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RESEARCH

Thoracoscopic Talc Pleurodesis in Malignant Pleural Effusions: impact of high frequency jet ventilation on outcome

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BEN AZIZ. M, EGO. A, DIGONNET. A, KHALIFE. M, HONTOIR. S, SOSNOWSKI. M
Institut Jules Bordet - Cancer Centre of the Brussels Free University (ULB), Brussels, Belgium

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CORRESPONDENCE AUTHOR: MOHAMMED BEN AZIZ
E-MAIL: mohammed.benaziz@bordet.be

CONFLICTS OF INTEREST
THERE ARE NO CONFLICTS OF INTEREST FOR ANY OF THE AUTHORS.

ABSTRACT:

Background:

Malignant pleural effusion is a complication of several types of advanced malignancy, which may significantly reduce the quality of life of patients.

Thoracoscopic talc pleurodesis is a feasible and effective treatment, but not devoid of complications such as respiratory complications. Airways management may play a role in the occurrence of these complications.

The purpose of the study is to evaluate the efficacy and safety of high frequency jet ventilation in the management of Thoracoscopic Talc Pleurodesis in Malignant Pleural Effusions.

Methods:

We performed a retrospective study on patients, who underwent Thoracoscopic Talc Pleurodesis in Malignant Pleural Effusions, with the objectives to substantiate the complications and possible influence of high frequency jet ventilation, on the occurrence of respiratory complications.

137 files were reviewed over a period of 11 years. Medical history, anaesthetic charts, intravenous fluid use, anaesthesia method and analgesia, records of complications and length of hospital stay were analysed. Patients were divided into 2 groups according to the intraoperative airways management for thoracoscopy: One Lung Ventilation (n = 112) or double lung high frequency jet ventilation (n=25).

Results:

The average age was significantly higher in the jet ventilation group (p =0.03)

Intraoperative high frequency jet ventilation was significantly associated with less frequent blood loss (p=0.049).

Respiratory complications such as pneumonia was found more often when intraoperative One Lung Ventilation was used (p = 0.023). No differences in the length of hospital stay but surgery time were significantly reduced (p<0.05).

Conclusions:

The use of intraoperative pulmonary high frequency jet ventilation in Thoracoscopic Talc Pleurodesis in Malignant Pleural Effusions may reduce blood loss, durations of surgery and postoperative respiratory complications. These findings should be confirmed in large prospectives study.

KEYWORDS: Pleurodesis , Pleural effusion, thoracoscopy, blood loss, pneumonia

INTRODUCTION

Lung cancer is the most common metastatic tumor to the pleura in men and breast cancer in women **(1).** Together, both malignancies account for 50%-65% of all malignant effusions **(2).**

Malignant pleural effusion (MPE) is the second leading cause of exudative pleural effusions after parapneumonic effusions **(3)**, it is common and can complicate most cancers, including one-third of patients with lung and breast carcinomas **(4)** and most (>90%) patients with malignant pleural mesothelioma. **(5)**

Brain cancer, breast cancer and bones cancer are the three serious forms of cancer which are taking many lives in Belgium.

Over 1.5 million pleural effusions occur in the United States every year as a consequence of a variety of inflammatory, infectious, and malignant conditions. Although rarely fatal in isolation, pleural effusions are often a marker of a serious underlying medical condition and contribute to significant patient morbidity, quality-of-life reduction, and mortality.

MPE is a common complication of advanced malignancy with a poor prognosis. It's estimated that MPE affects more than 200.000 people each year in the United States (**6**). Progressive dyspnea is the most common symptom in patients with MPE followed by cough and chest pain that affect the quality of life **(7).**

The discovery of malignant cells in pleural fluid and/or parietal pleura signifies disseminated or advanced disease and a reduced life expectancy in patients with cancer **(8).** Median survival following diagnosis ranges from 3 to 12 months and is dependent on the stage and type of the underlying malignancy **(9).**

The best way to prevent the accumulation of pleural fluid is not known. In general, the two main procedures available are the implantation of an indwelling pleural catheter and the creation of a pleurodesis.

Pleurodesis is a procedure aiming at the adhesion of the visceral and parietal pleura that prevents the accumulation of MPE and subsequently improves symptoms. It is created when an inflammation producing material is injected into the pleural space. This can be done either through a chest tube or at the time of thoracoscopy. Agents used to produce the pleural inflammation include talc, tetracycline derivatives silver nitrate, povidone, and antineoplastics **(10).**

The worldwide standard therapy for controlling malignant pleural effusions is pleurodesis with talc, as talc has been reported to have a better success rate and a lower incidence of side effects than other agents **(11).**

Talc is hydrated magnesium silicate powder that includes various types of minerals used for chalks and cosmetics. Concerns have been raised that intrapleural talc administration may cause acute respiratory

Distress syndrome; however, studies have revealed that using talc with a large particle size does not lead to systemic inflammation **(12).**

A Cochrane review demonstrated that talc was the most effective sclerosant comparing with other sclerosants and a significant reduction in MPE recurrence **(13).**

Another systemic review revealed that talc tended to be associated with fewer recurrence of MPE when compared with other sclerosants, but there was no significant difference **(14)**

On the other hand, a few complications of talc pleurodesis existed, such as acute respiratory failure, pneumonia, and treat-related death **(15)**

In our institution we use Thoracoscopic Talc Pleurodesis in Malignant Pleural Effusions, this procedure is not devoid of complications such as Blood Loss, pain, infection and respiratory complications. Careful screening of patients is mandatory. thoracoscopic talc poudrage pleurodesis, should be performed in patients with malignant pleural effusion, especially those with life-expectancy longer than one month **(16)**

Intraoperative Airways management may play a role in the occurrence of these complications.

One Lung Ventilation with Broncho-cath double lumen or pulmonary high frequency jet ventilation is used to maintain an adequate oxygenation during anesthesia and to facilitate the surgical procedure. High frequency jet ventilation is characterized by delivery of small tidal volumes (1-3mls/kg) from a high pressure jet at supraphysiological frequencies (1-10Hz) followed by passive expiration. HFJV is indicated when it offers advantages over conventional ventilation. These indications fall into two main categories; to facilitate surgical access and to optimize pulmonary function.

The purpose of our retrospective study is to assess the efficacy and safety of high frequency jet ventilation in the management of airways during Thoracoscopic Talc Pleurodesis in Malignant Pleural Effusions, and to evaluate this procedure of ventilation on patient's outcome.

MATERIALS AND METHODS

After the approval of the Ethics Medical Committee, we reviewed the medical records and the anesthesiology chart of all patients with Thoracoscopic Talc Pleurodesis in Malignant Pleural Effusions from January 2004 to December 2014 at Jules Bordet Institute.

One hundred thirty seven patients with Malignant Pleural Effusion were treated by Thoracoscopic Talc Pleurodesis. The procedure was performed by different experienced surgeons.

The following patient characteristics were searched: age, gender, weight, height, body mass index(BMI), American Society of Anesthesiologists (ASA) score, past medical history, cardiovascular risk factor including diabetes , smoking and alcohol and other co-morbidity factors such as Chronic lung disease, chronic pulmonary obstructive disease, Tuberculosis , Asbestosis , Aspergillosis and Fibrosis.

Primitive tumor characteristics and their definitive histopathological examinations were noted.

Intraoperative data were also collected: operative and anesthesia time, type of anesthesia with the product used and their dosages, type and quantity of fluid resuscitation, hemodynamic data and intraoperative blood loss, transfusion and diuresis.

Postoperative complications were divided into respiratory complications, cardiovascular complication, digestive complication, urinary complication and infectious complications.

All these characteristics were represented in Table 1 and Table 2 according to the type of intra operative airways management for thoracoscopy : one lung ventilation with a bronchocath double lumen (**group DB**) or double lung high frequency jet ventilation (**group JV**).

Anesthesia method was distributed with either volatile agents or propofol based total intravenous anesthesia. Sufentanil or remifentanil was used to provide perioperative analgesia.

Patients were invasively monitored, with an arterial line, and eventually a central venous line and a Core Temperature measurement. Operating room temperature was maintained above20◦C and administered fluids warmed if needed. Hemodynamic monitoring base includes cardiac monitoring by electrocardiogram (ECG), noninvasive blood pressure (NIBP), oximeter, capnography (ETCO2: end-expiratory carbon dioxide concentration), bispectral index (indicating the level of sedation and guiding the administration of anesthetics agents to maintain adequate hypnotic level). The patient's body temperature is kept constant by a heating blanket.

Anesthesia was induced with propofol or etomidate and rocuronium.

Tracheal intubation with an endotracheal tube or Broncho cath double-lumen tube was performed with the aid of fiberoptic bronchoscopy.

In the high frequency jet ventilaltion group only total intravenous anesthesia was performed with propofol and remifentanil using a Target Controlled Infusion pump under Bispectral Index. Monitoring was carried out with 100% O2. After the induction, the arterial blood gas analysis under two lung ventilation with a tidal volume of 8 mL/kg and a respiratory rate of 10 breaths/min was acceptable.

To maintain adequate ventilation and oxygenation for video assisted thoracoscopic, two methods were used in our study:

Broncho cath double-lumen tube: it is basically made up of two small lumen endotracheal tubes of unequal length fixed side by side. The shorter tube ends in the trachea, while the longer one is placed in either the right bronchus in order to selectively ventilate the left or right lung respectively.

Classic endotracheal tube associated with high frequency jet ventilation: before video assisted thoracoscopic surgery the endotracheal tube performed after the induction of anesthesia is disconnected from the respirator and a probe is inserted into the endotracheal tube and connected to the high frequency jet ventilation machine to provid à smal volume tidal (15 to 25 ml) with à high frequency (150 to 200 breats /min)

In total, 137 patients were included in the study: 112/137 patients were offered one lung ventilation by double-lumen broncho cath tube (group DB) versus 25/137 patients were given double lung high frequency jet ventilation (group JV) for Thoracoscopic Talc Pleurodesis in Malignant Pleural Effusions.

Variables were presented in term of median and interquartile range (IQR). In order to compare the two groups, were tested continuous variables for normality (Shapiro-Wilk).

After excluding a normal distribution, a nonparametric Mann-Whitney test was thus used (Minitab 15 for Windows).Chi square test was used for non-continuous variables. All of the tests were two-sided and performed with a 5% alpha risk.

RESULTS AND DISCUSSION

Table 1 reports the preoperative characteristics of patients in group DB and group JV.

No statistically significant difference was noted between patients in group DB and patient in group JV in terms of, gender, BMI, ASA score, Raison of thoracoscopy, medication use, comorbidity factors and the primary site of cancer except for kidney primitive which is more frequent in group JV.

The average age was significantly higher in the jet ventilation group (p =0.03).

In addition, intraoperative variables were not statistically different between the two groups except for blood loss (*P* = 0.049) , durations of anesthesia (p=0.0001) and surgery(*P* =0.0002) as reported in **Table 2 , Fig 1** .

Patients with complications were noted more frequently in the group DB compared to group JV (44.6% vs 24 %, *P* = 0.057) as reported in **Table 3**

Respiratory complications were more frequent in the group DB compared to group JV (42% vs.20%, *P* = 0.040) (**Figure 2)** and pneumonia (**Figure 3)** was found more often when Broncho cath double-lumen tube was used (p=0.023), while there were no statistically significant difference for others respiratory complication such as immediate respiratory failure or other complications.

The method of airways ventilation for Video assisted thoracoscopic surgery was associated with neither the length of hospital stay nor the occurrence of hospital mortality as reported in **Table 3.**

There were no other statistically significant differences between groups regarding mean oxygen saturation in the first post-operative day (**Table 4)**, time of the pleural air leak in postoperative time, the amount of fluid drained from the pleura and the average drainage period (**Table 2** and **3**)

Table 1. Patient preoperative characteristic distributed between the two groups

	Broncho-cath double lumen Group DB n = 112		Jet Ventilation Group JV n = 25			Test
	n	%	n	%	p	
Gender male /female (male %)	29/83	25,9	6/19	0,24	0,8444	Chi-Square
Age mean (median, IQR)	59 (50;66)		65 (55;75)		0,0365	TTEST
BMI mean(median, IQR)	24 (20;27)		22 (20;25)		0,4835	TTEST
ASA III (n,%)	112 100%		25 100%		1,000	Fisher's Exact Test
indications for thoracoscopy:						
Biopsy	77	68,8%	14	56,0%	0,2223	Chi-Square
Wedge resection	3	2,7%	0	0,0%	1,0000	Fisher's Exact Test
Drainage and Talcage	32	28,6%	11	44,0%	0,1328	Chi-Square
primitive tumor:						
Pulmonary	14	12,5%	3	12,0%	1,0000	Fisher's Exact Test
Kidney	0	0,0%	2	8,0%	0,0322	Fisher's Exact Test
Breast	57	50,9%	14	56,0%	0,644	Chi-Square
ORL	10	8,9%	0	0,0%	0,5919	Fisher's Exact Test
Digestive	7	6,3%	2	8,0%	1,0000	Fisher's Exact Test
Gynaecological (other than Breast)	7	6,3%	2	8,0%	0,6682	Fisher's Exact Test
Bladder	0	0,0%	1	4,0%	0,1825	Fisher's Exact Test
Blood	4	3,6%	0	0,0%	1,0000	Fisher's Exact Test
Bone	5	4,5%	1	4,0%	1,0000	Fisher's Exact Test
Melanoma	5	4,5%	0	0,0%	0,5844	Fisher's Exact Test
Neuroendocrine	1	0,9%	0	0,0%	1,0000	Fisher's Exact Test
Prostate	2	1,8%	0	0,0%	1,0000	Fisher's Exact Test
Generalized neoplasia	75	67,0%	15	60,0%	0,7766	Chi-Square
Comorbidity:						
Chronic lung disease	12	10,7%	2	8,0%	1,0000	Fisher's Exact Test
CPOD	7	6,3%	2	8,0%	0,6376	Fisher's Exact Test
Tuberculosis	1	0,9%	0	0,0%	1,0000	Fisher's Exact Test
Asbestosis	1	0,9%	0	0,0%	1,0000	Fisher's Exact Test
Aspergillosis	1	0,9%	0	0,0%	1,0000	Fisher's Exact Test
Fibrosis	2	1,8%	0	0,0%	1,0000	Fisher's Exact Test
Diabetes mellitus	8	7,1%	2	8,0%	1,0000	Fisher's Exact Test
Tabacco	37	33,0%	4	16,0%	0,1085	Chi-Square
Alcohol	24	21,4%	4	16,0%	0,5428	Chi-Square
CAD	1	0,9%	0	0,0%		
Preoperative Anticoagulation	10	8,9%	5	20%		
Corticosteroids Drugs	42	37,5%	5	20%		

Table 2. Comparison of intra-operative data between the two groups.

	Broncho-cath double lumen **Group DB n = 112**	**Jet Ventilation** **Group JV n = 25**	**P**	**Test**
<u>Drainage volume (mL):</u>				
median, IQR	1000 (312.5; 1600)	1650 (500;2375)		
mean	1133	1544	0,0977	TTEST
<u>Blood Loss (mean, mL):</u>	657,27	0	0,0495	TTEST
<u>Infusion (mL)</u>				
Cristalloïd (mean, mL)	1303,6	1104	0,0589	TTEST
Colloid (mean, mL)	218,75	300	0,2275	TTEST
Red Cells (n patients transfused)	4	1	1,0000	Fisher's Exact Test
<u>Durations:</u>				
Anesthesia (mean, mn)	158	112	<.0001	TTEST
Surgery (mean, mn)	88	65	0,0002	TTEST

Fig 1 anesthesia and surgery time between the 2 groups

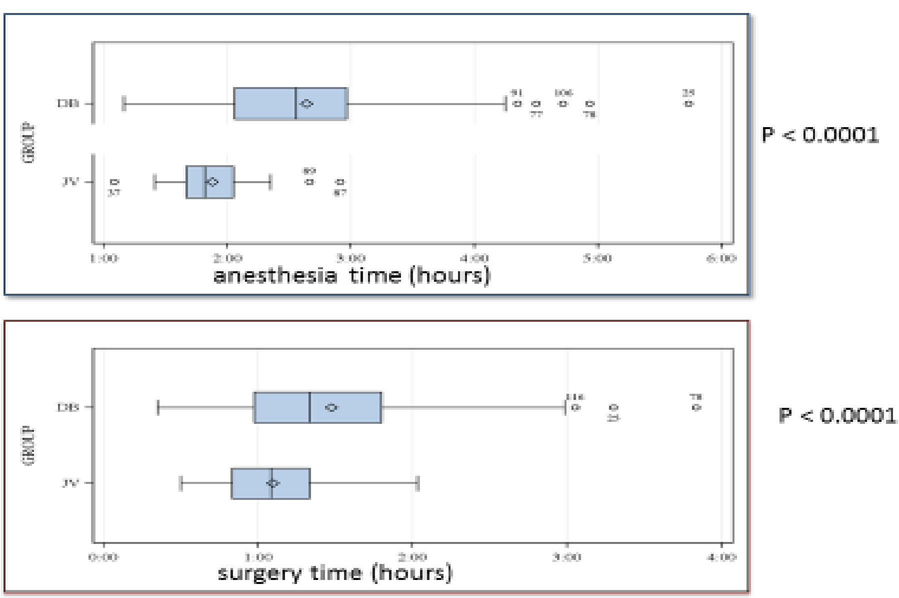
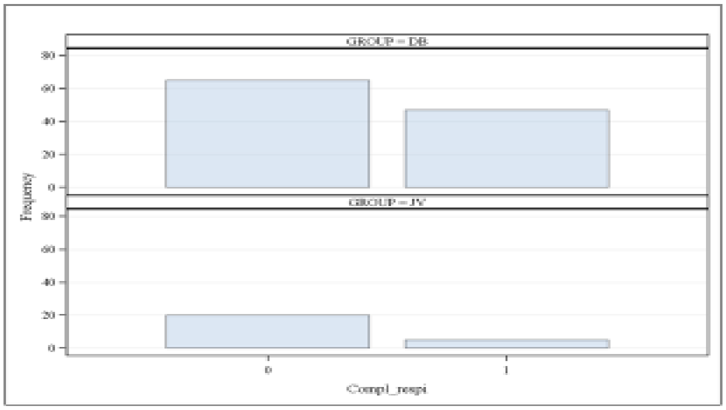


Fig 2. Patients with respiratory complications in the 2 groups

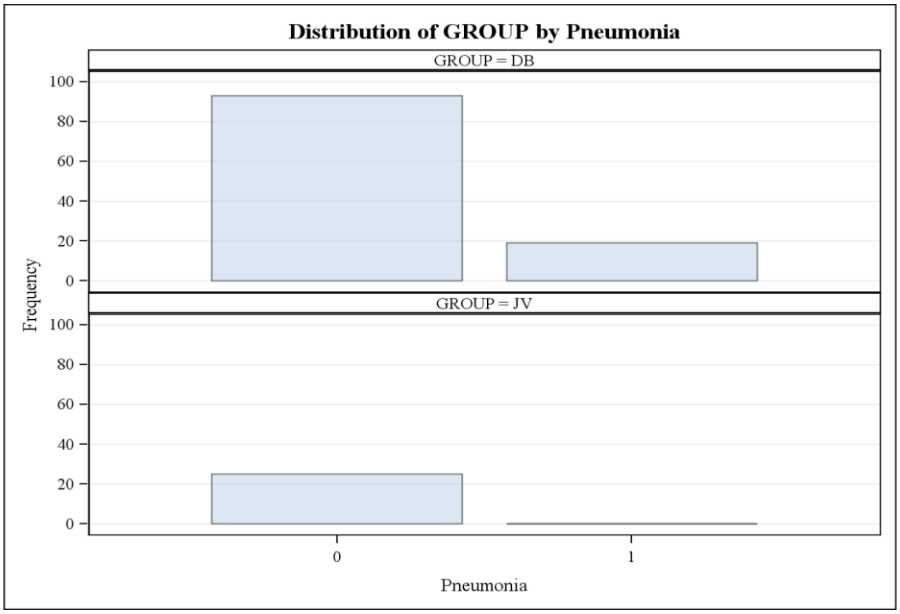


P = 0.04

Table 3. Postoperative complications in group 1 and group 2.

	Broncho-cath double lumen Group DB n = 112		**Jet-ventilation Group JV n=25**			
	n	%	n	%	p	Test
Patients with complications	50	44,6%	6	24,0%	0,0577	Chi-Square
Respiratory	47	42,0%	5	20,0%	0,0407	Chi-Square
Infectious	22	19,6%	1	4,0%	0,0773	Fisher's Exact Test
Pneumonia	20	17,9%	0	0,0%	0,0239	Fisher's Exact Test
Pleural infection	2	1,8%	1	4,0%	0,4563	Fisher's Exact Test
Immediat Respiratory failure	6	5,4%	2	8,0%	0,6376	Fisher's Exact Test
Radiology	16	14,3%	4	16,0%	1,0000	Fisher's Exact Test
Worsening effusion	9	8,0%	3	12,0%	0,7201	Fisher's Exact Test
Major subcutaneous emphysema	2	1,8%	0	0,0%	1,0000	Fisher's Exact Test
Atelectasis	5	4,5%	1	4,0%	1,0000	Fisher's Exact Test
Other	9	8,0%	1	4,0%	1,0000	Fisher's Exact Test
Urinary	3	2,7%	1	4,0%		
Cardiovascular	4	3,6%	0	0,0%		
Pulmonary embolism	4	3,6%	0	0,0%	0,5844	Fisher's Exact Test
Digestive	1	0,9%	0	0,0%		
pseudomembranous colitis	1	0,9%	0	0,0%	1,0000	Fisher's Exact Test
Sepsis X origin	1	0,9%	0	0,0%	0,1825	Fisher's Exact Test
Lengts of stay						
ICU (mean, day)	2,24		1,96		0,4733	TTEST
Hospital (mean, day)	11,33		12		0,8259	TTEST
Hospital mortality	9	8,0%	1	4,0%	0,6889	Fisher's Exact Test

Fig 3. Patients with pneumonia frequency in the 2 groups



P=0,02

	Broncho-cath double lumen Group DB n = 112	Jet-ventilation Group JV n=25	p	
SpO2 (%)	97,3	97,52	0,8194	TTEST
FiO2	0,45	0,4	0,3233	TTEST
SpO2/FiO2	255,2	272,9	0,3239	TTEST

Table 4. Mean oxygen saturation in the first post-operative day .

DISCUSSION:

To optimize the working conditions for the surgeon in Thoracoscopic Talc Pleurodesis, one lung ventilation (OLV) using a double-lumen tube (DLT) or different types of bronchial blockers **(17)** is usually employed.

However, OLV can be associated with a number of serious complications, varying from difficulty in placement of the DLT to more serious but rare complications such as laceration of the tracheal mucosa leading to tracheal rupture, and barotrauma.

Moreover, it also can lead to severe pneumothorax or complications arising during exchange of a DLT to a conventional single-lumen tube, deployed for postoperative ventilation **(18).**

High-frequency jet ventilation (HFJV) was introduced into clinical practice in 1977 by Klain and Smith, initially named “fluidic technology.” **(19)** Today its use is favored in otolaryngology for diagnostic or therapeutic procedures during rigid bronchoscopy.

Although the primary aim of ventilating both the lungs is accomplished, this ventilation strategy employs very small lung excursions, resulting in minimal rise in intrathoracic pressure.

In our retrospective study, high frequency jet ventilation in Thoracoscopic Talc Pleurodesis made taking off the pleura easier, providing better operating conditions and smaller injury of the lung. This resolved in a significantly shorter operating period. In contrast, in the one lung ventilation group, difficult operating conditions led to traumatization of the lung, greater intraoperative blood loss and longer operating time.

Average age was significantly higher in the jet ventilation group in our study, aging generates important changes in the structure and function of the respiratory system. There is a reduction in the elastic recoil of the lung causing "senile emphysema", a condition characterized by reduction in the alveolar surface area without alveolar destruction, which is associated with hyperinflation, increased lung compliance and reduction in alveolar-capillary diffusing capacity. In our study paradoxically less respiratory complications was found in this group.

The use of HFJV for lung ventilation can be advantageous. The non-dependent lung is held slightly distended, so minimizing shunt by increasing mean airway pressure, aiding perfusion and allowing carbon dioxide removal without necessity for large volume excursions. Kazuo Abe has shown that Selective HFJV of the non-dependent lung, while the dependent lung is ventilated with conventional intermittent positive-pressure, increases PaO2 compared with simple collapse of the non-dependent lung and conventional ventilation of the dependent lung **(20).**

High-frequency jet ventilation (HFJV) has been reported to have better oxygenation effects than continuous positive airway pressure (CPAP) in patients undergoing resection of thoracoabdominal aortic aneurysm **(21).** It is well known that the application of CPAP to the non-ventilated lung is useful for maintaining arterial oxygenation during OLV.

HFJV has been shown to recruit alveoli through the positive end-expiratory Pressure (PEEP) effect it generates **(22),** and this method could reopen some lung areas and reduce the risk of arterial hypoxemia during OLV. Crimi et al. **(23)** reported a dramatic improvement in arterial oxygenation and unchanged hemodynamics with the application of HFJV to the non-dependent lung and ventilation of the dependent lung with intermittent positive pressure, in patients with one-lung injury. In addition, the rate of carbon dioxide elimination can be regulated with HFJV by changing the driving gas pressure and the respiratory rate.

Godet et al. **(21)** studied the effectiveness of HFJV and CPAP on respiratory parameters in 20 patients undergoing resection of thoraco-abdominal aortic aneurysm and reported that differential ventilation with CPAP did not improve any of the respiratory parameters.

In Contrast, they found that differential ventilation with HFJV improved respiratory parameters and concluded that because HFJV improved gas exchange without affecting surgical comfort, differential ventilation with HFJV is superior to differential ventilation with CPAP.

HFJV could reopen some lung areas and reduce the risk of arterial hypoxemia and may be responsible of less respiratory infections such as pneumonia as reported in our study.

In Thoracoscopic Talc Pleurodesis under one lung ventilation (OLV), hypoxemia may occur because of shunting of the blood via the non ventilated lung as well as by surgery-induced compression of the mediastinum **(24).** In some cases of severe hypoxemia, the collapsed lung must be reinflated to restore tissue oxygenation, thus interrupting the surgical procedure. Operative hypoxemia and the duration of one-lung ventilation are even related to the development of postoperative acute respiratory distress syndrome **(25).**

Pulmonary complications such as pneumonia and respiratory insufficiency are among the most frequently reported complications that develop after esophagectomy **(26)**. In 1992, Crozier et al **(27)** reported an incidence of pneumonia in half of their patients.

In 1997, the British National Confidential Enquiry into Perioperative Death reported deficiencies in the management of double-lumen tubes (DLTs) during esophagectomy **(28)** High-frequency jet ventilation (HFJV) to two lungs has been successfully used in several fields of thoracic surgery **(29).** To reduce the problems of hypoxemia and mal positioning of the DLT and in an attempt to decrease the incidence of postoperative pneumonia after esophagectomy (by decreasing the areas of atelectasis and shunting), the authors have begun using HFJV during esophagectomy at their institution **(30).**

CONCLUSION:

HFJV seemed to be a safe and feasible method of ventilation for Thoracoscopic Talc Pleurodesis in malignant pleural effusions. To further establish its safety and efficacy, investigations with a larger study population would be necessary.

The use of intraoperative double lung HFJV in Thoracoscopic Talc Pleurodesis in Malignant Pleural Effusions may reduce intraoperative blood loss, durations of surgery and respiratory complications. It is may be an alternative method of lung ventilation in thoracoscopic surgery, in which disruption or significant reduction of mobility of the operated lung is important.

These findings should be confirmed in large prospective studies using specific guidelines. The relatively low number of serious complications denotes an adequate preoperative screening and stresses the importance of adequate maintenance of parameters throughout the perioperative process.

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