



The benefits of digital drainage system versus traditional drainage system after robotic-assisted pulmonary lobectomy

Kristina Jacobsen¹, Steven Talbert², Joseph H. Boyer³

¹Division of Cardiothoracic Surgery, AdventHealth, Orlando, FL, USA; ²UCF College of Nursing, University of Central Florida, Orlando, FL, USA;

³Division of Cardiothoracic Surgery, Director, AdventHealth Cardiovascular Institute Robotics and Minimally Invasive Cardiothoracic Surgery, Orlando, FL, USA

Contributions: (I) Conception and design: All authors; (II) Administrative support: S Talbert; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: K Jacobsen, S Talbert; (V) Data analysis and interpretation: K Jacobsen, S Talbert; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Kristina Jacobsen, PhD, APRN. 601 E. Rollins St., Orlando, FL 32803, USA. Email: Kristina.Jacobsen@Adventhealth.com.

Background: Postoperative air leaks are the most common complication after a pulmonary resection. There is no data in the literature comparing the traditional and digital chest drainage system after a robotic-assisted pulmonary lobectomy.

Methods: This was a retrospective, correlational study. Medical records from 182 eligible robotic-assisted lobectomy patients were evaluated to determine the association between digital and traditional chest tube drainage systems (CTDS) with postoperative chest tube days, hospital LOS, chest tube reinsertion during hospitalization, and 30-day readmission for pneumothorax. Multiple regression was used to determine the association between CTDS while controlling for confounding variables.

Results: No differences were noted between groups for age, gender, BMI, smoking, adhesions or neoadjuvant therapy. Patients with digital drainage systems had significantly shorter chest tube duration than those with traditional drainage systems (2.07 *vs.* 2.73 days, $P=0.003$). After controlling for age and BMI, CTDS was not found to be a significant predictor of CT duration. Digital drainage system were also associated with significantly shorter hospital LOS (4.02 *vs.* 5.06 days, $P=0.01$) After controlling for age, BMI, and presence of post-op a-fib, use of a digital CTDS was significantly associated with 1 day shorter hospital LOS. Chest tube reinsertion occurred four times more frequently with traditional drainage systems, but the difference did not achieve the level of statistical significance ($P=0.059$). The frequency of readmission due to pneumothorax was very low (1 patient per group), which prevented comparative statistical analysis.

Conclusions: In the digital drainage system there are shorter chest tube days and hospital length of stay after a robotic-assisted lobectomy. The decision to remove chest tubes in the traditional drainage system is burdened with uncertainty. The digital drainage system reduces intraobserver variability allowing for improved decision making in chest tube removal. Both CT duration and hospital LOS were shorter using unadjusted analyses. Type of CTDS was not significantly associated with CT duration after controlling for age and BMI. However, after controlling for age, BMI, and post-op atrial fibrillation, use of the digital CTDS was associated with a 1 day reduction in hospital LOS.

Keywords: Digital drainage system; robotic-assisted thoracoscopic surgery; lobectomy; air leak

Submitted Jun 30, 2019. Accepted for publication Nov 12, 2019.

doi: 10.21037/jtd.2019.11.69

View this article at: <http://dx.doi.org/10.21037/jtd.2019.11.69>

Introduction

Alveolar air leaks after a pulmonary lobectomy are a considerable cause of morbidity, increased number of chest tube days and longer length of hospital stay (LOS) that significantly increase costs (1). The literature reports air leaks in 28–60% of patients immediately postoperatively, 26–48% on postoperative (POD) day 1, 22–24% of patients on POD 2, and 8% on POD 4 (2). Up to 5% of patients still have an air leak when they are ready for discharge (3). Various intraoperative techniques are used to help prevent air leaks, including pleural tents, buttressing of the suture or staple lines, visceral sealants and glue and different strategies with chest tube management (1,4). Postoperative air leaks are evaluated differently with the information provided by the traditional and digital chest tube drainage systems (CTDS).

Air leak assessment using the traditional CTDS consists of visualizing bubbles in the water seal chamber. It is an immediate, subjective reading that can vary among clinicians. The clinician's evaluation of whether an air leak is present is contingent on when the chamber is visualized. In the traditional system, the air leak decision is burdened with uncertainty because the chamber was not continuously monitored, allowing a small, intermittent air leak to go unrecognized. Differing opinions and the inability to accurately ascertain an air leak can lead to longer chest tube days and increased hospital LOS (5-7).

Digital CTDS air leak assessment is a quantified measure that is both continuous and objective. It reduces interobserver variability which improves decision making regarding chest tube removal (4,8-11). Having the information provided by the digital system reduces uncertainty surrounding the decision of when it is appropriate to remove the chest tube. It shifts the decision from one based heavily on gestalt to one guided by valid and reliable patient-specific information.

According to the National Institute for Health and Care Excellence (NICE), after a pulmonary resection, adopting the Thopaz digital system is supported by the evidence. The digital system can decrease hospital LOS, reduce chest tube drainage time and improve safety. It has been shown to improve clinical decisions by objective monitoring. The cost savings with the Thopaz system is attributable to the reduced LOS in the hospital (12). Comparing the two CTDS in the robotic-assisted thoracoscopic surgical approach (RATS) has not yet been studied. This information can provide more relevant clinical data to the body of knowledge where open thoracotomies and

VATS pulmonary resections have previously been studied comparing these two systems.

The aim of this retrospective study was to compare two CTDSs on chest tube days, hospital length of stay, reinsertions of chest tube during hospitalization and readmission due to pneumothorax after RATS lobectomy.

Methods

Ethics

Institutional review board (IRB) approval was obtained from Florida Hospital, IRB 1312924-1 and The University of Central Florida SBE-18-14487.

Design

This study is a retrospective, descriptive, correlational design to evaluate the association between digital and traditional CTDS with postoperative chest tube days, hospital LOS, chest tube reinsertion during hospitalization, and 30-day readmission for pneumothorax following a RATS lobectomy.

Setting

The same cardiothoracic surgeon performed all RATS lobectomies. All subjects underwent elective surgery at a quaternary care hospital in Orlando, Florida.

Sample

All adult lung cancer patients admitted to the hospital for a RATS pulmonary lobectomy, lobectomy with wedge resection, or bilobectomy due to an incomplete fissure between January 2014 and December 2017 were eligible for inclusion in this study.

Exclusion criteria were as follows: patient younger than 18 years, post-operative mechanical ventilation, previous thoracic surgery, robotic-assisted requiring conversion to open thoracotomy, more than one type of drainage system used, patient discharged home with a chest tube, more than one chest tube placed perioperatively (6 patients), or post-operative death (1 patient).

Surgical procedure

An experienced robotic thoracic surgeon defined as a board certified/eligible thoracic surgeon who has performed, as

primary operator, 50 or more robotic cases within the past three years, utilized a DaVinci Xi (Intuitive Surgical Inc., Sunnyvale, CA, USA) console while employing a four-port technique as previously described (13). There were four 8 mm robotic ports including the camera port and a 15 mm accessory port for CO₂ insufflation and specimen egress. The insufflation system used in this accessory port was the AirSeal insufflator to maintain constant positive pressure within the chest cavity to maintain a pressure of 10–15 mmHg, increasing up to 20 mmHg if necessary, with a flow of 6 mL/min until the lung is deflated. This accessory port was placed midway between the camera port and the more anterior port of the robotic arm caudal to the axial plane of the camera port, yet cephalad to the costal margin. It was used to retrieve lymph nodes and small specimens, needles, and sponges; it later served as the site of non-robotic stapler insertion. By enlarging the skin to 20–25 mm later in the operation it became a working port to remove the lobe of the lung. The specimen was then removed using the Endo Catch (Covidien). All of the stapling and specimen retrieval was accomplished via the accessory port(s).

Progel sealant was routinely used to prevent intraoperative leaks from January 2014 through November 2015 when it was no longer available. No buttressed staple lines or pleural tents were used. A single apical 24F (BLAKE® Silicone Drains, Ethicon, Inc., Somerville, NJ, USA) chest tube was placed anteriorly at the end of the procedure via the most anterior 8 mm port.

Clinical course

CTDS management and air leak evaluation

In both the digital and traditional chest drainage systems, –20 cmH₂O suction was applied for the first 8 hours post-operatively then the patient's chest tube was placed to waterseal. With the traditional system, waterseal was the removal of suction and with the digital system, suction was placed to a physiologic mode of –8 cmH₂O which is the normal intrapleural pressure at the end of inspiration (14). Air leak evaluation was completed and charted by registered nurses (RN) every 15–30 minutes during the first post-operative hour in the post-anesthesia care unit (PACU). Air leak evaluations were then completed every hour for 1–2 hours. Patients were then transferred to the cardiothoracic step-down unit where air leak evaluations were completed by RNs every 4 hours until chest tube removal. All nurses had been trained in using the digital system and passed competency exams for this device.

Evaluation for pneumothorax or effusion

If the immediate post-operative chest X-ray in the PACU showed a pneumothorax of greater than 20–30% of the hemithorax, suction was maintained throughout the night and reassessed by the post-op day (POD) 1 morning chest X-ray. Pleural effusion threshold for removal was 400 mL/day. The chest tube was not clamped on any patient.

Chest tube removal decision

The decision to remove the chest tube was made by the cardiothoracic nurse practitioner, physician's assistant, the surgeon, or some combination of all three.

Digital CTDS group

- ❖ Air leak flow was less than 50 mL/min for at least 6 hours;
- ❖ Patient ambulated with no air flow spikes >50 mL/min;
- ❖ Morning chest X-ray showed sufficient expansion;
- ❖ Pneumothorax <20–30% of the hemithorax;
- ❖ No dyspnea on exertion;
- ❖ SPO₂ >92% without supplemental oxygen (unless oxygen dependent preoperatively).

Traditional CTDS group

- ❖ No bubbles observed or recorded in the waterseal chamber for at least 6 hours immediately post-operative;
- ❖ Morning assessment on POD 1 no bubbles observed with the patient coughing 2–3 times;
- ❖ Morning chest X-ray showed sufficient expansion;
- ❖ Pneumothorax <20–30% of the hemithorax;
- ❖ No dyspnea on exertion;
- ❖ SPO₂ >92% without supplemental oxygen (unless oxygen dependent preoperatively).

Statistical analysis

Continuous data were presented as means and standard deviation. Normal distribution of variables was evaluated by Shapiro-Wilk normality test. If continuous data were normally distributed, comparisons were made using the students *t*-test. Non-normally distributed continuous variables were compared using Mann Whitney U test. Categorical data were summarized as n and percentages. Comparisons of categorical data were made using the chi-squared or Fisher's exact test. Odds ratios with 95% confidence intervals were computed for categorical level outcomes. Multiple linear regression was used to

Table 1 Patient characteristics

Variable	Traditional (n=66)	Digital (n=116)	P value
Age	68.5±10.6	67.2±11.1	0.453
Gender, n (%)			0.914
Male	25 (37.9)	43 (37.1)	
Female	41 (62.1)	73 (62.9)	
BMI (kg/m ²)	27.8±6.0	28.4±5.9	0.485
Smoking status (yes), n (%)	60 (90.9)	91 (78.4)	0.079
Lobectomy, n (%)			0.315
Right upper lobe	14 (21.2)	35 (30.2)	
Right middle lobe	3 (4.5)	12 (10.3)	
Right lower lobe	15 (22.7)	24 (20.7)	
Left upper lobe	18 (27.3)	21 (18.1)	
Left lower lobe	9 (13.6)	17 (14.7)	
Lobectomy + wedge resection	5 (7.6)	5 (4.3)	
Bilobectomy	2 (3.0)	2 (1.7)	
Pleural adhesions, n (%)	17 (25.8)	30 (25.9)	0.988
History of neoadjuvant therapy, n (%)	2 (3.0)	6 (5.2)	0.713
Cardiac complication, n (%)	5 (7.6)	6 (5.2)	0.513

Continuous variables are expressed as mean ± standard deviations with P values from Student's *t*-test. Categorical variables are expressed as count (percentages) with P values from chi-square.

determine the association between CTDS and continuous level outcomes while controlling for known confounding variables. An α -level of 0.05 was used to establish statistical significance.

Results

Demographics

During 2014–2017, RATS lobectomies were performed on 182 eligible patients. The majority of patients (92.3%) underwent a lobectomy. Lobectomy with wedge resection was required in 5.5% of patients while bilobectomies compromised 2.2% of the study population.

A summary of the patient demographic characteristics is shown in *Table 1*. The study population was majority female (62.6%) with mean age of 68±11 years. The digital CTDS was used in a larger proportion of patients (63.7%). The groups did not differ significantly in terms of age, gender, BMI, smoking, adhesions or neoadjuvant therapy. Cardiac complication defined as postoperative atrial fibrillation was

included and was not statistically significant.

Patient outcomes

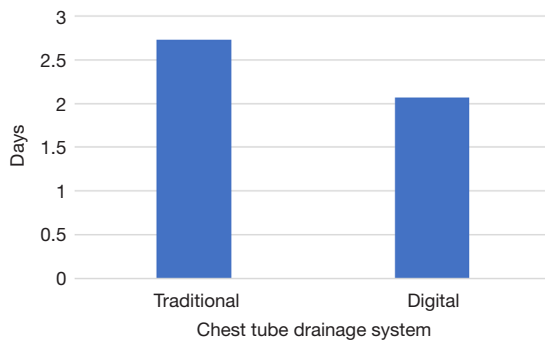
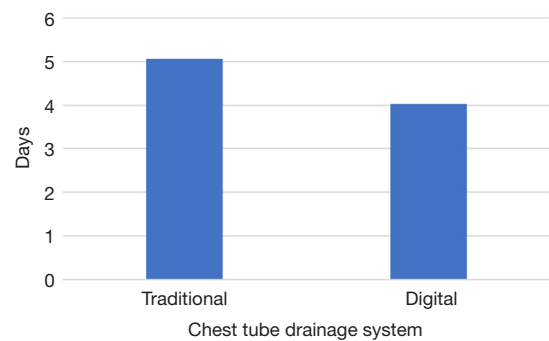
Chest tube duration was significantly shorter with digital CTDS use (see *Table 2* and *Figure 1*). Patients with the digital CTDS had a mean chest tube duration of 2.07 days compared with 2.73 days for the traditional CTDS ($P=0.003$).

Hospital length of stay was also significantly reduced with the digital CTDS (see *Table 2* and *Figure 2*). Patients using the digital CTDS had a mean hospital length of stay of 4.02 days compared with 5.06 days with the traditional CTDS ($P=0.010$). Although chest tube reinsertion occurred four times more frequently with traditional CTDS use, the difference did not achieve the level of statistical significance (Fisher exact =0.059; OR =0.14, 95% CI: 0.02 to 1.23). The frequency of readmission due to pneumothorax was very low (1 patient per group), which prevented comparative statistical analysis.

Table 2 Primary outcomes

Drainage system	Traditional (n=66)	Digital (n=116)	P value	OR
Chest tube (days)	2.73±3.0	2.07±1.99	0.003	N/A
Hospital stay (days)	5.06±4.21	4.02±3.00	0.010	N/A
Chest tube reinsertion during hospitalization	4 (6.1)	1	0.059	0.14 (95% CI: 0.02 to 1.23)
Readmission for pneumothorax	1	1	N/A	N/A

Continuous variables are expressed as mean ± standard deviations with P values from Mann Whitney U test. Categorical variables are expressed as count (percentages) with P values from the Fishers exact tests.

**Figure 1** Mean chest tube days in the traditional and digital chest drainage systems.**Figure 2** Mean hospital length of stay in the traditional and digital chest drainage systems.**Table 3** Multiple regression of CT duration using age, BMI, and CTDS

Variable	B	Std. Error	β	t	P value
Constant	2.524	1.548		1.630	0.105
CTDS	-0.495	0.361	-0.099	-1.373	0.172
Age	0.033	0.016	0.152	2.061	0.041
BMI	-0.074	0.030	-0.182	-2.470	0.014

CTDS, chest tube drainage system; BMI, body mass index.

Chest tube duration

Two sample characteristics were significantly associated with CT duration, age ($R=0.197$, $P=0.008$) and BMI ($R=-0.217$, $P=0.003$). A multiple regression was run to predict CT duration using age, BMI, and CTDS. The model significantly predicted CT duration, $F(3, 178) = 5.191$, $P=0.002$, adj. $R^2=0.065$. After controlling for age and BMI, CTDS type was not found to add significantly to the prediction (Table 3).

Hospital LOS

Three sample characteristics were significantly associated with hospital LOS, age ($R=0.166$, $P=0.012$), BMI ($R=-0.184$, $P=0.006$), and presence of post-op a-fib ($P=0.001$). A multiple regression was run to predict hospital LOS using age, BMI, and CTDS. The model significantly predicted CT duration, $F(4, 177) = 4.696$, $P=0.001$, adj. $R^2=0.076$. After controlling for age, BMI, and presence of post-op a-fib, use of a digital CTDS significantly reduced predicted

Table 4 Multiple regression of hospital LOS using age, BMI, presence of post-op Afib, and CTDS

Variable	B	Std. Error	β	<i>t</i>	P value
Constant	4.997	2.042		2.447	0.015
CTDS	-1.114	0.476	-0.168	-2.342	0.020
Age	0.031	0.021	0.107	1.450	0.149
BMI	-0.080	0.039	-0.148	-2.022	0.045
Afib	1.693	0.968	0.126	1.748	0.082

CTDS, chest tube drainage system; BMI, body mass index; Afib, atrial fibrillation.

hospital LOS (*Table 4*).

Discussion

Main findings

Postoperative air leaks after a pulmonary resection continue to be problematic for the patient and frustrating for the surgical team. Patients using the digital CTDS had nearly a one day decrease in chest tube days and a full day shortened hospital LOS. This finding is consistent with previous studies, even when more conservative chest tube removal flow threshold criteria were used (1,10). This decrease in chest tube days and hospital length of stay may be strongly influenced to the objective data collection and reduced uncertainty associated with the digital system in air flow readings.

A concern for pneumothorax after chest tube removal or readmission due to a pneumothorax has been presented in the literature. One of the most frequent causes of readmission to the hospital after a pulmonary lobectomy is the occurrence of a pneumothorax (15). The American College of Surgeons National Surgical Quality Improvement Program evaluated 9,510 patients admitted between 2012 and 2015 for a 30-day related, unplanned postoperative readmission after an anatomic lung resection for primary lung cancer. They compared thoracoscopic versus open resection and found a pneumothorax occurred in 17.6% of patients (16). Unexpected postoperative readmissions are a primary burden financially to the healthcare system and as part of the Affordable Care Act, mandates public reporting of hospital readmission rates with monetary penalties with the Hospital Readmission Reduction Program (17).

In one study that extracted data from the Surveillance Epidemiology and End Results (SEER) database, evaluated 11,432 patients, age 65 or older admitted for pulmonary

resection for lung cancer. The 30-day readmission rate was 12.8%. Of the readmitted patients, 13.7% were due to a pneumothorax (17).

Our experience in this study revealed that a pneumothorax after chest tube removal was a rare event. Our readmission rate due to a pneumothorax was substantially lower than previously reported data.

There are no standards with pleural fluid drainage and chest tube removal. Our study used 400 mL/24 hours. Previous study findings described 450 mL/24 hours as a safe threshold of pleural fluid drainage for chest tube removal in over 2,000 patients after a pulmonary resection (18).

Robotic-assisted thoracoscopic surgery

Evaluating CTDS options following RATS can positively impact postoperative care. However, such a comparison has not yet been completed in this unique and growing patient population. Robotic thoracic surgery has rapidly gained popularity among thoracic surgeons. The U.S. National Cancer Data Base reported a tripling in the percentage of robotic lobectomies from 2010 to 2012 (3% vs. 9%) (19). A recent analysis predicts robotic lobectomies have nearly doubled again to 15% in 2015 (19). As this patient population continues to grow, evaluation of clinical decisions and care processes will have correspondingly increased impact. Furthermore, such evaluations can effectively guide postoperative air leak management by the thoracic surgery team as they collaborate to improve patient outcomes. This study will add to the literature by including another surgical approach when comparing two different chest drainage system and air leak management.

Limitations

Our study included one surgeon at a single-center study.

Although this reduces variability intraoperatively and in postoperative chest tube management, it limits the generalizability of the result and a multi-institutional study is superior. This investigation is limited by the data accuracy and quality of completeness of the primary database. Retrospective data lacks randomized sampling allowing for equal number of participants in each group. Our study had unequal groups that may have influenced the outcome variables. Selection bias cannot be excluded. Our low occurrence of postoperative pneumothorax and readmission may require a larger patient population to increase statistical power and allow for stronger conclusions to be made. The cost savings of a decreased hospital length of stay and the increased cost of the digital system were not evaluated but should be addressed in future evaluations. The argument against robotic thoracic surgery costs compared to open thoracotomy and VATS could be addressed with a randomized controlled study in the future. Progel was only used on a small sample of patients and statistical analysis would be underpowered. Preoperative pulmonary function tests were not routinely done on all patients included in this study. Patients' respiratory system function should be evaluated with measurements of forced expiratory volume in 1 second (FEV1) and carbon monoxide lung diffusion capacity (DLco) before surgery. Impaired lung function would be useful in evaluating the risk of complications, such as a postoperative air leak. Measuring chest tube removal in hours instead of days could have created a more meaningful difference in time. Someone whose tube is pulled at 26 hours (2 days) is scored the same as someone whose tube is pulled at 42 hours (2 days). Retrospective data is limited in what is available in the charts. We believe that is why we see a larger difference in hospital LOS but not in chest tube duration.

Conclusions

Our study demonstrated shorter chest tube days and hospital length of stay in the digital CTDS after a RATS lobectomy by improved chest tube management. These findings are consistent with previous research. This retrospective study can be used to validate the necessity of a multicenter randomized study.

Acknowledgments

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Institutional review board (IRB) approval was obtained from Florida Hospital, IRB 1312924-1 and The University of Central Florida SBE-18-14487.

References

1. Miller DL, Helms G, Mayfield W. Digital drainage system reduces hospitalization after video-assisted thoracoscopic surgery lung resection. *Ann Thorac Surg* 2016;102:955-61.
2. Mueller MR, Marzluf B. The anticipation and management of air leaks and residual spaces post lung resection. *J Thorac Dis* 2014;6:271-84.
3. Cerfolio RJ, Bass C, Pask A, et al. Predictors and treatment of persistent air leaks. *Ann Thorac Surg* 2002;73:1727-30.
4. Cerfolio RJ, Bryant A. The benefits of continuous and digital air leak assessment after elective pulmonary resection: a prospective study. *Ann Thorac Surg* 2008;86:396-401.
5. Baringer K, Talbert S. Chest drainage systems and management of air leaks after a pulmonary resection. *J Thorac Dis* 2017;9:5399-403.
6. Cerfolio RJ, Varela G, Brunelli A. Digital and smart chest drainage systems to monitor air leaks: the birth of a new era? *Thorac Surg Clin* 2010;20:413-20.
7. McGuire AL, Petrcich W, Maziak D, et al. Digital versus analogue pleural drainage phase 1: prospective evaluation of interobserver reliability in the assessment of pulmonary air leaks. *Interact Cardiovasc Thorac Surg* 2015;21:403-7.
8. Brunelli A, Cassivi SD, Salati M, et al. Digital measurements of air leak flow and intrapleural pressures in the immediate postoperative period predict risk of prolonged air leak after pulmonary lobectomy. *Eur J Cardiothorac Surg* 2011;39:584-8.
9. Marjanski T, Sternau A, Rzyman W. The implementation of a digital chest drainage system significantly reduces complication rates after lobectomy—a randomized clinical trial. *Pol J Thorac Cardiovasc Surg* 2013;2:133-8.
10. Pompili C, Detterbeck F, Papagiannopoulos K, et al.

- Multicenter international randomized comparison of objective and subjective outcomes between electronic and traditional chest drainage systems. *Ann Thorac Surg* 2014;98:490-6.
11. Varela G, Jiménez M, Novoa N, et al. Postoperative chest tube management: measuring air leak using an electronic device decreases variability in the clinical practice. *Eur J Cardiothorac Surg* 2009;35:28-31.
 12. Nice.org.uk. Medical Technologies Guidance. Overview Thopaz+ portable digital system for managing chest drains [Internet]. 2019 Nov 7. Available online: <https://www.nice.org.uk/guidance/mtg37>
 13. Cerfolio RJ. Total Port Approach for Robotic Lobectomy. *Thorac Surg Clin* 2014;24:151-6.
 14. Schwartzstein R, Parker M. Respiratory physiology: a clinical approach. Philadelphia: Lippincott Williams & Wilkins, c2006.
 15. Pompili C, Miserocchi G. Air leak after lung resection: pathophysiology and patients' implications. *J Thorac Dis* 2016;8:S46-54.
 16. Bhagat R, Bronsert M, Ward A, et al. National analysis of unplanned readmissions after thoroscopic versus open lung cancer resection. *Ann Thorac Surg* 2017;104:1782-90.
 17. Hu Y, McMurry T, Isbell J, et al. Readmission after lung cancer resection is associated with a 6-fold increase in 90-day postoperative mortality. *J Thorac Cardiovasc Surg* 2014;148:2261-2267.e1.
 18. Cerfolio RJ, Bryant A. Results of a prospective algorithm to remove chest tubes after a pulmonary resection with high output. *J Thorac Cardiovasc Surg* 2008;135:269-73.
 19. Kocher GJ. Robotic-assisted thoracoscopic surgery: state of the art and future perspectives. *J Thorac Dis* 2017;9:1855-7.

Cite this article as: Jacobsen K, Talbert S, Boyer JH. The benefits of digital drainage system versus traditional drainage system after robotic-assisted pulmonary lobectomy. *J Thorac Dis* 2019;11(12):5328-5335. doi: 10.21037/jtd.2019.11.69