The Influence of Airway Closure Technique for Right Pneumonectomy on Wall Tension During Positive Pressure Ventilation: An Experimental Study

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Bronchopleural fistula (BPF) remains a significant source of morbidity and mortality after right pneumonectomy (RPN). Postoperative mechanical ventilation represents a primary risk factor for BPF. We undertook an experiment to determine the influence of airway diameter on suture line tension during mechanical ventilation after RPN. RPN was performed in 6 fresh human adult cadavers. After initial standard bronchial stump closure (BSC), the airway suture lines were subjected to 5 cm H_2O incremental increases in airway pressures beginning at 5−40 cm H_2O. To minimize airway diameter, a carinal resection was then performed with trachea to left main bronchial anastomosis and the airway suture lines subjected to similar incremental airway pressures. Wall tension (N/m) at the suture lines was measured using piezoresistive sensors at each pressure point. As delivered airway pressure increased, there was a concomitant increase in wall tension after BSC and carinal resection. At every point of incremental positive pressure, wall tension was however significantly lower after carinal resection when compared to BSC ($P < 0.05$). Additionally the differences in airway tension became even more significant with higher delivered airway pressure ($P < 0.001$). Airway diverticulum after BSC leads to significantly increased tension on the bronchial closure with positive airway pressure as compared to a closure which minimize airway diameter after RPN. This supports the role of Laplacian Law where small increases in airway diameter result in significant increases on closure site tension. Techniques which reduce airway diameter at the airway closure will more reliably reduce the incidence of BPF following RPN.

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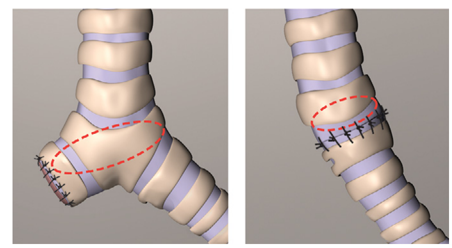
Keywords: Right pneumonectomy, Bronchopleural fistula, Carinal resection, Wall tension, Stump, Diverticulum



Airway diameter after bronchial closure versus trachea to left main bronchial anastomosis.

Central Message

Standard bronchial closure after right pneumonectomy leads to significantly higher suture line tension with positive airway pressure compared to a closure technique which minimizes airway diameter.

Perspective Statement

Bronchopleural fistula remains a significant source of morbidity and mortality after right pneumonectomy. We undertook an experimental study which demonstrates a significant and underappreciated risk a large airway diameter poses to suture lines after standard bronchial stump closure during positive pressure ventilation as compared to an airway closure technique which minimizes airway diameter.

Abbreviations: BSC, bronchial stump closure; BPF, bronchopleural fistula; FEV1, forced expiratory volume (1 second); N, Newton; P, pressure; PPS, positive pressure support (continuous positive airway pressure or positive pressure ventilation); PPV, positive pressure ventilation; RPN, right pneumonectomy; R, radius; T, wall tension; W, wall thickness

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INTRODUCTION

It has been well established that pneumonectomy is associated with higher morbidity and mortality as compared to lobar resections. A query of the Society of Thoracic Surgeons database involving 1267 pneumonectomies found 30.4% of patients experienced at least one major adverse event postoperatively including pneumonia, adult respiratory distress syndrome, and prolonged mechanical ventilation with an overall mortality of 5.6%.[1] Right pneumonectomy (RPN) has additionally been associated with higher risks as compared to left pneumonectomy due to several factors including loss of a larger lung resulting in less pulmonary reserve as well as the entirety of right heart output going through a smaller lung with an increased propensity for right heart failure and/or postpneumonectomy pulmonary edema. Finally, RPN is notoriously associated with a higher risk of bronchopleural fistula (BPF).[2−6]

BPF represents a devastating complication typically leading to a virulent combination of ipsilateral empyema, sepsis, and internal aspiration of contaminated fluid into the remaining contralateral lung. BPF following RPN has a reported overall incidence between 2.4 and 7.0%, with one study indicating up to a 12% BPF rate.[1,3,4,7−10] BPF-related mortality ranges between 13.3 and 31.6%.[4,7,10] The true incidence of BPF may well however be underestimated due, for example, to patients requiring prolonged mechanical ventilation ostensibly succumbing to contralateral lung pneumonia however a small underlying BPF either goes undetected or once detected goes untreated due to end-stage cardiopulmonary failure. Late BPF also occur after initial perioperative recovery and may not be captured in short-term datasets.[11]

Anatomic factors thought to be responsible for the increased incidence of BPF after RPN include lack of natural mediastinal soft tissue coverage over the bronchial stump, a watershed bronchial blood supply to the stump owing to its anatomical location in relation to a leftward descending thoracic aorta which can be further compromised by mediastinal lymph node dissection, and a larger membranous to cartilaginous closure interface. Nonanatomic risk factors which have been identified include chronic obstructive pulmonary disease, poor postpneumonectomy FEV1, preoperative chemoradiation therapy, diabetes, and positive pressure ventilation (PPV).[5,6,8,9,12] There is little debate that postoperative mechanical ventilation subjects the bronchial stump closure (BSC) line to increased wall tension. We speculate however that due to the large airway diameter at the carina after standard BSC that this closure technique may be subject to significantly increased wall tension during PPV, as described by Law of Laplace, which is under appreciated, predisposing to BPF. Using a human cadaver model, we undertook an experiment to determine the amount of wall tension airway closures are subjected to during PPV after BSC as compared to the airway suture lines after carinal resection with end-to-end trachea to left main bronchial anastomosis which minimizes airway diameter.

METHODS

RPN With BSC Followed by Carinal Resection With Trachea to Left Main Bronchial Anastomosis

Six fresh/frozen adult human cadavers were utilized for this study. The cadavers were thawed for 72 hours then intubated with a standard 7.5 mm endotracheal tube and placed in the left lateral decubitus position. A right posterolateral thoracotomy was performed through the 5th intercostal space. After standard lung mobilization, the main pulmonary artery and pulmonary veins were divided. The azygous arch was excised. All paratracheal and subcarinal lymph nodes were removed. The right main bronchus was divided 1 cartilaginous ring distal to the carinal with a scalpel. The right lung was removed from the chest. The circumference of the right and left main stem bronchi, trachea just proximal to the carina, and length of the residual right main stem bronchus were measured**.** The bronchial stump was closed with interrupted 3−0 vicryl sutures (Ethicon Inc, Somerville NJ) beginning with a suture at the middle of the orifice to initially align the cartilaginous and membranous walls (Fig. 1). Two tension sensors (see Sensors below) were attached to the closure by tying sutures over the sensors. After measurement of wall tension at baseline then during incremental increases in airway pressures (see Measurements below), the carina was resected using a scalpel, 1 cartilaginous ring proximal to the carina on the trachea and the left main bronchus flush with the carina. An end-to-end trachea to left main bronchial anastomosis was also performed with interrupted 3−0 vicryl sutures beginning with an aligning suture placed at the right cartilaginous-membrane junction (Fig. 2). To account for the diameter discrepancy, sutures were advanced 2 mm on the left main stem bronchus and 3 mm on the trachea. Similar to bronchial closure, 2 tension sensors (one on the cartilaginous wall and one on the membranous wall) were attached to the airway anastomosis by tying sutures over the sensors. Measurements of wall tension at baseline then during incremental increases in airway pressure were repeated.

Wall Tension Sensors

Deformable wall tension sensors were fabricated from a conductive, carbon filled, polyethylene 3 mm thick foam with an open pore size of ~100 μm (All-Spec Inc, Wilmington, NC).[13,14] The foam is piezoresistive, which increases conductivity when external pressure reduces the gaps in the porous structure (Fig. 3). The foam was cut into 20 × 5 × 3 mm pieces using a CO_2 laser (MT3050D, MornTech Inc, Jinana, China). A copper wire (0.2 mm diameter) was attached to each end of the sensors, separated by 15 mm. The resistance of each of the sensors was measured at baseline before positive pressure was introduced into the airway to serve as a reference value for estimation of the absolute change in electrical resistance as a function of wall tension. The resistance value of the sensors was measured by an open-source microcontroller prototyping platform (Mega 2560, Arduino Inc, Ivrea, Italy) using the

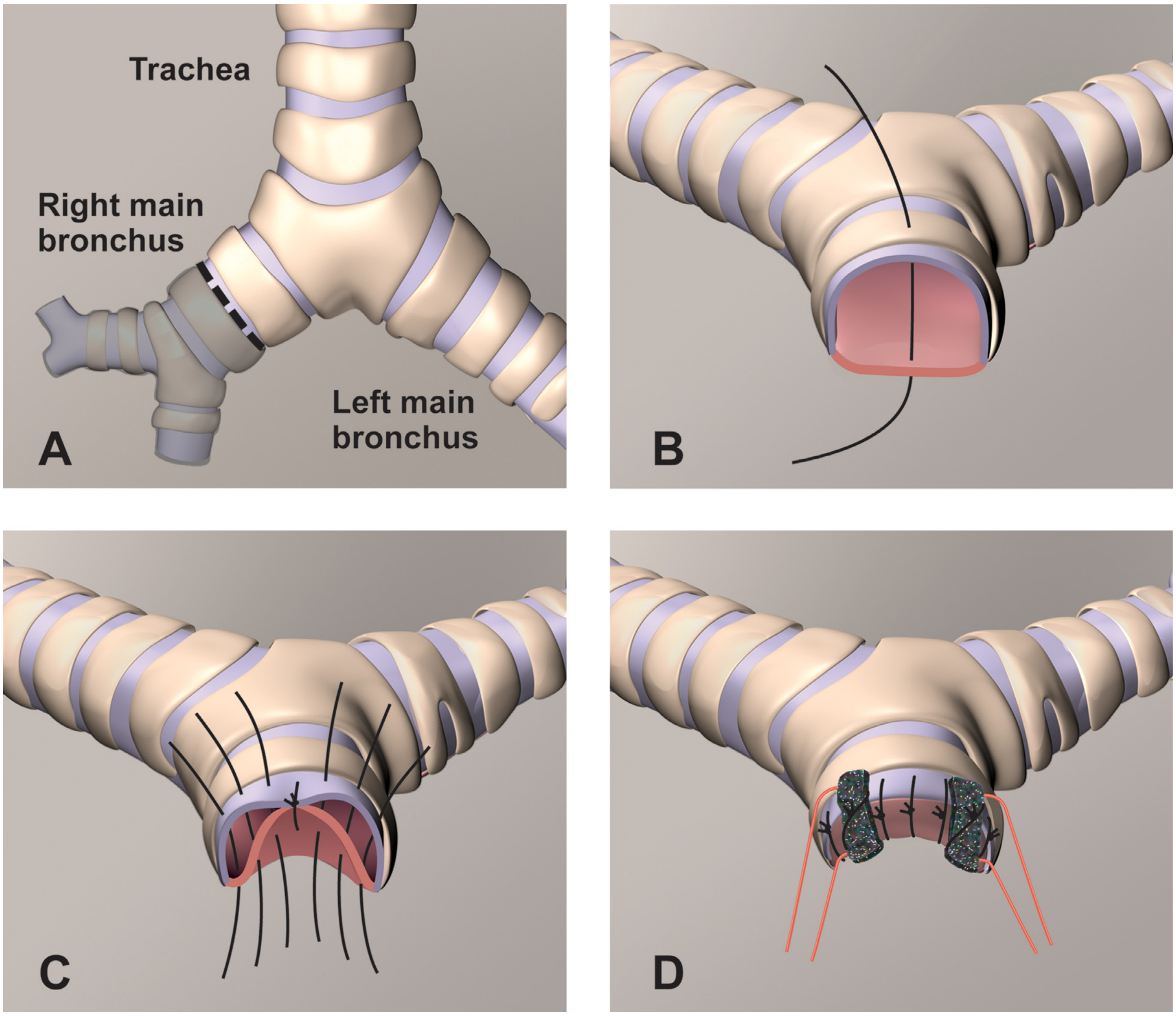

Figure 1. Technique of right bronchial stump closure. (A) Site of right main bronchus division. (B) An initial suture is placed in the middle aspect of the open airway to align the cartilaginous and membranous walls. (C) The aligning suture is tied then interrupted sutures placed on either side of the initial suture. (D) The remaining sutures are sequentially tied, 2 sutures of which are tied over sensors.

MATLAB/Simulink software package (MathWorks Inc, Natick, MA). Measurements from 2 sensors were simultaneously recorded and used to obtain an average value of wall tension.

Positive-Pressure Delivery and Wall Tension Measurements

Airway pressure was delivered and measured using a flow resuscitation device (Airlife, Carefusion Inc, San Diego, CA). Airway pressures were incrementally increased by 5 cm H_2O every 10 seconds beginning with an airway pressure of 5 cm H_2O and increasing the pressure by 5 cm H_2O every 10 seconds until a pressure of 40 cm H_2O was obtained. Measurements were recorded and averaged for 2 cycles at baseline and each of the 8 pressure points for both the standard bronchial closure and the end-to-end trachea to left main bronchial anastomosis. Finally, wall tension measurements were averaged for all 6 experiments at each of the 8 pressure points for both closure techniques.

Statistical Analysis

Wall tensions were averaged for the 6 experiments at baseline and each pressure point for both the standard bronchial closures and end-to-end trachea to left main bronchial anastomoses. Average percentage differences in wall tension between the 2 airway closure techniques were calculated at each pressure point. Paired *t* tests were used to assess the differences in mean wall tension and percentage differences in mean wall tension at each pressure point between the 2 airway closure techniques.

RESULTS

The average age at death of the 6 cadavers (female n = 5, male n = 1) was 73.8 ± 15.8 years (range 52−93 years). Mean

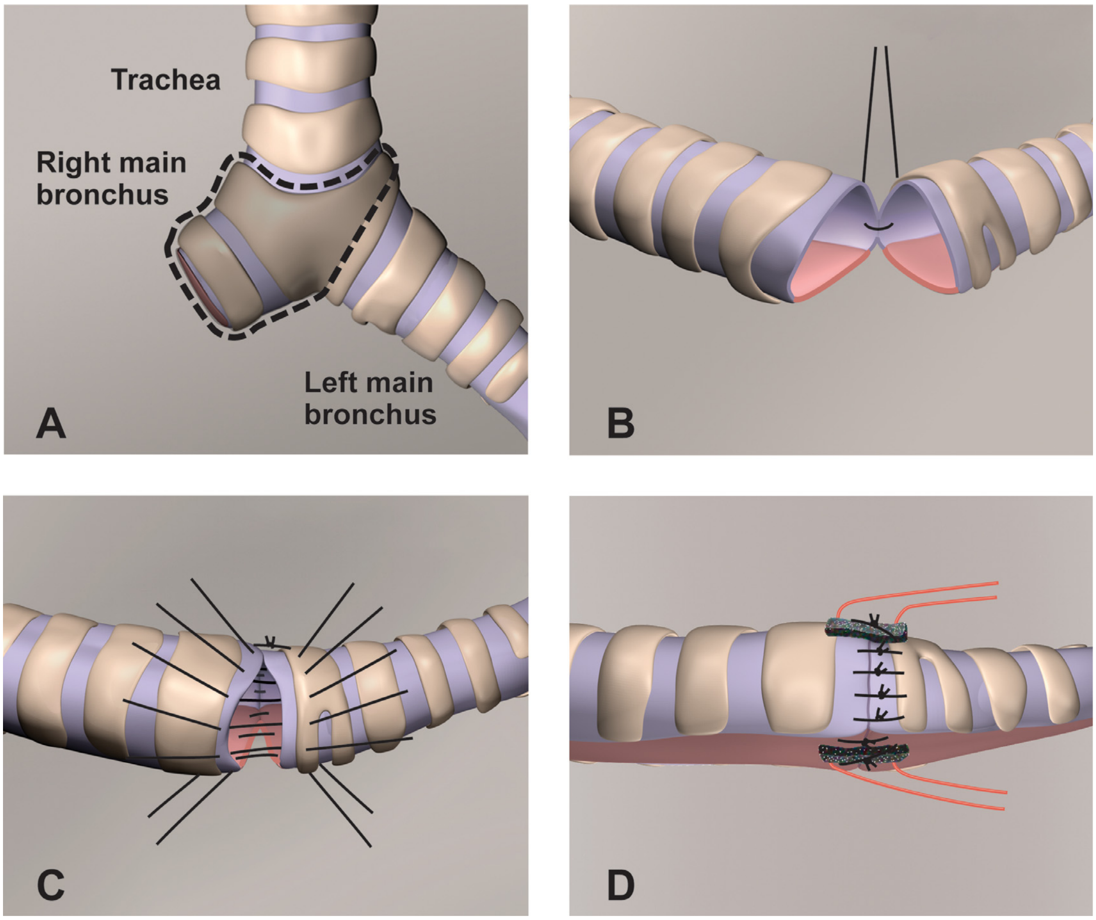

Figure 2. Technique of end-to-end trachea to left main bronchial anastomosis. (A) Site of carinal resection. (B) An initial suture is placed beginning at the right cartilaginous-membrane junction. (C) Interrupted sutures are placed and tied around the cartilaginous wall counter clockwise until approximately half of the anastomosis is complete. To account for the diameter discrepancy, sutures are advanced 2 mm on the left main stem bronchus and 3 mm on the trachea. One suture is tied over a sensor. The remaining sutures are then placed open through the cartilaginous and membranous walls. (D) These sutures are then sequentially tied beginning on the cartilaginous wall and finishing on the membranous wall, one membranous wall suture is tied over a sensor.

tracheal circumference was 6.98 ± 0.45 cm. Mean right main stem and left main stem bronchial circumferences were 6.23 ± 0.86 and 5.43 ± 0.53 cm, respectively. Mean right bronchial stump length was 1.48 ± 0.15 cm. As delivered airway pressure was increased, there was a concomitant increase in wall tension at both the BSC and trachea to left main bronchial anastomoses (Fig. 4). Wall tension began at 25.0 Newton/meter (N/m) and ended at 69.6 N/m over the range of pressures

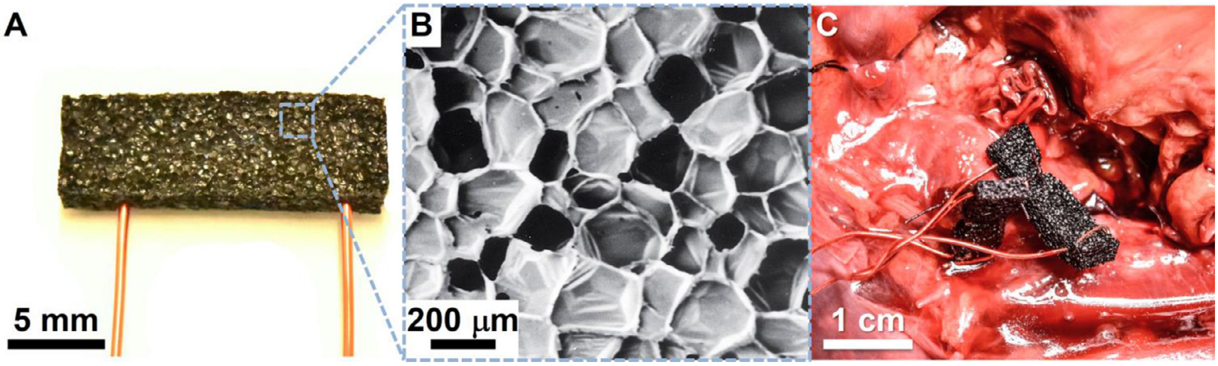

Figure 3. Wall tension sensors. (A) Representative sensor with copper wires attached. (B) Scanning electron micrograph showing sensor porous microstructure. (C) Standard bronchial stump closure with sutures tied over sensors.

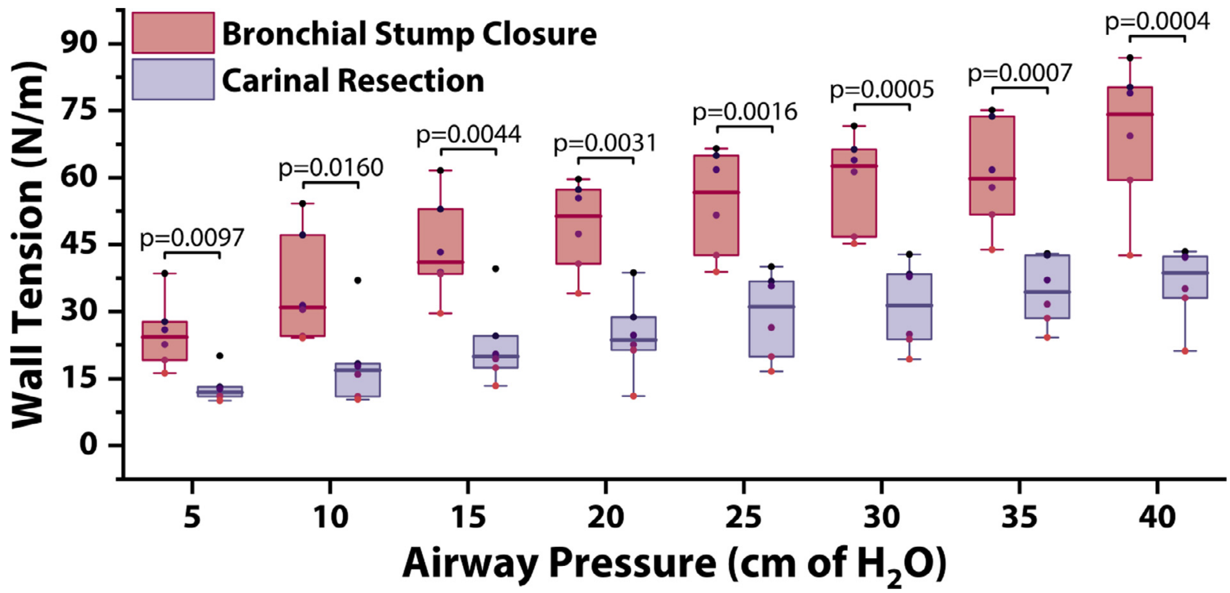

Figure 4. Average wall tension at airway suture line (N/m, n = 6) following right pneumonectomy after standard bronchial stump closure (red), then after carinal resection with trachea to left main bronchial anastomosis (blue) during incremental increases in delivered airway pressure. The upper and lower borders of each box represent upper and lower quartiles respectively. The middle horizontal line inside a box represents the median. The upper and lower whiskers represent the maximum and minimum values of non-outliers. Outliers are defined as being outside 1.5 times the inter-quartile range above the upper quartile or below the lower quartile. (Color version of figure is available online at http://www.semthorcardiovascsurg.com.)

delivered at the BSC. With respect to the trachea to left main stem bronchial anastomoses, measured wall tension began at 13.0 N/m and ended at 36.2 N/m over the range of pressures delivered. At every point of incremental positive pressure, wall tension was significantly lower in the trachea to left main bronchial anastomosis when compared to BSC (Figs. 4 and 5. Fig. 6). Additionally, the differences in airway tension became more statistically significant with higher airway pressures. The average reduction in wall tension after carinal resection compared to standard BSC at each pressure point was 47.4 ± 2.1% (range 43.1% to 50.0%) which were also highly statistically significant (Table 1).

DISCUSSION

Although over the past decade clear advances have been made in the field of medical oncology for the treatment of pulmonary malignancies, surgery remains the mainstay for disease-free long-term survival. However, the relatively high

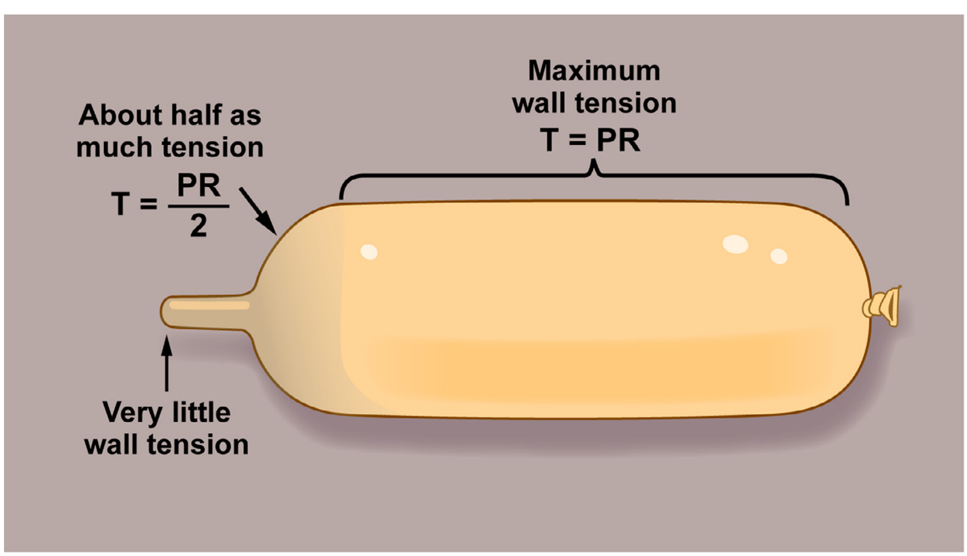

Figure 5. The Law of Laplace and Pascal's Principle demonstrated in a cylindrical balloon which is not totally inflated. Although pressures throughout the balloon are equal, wall tension is maximal at the longest radius. As the balloon radius tapers leftward, the wall tension progressively reduces until there is very little wall tension at the balloon tip.

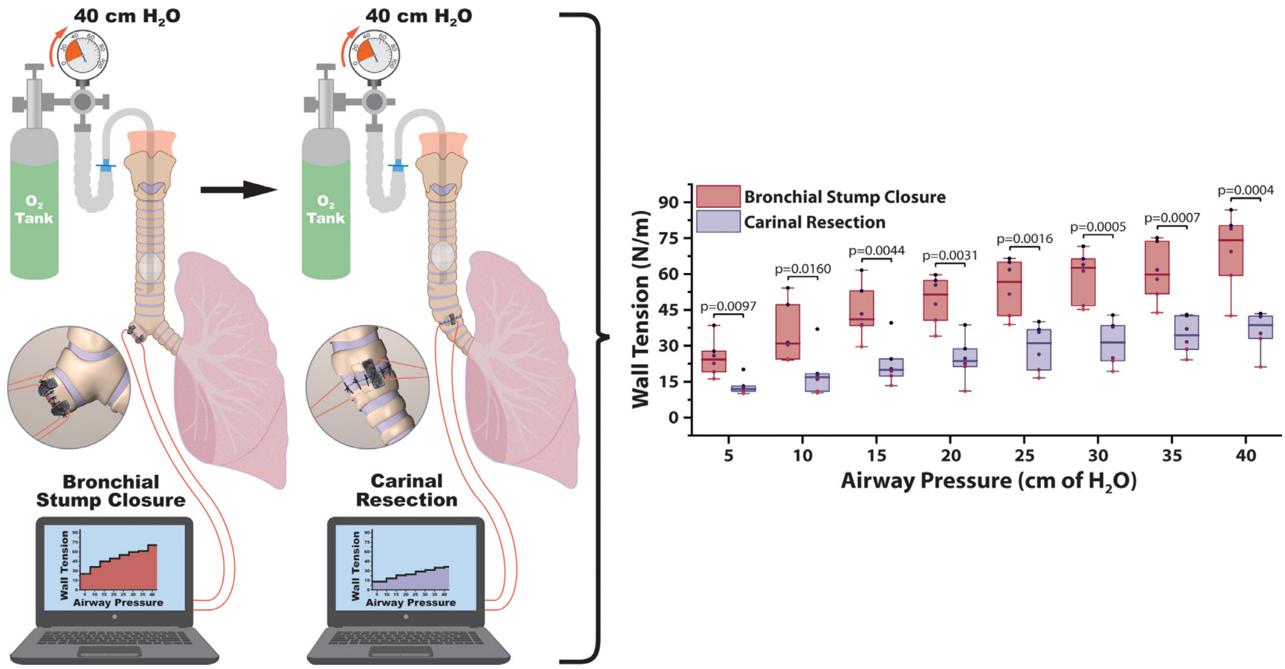

Figure 6. Experimental design showing method of recording wall tension using piezoresistive sensors at the airway suture line following standard bronchial stump closure (left) then subsequent carinal resection with tracheal to left main bronchus anastomosis (right) for right pneumonectomy. Wall tension (N/m) was measured at incremental 5 cm H_2O increases in delivered airway pressures (range 5 cmH_2O to 40 cmH_2O) after both closure techniques. The wall tension following tracheal to left main bronchus anastomosis was significantly lower as compared to bronchial stump closure at every point of delivered airway pressure. Airway closure techniques which minimize airway diameter may significantly reduce wall tension and subsequent bronchopleural fistula following right pneumonectomy particularly in patients who require postoperative positive pressure respiratory support. (N/m, Newtons per meter).

morbidity and mortality of pneumonectomy has undoubtedly contributed to a trend where removal of the entire lung is avoided. Data from the National Cancer Database found a significant decline in the use of pneumonectomy for locally advanced lung cancer, which is the primary indication.[15] The increased use of parenchymal sparing sleeve resections for select cases has likely also been responsible for this decline however pneumonectomy not infrequently remains the best option for successful extirpation.[16] Development of surgical techniques and postoperative care strategies designed to minimize the risks of pneumonectomy, including decreasing the incidence of BPF, would therefore seem worthy of study. Minimally invasive thoracoscopic and robotic techniques have more recently been utilized for pneumonectomy. A multicenter retrospective analysis involving 359 pneumonectomy patients, 124 of whom underwent a thoracoscopic approach, however found no difference in perioperative morbidity or survival.[17] Although study using minimally invasive pneumonectomy

Table 1. Measured Average Wall Tension at the Airway Closure Suture Lines After Right Pneumonectomy With Incremental Increasing Airway Pressures From 5 cmH_2O to 40 cmH_2O (8 total increments) for Standard Bronchial Stump Closure Then Subsequent Carinal Resection With Trachea to Left Main Bronchus Anastomosis

Airway Pressure (cm of H_2O)	Wall Tension for BSC (N/m)	Wall Tension for Carinal Resection (N/m)	*P* Value	Reduction in Wall Tension by Carinal Resection (%)
5	25.04	13.04	0.0097	47.94
10	35.31	18.42	0.0160	47.83
15	44.13	22.49	0.0044	49.03
20	49.10	24.55	0.0031	50.01
25	54.41	29.26	0.0016	46.22
30	59.19	31.19	0.0005	47.30
35	60.68	34.52	0.0007	43.11
40	69.59	36.23	0.0004	47.93

P values given for difference in average wall tension between both techniques per increment pressure as well as percent reduction in wall tension. (N/m Newtons per meter).

techniques is ongoing, one might speculate that the large cardiopulmonary "insult" of complete lung removal, impacts outcomes more than the specific surgical approach. As many locally advanced lung cancer patients who would normally require pneumonectomy are currently being treated with definitive chemoradiation therapy followed by immunotherapy, expectations are that surgeons will be asked to evaluate select patients with locally persistence or recurrent disease for "salvage" surgery. Optimal airway closure techniques and postoperative care strategies need consideration in these challenging cases to avoid disastrous complications.

A variety of surgical techniques have been described to diminish the risks of BPF following RPN. Several series have suggested the superiority of mechanical stapler as compared to suture closure of the bronchial stump to reduce the incidence of BPF.[5,12,18] Prior to the introduction of mechanical staplers, Sweet in 1945 defined the principles of manual bronchial closure which includes minimizing bronchial trauma, preserving bronchial blood supply, careful approximation of the bronchial edges, and providing adequate tissue reinforcement, all of which still hold true today regardless of the closure technique.[19] Soft tissue reinforcement of the bronchial closure line has been described using several rotational flaps including pericardium[20,21], intercostal muscle[22], pleura[23] and even transposed skeletal muscle in patients deemed high risk.[24,25] While soft tissue bronchial stump coverage seems prudent after RPN, convincing data with respect to BPF risk reduction is lacking.

Postoperative mechanical ventilation has been identified as a critical risk factor for BPF after pneumonectomy and avoidance of postoperative mechanical ventilation has therefore been advocated.[4,7,8,26,27] Temporary PPS is however not infrequently needed and delaying PPS to avoid BPF may exacerbate cardiorespiratory failure thus paradoxically reducing the likelihood of a successful outcome.[28] Our data demonstrate that the risks of BPF as a result of PPV after standard BSC may not only be underappreciated but also potentially ameliorated by minimizing airway diameter at the closure site. The Law of Laplace states that wall tension (T) in a container is dependent on radius (R), pressure (P), and wall thickness (W). The following equations are derivations of the law:

$$T = \frac{P \times R}{2 \times W} \text{ for a sphere}$$

$$T = \frac{P \text{ x } R}{W} \text{ for a cylinder}$$

The Law of Laplace is well known to be responsible for human pathophysiology including for example rupture of arterial aneurysms and colonic diverticula, where small increments in radius generate significantly higher wall tension.[29] With respect to airway dynamics, Pascal's Principle states that the pressure of gas is equalized in a closed container regardless of container geometry. Therefore, a combination of Law of Laplace and Pascal's Principle describe the effect of airway diameter on wall tension at the BSC and trachea to left main bronchial anastomosis. We have pictorially described this effect using a cylindrical balloon which is subtotally inflated (Fig. 5). Wall tension reaches a maximum at the largest balloon diameter and a minimum in the areas of the balloon with shorter diameters despite equalized internal pressure. The carinal geometry is, however, neither a sphere nor a cylinder; moreover, the cartilage and membrane walls do not have equivalent mechanical compliance. Therefore, although an analytical derivation of the Law of Laplace cannot be easily applied to accurately calculate wall tension at the carina, there is little argument that there exists a larger airway diameter after BSC as compared to trachea to left main bronchial anastomosis. Our finding that differences in wall tension at the airway closure site became progressively more significant at higher airway pressures supports the concept that Laplacian Law applies to the diverticulum at the BSC. Of note, airway suture lines can be subjected to high pressures not only from PPV but in nonventilated patients during coughing and Valsalva maneuvers. One might speculate that a stapled BSC would be relatively more resistant to dehiscence when subjected to high wall tension as compared to suture closure. The BSC site however will still be subject to similar high wall tension during PPS completely independent of closure technique. While soft tissue coverage of the bronchial closure after RPN is an accepted and reasonable practice, if high wall tension is imposed on the BSC resulting in dehiscence, it would seem that soft tissue coverage would likely be of little value to prevent development of a postoperative BPF.

A long bronchial stump has also been cited as a risk factor for postpneumonectomy BPF. Although strict comparison is difficult, reported results of surgical techniques which eliminates the stump, seem to have diminished rates of BPF as compared to techniques where the stump remains. While closure of the right main stem bronchus "flush" at the carina could be considered to minimize airway diameter, this approach will still leave a relatively large carinal "volume" as well as at least in theory result in more distraction tension on the membranous/cartilaginous wall closure interface as compared to bronchial closure 1 centimeter distal to the carina. In 1965 Jack described a "tracheal closure" technique resecting the right bronchial stump and employing a long posterior membranous flap for closure at the carina.[30] Success with Jack's technique or modifications thereof has been reported in other series.[4,31,32] Another bronchial exclusion method, carinal wedge resection, initially described by Fahimi et al. was developed to both preserve airway vascularity and reduce tension on the suture line.[33] This "carinoplasty" technique was performed on 51 consecutive patients undergoing RPN at our institution with only 2 (3.9%) complicated by BPF despite 17 of these patients requiring PPS for an average of 13 days.[34] A subsequent larger review of our experience over 18 years with 145 RPNs revealed a 3.6% mortality after wedge carinal resection technique as compared to an 11.6% mortality in patients undergoing BSC.[9] While in our experience the carinoplasty technique had low rates of BPF, BPF still occurred and it was occasionally difficult to properly align the cartilaginous walls during closure.

Since 2009, we have routinely been using carinal resection with end-to-end trachea to left main stem bronchial anastomosis buttressed with a rotational flap of debulked anterior mediastinal fat for airway closure after RPN. The trachea can be anastomosed to the left main bronchus after segmental carinal resection with little if any tension. Moreover, after careful carinal resection the blood supply to the trachea and left main bronchus airway walls is typically robust and cartilage-to-cartilage and membranous-to-membranous walls accurately approximated to maintain laminar flow. We have frequently placed high risk RPN patients on PPS through a temporary tracheostomy on the evening of surgery with weaning to tracheostomy collar planned on the first postoperative day. Intermittent PPS is administered as needed thereafter through the tracheostomy without sedation and reintubation. Surgical tracheostomy closure is done under local anesthesia with sedation if the patient has been weaned from PPS within 5 days of surgery otherwise the tracheostomy is ultimately downsized and removed for secondary healing prior to discharge. To date, 24 patients have undergone right carinal pneumonectomy at our institution. Twelve (50%) of these patients received chemoradiation therapy, 5 of whom received definitive chemoradiation therapy, prior to institutional referral. No patient experienced BPF with an average postoperative PPS time of 5 days (range 1−32 days) [unpublished data]. There have been 2 operative deaths, one death secondary to acute pulmonary embolism after hospital discharge but within 30 days of surgery who underwent RPN for extensive mediastinal fibrosis obstructing the right hilum. The other patient died of contralateral lung failure after completion RPN for an end stage aspergillius infection following remote upper lobectomy. A recent report from the Massachusetts General Hospital also demonstrated low operative risks of carinal resection and additionally showed decreasing mortality in other contemporary series.[35] Although technically more challenging than BSC, after a brief learning curve, carinal resection with trachea to left main stem bronchial anastomoses can usually be done with little additional operative time. Results appear excellent with respect to the incidence of BPF and mortality in the current era however further study is needed for routine use.

There are limitations to this experiment. A cadaveric airway may well have different compliance characteristics as compared to normal human tissue. One could speculate however that tissues from a normal human airway are likely more compliant and therefore more susceptible to increased wall tension during PPV or coughing and Valsalva maneuvers in nonventilated patients therefore underestimating the impact of our findings. Next, the wall tension sensors were fixed with sutures used to close the airway. The reported tension values were therefore a direct measurement of tension experienced by the suture itself which was used as a surrogate for wall tension at the site of airway closure. We believe this measurement technique accurately reflected changes in wall tension over all pressure points. Accordingly however precise baseline wall tension measurements could not be assured. Finally, given the relative degradation of airway tissues used in this study, not surprisingly we occasionally observed air leaks through suture holes at the higher range of ventilating pressures. These air leaks were small, infrequent, and equally observed in both airway closure techniques and likely did not impact findings.

Many risk factors have been cited for BPF after RPN. While further experimental studies are justified, based on physical laws these data demonstrate a significant and underappreciated risk a large airway diameter after BSC represents particularly in patients who require PPV. Accordingly airway closure techniques, which eliminate the bronchial stump, should reduce the reluctance to use PPV after RPN. Carinal resection with trachea to left main stem bronchial anastomosis would have benefits including excellent vascularity at the airway suture line, cartilage-to-cartilage/membrane-to-membrane wall continuity, and reducing airway diameter to a minimum. Although technically more challenging, carinal RPN has at least these theoretic advantages over BSC for RPN for routine airway closure. Further clinical studies seem justified in this regard. This airway closure approach should be included in surgical options for patients at risk for BPF including patients who have received prior radiation therapy or predictably will be in need of PPV.

Acknowledgments

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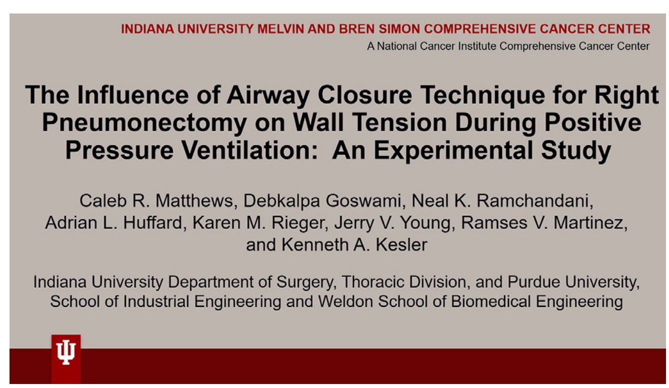
SUPPLEMENTARY MATERIAL

The following is the supplementary data to this article:



Video 1. Discussion of experimental rational, conduct of the experiment, and potential clinical implications of the results.

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