 8
Esophageal pressure (cmH <sub>2</sub> O)	6.7 ± 1.8	-11.3 ± 1.9*	-8.5 ± 1.5	-10.6 ± 1.7†
Gastric pressure (cmH <sub>2</sub> O)	1.26 ± 0.42	0.38 ± 0.67*	-0.74 ± 0.89	0.83 ± 0.83†
Transdiaphragmatic pressure (cmH <sub>2</sub> O)	-5.4 ± 1.6	11.7 ± 2.4*	7.7 ± 1.5	11.5 ± 1.9†
Airway pressure (cmH <sub>2</sub> O)	19.3 ± 5.3	-3.7 ± 0.4*	-2.0 ± 0.5	-2.8 ± 0.7
Tidal volume (ml)	457 ± 102	433 ± 103	390 ± 78	555 ± 75†
Minute ventilation (l/min)	4.26 ± 1.18	7.02 ± 0.79	5.64 ± 0.46	7.00 ± 0.85†
Respiratory frequency (breaths/min)	8.9 ± 0.5	18.1 ± 2.7*	16.2 ± 1.9	13.2 ± 1.5
Ribcage motion (AU)	0.18 ± 0.04	0.15 ± 0.03	0.09 ± 0.02	0.12 ± 0.03
Abdominal motion (AU)	0.25 ± 0.08	0.44 ± 0.06*	0.56 ± 0.04	0.78 ± 0.12
Ribcage motion (% tidal volume)	43.1 ± 8.8	43.5 ± 7.1	42.5 ± 9.3	26.4 ± 9.1
Maximal inspiratory pressure (cmH <sub>2</sub> O)			-38.3 ± 8.0	-51.8 ± 9.6†
Forced vital capacity (l)			1.37 ± 0.16	1.68 ± 0.20†

Results are mean ± SE.

% L<sub>FRC</sub> = length change as percent of length at functional residual capacity; EMG = electromyographic activity; AU = arbitrary units.

\*  $P < 0.05$ , mechanical ventilation versus spontaneous ventilation.

†  $P < 0.05$ , after versus before lidocaine injection.

ventilation, supine and 30° head-up posture, and before and after epidural blockade were done using a Wilcoxon matched-pairs test.<sup>18</sup> A  $P$  value less than 0.05 was considered to indicate statistical significance.

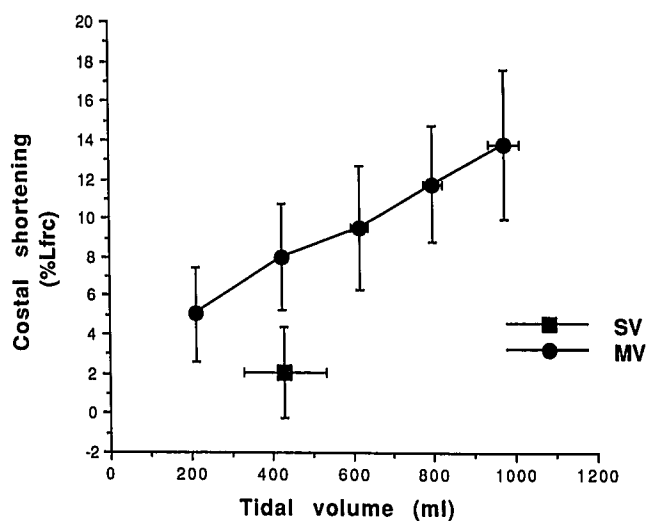
## Results

We obtained reliable sonomicrometric signals in five of six patients. In one patient (no. 1, table 1) a small sonomicrometric signal-to-noise ratio precluded accurately recording all measurements on the strip chart recorder, but they were observed on the oscilloscope. In this patient, the trend and variation of the signals with each intervention were similar to those of the other patients, and we included stable sonomicrometric measurements from this patient in our study. Diaphragmatic shortening during direct electrical stimulation at the time of implantation was  $9.9 \pm 3.4$  L<sub>FRC</sub> during single twitch stimulation and  $29.6 \pm 5.1$  L<sub>FRC</sub> during 100 Hz tetanic stimulation.

### Effects of Mechanical Ventilation

The results are summarized in table 2. During controlled MV, the costal diaphragmatic EMG signal was

abolished. Costal shortening increased linearly with ventilator  $V_T$  ( $\%L_{FRC} = 2.81 \pm 1.12 \times 10^{-2} V_T$  (ml);  $r = 0.99$ ,  $P < 0.05$ ), as shown in figure 2. Furthermore, costal shortening during MV ( $7.9 \pm 3.0$  L<sub>FRC</sub>) ex-



**Fig. 2.** The relationship between costal shortening and tidal volume during mechanical and spontaneous ventilation ( $n = 5$ , results are expressed as mean ± SE).

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ceeded costal shortening during spontaneous ventilation ( $2.1 \pm 2.3 \%L_{FRC}$ ;  $P < 0.05$ ) at the same  $V_T$  ( $433 \pm 103$  vs.  $457 \pm 102$  ml, respectively), while costal resting length did not change. In all patients, costal shortening decreased during spontaneous ventilation (SV; fig. 3). When patients breathed spontaneously,  $P_{cs}$  became more negative (from  $6.7 \pm 1.8$  (MV) to  $-11.3 \pm 1.9$  cmH<sub>2</sub>O (SV);  $P < 0.05$ ) and  $P_{di}$  significantly increased (from  $-5.4 \pm 1.6$  (MV) to  $11.7 \pm 2.4$  cmH<sub>2</sub>O (SV);  $P < 0.05$ ), while  $P_{gas}$  decreased (from  $1.26 \pm 0.42$  (MV) to  $0.38 \pm 0.67$  cmH<sub>2</sub>O (SV);  $P < 0.05$ ).

Because  $R_f$  increased and comparisons were made at similar  $V_{Ts}$ ,  $V_E$  increased during spontaneous ventilation as compared to MV, from  $4.26 \pm 1.18$  to  $7.02 \pm 0.79$  l/min ( $P < 0.05$ ).

In spontaneously breathing patients, transition from the supine to  $30^\circ$  head-up position did not change costal resting length, shortening fraction, EMG activity, breathing pattern, or respiratory pressures.

#### Effects of Thoracic Epidural Blockade

Respiratory measurements are summarized in table 2. Costal resting length and shortening did not change

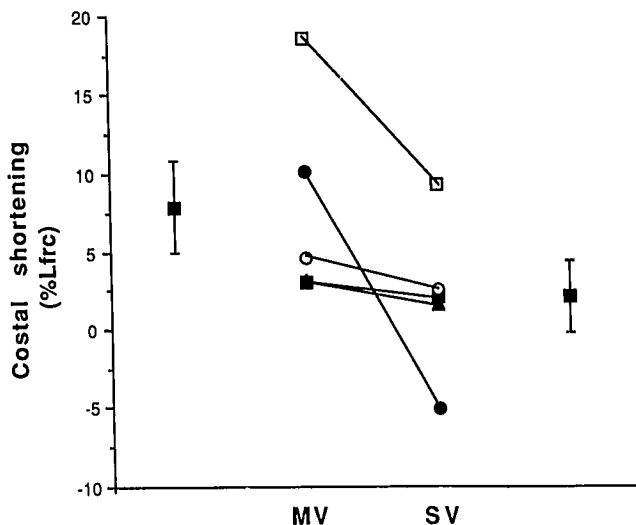


Fig. 3. Individual data, for five patients, of costal shortening during mechanical ventilation at a tidal volume of  $457 \pm 102$  ml and spontaneous ventilation at a tidal volume of  $433 \pm 103$  ml. The group mean and standard error is represented by the symbol with vertical bar adjacent to each group of individual data points. Patient 6 developed diaphragmatic lengthening during inspiration. Open square = patient 1; open triangle = patient 2; closed square = patient 3; closed triangle = patient 4; open circle = patient 5; closed circle = patient 6.

after epidural blockade. Three patients (nos. 4, 5, and 6) demonstrated paradoxical motion (segmental lengthening upon inspiration) of the costal diaphragm after epidural blockade (fig. 4). An example of paradoxical lengthening of the costal diaphragm after epidural block is shown in figure 5. No change in costal diaphragmatic EMG activity was observed after the injection of lidocaine.

Compared to values before epidural anesthesia,  $V_T$  and  $V_E$  significantly increased (from  $390 \pm 78$  to  $555 \pm 75$  ml and from  $5.64 \pm 0.46$  to  $7.00 \pm 0.85$  l/min, respectively; both,  $P < 0.05$ ), while  $R_f$  did not change. The FVC and MIP both increased significantly after epidural blockade (from  $1.37 \pm 0.16$  to  $1.68 \pm 0.20$  l and  $-38.3 \pm 8.0$  to  $-51.8 \pm 9.6$  cmH<sub>2</sub>O; both,  $P < 0.05$ ). This pattern was observed in each patient.

After epidural anesthesia,  $P_{cs}$  decreased (from  $-8.5 \pm 1.5$  to  $-10.6 \pm 1.7$  cmH<sub>2</sub>O;  $P < 0.05$ ), while  $P_{gas}$  and  $P_{di}$  increased (from  $-0.74 \pm 0.89$  to  $+0.83 \pm 0.83$  cmH<sub>2</sub>O and  $7.7 \pm 1.5$  to  $11.5 \pm 1.9$  cmH<sub>2</sub>O, respectively; both,  $P < 0.05$ ). Pressure measurement values for each patient are given in figure 6.

No significant changes were observed in rib cage and abdominal displacements as a percentage of  $V_T$  before and after epidural anesthesia.

#### Discussion

The major results of this clinical study are: (1) sonomicrometry measured diaphragmatic segment length changes in patients after thoracic surgery; (2) passive costal shortening during MV was greater than active shortening during spontaneous ventilation at a similar  $V_T$ ; and (3) after thoracic surgery, thoracic epidural anesthesia using 2% lidocaine did not increase diaphragmatic shortening. Epidural anesthesia increased  $P_{di}$ s and augmented  $V_T$ , vital capacity, and MIP, but decreased tidal diaphragmatic shortening, and in three of six patients, produced paradoxical inspiratory lengthening of the costal diaphragmatic segment.

Our measurements of regional diaphragmatic shortening using sonomicrometry directly documented regional diaphragmatic shortening in patients after thoracic surgery. Maeda *et al.*<sup>19</sup> demonstrated that diaphragmatic function was impaired in patients after a pulmonary resection, and many studies<sup>2,20</sup> have demonstrated reduced diaphragmatic function after upper abdominal surgery. However, previous assessments of diaphragmatic shortening and its function have been

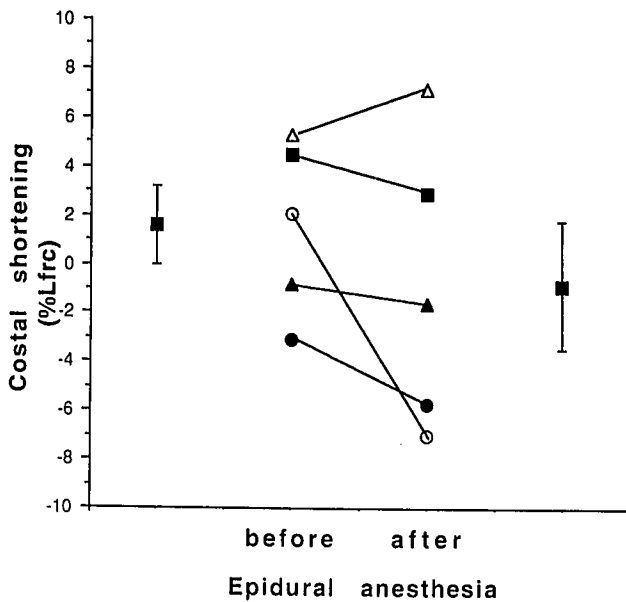


Fig. 4. Individual measurements of costal shortening before and after epidural anesthesia at a tidal volume of  $390 \pm 78$  ml and  $555 \pm 75$  ml, respectively, for five patients. Patient symbols as in figure 3. Three patients (nos. 4, 5, and 6) developed paradoxical inspiratory shortening.

based upon indirect measurements. Diaphragmatic displacement has been inferred from changes of lung gas volumes,<sup>21,22</sup> relative displacement of the rib cage and abdomen,<sup>23,24</sup> or by measuring variations of  $P_{di}$  or the ratio of  $\delta P_{gas}/\delta P_{di}$ .<sup>6,20</sup> To attempt to reduce some of the difficulties encountered by these indirect diaphragmatic measurements, we developed an awake sheep model employing sonomicrometry with transthoracic implantation to enable us to accurately determine diaphragmatic length changes after various interventions.<sup>5,8</sup> These consistent and reliable animal studies allowed us to safely and temporarily implant sonomicrometer crystals into patients undergoing thoracic surgery.

The sonomicrometer signals provided data from one small area of one hemidiaphragm. Although Sprung *et al.*<sup>25</sup> have demonstrated differences in shortening between different diaphragmatic regions in the same animal, these differences become less important when similar regions are studied in many animals.<sup>25-27</sup> Our sonomicrometry data for each subject were directionally consistent between each intervention despite implantation into either right or left costal diaphragmatic region. We believe the similarity of data between sub-

jects accurately represents the shortening of the lateral costal diaphragmatic region in humans.

The first phase of our study examined regional diaphragmatic shortening during mechanical and spontaneous ventilation in patients after a thoracotomy. We hypothesized that differences between mechanical and spontaneous ventilation might demonstrate diaphragmatic inhibition. During controlled MV, the lack of respiratory muscle drive was evidenced by the absence of both diaphragmatic EMG activity and changes in the pressure signals that are indicative of inspiratory efforts. When lung volume was increased by a mechanical inspiration, the costal diaphragmatic segment shortened passively and the degree of shortening was correlated with the  $V_T$ . During spontaneous ventilation, costal segmental shortening was less than during MV at an equivalent  $V_T$  (figs. 2 and 3). In one spontaneously breathing patient, we observed costal paradox with costal diaphragmatic lengthening during inspiration (fig. 3). This pattern was noted occasionally in our sheep model on the first postoperative day after thoracotomy.<sup>5</sup> In the other five patients, the costal segment shortened synchronously with inspiration. Although hypercapnia has been reported to depress diaphragmatic contractility, and our sedated patients were probably hypercapnic, we doubt hypercapnia was the primary cause for the reductions of diaphragmatic shortening during spontaneous breathing.

Phrenic nerve conduction is believed to be normal after a thoracotomy in humans.<sup>19,28</sup> In the operating room, the costal diaphragmatic segment of our patients shortened during direct electrical stimulation of the muscle (9.9 % $L_{FRC}$  single twitch, 29.6 % $L_{FRC}$  tetanic stimulation). In our previous sheep studies after a thoracotomy, diaphragmatic shortening during spontaneous ventilation increased during recovery despite a constant level of maximal electrically stimulated shortening.<sup>5</sup> Thus, based upon these previous studies,<sup>19,28</sup> our differences of costal shortening between mechanical and spontaneous ventilation most likely are due to factors proximal to the phrenic nerve, but we cannot exclude the possibility of functional abnormalities within the phrenic nerve due either to the surgery or the concomitant cancer.

Previous studies have suggested that inhibition of diaphragmatic contraction after thoracotomy is secondary to reflexogenic inhibition of phrenic neural activation rather than due to pain alone.<sup>7,20,29</sup> In patients after upper abdominal surgery, Simoneau *et al.*<sup>20</sup> re-

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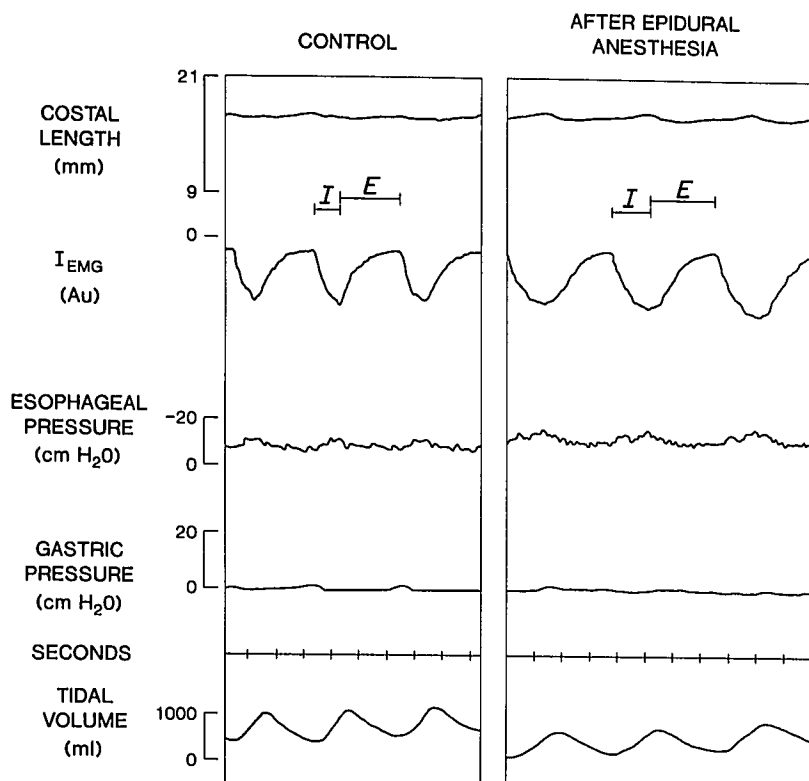


Fig. 5. Data recording from one patient (no. 5) during spontaneous ventilation in the 30° head-up position before (control) and after thoracic epidural anesthesia. Paradoxical lengthening of the costal diaphragm developed after epidural blockade, without changes of resting length, integrated electromyogram activity, or tidal volume. In this patient, gastric pressure increased near the end of expiration in the control period, suggesting activation of expiratory abdominal muscles. This was eliminated after epidural blockade.

ported that diaphragmatic dysfunction was not affected by epidural injection of fentanyl. Clèrgue *et al.*<sup>29</sup> demonstrated that the rapid, shallow postoperative breathing pattern was not modified by intrathecal injection of morphine (2 and 5 mg). Mankikian *et al.*<sup>7</sup> reported that diaphragmatic inhibition was partially reversed by thoracic epidural blockade with 0.5% bupivacaine. Taken together, these studies suggested that pain perception is probably not the key mechanism underlying postoperative diaphragmatic dysfunction and that reflexes inhibiting phrenic motor activity are probably responsible for diaphragmatic dysfunction. After upper abdominal surgery in humans, inhibitory reflexes may originate from visceral stimulation and/or increased abdominal wall tone and could ascend through the spinal cord, vagus nerve, or phrenic nerve. Partial reversal of diaphragmatic inhibition with epidural blockade of the thoracic spinal cord after abdominal surgery may be related to direct or indirect interruption of spinal afferent pathways.<sup>7</sup>

In our patients, the respiratory effects of epidural anesthesia were assessed by measuring several respi-

ratory parameters (table 2). We noted  $V_T$ , FVC, and MIP increased, while the  $R_f$  tended to decrease, maintaining a constant  $V_E$ .  $P_{gas}$  and  $P_{di}$  increased, while  $P_{es}$  decreased after epidural blockade (fig. 6). However, no improvement of costal shortening (fig. 4) or EMG activity was observed. Indeed, costal shortening decreased, and in three of six patients, paradoxical inspiratory motion was noted after epidural blockade. The failure of regional diaphragmatic shortening to increase after epidural blockade and the fact that diaphragmatic activation did not increase, despite increases of  $P_{es}$ ,  $P_{di}$ ,  $V_T$ , FVC, and MIP, suggest that diaphragmatic contraction could not overcome the increased external forces placed upon it by the other respiratory muscles. The maintenance of a nearly constant resting length and the absence of a consistent change in rib cage expansion in our patients limited the compensatory mechanisms that could alter diaphragmatic shortening. However, we are unable to determine whether recruitment of accessory muscle contraction, maintenance of intercostal muscle motor function, or contraction of other diaphragmatic regions



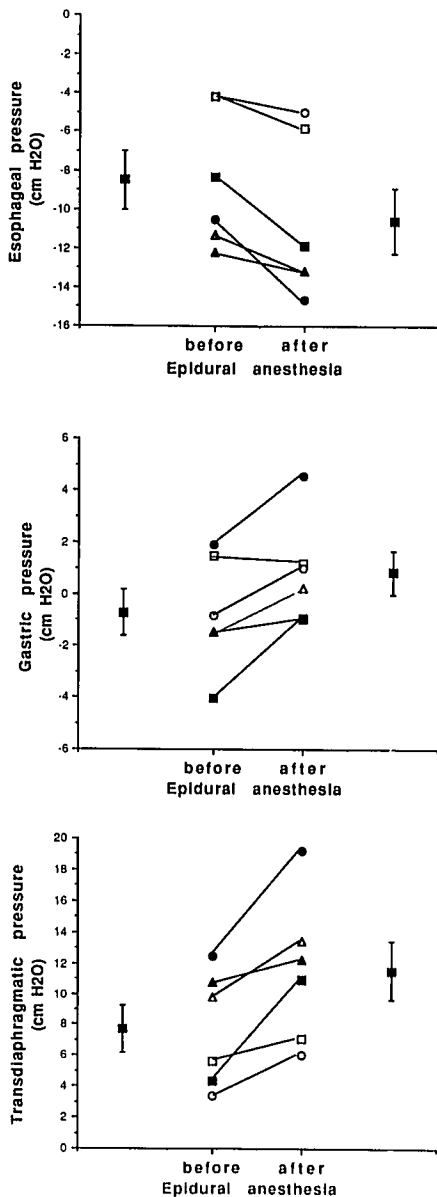


Fig. 6. Individual measurements of esophageal, gastric, and transdiaphragmatic pressures before and after epidural anesthesia at a tidal volume of  $390 \pm 78$  and  $555 \pm 75$  ml, respectively, for six patients. Patient symbols as in figure 3.

led to the apparent persistence of rib cage expansion after epidural blockade. Despite the limitations of our chest wall measurements, our results do not support the view that thoracic epidural anesthesia can interrupt the inhibitory afferents responsible for diaphragmatic inhibition.

In our sheep model, we evaluated the effects of thoracic epidural anesthesia using 2% lidocaine after a thoracotomy.<sup>10</sup> We observed a significant increase of both costal and crural diaphragmatic shortening, from  $8.7 \pm 0.7$  to  $18.1 \pm 1.0$  %L<sub>FRC</sub> and from  $4.9 \pm 0.5$  to  $10.4 \pm 2.0$  %L<sub>FRC</sub> ( $P < 0.05$ ), respectively. However, the costal and crural shortening increases were associated with an increased costal resting length from  $23.0 \pm 1.1$  to  $28.2 \pm 1.5$  mm ( $P < 0.05$ ), while crural resting length did not change. After injection of 2% lidocaine, regional EMG and  $P_{di}$  were not altered during quiet breathing, but  $V_T$  was increased (from  $235 \pm 16$  to  $283 \pm 28$  ml,  $P < 0.05$ ) and rib cage expansion was almost abolished. While epidural infusion of 2% lidocaine increased the  $V_T$  without changing diaphragmatic EMG activity in both our sheep and patient studies, diaphragmatic segmental shortening increased in the sheep but decreased or became paradoxical in the patients. Epidural lidocaine markedly reduced rib cage expansion in the sheep but had only a minor effect on rib cage expansion in patients (table 2). We postulate that the differences in diaphragmatic shortening after epidural blockade were due to the different effects of the epidural on rib cage expansion and its ability to lower  $P_{cs}$ .

We had postulated that, after thoracic surgery, the addition of a thoracic epidural anesthetic, by interrupting inhibitory afferents conducted by the thoracic spinal cord, would reduce phrenic inhibition and improve diaphragmatic function. However, an epidural anesthetic also can alter the function of other inspiratory (intercostal and accessory) or expiratory (intercostal and abdominal) respiratory muscles and, as discussed below, the interaction of the rib cage with the diaphragm. The respiratory inductance plethysmograph measurements were included to assess changes in respiratory muscle function, but in this study, many factors may have impaired their ability to infer respiratory muscle function (see appendix). Therefore, to emphasize the uncertainties of the respiratory inductance pneumograph data, we have presented the results in two forms, as uncalibrated excursions (measured in units of voltage) and as the rib cage fraction of  $V_T$ .

The interaction of the diaphragm with the rib cage muscles during inspiration may be explained by their mechanical linkages and by the relationship between contractile force and speed of muscular shortening. Ward *et al.*<sup>30</sup> have proposed that, during inspiration, the intercostal and accessory muscles operate mechan-

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ically in series with the costal diaphragm. The contraction of two muscles mechanically arranged in series will generate an equal contractile force in each muscle, but the change in the length of each muscle will be additive.<sup>31</sup> If one muscle were stronger than the other, then even if both were stimulated equally, the stronger would shorten and the weaker would lengthen, or shorten less than the stronger one. Such a situation could occur if an epidural anesthetic were to alter the motor activation of the intercostal and/or accessory muscles relative to the diaphragm. Since the activation of the diaphragm was unchanged in both our patient and sheep epidural studies, an increase in rib cage contractile force would lead to decreased diaphragmatic shortening, whereas a decrease in rib cage contractile force would lead to increased diaphragmatic shortening.

Similarly, differences in the rates that two muscles arranged in series change their length can result in equalization of previously unequal contractile forces. The force-velocity curve indicates that, for a constant level of muscle activation, changes in the rate of diaphragmatic length change also affect its apparent contractile force. If inspiratory time (or muscle contraction time) is constant, a reduction in the shortening of an actively contracting muscle leads to slower average shortening rate and an increase in contractile force, while an increase in shortening rate leads to a decrease in contractile force. However, if a contracting muscle is stretched, its contractile force exceeds the force it would exert if no length change occurred.

By assuming the diaphragm operates mechanically in series with the intercostal and accessory muscles and that the force-velocity relationship applies to the diaphragm, we can explain the divergent results of our two studies. In the sheep study, diaphragmatic shortening increased after epidural injection of 2% lidocaine, while rib cage expansion decreased and tidal  $P_{es}$  changes were less negative.<sup>10</sup> By contrast, in our patients after epidural injection of 2% lidocaine, diaphragmatic shortening decreased or became negative (paradoxical lengthening), while tidal  $P_{es}$  changes became more negative. This suggests that the rib cage or accessory muscles may have generated a greater force (despite a possible reduction of rib cage contribution to breathing, as judged from the Resptrace) that led to tidal lengthening of the diaphragm in three patients and to reduced tidal shortening in the other three patients.

The analysis and interpretation of our data has presumed that sonomicrometers produce representative shortening measurements for the entire diaphragm. The limitations of this assumption are described above. Similarly, we have assumed that our measurements of esophageal and  $P_{gas}$  represent the pressures within the pleural space and abdomen, respectively. Such global measurements may not reflect local forces within the diaphragm<sup>27</sup>; following a thoracotomy with pulmonary resection, neither esophageal nor  $P_{gas}$  may define the pressure acting upon either hemidiaphragm. Until the interrelationship of local forces and global pressure measurements is defined, clinical studies will be limited to inferences based upon global pressure measurements.

Changes of body posture are known to alter functional residual capacity and the relative tidal displacement of the rib cage and abdominal compartments. It has been postulated that the action of gravity on the chest wall determines the resting length of the diaphragm and modifies the compliances of the rib cage and abdominal compartments.<sup>32,33</sup> Increased neural stimuli (operational length compensation) or activation of expiratory muscles (operational length restoration) are believed to compensate for alterations in resting diaphragmatic length.<sup>11</sup> Studies in dogs have demonstrated that both the costal and crural segments show a compensatory increase in neural drive to decreases in resting length induced by transition from the supine to 45° head-up posture<sup>34</sup> and that phasic expiratory contraction of the abdominal muscles can compensate for changes of diaphragmatic length.<sup>35</sup> Therefore, we expected that changing the patient's position from supine to 30° head-up would alter diaphragmatic resting length, and diaphragmatic shortening would either change or be maintained by a compensatory reflex. However, in our study, no change in costal resting length was observed when changing posture, and we did not observe an increased diaphragmatic EMG. This may indicate that a 30° positional change is insufficient to alter diaphragmatic segmental function after a thoracotomy.

We conclude that thoracotomy and pulmonary resection markedly impair active diaphragmatic segmental shortening in patients and, although thoracic epidural anesthesia does not reverse this impairment, it improves other measurements of ventilatory function.

## Appendix

The respiratory inductance pneumograph (Respirace) measures changes in the size of the rib cage and abdomen during respiration and may be used to infer the actions of respiratory muscle groups. Use of this device presumes that a measurement at one location on either the rib cage or the abdomen is representative of all other locations on that structure, that the pneumograph belts are applied directly against the body surface, that changes in lung volume are the only variable changing rib cage and abdominal size, that position changes do not affect calibration coefficients, and that pneumograph results are independent of the calibration procedure. In this study, we were not able to satisfy all of these requirements: the thoracostomy tubes precluded applying the bands directly to the chest wall surface; slippage of the bands during transitions between supine and 30° head-up position could have altered the volume-motion coefficients; the epidural blockade could have altered the level of inspiratory action of the intercostal muscles relative to the accessory muscles, leading to differences in the expansion between the upper and lower portions of the rib cage<sup>36</sup>; and the calibration technique proposed by Sackner *et al.*<sup>16</sup> may be limited if only five breaths are analyzed. All of these limitations were manifested when we determined the fractional rib cage contribution to  $V_T$  during MV even when we used another calibration approach.<sup>37</sup> When the approach of Sackner *et al.*<sup>16</sup> was used to assess rib cage motion of each patient during the random application of  $V_T$ s between 200 and 1,000 ml, the standard deviation about the mean rib cage contribution, expressed as a percentage of  $V_T$ , for each patient was 16.6%, and the difference about each patients' mean value demonstrated no consistent pattern with increasing  $V_T$ . Similarly when the technique described by Abraham *et al.*<sup>37</sup> was used to analyze chest wall motions for each of the four conditions for each subject, it did not provide a uniform volume-motion coefficient.

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