ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

MASTER UNIVERSITARIO DI II LIVELLO

MINIMALLY INVASIVE AND ROBOTIC PEDIATRIC SURGERY

Uniportal video-assisted thoracoscopic surgery (U-VATS) for primary spontaneous pneumothorax: early results and comparison with three-port video-assisted thoracoscopic surgery (VATS)

Relatore
Ch.mo Prof. M. Lima

Presentata da
Dott.ssa Valentina Montano

ANNO ACCADEMICO 2021-2022

PART I

PART II

PART III

PART IV

PART V

PART I

INTRODUCTION

Thoracoscopy is the minimally invasive technique applied in the vast majority of thoracic surgery. Despite technical safety and feasibility were advocated by many authors,[1,2,3,4] uniportal video-assisted thoracoscopic surgery (U-VATS) is still little used in paediatric surgery, especially for major surgeries, and reports in literature are limited.[5]

U-VATS is performed through a 2-3 cm single incision, with camera and operative instruments entering the pleural cavity in a parallel manner.

Procedure, specimen retrieval and chest drain insertion, are all carried out gasless from the single port.[6]

U-VATS was initially described in adults, limited to diagnostic procedures and pneumothorax treatment, by Rocco et al;[7] nowadays, the procedure has been widely extended in complex thoracic surgery, demonstrating to be safe and feasible in adults, and many publications have highlighted its benefits, including shorter hospital stay, earlier chest tube removal, reduced complication rates, and equivalent cancer-free survival, compared to thoracotomy, with a better cosmetic result, if compared to multiportal approach.[8]

The aim of this study is to show the preliminary results of a “Uniportal-VATS program” for primary spontaneous pneumothorax (PSP), started in 2019 at Filippo Del Ponte Children’s Hospital, in Varese.

After a general part, where the state of the art in medical and surgical management of PSP is described, we explain uniportal technique, with its “tips and tricks”, and show the preliminary results of our U-VATS surgeries; furthermore we make a comparison of two cohorts of patients, in order to illustrate the advantages and limits of the uniportal technique compared to ,the well-known, multiportal video-assisted thoracoscopic surgery (VATS): cohort A, with patients from Varese’s U-VATS program, and cohort B, made up of patients underwent standard VATS, in Bologna, at Policlinico S.Orsola-Malpighi Children’s Hospital.

PRIMARY SPONTANEOUS PNEUMOTHORAX

Definition

PSP is defined as "presence of air in pleural space" occurring neither with an underlying lung disease nor a trauma.
The incidence of PSP in the paediatric population is low than in adult, and it has been reported to be around 3.4/100,000 children, with a male to female ratio of 4:1 and a peak of incidence during the adolescence.[9]
However, it has been reported a higher recurrence rate in the paediatric population, compared with adults (50–60% vs 30–50%).[10]

Typically, PSP and associated bullous/blebs disease is a condition that usually occurs in thin and tall adolescents, and boys are more often affected than girls.[9,11]
There may be a familiar component, and there are well-known associations:

- Marfan syndrome;
- Ehlers-Danlos syndrome;
- Alpha-1-antitrypsin deficiency;
- Homocystinuria;

Classification

PSP can be classified as *symptomatic* or *non-symptomatic* as well as *large* or *small*. The two categories are not necessarily associated: a small pneumothorax (PNX) can be symptomatic, while a large one can be completely asymptomatic.
The categories are defined in advance and have an impact on the diagnostic and therapeutic choices.
Sudden chest pain, acute onset and dyspnea (of varying degrees, from simple discomfort to shortness of breath, cough, tachypnea or fatigue) are the main symptoms associated with PSP.[10] In addition, the PSP is considered symptomatic in case of high cardiac frequency and respiratory frequency.[10]

The British Thoracic Society guidelines suggest defining a PNX as "*large*" if there is a "*2 cm gap between the lateral lung edge and the chest wall at the level of the hilum*".[9] The American College of Chest Physicians guidelines, on the other side, consider a "*large*" pneumothorax when there is an "*apical distance of 3 cm between the thoracic wall and the lung*".[9]

***"**Tension"* PNX occurs when intra-pleural air accumulates with mediastinal shift and progressively hemodynamic compromise.[12]

Etiophatology

The formation of bullae (*Fig.1*) is most likely to be multifactorial, including physical characteristics, smoking, anatomic abnormalities of the bronchial tree, sex differences, genetic factors, and growth.[13]
The seasonal pattern of the onset of PSP, higher in spring and summer seasons, has been explained with atmospheric changes in term of pressure and temperature, but the exact impact of weather determinants is not clear.[14]

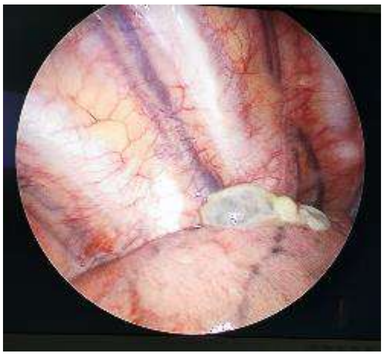


Fig.1 *Apical pulmonary bullae.*

The development of blebs is a dynamic process, that often continues throughout adolescence. Previous studies have suggested that growth during adolescence causes a rapid increase in the vertical dimension of the thorax, compared to the horizontal dimension. This rapid increase causes an increase in negative pressure at the apex of the lung, which may lead to formation of bullae and may cause PSP upon rupturing.[13,15]

At the histopathological analysis on the surgical specimen, the pneumothorax-associated fibroblastic lesions (PAFL) are defined as a fibrosis located on the peripheral pleura classically associated with wedge-shaped septa and with fibroblastic foci disseminated on the visceral face. PAFL are not ubiquitous but were found in 50% of patients under 20 years of age and were absent in secondary pneumothoraces.[14] It is uncertain if PAFL are the result of a previous healing process or the expression of emphysematous-like changes (ELC) based on connective tissue disorders.

Imaging

An upright *chest X-ray* (CXR), performed in maximum inspiration, is the first choice of investigation for the diagnosis of PNX. Posterior CXR, in expiration, is chosen for the search of small layer of PNX.[10]

Typically radiographs demonstrate (*Fig.2*):

- Visible visceral pleural edge is seen as a very thin, sharp white line;
- No lung markings are seen peripheral to this line;
- Peripheral space is radiolucent, compared to the adjacent lung;
- Lung may completely collapse;
- Mediastinum should not shift away, unless a tension PNX is present;
- Subcutaneous emphysema and pneumomediastinum may also be present;

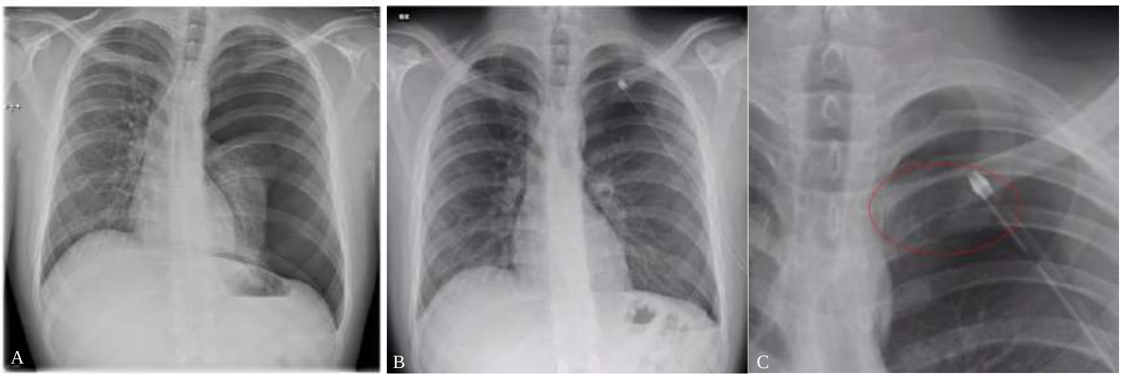


Fig.2 A. *Massive left PNX;* ***B.*** *Residual left PNX, with chest tube;* ***C.*** *Apical bulla (red circle).*

Lateral-lateral projection performed in up-right position and on inspiration may be useful in defining particular cases of PSP, where the air layer is mainly located anteriorly or posteriorly. [10]

In clinical practice, *chest ultrasound* is indicated in selected situations, for example in post-traumatic events or as first approach in pregnant patients, to minimize exposure to radiation. Current data in the literature indicate an increasing application of the ultrasonography (US) with PSP in the paediatric population;[14] because of its portability and the absence of ionizing radiations, some authors point out its usefulness especially for children and adolescents.

The results of a recent meta-analysis revealed a higher sensitivity and similar specificity in the use of US compared with CXR.[14] On the other hand, the use of US, as a reliable tool for the diagnosis of PSP, is limited because its accuracy is strongly dependent on the operator's skills.

We consider US useful in post-operative time, to reduce X-ray exposure but, at the same time, to evaluate re-expansion of the lung daily; for this reason, all the surgeons of our team have been trained by practical courses on thoracic ultrasound.

The role of *computed tomography* (CT) scan for the first episode of PSP is controversial and generally this method is not considered a first-line diagnostic tool, especially with paediatric patients. CT scans are, in fact, not encouraged by paediatricians and paediatric surgeons, due to the risk of radiation exposure. This exposure has been calculated to be approximately 68 times the effective dose of a traditional CXR.[14] But, at the same time, it has been reported that in children who develop recurrent PSP, half will have recurrence on the contralateral side.[13]

Thanks to the very high morphological definition of the anatomical structures, CT can be considered the "gold standard" for the diagnosis of PNX. In particular, high-resolution thin-layer CT (HRCT; *Fig. 3*), with 1 mm of slice thickness, ensures maximum sensitivity in the identification of sub-pleural bullae, ranging between 94% and 97%.[2]

In practice, CT is indispensable for the definition of complex PNX, as in case of patients with severe bullous dystrophies.

The role of air-containing lesions (blebs/bullae) in the etiopathogenesis and in the risk of recurrence of PSP has also been debated, along with the need of performing a HRCT in children with a first episode of PSP. It has been reported an incidence of air-containing lesions at HRCT ranging from 31 to 100% in children with PSP.[14] Moreover, the recurrence rate of PNX in these children has been reported to range between 50 and 100%, suggesting an important role of the blebs in the risk of recurrence[9] and the importance of CT scanning at first PSP episode, to identify contralateral blebs or bullae, for assessing the risk of recurrence.

Our PSP protocol provides for a CT scan after first episode of PNX, just before discharging the patient or few days later, to find any residual blebs and to schedule an elective apicectomy.

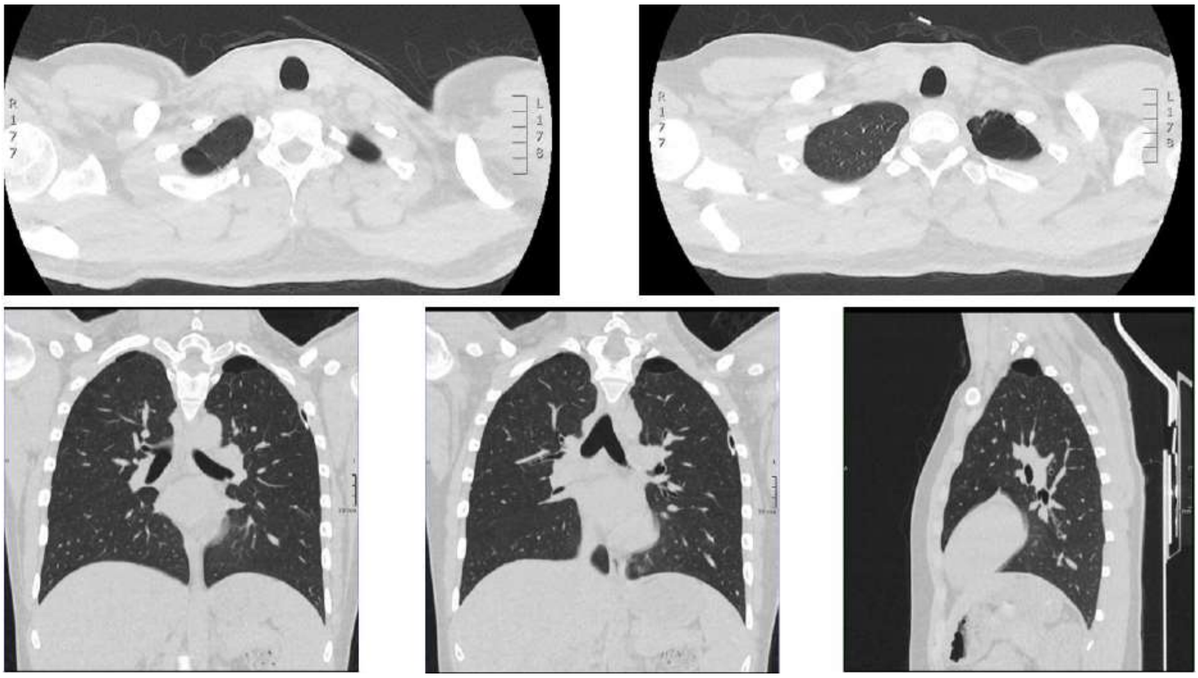


Fig.3 *HRCT of a patient with bilateral apical bullae in axial (up), coronal and sagittal (down) window.*

Nuclear magnetic resonance investigation protocols are unable to produce images qualitatively comparable to those obtained with CT.

Therapeutic Management

Guidelines exist, from the British Thoracic Society and American College of Chest Physicians, regarding the management of PSP in adults. However, there is not a consensus regarding the strategy of treatment of PSP in children up to now.[9]

The first aim in treating a PNX is to allow the collapsed lung to re-expand. The method for achieving this goal is to relieve the pressure in the intra-pleural space, draining out the air in order to avoid a tension PNX, that could lead to hemodynamic instability.
The second aim may be to prevent recurrences.
The choice of optimal treatment depends on the severity of the collapsed lung, on the persistence of air leaks and on the clinical history of the patient.

To calculate the size of PNX many methods have been proposed, but the accuracy of these equations has been questioned.[14] The most used are the Light index, the Collins and the Rhea methods, all based on the estimated volume on the upright CXR.

After having defined the volume of PNX, two options are widely accepted for treatment: in conservative management, different choices are provided, from the simple observation with oxygen administration, to the aspiration of the intra-pleural air through needle, pig-tail catheter and other types of chest tubes. Patients are eligible for conservative treatment at the first episode of PSP or if they are clinically stable and asymptomatic, with a small, non-hypertensive pneumothorax (<20% at Light index).
In non-surgical treatments, the recurrence rate, in adult, after the first attack, is 25- 30%[16] while in children has been reported up to 60%.[10]

The second option is surgical treatment, that can be carried out through a bullectomy/apicoectomy, pleurectomy, mechanical or chemical pleurodesis.
These procedures are proposed to adult patients affected by recurrences and/or large bullae, or by persistent air leaks resulting in a failed lung re-expansion after non-invasive therapy.[14]

Up till now, the management of paediatric PSP is mainly based on the clinical conditions of the patients, with some authors suggesting an early surgical procedure due to the high risk of recurrence.[9]

Conversely, others prefer an initial non-operative treatment, as recommended by the current available guidelines (ACCP, BTS), with O2 administration, needle aspiration and/or chest drain, reserving surgery in case of recurrence or persistent air leak.[9]

Paediatric guidelines are still lacking and children with PSP are commonly managed according to the experience and preference of different clinicians.[9]

NON-OPERATIVE TREATMENTS

It has long been known that patients with small PSP, without significant symptoms, can be observed, without problems; there are no randomized studies that unequivocally address treatment in this particular situation.[10]
In absence of symptoms, radiographic control at least every two days is advisable.[10]

The administration of oxygen, in continuous flow (2–4 L/min) through non-rebreathing face mask or nasal cannula, is the treatment of choice. The purpose of this procedure is based on a trans-pleural gradient, which reduces the partial pressure of nitrogen on the alveolar side, and leads to a diffusion of nitrogen into the alveoli and a progressive resorption of the PNX.

Needle aspiration is accepted if small PNX has a volume ranging between 20% and 40%, with Light Index. Needle thoracentesis is performed following various protocols, by a simple manual aspiration, with a 16-gauge needle inserted at the level of the second intercostal space crossing the midclavicular line. The pig-tail catheter with a diameter of 8-Fr can be placed by a Seldinger manoeuvre to repeat the aspiration.[14]

PLEURODESIS

Pleurodesis can be performed using several techniques: partial apical pleurectomy and pleural abrasion, electrocoagulation hook from the second through the fifth intercostal space, Vicryl mesh, talc effusion pleurodesis, etc.

The first technique used for pleurodesis in adult was a complete parietal pleurectomy, which is not recommended for young patients due to the increased risk of bleeding and

of intercostal nerve damage.[13] Moreover, pleurectomy can make secondary thoracotomy extremely difficult, and performance of an apical pleurectomy alone will not prevent recurrence in the lower part of the chest.[13]
Currently, the most consolidated techniques are the mechanical and the chemical pleurodesis.[14]

Mechanical pleurodesis is performed by an abrasion on pleural surface, using sterile materials, such scratch-pad (*Fig.4*) or a gauze, swabs or scrapers, through VATS access, to initiate an inflammatory response, which results in the formation of adhesions and prevents the lung from collapsing in situations of recurrence. Electric rotating brushes have also been described.[14]

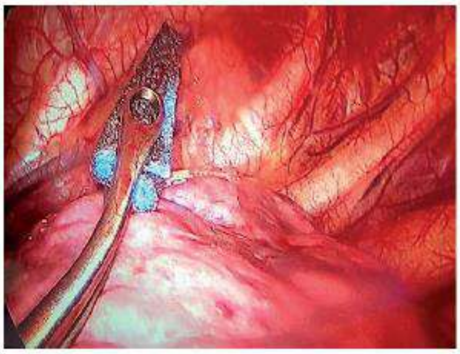


Fig.4 *Mechanical pleurodesis with scratch-pad.*

The treatment is effective when haemorrhagic spots and mild bleeding appear from the parietal pleura. Pleural lesions can be made by electrocautery or argon beam as well, to decrease the risk of excessive bleeding, that may happen with the abrasive technique. Care should be taken when working at the apex, as a Horner's syndrome can occur if there is any injury to the stellate ganglion of the sympathetic chain.
Additional operative complications include bleeding, particularly from intercostal or mammary vessels, and pain.[17]

Chemical pleurodesis is performed by various agents, with irritant and sclerosant properties: the most common are talc, povidone iodine, silver nitrate and minocycline.
Talc poudrage is rarely performed, even though available data show that both VATS bullectomy plus pleurodesis and medical talc poudrage without bullae treatment are

equally effective.[13] Talc poudrage has two main drawbacks: the risk of postoperative pleural infection and the creation of tight adhesions that are difficult to free.
Minocycline has been introduced in clinical practice for its cost and its solubility, which permits administration through the small-bore tubes, allowing outpatient management.[14] On the other hand, a more intense chest pain has been observed after minocycline pleurodesis.[14]

In a recent meta-analysis, it has not yet been identified a pleurodesis method that can be considered definitively superior to others, despite the fact that pleural talcage, during thoracoscopy, seems to guarantee a lower rate of relapses, in absence of adverse effects.[10] In a recent Japanese single-center retrospective article a recurrence rate of 9.6% after thoracoscopic resection of the bullous area is documented without the addition of other surgical measures. Indeed, it has been shown that 63,9% of patients developed new sub-pleural bullae after bullectomy.[10] An additional pleurodesis procedure is advisable in order to minimize relapses, despite the evidence of the effectiveness of this procedure is not yet based on absolute levels of evidence.

CHEST DRAIN

Symptomatic patients with PSP, patients with tension PNX, albeit with minimal symptoms, and patients with bilateral PSP should undergo pleural drainage.

The first study in children's population which proved the efficacy of the small-bore in comparison with large-bore drains was published in 2002 by Dull *et al*.[14] The results were favourable for the pain control but the length of hospital stay (LOS) was not significantly different among the two groups. Kuo *et al.* analysed a cohort of 41 adolescents (<18 years old) treated with a conservative procedure. They found a success rate of more than 50% that was not dependent on the calibre of the tube. LOS and recurrence rates overlapped between the patients treated with small and large-bore drains.[14]
The authors pointed out the potential advantages of the small-bore drains, because insertion does not require large incision on the chest wall, resulting in less pain and more aesthetic wounds.

There is no evidence on the utility of suction applied to drains. Lung re-expansion is achieved in up to 70% of patients with chest tube drainage alone by day 3, without suction.[14]

It should be noted that the immediate application of suction, after the insertion of the chest tube, can lead to acute pulmonary edema, because of re-expansion; this event appears more frequent in young-adult and in massive PNX untreated for more than 7 days.[10]

A retrospective multicenter study by Soccorso et al in 2015 based on 50 paediatric cases showed that 53% of children treated by needle aspiration recurred and ultimately required a chest drain.[18] Thus, the authors suggested to directly insert a chest tube in children to reduce the risk of repeat procedures and anesthesia.

The most recent Cochrane review demonstrates a significant advantage of chest tube over needle aspiration (risk ratio 0.78) albeit with a higher rate of adverse events.[10]
The criteria for removing the chest tube are not uniquely defined; closing the drain before its removal is not a shared practice among surgeons, but it increases considerably the certainty of the cessation of air-leak.[10]

An early VATS has also been proposed to avoid the risk of recurrence and thus to reduce the total hospital stay in children who should undergo a chest tube insertion for the first episode of PSP.[18]

SURGERY

Surgical techniques will be treated in part II

PART II

UNIPORTAL-VATS

Our experience and surgical tips

Since the paediatric surgery department was established, in November 2017, at Varese Children's Hospital, a program for minimally invasive thoracic surgery (MIS-T) has been developed, using standard multiportal thoracoscopic technique to treat thoracic diseases in children and adolescents.

Since December 2019 uniportal technique gained our attention, so we decided to start a uniportal-MIS-T program. Currently, at our center, this program is used exclusively for patients with PSP caused by congenital bullous dysplasia, who require apicoectomy.

As part of this program a fixed surgical team (U-Team) was formed, initially consisting of two paediatric surgeons, a third one was added later; The U-Team visited a high volume thoracic hospital (for adult patients), to observe and learn about uniportal apicoectomy, thanks to a skilled thoracic surgeon; afterwards the same surgeon come to our children's hospital, to supervise the U-Team during the first surgeries, as experienced team leader; this practice was very helpful for gaining confidence in uniportal technique.

After referring to the emergency room with PSP, and receiving immediate adequate treatment, all patients were evaluated with HRCT and if residual apical blebs/bullae were found they were entered into the U-VATS program for scheduled apicoectomy, or for urgent apicoectomy, if the PNX wasn't resolved despite drainage.

We think, as supported by literature, that U-VATS allows performing all the main surgical steps recommended for treating patients affected by bullous dysplasia, with the same clinical advantages of the traditional three-port VATS. At the same way of multiport technique, it achieves the exploration of the chest cavity and the lung parenchyma to find blebs/bullae, to resect the diseased areas of the lung, and to perform adequate pleurodesis procedures (e.g. mechanical parietal pleural abrasion, talc poudrage, pleurectomy, etc.).[19]

Otherwise, from the standard three-port VATS approach - where the lesion represents the peak of an ideal pyramid, and the camera and instruments are placed in correspondence of the other three pinnacles - the uniportal VATS technique implies that the target, the thoracoscope, and the instruments all lie in the same sagittal plane. Although the single incision is the fulcrum where the parallel devices reach the target, arranging themselves in a cranio-caudal direction, the surgeon should be free to move inside the chest cavity without the boundaries due to an unfavourable geometry.

Patient is under general anaesthesia, with one–lung ventilation and patient decubitus is in lateral position, with a tissue roll under the chest to avoid the hip curve and to facilitate a 15 to 20° recumbent position (*Fig.5*).[20] Asepsis is obtained as per routine thoracotomy.

Fig.5 *Positioning of patient of Cohort A in lateral decubitus.*

A 20-30 mm single access is made in the fourth–fifth intercostal space with no carbon dioxide (CO2) insufflation. Local infiltration with 0.5% levo-bupivicaine is given pre-emptively, prior to creating the port (IV-V-VI intercostal space).

It's important to assess the thoracic cavity without muscular section and without rib spreading, using only a wound protector/retractor (Alexis® wound protector/ retractor; Applied Medical, CA, USA) size S or XS, with a 30°- 5 mm thoracoscope, and two parenchymal graspers. Alexis allows to achieve the best field exposure with the minimum associated local tissue trauma. Once the pleural cavity is entered, the surgical team distributes in a convenient fashion to the target area (*Fig.6*).

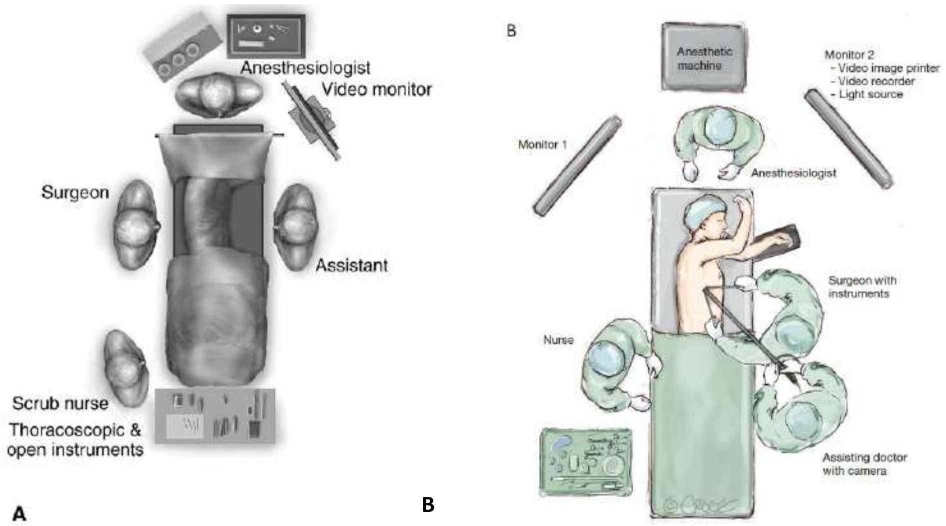


Fig.6 ***A.*** *Surgical team distribution when surgery starts.* ***B****. Surgical team distribution once the pleural cavity is entered.*

With Uniportal VATS, the target lesion in the chest cavity is addressed along a cranio-caudal approach, which enables the surgeon to obtain thoracoscopic visualization and operate through a single port. Compared with standard VATS, with the attendant "baseball diamond" placement of ports to achieve a latero-lateral approach, the ensemble of thoracoscope and operative instruments is rotated 90° on the vertical— or sagittal— axis. This principle is maintained in all applications of this procedure and this approach is facilitated by the utilization of articulating devices ("roticulator"), which offer the ability to deploy and rotate their intrathoracic parts, so that mutual interference of the operative instruments is avoided and a 360° manoeuvrability is obtained (*Fig.7*).[20] Our trick, at this point, is to put a simple stitch (silk n.2) in the third superior of the access, to create a separation between 1/3 upper and 2/3 inferior; this stitch serves as a support deck for the camera, preventing it for falling inside, and facilitates the movements of the instruments and avoids collision with the camera (*Fig.8*).

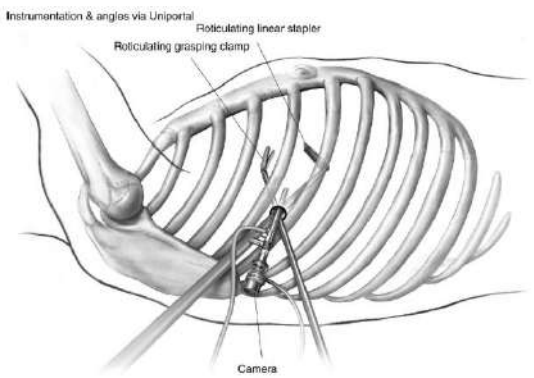


Fig.7 *Roticulating instruments for uniportal VATS.*

Fig.8 *Silk stitch divides in two parts the access and supports the camera.*

The first step, after the gasless chest cavity exploration to search any air leak, is the resection of parenchymal dystrophies: the thoracoscope, the stapler, and the straight parenchymal grasper could be simultaneous introduced (*Fig.9*).[19] When the target area on the lung is easily identified, lung manipulation is reduced to a minimum, but enough to inspect the lung for other emphysematous changes.

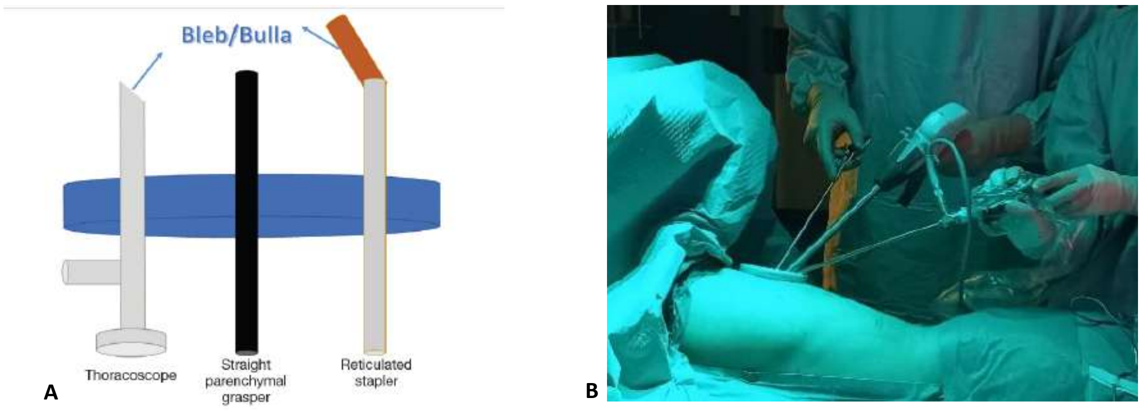


Fig.9 A*. Schematic image show how the 30° thoracoscope, reticulated stapler, and straight parenchymal grasper are simultaneously introduced in the single incision access, protected by a wound retractor.*
B*. Intra-operative image of the instruments simultaneously introduce through the single access.*

Blebs will be air-filled areas of the lung less than 1 cm in size compared to bullae, which are greater than 1 cm in size. The most common technique is to place the endograsper on the bleb/bullae and deploy the endostapler,[20] in order to fully expose the diseased area. There should be a good margin with the stapler passing through only the "healthy" pulmonary tissue, in patients with PSP. Before doing it we often disconnect the bulla from the pleura with a swab. The jaws of the endostapler are open inside the chest and positioned, upwards, just caudal to the bleb/ bullae to remove (*Fig.10e*).
The endostapler is fired and the specimen is then extracted by the same incision, using an endobag or directly with a long Roberts’ clamp.[20]

Pleurodesis can be performed using several techniques, we prefer electrocoagulation hook from the second through the fifth-seventh space associated with pleural abrasion with abrasive tissue.
Our “trick” for pleurodesis is to use the monopolar electrode with a long shaft and bend the metal tip to give a curvature such as to reach a greater portion of the circumference of the hemithorax (*Fig.10G*).

Another "trick", to optimize the costs and not need to buy a dedicated instrument for pleural abrasion, is to use the abrasive scratch-pad which is usually used for clean the tip of monopolar; the abrasive sponge is cut into squares and mounted on a grasping De Bakey for U-VATS; this is an "inexpensive way" to deal with this part of the procedure (*Fig. 10H*). We complete the surgery with the hydropneumatic control of the pulmonary section line, the control of haemostasis and the placement of the thoracic tube, under visual control, by the uniportal access. At last, the skin is closed with simple stitches.

For the chest tube withdrawal our preferred protocol, according to the current literature, is 48 hours of suction at 20 mmHg, then 24 (or 48) hours without suction, and, finally, chest tube removal at postoperative day four (or five), than the patient is discharged the following day. We check lung re-expansion every day with ultrasound, to minimize X-ray exposure, and with CXR every 48-72 hours or before removing the chest tube.

Fig.10 shows the principal steps of the procedure (Patient 2 of the U-VATS Program)

Fig.10 **A**. *Lateral Decubitus with self-locking vacuum mattress;* ***B****. Measurement of the incision;* ***C****. Uniportal access with Alexis S size and silk stich to support the camera;* ***D****. Apical bullae;* ***E****.10 mm Endostapler closed under the bullae;* ***F****. Specimen;* ***G.*** *Pleurodesis with the tip of the coagulator bent;* ***H****. Pleural abrasion with abrasive tissue (scratch-pad)* ***I****. Insertion of a chest tube;* ***J****. drainage set.*

Technical considerations and limitations of uniportal VATS in paediatric population

The morphology of the paediatric chest changes with age (*Fig. 11*). In neonates, the thorax has a trapezoidal morphology and the ribs are horizontal with greater length in anteroposterior diameter. In the older children, the thorax is more rectangular and the vertical diameter is greater, resembling the adult's chest. In addition, the child's thorax is more flexible than in adults.[5]

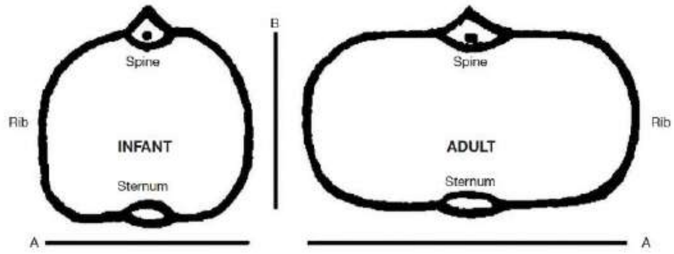


Fig.11 *Thoracic morphology according to age. In neonates and infants the thorax has trapezoidal morphology. In the older children and adults, the thorax is rectangular and the transversal diameter (A) is greater than anteroposterior diameter (B).*

The diaphragm in children is positioned at a "higher level" than in adults. For this reason, diaphragm position should be considered when incisions are planned for thoracic surgery.

Working space is limited for VATS in children and the lung dimensions have to be taken into consideration as an issue when performing this technique. Lungs and airway in children are not fully developed at birth. The structural integrity of the airway improves after birth as the flexible cartilage of the infant's larynx and trachea becomes more rigid.[5]

Single lung ventilation is more difficult in infant or small children if compared with adults. A double lumen-tube is too prominent for patients with less than 30 kg, however different options as bronchial blocker or selective intubation of the contralateral bronchus can be achieved. Ventilator-dependent patients and those with significant cardiac defects can tolerate a limited period of partial lung collapse necessary to perform most of thoracic procedures.[5]

The risk of developing deformities like scoliosis, scapular winging and muscle weakness after thoracic surgery is high, but no thoracic deformities after U-VATS have been reported. Any damage to the innervation of serratus anterior muscle and no need costal resection have been described.[5]

Thoracoscopy has been limited in low weight patients due to both the reduced space in thorax and the absence of specific material for this age.

Fernandez-Pineda et al. reported the approach by single port, but with access through two intercostal spaces (camera trough upper intercostal space and instrumentation trough lower intercostal space).[12] With this approach, they conserved functional and aesthetic advantages of U-VATS, however camera mobility was not conditioned by instrumental mobility (*Fig.12*).

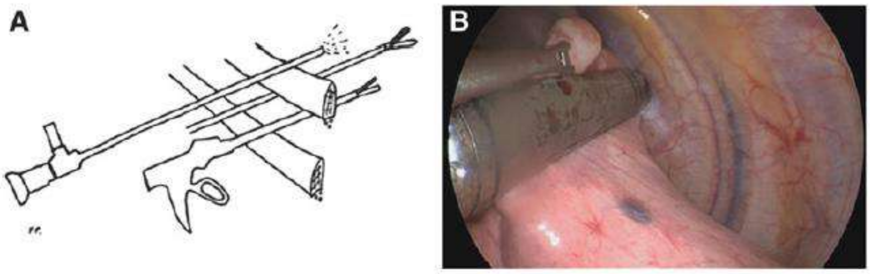
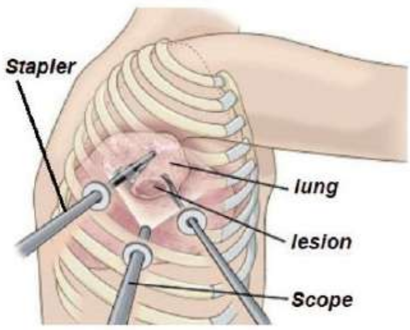


Fig.12 A. *Diagram of the thoracoscope in the superior intercostal space relative to the working instruments.*
B. *Thoracoscopic view with parallel instrumentation between endograsper and endostapler.*

The initial setting for standard multiportal-VATS is similar to U-VATS: patients is under general anesthesia with one-lung ventilation and is placed in lateral decubitus (*Fig.13*).

Fig.13 *Patient of Cohort B in lateral decubitus.*

The first incision is typically placed in the fifth or sixth interspace in the midaxillary line. Two additional incisions can typically be made in the fourth interspace in the anterior axillary line, as well as the fifth interspace in the auscultatory triangle [21] (*Fig.14 A*). There have been modifications to this strategy over the years, with variations in the number and position of the incisions (*Fig.14 B*)



A

B

Fig.14* A.** *Position of three ports* ***B. *Position of four ports.*

Once safely in the chest the lungs are carefully inspected to identify any bullous changes and to detect the source of the air leak. Adhesions should be identified and lysed to allow for complete evaluation of the lung.

Care should be taken to obtain haemostasis if any bleeding from the adhesions is encountered. Bullae that are identified can be stapled using an endo-stapler without crossing over any portion of the bullae in the staple line, as this may increase risk of recurrence. As already said for U-VATS, also in VATS there should be good margin with the stapler traversing only "healthy" lung tissue. The Specimen exit through the 10 mm camera access.

As alternative option to endostapler resection, ablation of blebs and bullae, with endoloop[22] with laser device (MBB 100 watt, Germany) [23] with the LigaSure vessel sealing system (LVSS) [24] (Valleylab, Boulder, CO., USA) and with radio-frequency device have also been described.[25]

Some authors suggest that a resection of the apical segment of the lower lobe should be systematically performed, because bullae at that level can be a potential risk for PSP recurrence after VATS. [26]

Lee *et al.* along with Haraguchi and colleagues proposed a coverage of the staple line with absorbable materials as an additional procedure.[27,28]

CO2 effects in VATS

CO_2 insufflation is used in VATS to achieve adequate exposure of intrathoracic structures and to facilitate the surgical procedure. Several authors have advocated insufflation of CO_2 to expedite collapse of the lung for visualizing the intrathoracic structures. The clinical impact of positive-pressure pleural insufflation during VATS procedures remains controversial. Several investigators have found no significant sequelae with its use, whereas others have reported major problems.[29] One of the sequelae of CO_2 insufflation is the development of hypercapnia, which has traditionally been avoided in an attempt to keep hemodynamic variables normal. Recent evidence of the role of excessive tidal stretch (volutrauma) has prompted clinicians to avoid the use of high-tidal volume (V_T) and to accept the resulting permissive hypercapnia.

Hypercapnia causes a variety of effects on cardiovascular function, mediating alteration in preload, afterload, contractility, and CO. The direct effect of hypercapnic acidosis on the heart and vascular smooth muscle is to reduce contractility. However, these direct effects are opposed by a neurohumeral effect, thus resulting in an increase in sympathomimetic output. This leads to an increase in HR, systemic vasodilatation, and decrease in left ventricular afterload, which results in an increase in CO.[30,31]

Jones et al.[32] demonstrated significant hemodynamic deteroriation in an animal model during CO_2 insufflation pressures of 5 mm Hg or more. More recently, Brock et al.[30], manteining normocapnia throughout the procedure, stated that CO_2 insufflation was associated with a clear deterioration in circulatory function.

A recent randomized controlled study published in March 2022[33] concluded that intrathoracic pressure overshoot can occur during thoracoscopic surgery (in adult) with artificial CO2 pneumothorax and may lead to cardiovascular adverse effects, which highly depends on the duration of the pressure overshoot (hypercapnia and acidosis). Another potential effect of capnothorax is that intraoperative venous bleeding may be covered when intrathoracic pressure exceeds venous pressure and the negative intrathoracic pressure during spontaneous inspiration could siphon blood into the pleural cavity.[33]

For Suarez-Pierre et al. CO2 insufflation has potential complications including arterial hypercapnia and related cardiovascular response, CO2 embolism, and hypotension resulting from impaired venous return.[34]
In contrast, Wolfer et al. found neither haemodynamic nor respiratory disturbances in 32 patients undergoing thoracoscopy with OLV and carbon dioxide insufflation. They concluded that low-pressure carbon dioxide insufflation (< 10mmHg) does not have adverse haemodynamic effects.[35]

Lee et al. in 2018 demonstrated, with a prospective randomized study for bleb resection, that CO2 insufflation did not produce a superior surgical field except at the beginning of surgery. CO2 insufflation required more time and resulted in higher mean PaCO2 and peak airway pressure. But they said also that a young and healthy lung and short operation time could be major factors for preventing hemodynamic deterioration.

Few studies have investigated the hemodynamic consequence of CO_2 insufflation, and all of these reports were done in adult thoracoscopy.[29] Little is known about the cardiovascular changes associated with artificial capnothorax during VATS procedures in paediatric patients.

In small children low pressure CO_2 insufflation should be sufficiently provided no desaturation occurs. Higher pressure may cause hemodynamic compromise and myocardial ischemia; the respiratory and cardiovascular system of a child have characteristics that differ from those of an adult: the lung has less functional residual capacity and lung mechanics in infants and young children are also not favourable in the lateral position, due to softer chest walls and relatively higher diaphragmatic positions.

Collapse volume is much closer to functional residual capacity (FRC), and both lung compliance and airway resistance are adversely related to lung size. Blood pressure is lower and heart rate is higher in infants. The infant's systemic vascular resistance is lower, a factor that well correlates with high metabolism and O_2 consumption. Cardiac output is also higher in infants, especially when calculated according to body weight. Heart rate plays a more important role in determining cardiac output. [36]
In anaesthetized patients in a lateral decubitus position during two-lung ventilation there is relatively good ventilation and a reduced perfusion in the nondependent lung, due to the gravitational distribution of the blood flow. On the other hand, the dependent lung is relatively hypo-ventilated while over-perfused. During one-lung ventilation an obligatory right-to-left trans-pulmonary shunt is created through the non-ventilated lung.[36]

Hypoxia may commonly occur in paediatric age, mainly during one-lung ventilation, hypercapnia may occur during thoracoscopic surgery, partly due to CO_2 absorption across the pleura, and partly because, even when lung exclusion is avoided, thoracoscopy brings about a mechanical constriction on the pulmonary parenchyma, reducing tidal volume, functional residual capacity, total lung capacity and pulmonary compliance;[36,37] factors such as lung exclusion, length of thoracoscopy, and preoperative parenchymal pulmonary abnormalities, may influence some vital parameters during thoracoscopy.[36]

Single Incision Thoracoscopic Surgery **(SITS)** takes a similar approach to U-VATS but it uses CO2 insufflation: a 2,5-3 cm incision is made obliquely at the anticipated chest tube site within a rib interspace (*Fig.15*).[21] Two trocars (either two 5mm or one 5mm and one 12mm) are placed, and one unsheathed 3 or 5mm instrument is passed adjacent to the trocars directly through the intercostal muscles.

This array allowed for visualization with a 5mm thoracoscope and tissue manipulation with two instruments.

Fig.15 *Single Incision Thoracoscopic Surgery (SITS).*

Novel new methods are also being discussed such as a subxiphoid uniport incision.[17] This type of incision is currently being studied to assess for a decrease in the amount of intercostal nerve injury, that is typically observed with intercostal incisions.

PART III

MATERIALS AND METHODS

This is a retrospective study, performed both on a prospective surgical database and retrospective analysis of medical charts, outpatient visits and imaging; this data were used for the comparison between the two cohorts.

The last part of this study includes data about late paraesthesia, sport activity and cosmetic result after U-VATS surgery, that were gathered by a telephonic interview, through a multiple choice questionnaire, sent in advance by e-mail.

Patients were also asked to assess their current activity (equal or lower than before surgery) and if they were currently using analgesic treatment. An opinion about cosmetic results at follow-up was asked separately also to the surgeons of the U-Team, and compared with patients' answers.

Population, procedures, and outcome

We have retrospectively reviewed data about U-VATS gasless procedures performed in our department, since the U-VATS program started (2019); we collected and analysed data about the following parameters:

- **Demographics**: gender, age, weight, height, familiarity and comorbidity;
- **Preoperative clinical presentation**;
- **Perioperative features**: operative time, technical problems during the performance of the procedure, intraoperative complications and conversion rate,
- **Postoperative outcomes**: chest tube duration, LOS, infections, air leak, need for redo-surgery, histopathological diagnosis, postoperative pain recurrence, paraesthesia and aesthetic result;

The same data were retrospectively reviewed for cohort B of patients operated in Bologna by a senior and skilled surgeon, using a well-known and standardised 3 trocars-technique, and both cohorts were compared for intraoperative characteristics and outcomes; we also have tried to investigate possible differences and consequences on systemic circulation during CO_2 insufflation vs Gasless surgery.

We considered as “recurrence of disease” a PSP, appeared on the same operated side, within 6 months of surgery; other cases of PSP manifested on the same operated side, but more than 6 months after surgery, were considered related to new bullae and counted as new lung surgeries. In fact, the higher risk of recurrence in children is not related to surgical failure, but it is often associated with the formation of new bullae.[13]

The postoperative pain was determined by the visual analogue scale (VAS, see *Form.1*), ranging from 0 to 10, and compiled by nurses during hospitalization.[4] But also with retrospective view of Medical Chart, examining post-operative narcotic usage, that provides a much more objective and verifiable source of data regarding post-operative pain.

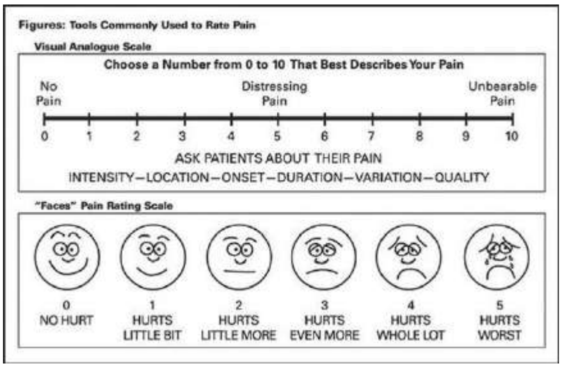
In the last part of the study, for Cohort A, a questionnaire-based survey was conducted by telephone interview, with questions regarding postoperative pain or paresthesia at home (1 week and 1-3-6 months after surgery), changes in sport activity and social life, perception and satisfaction of the scar. The content of the questionnaire was generated specifically for the assessment of U-VATS post-operative period. A single surgeon performed all the interviews, explaining the pain scale (VAS) and aesthetic scale, dividing patient in 3 groups: 0-6 months after surgery, 6-12 months after surgery, more than 12 months after surgery.

Paraesthesia was defined according to the criteria and descriptions reported by Sihoe[38]: participating patients were asked if they could recall the wound pain after surgery, and if they experienced any paresthetic discomfort in addition to that pain. “Paresthesia” has been defined as any numbness or disordered sensation causing chest wall discomfort, which the patient can distinguish clearly from the wound pain. Patients, with such paresthesia, were asked to describe the site and the characteristics of any paresthetic discomfort. Patients were also asked to subjectively grade the severity of any paresthesia on a 10-points analogue scale (with 1 being minimal discomfort and 10 being the worst discomfort imaginable). We regard paresthesia severity of 1–3 on the 10-point scale to be ‘mild’, 4–7 to be ‘moderate’ and 8–10 to be ‘severe’. Affected patients were also questioned regarding the perceived effect of the discomfort on their daily lives. An opinion on the aesthetic results, in a scale from 0 to 10 points, was asked to the patients and also to the U-Team surgeons, to compare the perception of the scars.

Form.1

VISUAL ANALOGUE SCALE

The visual analogue scale (VAS) represents a method of assessment of a 'feeling'. It consists of a 100 mm long line (designated dolorimeter). The left end signifies 'no pain' and the right 'unbearable pain'. It also requests the transfer of a sensation into another dimension.[39]



A Visual Analogue Scale (VAS) is one of the pain rating scales used for the first time in 1921 by Hayes and Patterson[40]. It is often used in epidemiologic and clinical research to measure the intensity or frequency of various symptoms. For example, the amount of pain that a patient feels ranges across a continuum from none to an extreme amount of pain. From the patient's perspective, this spectrum appears continuous ± their pain does not take discrete jumps, as a categorization of none, mild, moderate and severe would suggest. It was to capture this idea of an underlying continuum that the VAS was devised.[41]

Scoring and Interpretation

Using a ruler, the score is determined by measuring the distance (mm) on the 10-cm line between the “no pain” anchor and the patient’s mark, providing a range of scores from 0–100. A higher score indicates greater pain intensity. Based on the distribution of pain VAS scores in post-surgical patients (knee replacement, hysterectomy, or laparoscopic myomectomy who described their postoperative pain intensity as none, mild, moderate, or severe, the following cut points on the pain VAS have been recommended: no pain (0–4 mm), mild pain (5-44 mm), moderate pain (45–74 mm), and severe pain (75–100 mm). Normative values are not available. The scale has to be shown to the patient otherwise it is an auditory scale, not a visual one. There is a recent study stated that" the preferred paper-based VAS item is with a horizontal, 8-cm long"[42]

Acceptability

The ability to accurately measure and interpret pain intensity is central to any research endeavors in the domain of pain. Research with children and adolescents is sometimes considered especially problematic because it is unclear whether young children can understand and follow the instructions, and because pain intensity in very young children can only be inferred from parental ratings[43] The most widely used method to empirically define thresholds has been developed by Serlin and colleagues[44]. According to their method, cut points optimal to classify pain intensity are those that best predict the level of functional interference.

RESULTS

Demographics

In Varese's Filippo Del Ponte Hospital, since December 2019 to September 2022, there were fourteen admissions in Emergency Room for PSP, that needed a non-conservative treatment.

Eleven patients were drained, in urgency, and three patients were already arrived with a chest tube, previously positioned in a peripheral hospital.

Once the acute PSP was solved (or not solved after a mean of 11,2 days of drainage) all the patients underwent CT scan, to find any residual blebs/bullae;

We found residual blebs/bullae in 7 patients (63,6 %), they represent our Cohort A, that counts 10 lung surgeries (*Table1*);

Patients	Lungs	Gender	Age (years)	Weight (kg)	Height (cm)	Side	Comorbidity
A-1	1	*Male*	17	54	174	Right	-
A-2a	2	*Male*	14	48	178	Left	Scoliosis, RBBB*
A-2b	3	*Male*	15	50	179	Right	‘’
A-3	4	*Male*	14	60	180	Left	
A-4a	5	*Male*	16	54	170	Left	Depression
A-4b	6	*Male*	16	57	170	Right	‘’
A-5a	7	*Male*	17	78	179	Left	-
A-5b	8	*Male*	17	82	180	Right	-
A-6	9	*Male*	16	53	184	Left	-
A-7	10	*Male*	17	57	173	Left	-

Table 1. *Demographic Data Cohort A – U-VATS technique* *RBBB: Right bundle branch block.

All patients were males; mean age at the time of operation was 15,9 years (range 14-17, median 16), mean weight was 59,3 kg (range 48-82, median 55,5) and mean height was 176,7 cm (range 170-184, median 178,5).

Uniportal-VATS was performed on the right side in 1 patient, on the left side in 3 patients and bilaterally in 3 patients, even if CT scan showed bilateral disease in 5 patients (sub-centimetric blebs were present in non-operated side). About comorbidity: patient 2 (A2) has scoliosis and right bundle branch block, and patient 4 (A4) was in therapy for depression with fluoxetine. No one of patients was studied for genetic syndrome.

Bologna's Cohort B had initially nine patients, but two patients were excluded from this study because they were out of paediatric age (20 years old both) and another patient was excluded because he had a PNX for a bronchopleural fistula after a thoracic operation (maybe iatrogenic fistula?); than we examined for Cohort B 6 patients (*Table 2*) and 13 lung surgeries (excluding redo - surgeries).

Patients	Lungs	Gender	Age (years)	Weight (kg)	Height (cm)	Side	Comorbidity
B-1a	1	*Female*	10	30	146	Right	PFO*, PNX* Father
B-1b	2	*Female*	11	30	146	Left	‘’
B-1c	3	*Female*	13	40	160	Left	‘’
B-2a	4	*Female*	16	57		Left	PDA* PNX* Brother
B-2b	5	*Female*	17	56		Left	‘’
B-3a	6	*Male*	13	85	190	Left	LMNA het.* OSAS-CRI* Dismorphism
B-3b	7	*Male*	13	85	190	Right	‘’
B-4a	8	*Female*	13	47	169	Left	
B-4b	9	*Female*	13	48	169	Right	
B-5a	10	*Male*	15	70	191	Left	
B-5b	11	*Male*	15	70	191	Right	
B-6a	12	*Female*	12	42		Right	E.D.s.*
B-6b	13	*Female*	13	42		Left	

Table 2. *Demographic Data Cohort B – Multi Portal Technique* *PFO:Patent Foramen Ovale; PNX: pneumothorax; PDA: Patent Ductus Arteriosus; LMNA Het: Heterozigosis LMNA; OSAS: Obstructive Sleep Apnea Syndrome; E.D.s: Ehler Danlos syndrome. CRI: Chronic respiratory insufficiency.

Four patients (9 lungs) were female and two patients (4 lungs) were male; mean age at the time of surgery was 13,4 years (range 10-17 years, median 13), mean weight was 54 kg (range 30- 85, median 48) and mean height was 172,4 cm (range 146-191, median 169). Surgery was performed bilaterally in 5 patients, and two times at left side for patient 1 (B1) and patient 2 (B2), respectively 21 and 11 months after the first surgery, so these pneumothoraces were not considered recurrences but new lung diseases.

B1 and B2 had a member of the family that experienced PNX too (33% familiar incidence); they both had a minimum cardiac left-right shunt: B1 for Patent Foramen Ovale (PFO) and B2 for Patent Ductus Arteriosus (PDA). Finally, B1 and B2 had been subjected of multiple genetic exams, for high suspicion of genetic syndrome, but all results were normal; Patient 3 (B3) had a LMNA heterozygosis with a severe scoliosis, dysmorphia of the rib cage, myopathy, asthma, OSAS with later chronic respiratory failure and micrognathy. Patient 6 (B6), had Elher Danlos syndrome, diagnosed after 3 PNX, and during the third surgery (second redo) the surgeon found a nylon thread into the parenchyma. Patient 4 (B4) was the only one who arrived in emergency room with a hypertensive PNX.

The two cohorts are homogeneous in term of height (*Fig.16*) and weight (*Fig.17*), while there is a difference statistically significant regarding age (*Fig.18*), because in Cohort B age is inferior than in Cohort A (***p-value 0,002*** with Student's t-test, *Table 3*). There was also a different regarding sex (*Fig.19*), because in group A all the patients were males, while in group B 69% were females (***p-value < 0,001*** Chi-squared tests). The operated sides were equally distributed (*P-value <0,*940 Chi-Squared Test. *Fig 20).*

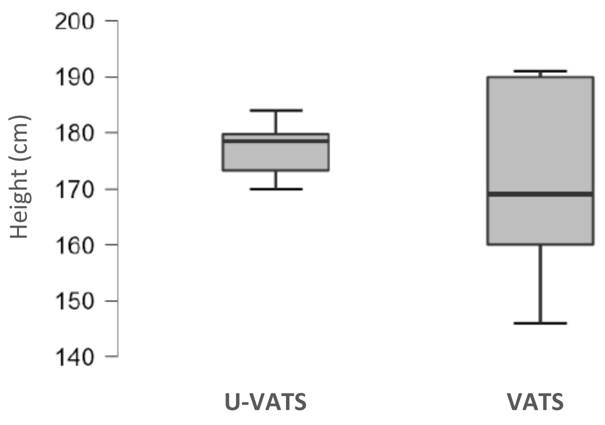


Fig.16 *Boxplots showing the distribution of heights between the two groups (p-value 0,501 Student's t-test).*

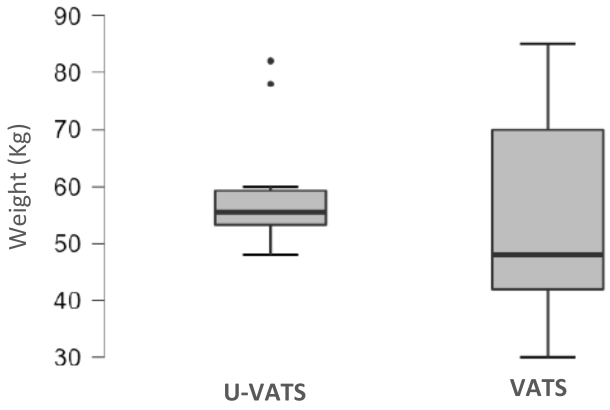


Fig.17 *Boxplots showing the distribution of weights between the two groups (p-value 0,439 Student's t-test).*

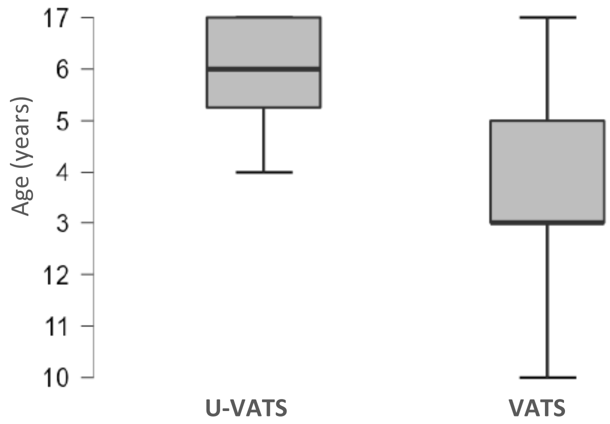


Fig.18 *Boxplots showing the distribution of ages between the two groups (**p-value 0,002** Student's t-test).*

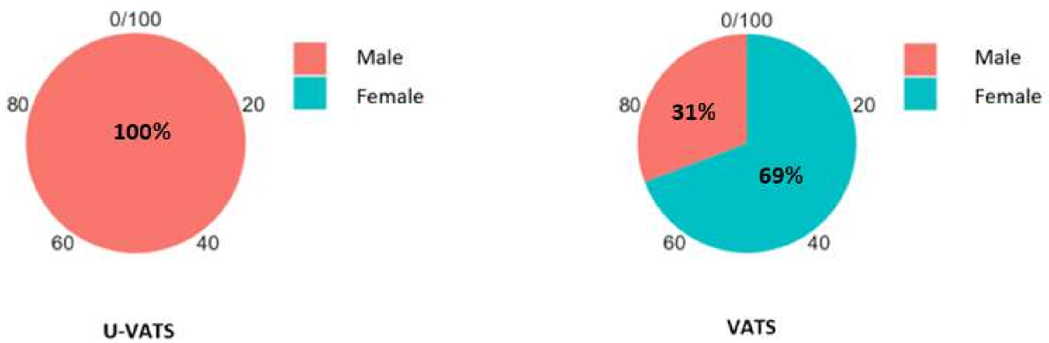


Fig.19 *Pie Chart showing the distribution of sex between the two groups (**P-value <0,001** Chi-Squared Test).*

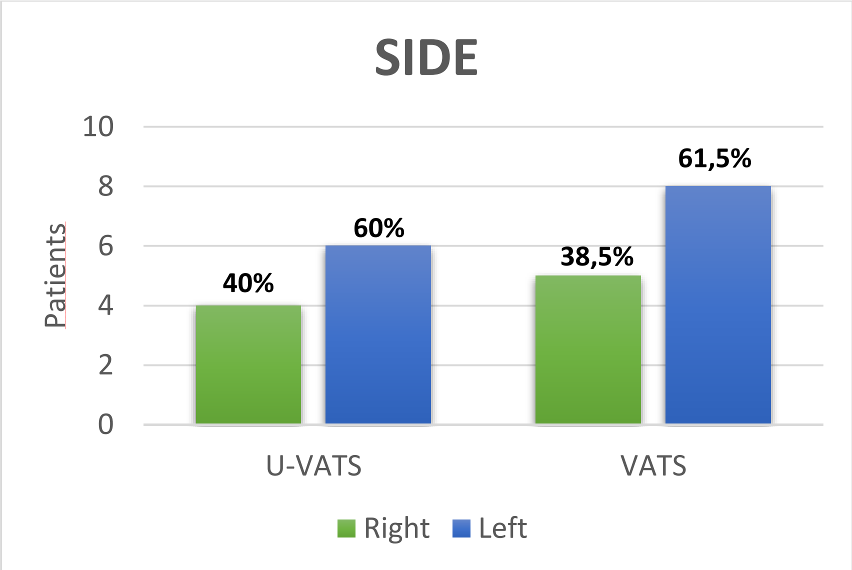


Fig.20 *Histogram showing the frequency of side between the two groups (P-value <0,940 Chi-Squared Test)****.***

	t	df	p
Age	3.599	21	0.002
Weight	0.789	21	0.439
Height	0.688	17	0.501

Note. Student's t-test.

Table 3. *Independent Sample T-Test of demographic data.*

Tables 4 summarizes the descriptive statistics of demographic data

	Age		Weight		Height	
	A	B	A	B	A	B
Valid	10	13	10	13	10	9
Missing	0	0	0	0	0	4
Median	16.000	13.000	55.500	48.000	178.500	169.000
Mean	15.900	13.385	59.300	54.000	176.700	172.444
Std. Deviation	1.197	1.938	11.480	18.637	4.692	18.981
Minimum	14.000	10.000	48.000	30.000	170.000	146.000
Maximum	17.000	17.000	82.000	85.000	184.000	191.000
25th percentile	15.250	13.000	53.250	42.000	173.250	160.000
50th percentile	16.000	13.000	55.500	48.000	178.500	169.000
75th percentile	17.000	15.000	59.250	70.000	179.750	190.000

Table 4. *Descriptive statistics of demographic data.*

Preoperative clinical presentation

In Cohort A: 4 patients (A1, A2, A3, A5) underwent U-VATS apicoectomy in urgency, after a mean time of 11,2 days (range 4-19) with a chest tube, without solving the PNX. 1 of them (A3) was re-admitted for a massive PSP, while he was waiting for elective surgery; finally, patients A4, A6, A7 were admitted for first PSP, which was resolved with a chest tube, they were then discharged and after a few weeks they had elective U-VATS apicoectomy and pleurodesis (*Table 5*).

CT scan showed bilateral disease in 5 patients and monolateral bullae in 2 patients; but we decided to operate bilaterally only 3 patients, because controlateral blebs were millimetric in patient A1 and A3.

Patient	Surgery	Days with chest tube before urgent Apicoectomy	Side of disease (CT Scan)
A1	1st. Urgency for 1St PNX*	9	Bilateral
A2	1st. Urgency for 1St PNX* 2nd. Elective C.L.*	13	Bilateral
A3	1st. Urgency for massive PNX*	4	Bilateral
A4	1st. Elective 2nd. Elective C.L.*		Bilateral
A5	1st. Urgency for 1St PNX* 2nd. Elective C.L.*	19	Bilateral
A6	1st. Elective		Left
A7	1st. Elective		Right

Table 5. *Preoperative clinical presentation - Cohort A *PNX: pneumothorax; C.L: contro-lateral.*

In Cohort B: 2 patients, B2 and B5, had elective surgery after some weeks from first PNX attack; 4 patients (B1, B3, B4, B6) were operated in urgency for unsolved air leak, after a mean time of 14,1 days with a chest tube (range 8-23). B6 had a contralateral PNX attack during a hospitalization for relapse, so she was operated in urgency both for left and right side.

B1 and B2 had also an urgent surgery for a second PNX attack, respectively after 21 months and 11 months from previous surgery and they had a chest tube respectively for 10 and 17 days before a second apicoectomy.

Finally, B1, B3, B4, B5 had elective surgery for contro-lateral lung, after CT scan showed bilateral disease (*Table 6*, recurrences are not in).

Patient	Surgery	Days with chest tube before Apicoectomy	Side of disease (CT Scan)
B1	1st. Urgency for 1St PNX* 2nd. Elective C.L.* 3rd. Urgency for 2nd PNX*	23 10	Bilateral
B2	1st. Elective 2nd. Urgency for 2nd PNX*	 17	Bilateral
B3	1st. Urgency for 1st PNX * 2nd. Elective C.L.*	8	Bilateral
B4	1st. Urgency for 1st PNX * 2nd. Elective C.L.*	12	Bilateral
B5	1st. Elective 2nd. Elective C.L.*		Bilateral
B6	1st. Urgency for 1st PNX * 2nd. Urgency for 1st PNX* C.L.*	13 16	Bilateral

Table 6. *Preoperative clinical presentation - Cohort *PNX: pneumothorax; C.L: contro-lateral.*

The samples between the two groups are homogeneous in terms of urgent *vs* elective surgeries (*Fig.21*), respectively 40% of urgent surgery in group A and 54% in group B (*p-value 0,510* with Chi-Squared Tests) and also in terms of day with pleural drainage without solving PNX (*Fig. 22)* before underwent urgent surgery (*p-value 0,423* with Student's t-test)

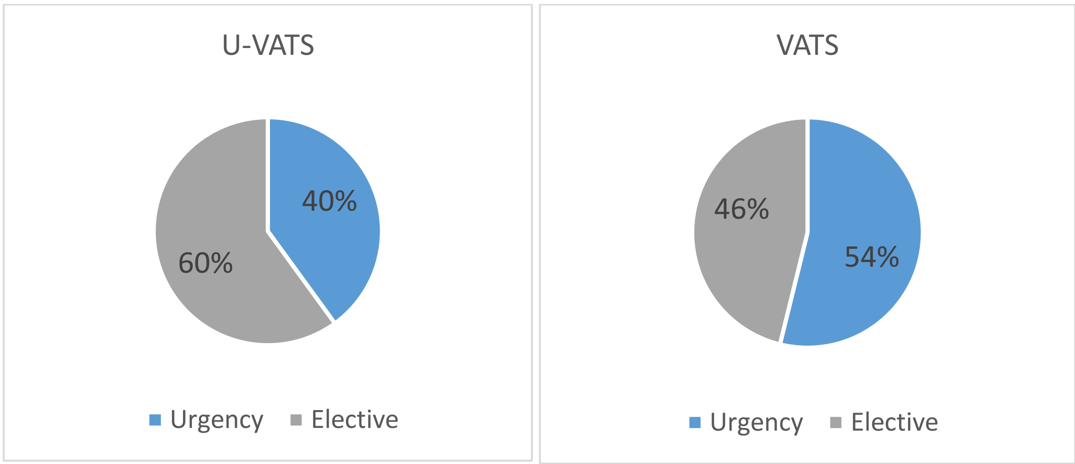


Fig.21 *Pie charts with the percentage of patients operated in urgency vs elective in the two groups (p-value 0,510 Chi-Squared Tests).*

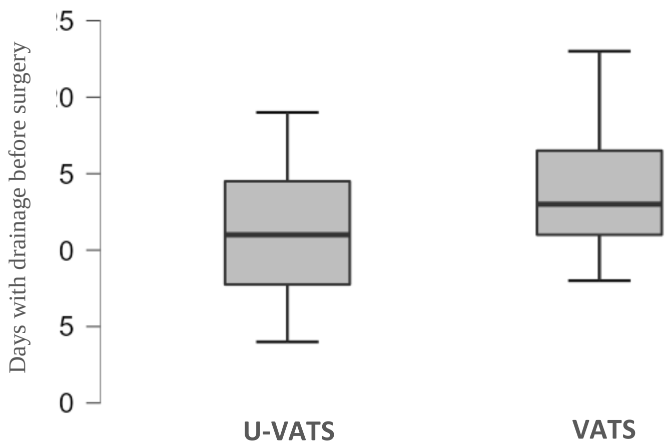


Fig.22 *Boxplots showing the distribution of "Days with drainage before surgery" between the two groups (p-value 0,423 Student's t-test).*

Peri-operative features

Both groups underwent standard patient monitoring (electrocardiography, oxygen saturation, non-invasive blood pressure, end-tidal CO2), general anaesthesia, and for intubation was used with all patients a double-lumen endotracheal tube (DLT).
Site of pathology was the apex of the affected lung for every patient in both groups.

Emphasizing the fact that, in B group, VATS technique was well known, because largely used for caring various lung diseases, and underlying also that in this group the surgeries were always performed by a senior surgeon, we found a surgical mean time of 85,3 minutes for U-VATS *vs* 68,1 minutes for VATS *(p-value 0,063* with Student's t-test) or 78,6 minutes for VATS, counting also the recurrences (*p-value 0,596* with Student's t-test) and time got better and better, during the U-MIS program, as the surgeries were performed, not only in terms of "personal time" but, we may say, as "U-Team time." (*Fig.23 A*).

Surgery's median time for Cohort A was 86 and the range of surgical time was from 62 to 127 (127 minutes were spending for the first patient of the U-MIS program); as anticipated, a curiosity is that the first apicoectomy made by a second and a third member of the U-Team, was respectively 85 and 88 minutes long, fully in line with the average of the first-surgeon after five surgeries, to highlight the easy learning and reproducibility of this technique and the "in-line" movements of the instrument.

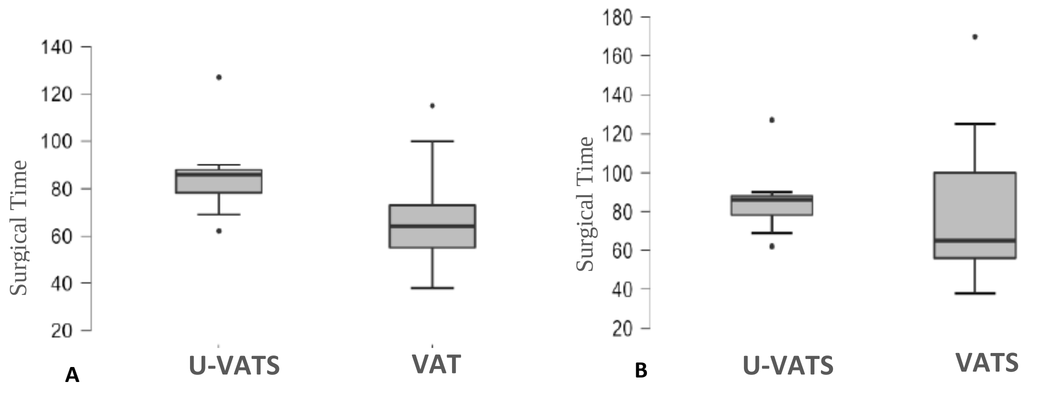


Fig.23 A. *Boxplots showing the distribution of surgical time between the two cohorts, without recurrences (p-value 0,063 with Student's t-test****)*** ***B.*** *Box Plot showing the distribution of surgery time between the two cohorts, with recurrences (p-value 0,596 with Student's t-test).*

All patients of Cohort A underwent the same gasless U-VATS surgery (*Fig.24 A*) and single-lung ventilation with a DLT; Uniportal access size was between 2 and 3 cm. All patients of this series had pleurodesis (*Fig.25A*) with monopolar coagulator from the II to the V or VII rib and anterior- lateral-posterior pleural abrasion with abrasive tissue of the first five intercostal spaces.

All patients of this group, after pleurodesis, had one chest tube positioned at the end of the surgery (*Fig.26 A*), size from 16 to 24 Charrière (Ch); all of them were awakened in the operating theatre (O.R.) and nobody required intensive care after surgery.

In this series, no conversions to open surgery were necessary and there were no complications during operation.

Group B comprehends patients underwent to Multiportal VATS and Robotic Surgeries (*Fig.24 B*), with a similar thoracoscopic approach and operative time; surgery's mean time was 68.1 minutes with a median of 64 and a range from 38 to 115 and it becomes of 78,6 minutes (median 65, range 38-170) if we count the recurrences.

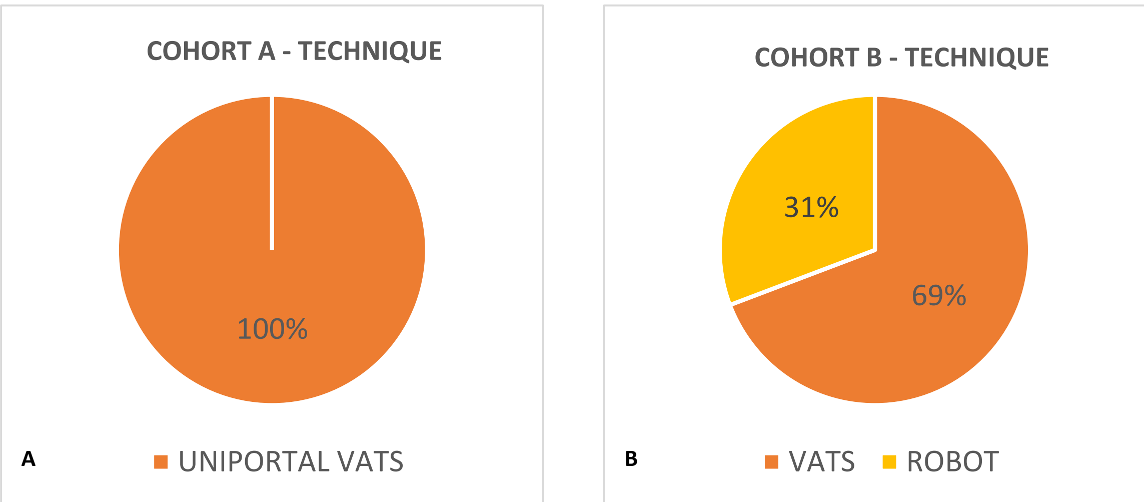


Fig.24 A. *Pie chart showing the percentage of patients operated with Uniportal technique, in Cohort A.*
B. *Pie chart showing the percentage of patients operated with VATS or with ROBOTIC technique, in Cohort B.*

Pleurodesis was made 5 times (38%, ***p-value 0,002*** Chi-Squared tests) (*Fig 25B*): 4 times after a second episode of PNX, in the same side of an already treated lung, and 1 time (B4) for a 1st episode of PNX.

In 3 surgeries (23%) two thoracic tubes were placed, in the other 10 surgeries only one chest tube was used (*Fig.26 B).*

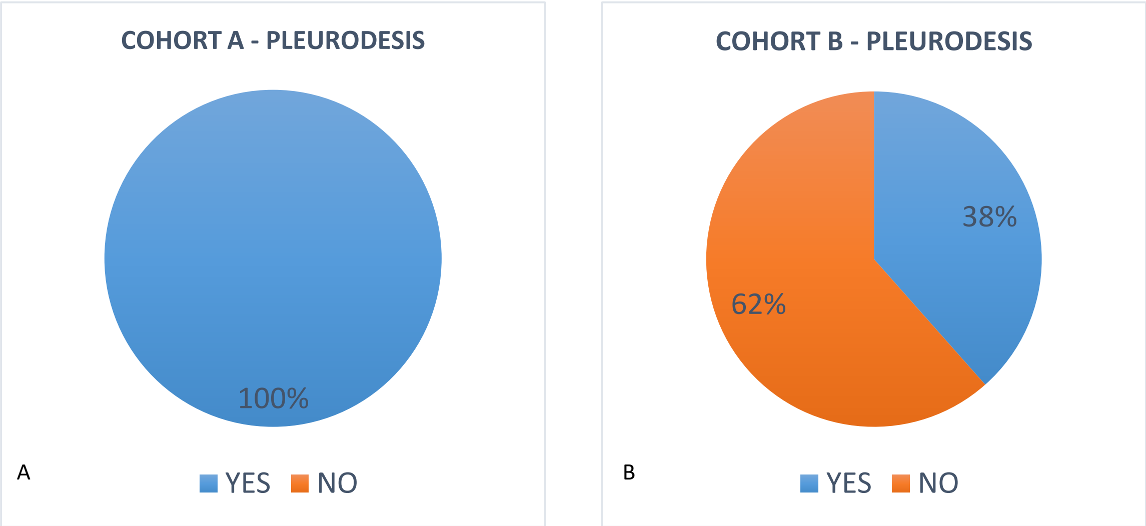


Fig.25 A. *Pie chart showing the percentage of patients underwent to pleurodesis , in Cohort A.*
B. *Pie chart showing the percentage of patients underwent to pleurodesis, in Cohort B* *(**p-value 0,002** Chi-Squared Tests).*

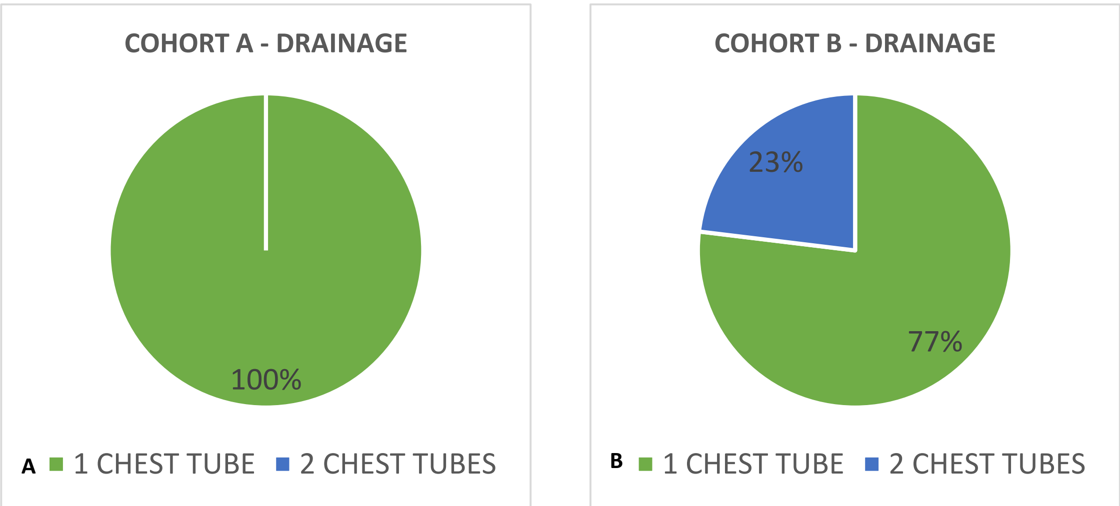


Fig.26 A. Pie chart showing the percentage of patients with 1 or 2 chest tube after surgery, in Cohort A.
B. Pie chart showing the percentage of patients with 1 or 2 chest tube after surgery, in Cohort B.

This cohort of patients had a different post-operative protocol, compared to Cohort A: all of the patients, except one (2 lungs), went in intensive care unit (ICU) for 1 or 2 days (***p-value* < *0,001*** Chi Squared Tests); for this different practice they were often not awakened in the O.R, but later in the ICU (*Fig.27*). Only patient B5 went directly to the ward after both surgeries, perhaps because he was operated on 11 years ago, and the ICU protocol was applied later; also in this series there was no need for conversion to open surgery and there were no complications during the procedure.

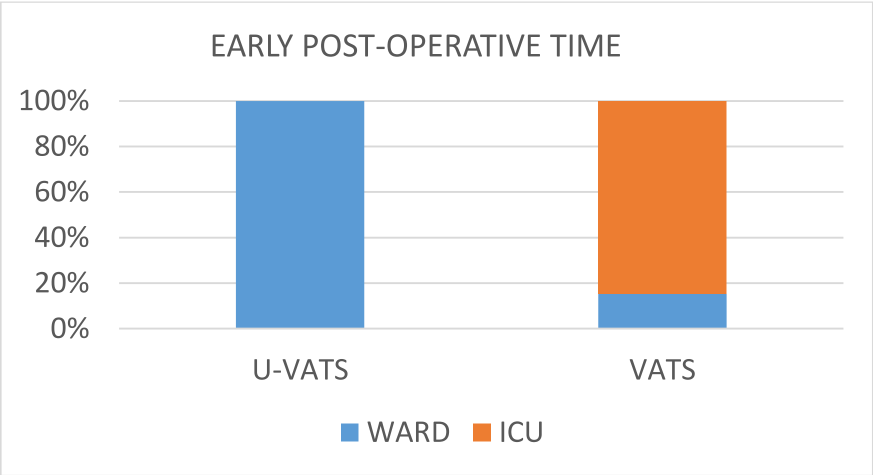


Fig.27 Histogram representing the patients who went to ICU* *vs* ward after surgery (***p value* < *0,001*** *Chi-Squared Tests*). *Intensive Care Unit

Anaesthesia time for cohort A and B (*Fig.28*) was respectively 176 minutes (range 130-240) and 200 minutes (range 150-240, without recurrences), difference not statistically significant (*p-value 0,075 with Student's t-test*).

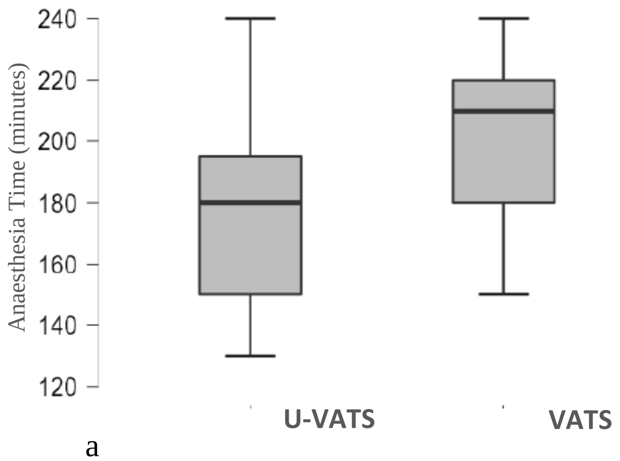


Fig.28 Boxplots showing the distribution of anaesthesia time between the two cohorts (*p value 0,075 Student's t-test*).

Table 7 summarizes the descriptive statistic of surgical and anaesthesia time.

	Surgical Time		Anesthesia time	
	A	B	A	B
Median	86.000	64.000	180.000	210.000
Mean	85.300	68.077	176.000	200.000
Std. Deviation	17.257	23.146	34.383	27.080
Minimum	62.000	38.000	130.000	150.000
Maximum	127.000	115.000	240.000	240.000
25th percentile	78.250	55.000	150.000	180.000
50th percentile	86.000	64.000	180.000	210.000
75th percentile	88.000	73.000	195.000	220.000
p-value *	0.063		0.075	

** Student's t-test*

Table 7. *Descriptive statistics of surgical and anesthesia time.*

Post-operative outcome

Outcomes for Cohort A, described in terms of median VAS (*Table 8*) at postoperative day (POD) 1, 2, and 3 were of 2 (range 0–6, mean 1,7), 2,5 (range 0–5, mean 1.9), and 0 (range 0–7, mean 0,9):

- in POD-1: 5 patients/10 surgeries had mild pain (VAS ≤ 3) and 1 patient had moderate pain (4 ≤ VAS ≤ 7);
- in POD-2: 5 patients/10 surgeries had mild pain (VAS ≤ 3) and 1 patient had moderate pain (4 ≤ VAS ≤ 7);
- in POD-3: 1 patient/10 surgeries had mild pain (VAS ≤ 3) and 1 patient had moderate pain (4 ≤ VAS ≤ 7);

Pain was treated with Non Steroidal Anti Inflammatory Drugs (NSAIDs) on request, with immediate pain relief.

Patient	VAS 1	THERAPY POD1		VAS 2	THERAPY POD2		VAS 3	THERAPY POD3	
A1	2	P x 4	K x 1*	3	P x 4	-	0	P x 4	-
A2a	0	P x 4	-	0	P x 4	-	0	P x 4	-
A2b	6	P x 4	I x 1*	5	P X 4	I X 2*	0	P X 4	I X 1*
A3	0	P x 4	I x 1*	3	P x 4	-	0	P x 3	-
A4a	2	P x 3	I x 2	2	P X 3	I x 2	2	P x 3	I x 1 *
A4b	2	P x 3	-	3	P x 3	-	7	P x 3	I x 1 *
A5a	3	P x 4	K x 3	3	P x 4	K x 3	0	P x 4	K x 1 *
A5b	0	P x 3	K x 2	0	P x 2		0	P x 2	
A6	2	P x 4	K x 2	0	P x 4	K x 2	0	P x 4	K x 2
A7	0	P x 4		0	P x 4		0	P x 4	
MEAN	1,7			1,9			0,9		
MEDIAN	2			2,5			0		

Table 8. Post-operative VAS of Cohort A and medications.
*****:Medication on request; **I:** Ibuprofen; **K**: Ketorolac; **P**: Paracetamol.

Standard pain-treatment protocol, for group A, was Paracetamol 3 or 4 times a day, for the first 3 post-operative days, and Ketorolac/Ibuprofen mostly on request; in POD 4 therapy with paracetamol was reduced to 2 times a day or, compatible with pain, on request and VAS was 0 at POD 4 for all the patients.

According to medical records, nobody in this group had uncontrolled thoracic pain during hospitalization.

After discharge we recommended paracetamol on request, maximum 4 times per day.

In Cohort A, for 8/10 surgeries was used only 1 prophylactic dose of antibiotic, given in O.R before starting the surgery, in fact the "Thoracic Protocol" provides only 1 prophylactic dose of antibiotic both for the insertion of the chest tube (for acute PNX treatment) and for apicoectomy.

The two patients, who had more days of antibiotic, were both transferred from another hospital with a chest tube already inserted, and an antibiotic therapy already started, so they continued the same therapy for four days, to complete the antibiotic cycle.

All patients had medication of the scar, and of the tube site, every 48 hours (or more often, if necessary) with povidone iodine or with sodium hypochlorite 0.05%.
No patients had infections either during hospitalization or at home, so no patients needed any antibiotic therapy at home.

Outcomes for Cohort B, described in terms of median VAS (*Table 9*) at POD 1, 2, and 3 were of 8 (range 0–8, mean 5), 1.5 (range 0–9, mean 3,2), and 0 (range 0–9, mean 2,1):

- in POD-1: 1 patient/13 surgeries had mild pain (VAS ≤ 3); 6 patients had severe pain (VAS ≥ 8) and 3 patients were under sedation;
- in POD-2: 1 patient/13 surgeries had mild pain (VAS ≤ 3); 3 patients had moderate pain (4 ≤ VAS ≤ 7); 2 patients had severe pain (VAS ≥ 8); and 1 patient was still under sedation;
- in POD-3: 2 patients/13 surgeries had mild pain (VAS ≤ 3), 3 patients had moderate pain (4 ≤ VAS ≤ 7) and 1 had severe pain (VAS ≥ 8).

Pain treatment for group B was not standardized and different from group A, especially because the 84,6% of patients spent from 1 to 5 post-operative days in ICU (median 1), some of them were under sedation in POD1 e POD2, most of them were under Opioid and Benzodiazepine, with epidural catheter of Levobupivacaine or Chirocaine, and often this therapy was continued even after returning to the ward. Also after POD4 some patients had moderate or severe pain.

Moreover, two patients complained about uncontrolled thoracic pain (no responsive to morphine) during hospitalization.

Patient	VAS 1	THERAPY POD 1			VAS 2	THERAPY POD 2			VAS 3	THERAPY POD 3		
B-1a	**0**	P x 3	Mor		**3**	P x 3	Mor		**0**	P x 3	Mor	
B-1b	**2**	P x 4	Mor	Mdz	**6**	P x 4	Mor		**0**	P x 4		
B-1c	**8**	P x 4	Ktp x 2 Ep. L	Ctm x 1	**0**	P x 4	Ktp x 2		**0**	P x 4	Ktp x 2	
B-2a	**0**	P x 3	Ctm x 1 K x 3	Mdz	**0**	P x 3	K x 3	Mdz	**0**	P x 3		Mdz
B-2b	**SED**	P x 4	Mor	K	**0**	P x 4	Mor		**9**	P x 4	Mor	
B-3a	**0**	P x 3	Mor Mdz	Ktp x 1	**0**	P x 3			**0**	P x 4		
B-3b	**8**	P x 4	Ktp x 1*	K x 3	**6**	P x 4		K x 2	**4**	P x 4		K x 2
B-4a	**8**	P x 4	Ktp X1*		**9**	P x 4	K x 3		**3**	P x 4	K x 3	
B-4b	**SED**	P x 3	I x 1	Ktp Ep.L	**0**	P x 3	K x 1	Ep.L	**2**	P x 3	Ep.L	
B-5a	**8**	P x 4	Ep. ChC	K x 3	**0**	P x 4	K x 3		**0**	P x 4	K x 3	
B–5b	**8**	P x 4	Ep. Chc I x 1*	Ctm x 1* K x 2*	**6**	P x 4	K x 2*		**5**	P x 4	K x 2*	
B- 6a	**8**	P x 4	Mor Mdz* En* Fen	K x 2 *	**8**	P x 4	Mor	K x 2* I x 3	**0**	P x 4	Mor	K x 2* I X 3
B–6b	**SED**	P x 2 Dip Mdz	K x 1 En*	Ep.L Fen	**SED**	P x 2	Dip Mdz	Ep.L	**4**	P x 2 Dip	K En* Mdz	Ep.L
MEAN	**5**				**3,2**				**2,1**			
MEDIAN	**8**				**1,5**				**0**			

Table 9. Post-operative VAS of Cohort B and medications.

SED: under sedation; *****: Medication on demand; **Ctm**: Contramal; **Dip**:diprivan; **Ep.Chc:**Epidural catheter of Chirocaine; **Ep.L:**Epidural catheter of Levobupivacaine; **En**:Delorazepam drops; **Fen**:Fentanest; **I**:Ibuprofen; **K**:Ketorolac; **Ktp:**Ketoprophen; **Mdz:** Midazolam; **Mor**:Morphine; **P**:Paracetamol.

Pain, in term of VAS, was inferior in group A at POD1 (***p-value 0,027*** Student's t-test), while the difference wasn't statistically significant in POD2 (*p-value 0,323* Student's t-test) and in POD3 (*p-value 0,290* Student's t-test) (*Fig.29*) but uniportal group consumed less narcotic medication (and no Opioids or Benzodiazepines) at every time point when compared to the multiportal group (*Fig.30*);

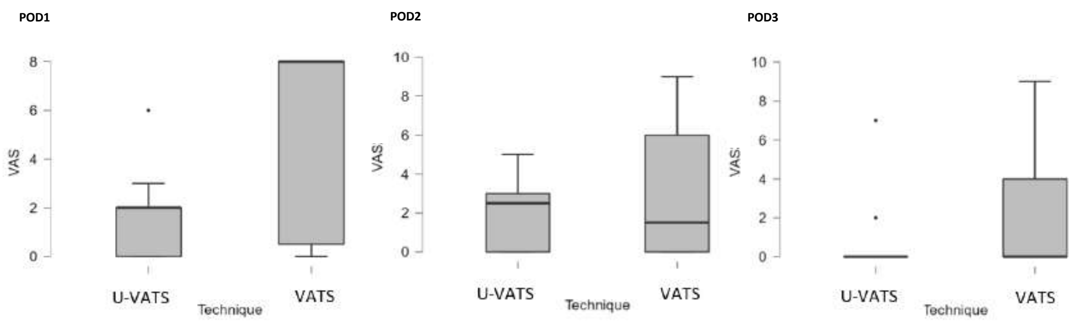


Fig.29 *Boxplots with the distribution of VAS at POD 1-2-3 in the two groups.*

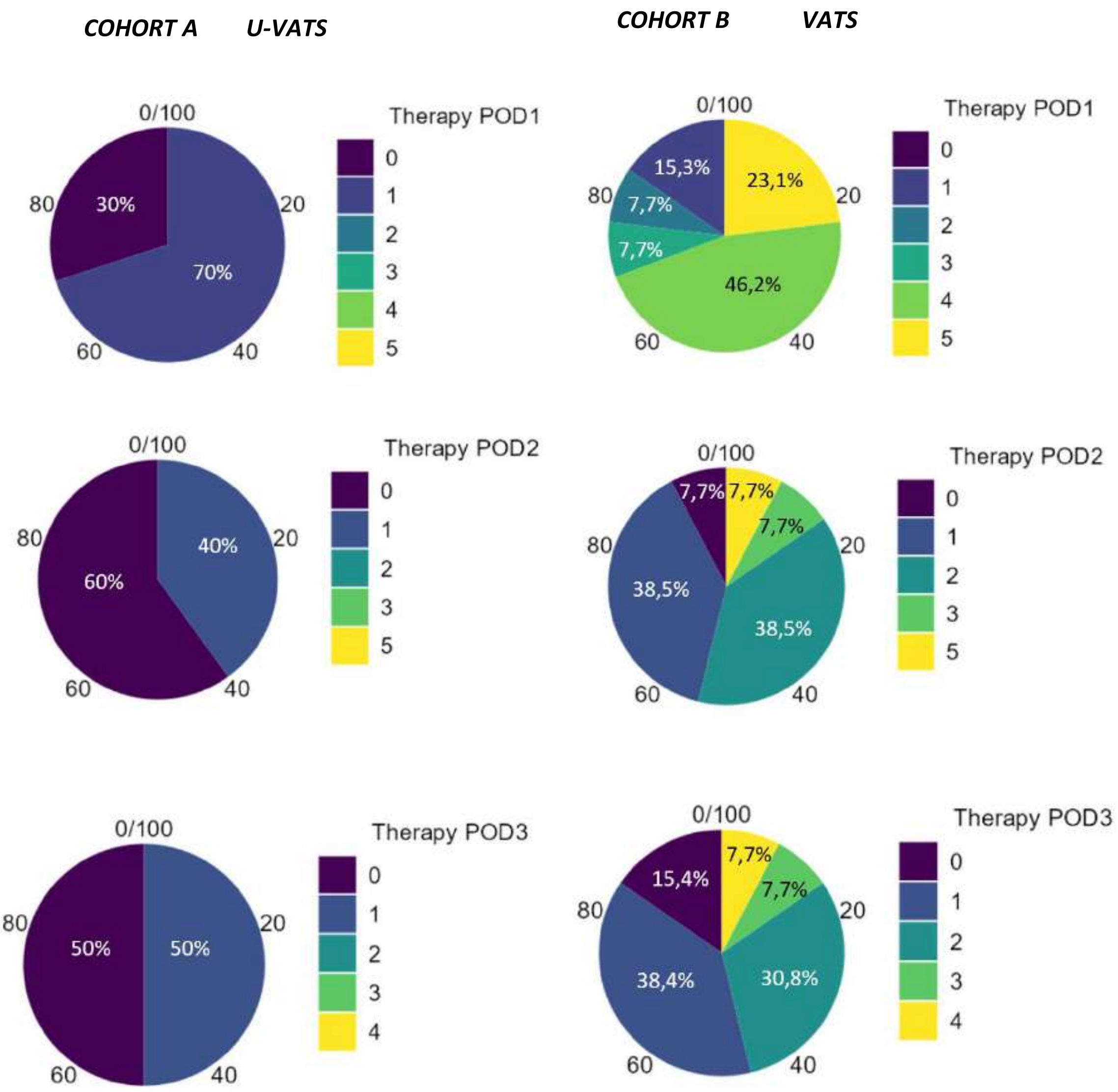


Fig.30 *Pie charts showing the medications used in post-operative days (POD) 1,2,3 in the two cohorts*.

Legend: 0= Paracetamol; 1= Paracetamol + NSAIDs (Ibuprofen, Ketoprophen, Ketorolac); 2= Use of Opioids or Benzodiazepines (BDZ); 3= Epidural catheter; 4= Mixed use of Opioids and/or BDZ and/or Epidural catheter; 5= Sedation.

Furthermore, all patients of Cohort B underwent antibiotic therapy for a mean of 7,9 days ± 3,8 SD after surgery (range 4-18 days, median 7), many of them have already had antibiotic treatment for many days before surgery (after chest tube insertion for PNX) and they continued the therapy also at home for a mean of 2,3 days ± 2,4 SD (range 0-7, median 2,5). Also in this group there were no infections during hospitalization or later.

Compared with Cohort A, in which the mean of antibiotic treatment during hospitalization was of 1,1 day ± 2,4 SD (median 0, range 0-7) and nobody continued antibiotic therapy at home, Cohort B had a significant major use of antibiotics (*Fig 31*) both during hospitalization and at home (***p-value* < *0,001*** with Mann-Whitney).

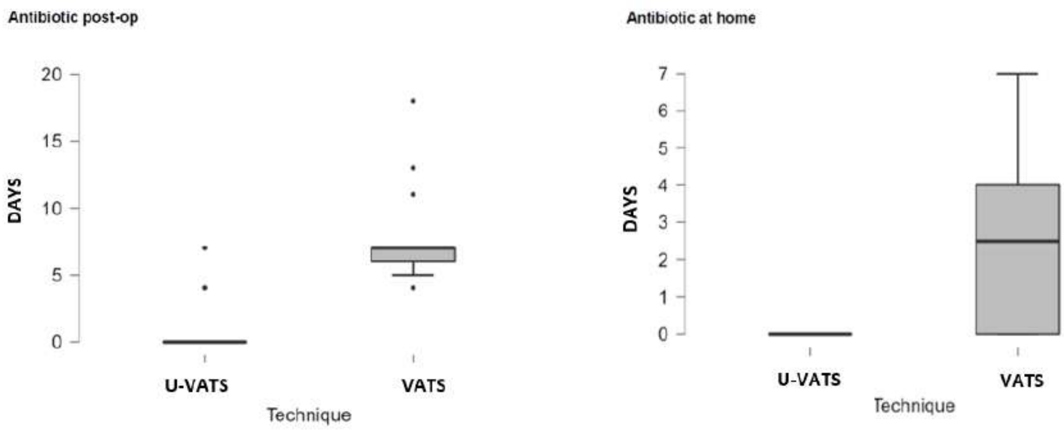


Fig.31 *Boxplots with antibiotic's use during hospitalization and at home*.

Mean chest tube duration after apicoectomy was of 4,8 days ± 0,9 SD (range 4–7, median 5) for cohort A and of 6,4 days ± 4 SD (range 1-17, median 5) for cohort B (*p-value 0,229* Mann-Whitney) (*Fig.32*)

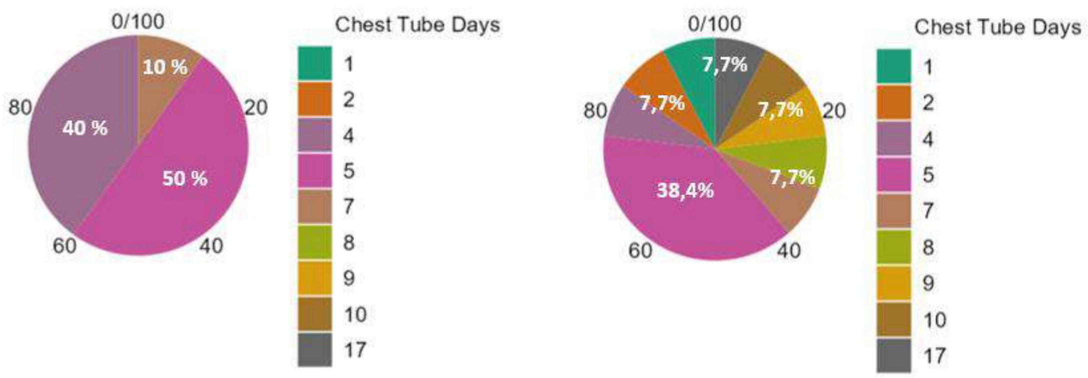


Fig.32 *Pie Charts showing the percentage of patient and the days they had chest tube after apicoectomuy (p-value 0,229 Mann-Whitney).*

Mean length of postoperative hospital stay was 5,7 days ±1,16 SD (range 4-8, median 5,5) for cohort A and 8,3 days ± 5 SD (range 4-23, median 6) for cohort B (*p-value 0,141* Mann-Whitney) (*Fig.33 A*).

Also total days of hospitalization were not statistically significant: median of 8 for Cohort A and 15 for Cohort B (*p-value* 0,348 Mann-Whitney) (*Fig.33 B*).

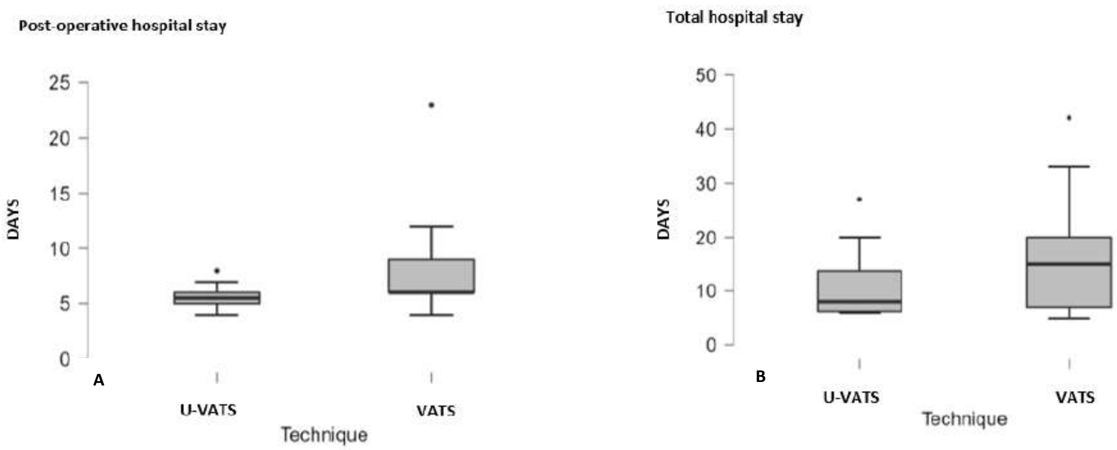


Fig. 33 *Boxplots comparing the days of hospitalization (A- post-operative ; B- total) between the two cohorts.*

Re-admission rate for recurrence (same side disease, before than six months after surgery) was 0% for group A and 15,3% for group B (*p-value 0,194* Chi-Squared Tests, *Fig.34)*, while the redo-surgeries (same side, more than six months after surgery) were 0% for group A and 23% for group B (*p-value 0,103* Chi-Squared Tests, *Fig 35*).

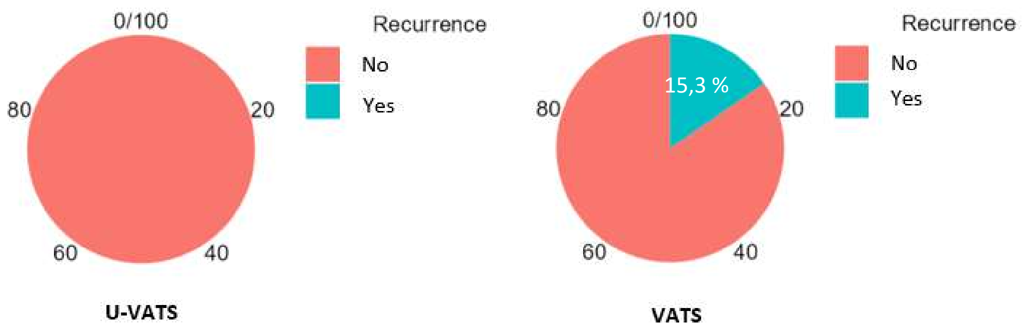


Fig.34 *Frequency of recurrence in both groups (p-value 0,194 Chi squared Tests).*

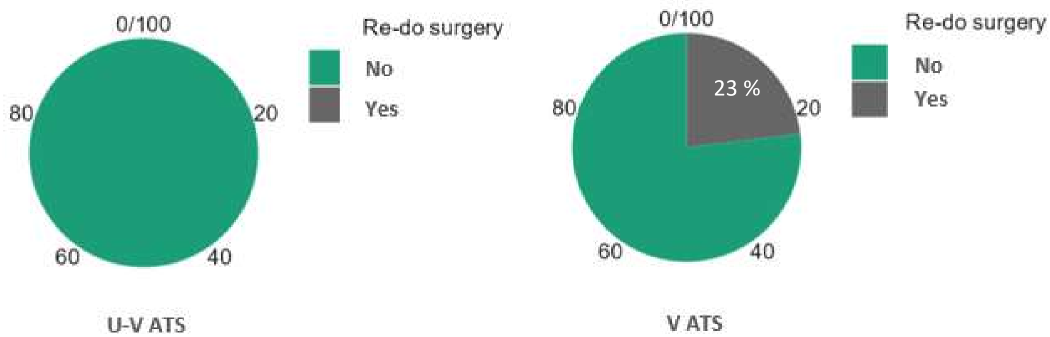


Fig.35 *Frequency of redo-surgery in both groups (p-value 0,103 Chi squared Tests)*

Table 10 summarizes the differences in terms of postoperative characteristics between the two groups.

	Post-operative Stay		Hospital Stay		Chest Tube Days		Antibiotic post-op	
	A	B	A	B	A	B	A	B
Median	5.500	6.000	8.000	15.000	5.000	5.000	0.000	7.000
Mean	5.700	8.308	11.300	17.308	4.800	6.385	1.100	7.923
Std. Deviation	1.160	5.089	7.181	11.856	0.919	4.073	2.424	3.883
P-value*	0.141		0.348		0.229		<0.001	

*Mann-Whitney U test.

Table 10. *Descriptive statistics of post-operative data*

In our clinical records there was no postoperative mortality or any severe complications after both techniques.

About mild complication during postoperative stay, we experienced, in Cohort A, a total of 2/10 (20%) lungs that were not totally expanded when the patients were discharged, 1 patient had also a mild tissue emphysema.

A2 and A6 described a symptom of hemithorax paresthesia during post-operative days.

At first visit in outpatient clinic, about 1 week after hospital discharge, no one had wound dehiscence and only 1 patient (A6) still complained of paraesthesia and muscular pain; his paraesthesia lasted a few months.

In cohort B a total of 10/13 (77%) lungs were not totally expanded when the patients were discharged (7/10 pneumothoraces were more than 2 cm); Patient B6, after first recurrence had sub-cutaneous emphysema, pleural effusion and residual asymptomatic mild PNX.

1 patient (B3) had sub-cutaneous emphysema and another patient (B4) had little pleural effusion. 1 patient (B5) had thoracic and right arm paresthesia since POD1.

We have incompletes data about outpatient-clinic controls, we know about 4 patients complaining for pain during the first week at home (and 2 of them still complaining after one month).

Table 11 shows mild complications in the first 30 days after surgery (complications after recurrence are not in); the difference of PNX at discharge is statistically significant with a ***p-value 0,007*** with Chi-Squared tests.

Cohort	Pnx At Discharge	Pnx At 1-Month	Sub-Cutaneous Emphisema	Pleural Effusion	Uncontrolled Pain	Thoracic Pain After Discharge	Paresthesia
A	20%	0%	10%	0%	0%	10%	20%
B	77% *	23%	7,7%*	7,7% *	15,3%	30,7%	7,7%
p-value	**0,007**	0,089				0,231	0,385

Table 11. *Mild complications in the first month after surgery. *Complications of B6 during recurrence are not in the percentage. P-value with Chi squared tests*

At 1 month-controls CXR was normal for 100% of patients in group A , while in group B 3 patients (23%) had still residual PNX (*p-value 0,089* Chi Squared Tests); one of these patients (B6) was also re-hospitalized after the CXR control to insert again a drainage, and it hesitates in subcutaneous emphysema, pleural effusion and a soon third massive PSP with another long hospitalization , eventually loss of haemoglobin such as to require transfusions; this patient ,during these dramatic events, had also a contralateral first PSP attack and underwent multiportal thoracoscopy for contralateral lung.

In 1 patient of group A (10%) the scar turned into a little keloid, but the patients didn't want to treat it. We have not information about the scars of B group.

The months of follow-up were homogeneous between the two groups (*p-value 0,136* Mann-Whitney), with a median of 13 months for Cohort A and 24 months for Cohort B. In group A and B respectively 20% and 23% of patients had a follow up inferior to 6 months, 20% and 15% had a follow up of 6-12 months, 60% and 61,5% of patients had a follow up of more than 12 months (*Fig.36).*

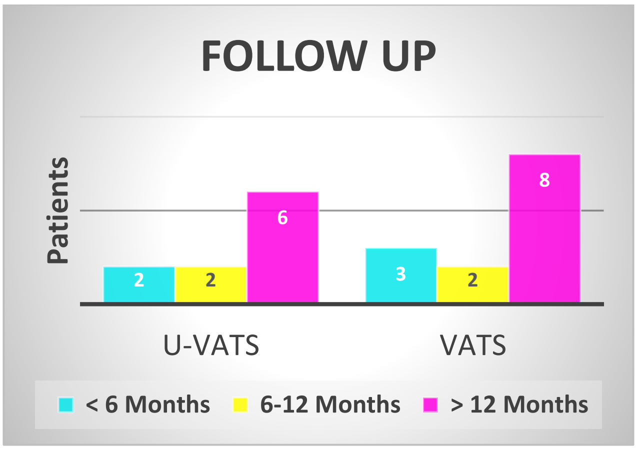


Fig.36 *Histogram comparing duration of follow up in the two groups.*

Hystologic results of the specimen were of subpleural emphysematous bubbles with chronic interstitial emphysema, flogistic pleura foci and reactive mesothelial hyperplasia fibrosis with in some cases granulocyte components and in other cases histiocyte-macrophage aggregates and rare plurinuclear giant cell; we found PAFL in 60% of specimens in Cohort A (no data about PAFL for Cohort B).

The loss of haemoglobin, calculates as "delta" between haemoglobin pre-surgery and haemoglobin 24 hours after surgery, was irrelevant in both cohorts (Cohort A mean δ 1.4, median 0.8; Cohort B mean δ 1.5 , median 1.5, *p-value 0,570* Mann-Whitney); only in cohort B 1 patient underwent transfusion during a duplex surgery for recurrence.
We calculated also the variation of pressure rate between T1, the moment of positioning the patient already sedated in lateral decubitus, and T2, after CO2 insufflation started (for U-VATS we considered T2 after the surgical access was done) and we found a significant difference in systolic blood pressure variation (SBP) major in cohort A (***p-value 0,017*** Mann Whitney); the variations of SBP were also between T1 and T3 (awakening) with ***p-value 0,004*** Mann-Whitney (*Fig 37*).

About end-tidal value at 3 time points there were not differences between the two groups (*p-value 0,177* and *0,180*).

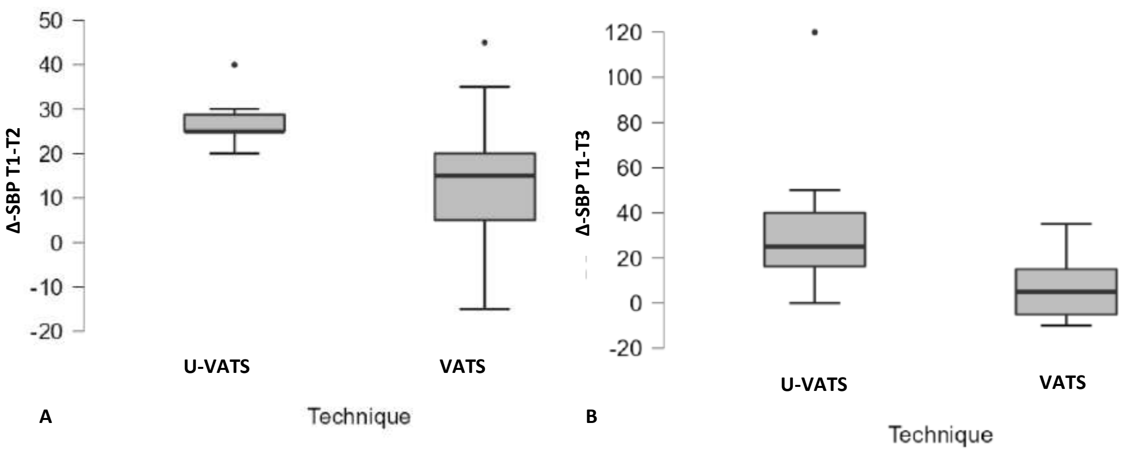


FIg.37 A *Boxplots SBP's variation between T1 (pre CO2 insufflation) and T2 (post CO2 insufflation/ surgery started)* ***B****: Boxplots SBP's variation between T1 and T3 (awakening).*

Five patients (7 surgeries) joined the questionnaire, which is composed of four part:

- Physical activity: sport done before surgery and time needed to resume usual activities;
- Pain: intensity (measured with VAS), duration (3 time points: 1-3-6 months) and how much pain affected the quality of life;
- Paresthesia: site, triggers, severity and duration;
- Scar: satisfaction of the appearance.

Physical activity: before U-VATS surgery 4 patients practiced some sport activities: A3 was a competitive soccer player, the others practiced sport 3 times for week (A2, A4) or occasionally (A7). Only 1 patient didn't practice any sport (A6).

3 patients were back to their routine activities in less than 2 months, 1 patient in 6 months and only 1 patient hadn't already started any activity, his last surgery had been made less than 6 months before questionnaire propose (*Fig.38*).

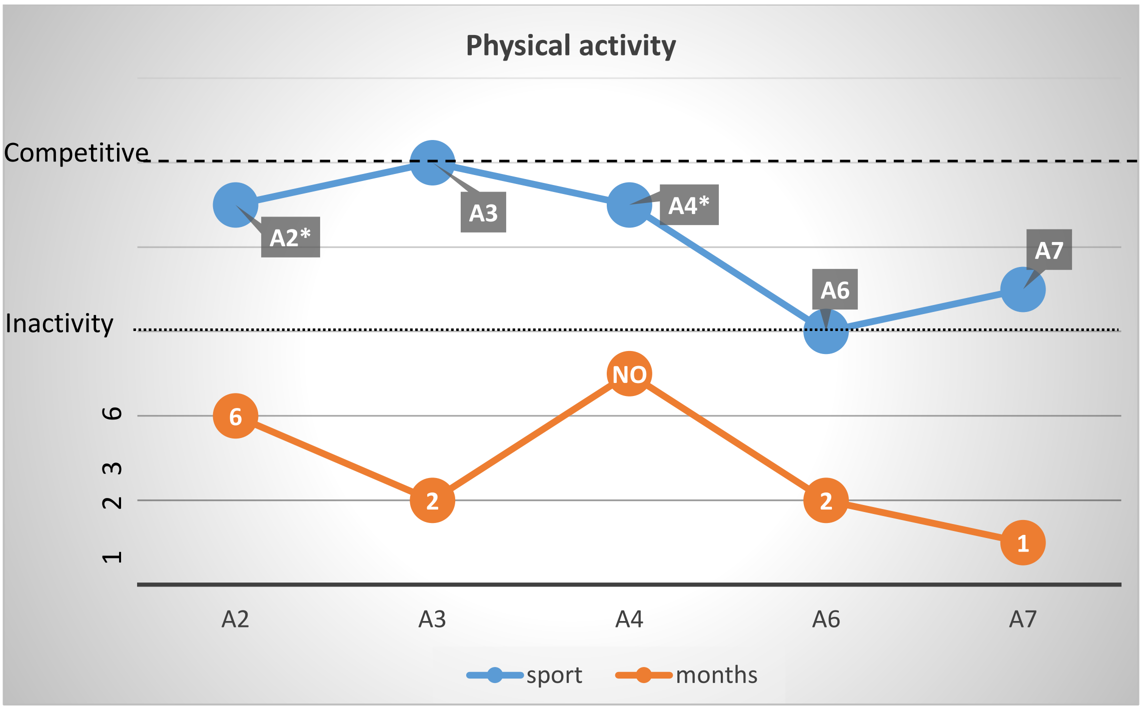


Fig.38 *The graph shows, in blue, the level of activity practiced by the patients of Cohort A; in Orange the months needed for the patients to be back to their routine activity. No correlation between the intensity of activity and the months waited. * Two lungs surgery*

***Pain intensity*:** the pain protocol after discharged provided only paracetamol on request; during the first week at home pain intensity, measured with VAS, had a median of 7 (range 2-9) and 5 patients (71%) needed to assume everyday paracetamol; after 1 month the pain interested still 4 patients (6 surgeries) but the intensity were decreased consistently, with a median VAS of 2 (range 0-5), moreover 3 patients complained about lower effort tolerance. In the 6th month post-operatively only 1 patient (14%) still complain about scar discomfort (*Fig.39*).

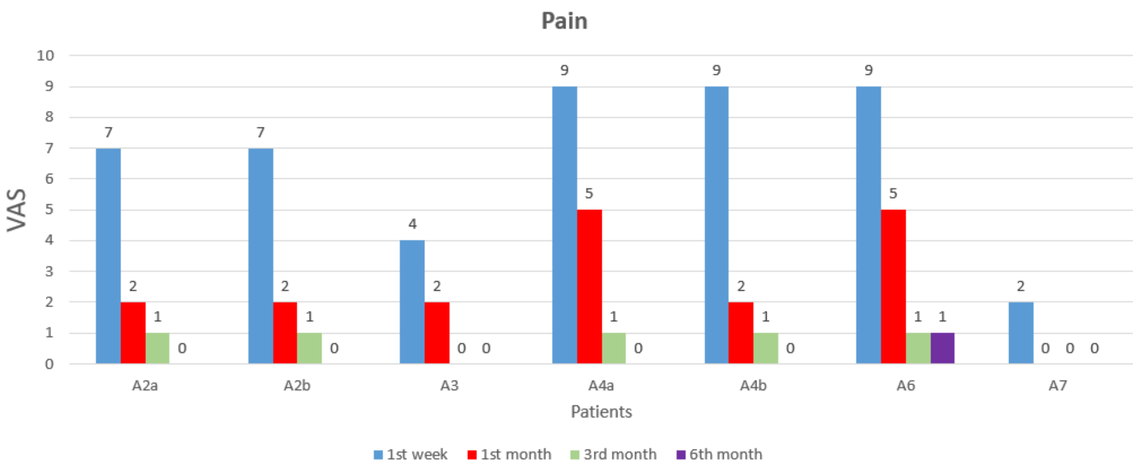


Fig.39 *Histogram shows pain score in the first 6 months after U-VATS surgery.*

Paresthesia: during the first month, in six surgeries the patients reported some symptoms at home, which were described as compatible with the term "paresthesia" that is to say " any numbness or disordered sensation causing chest wall discomfort, distinguishable from pain"; 3 patients (42,8%) during the first month had a sensation of numbness or/and pins and needles or electric shock (in the anterior thorax , art and scar), 1 patient (14%) had hyperesthesia localized in the anterior thorax and 1 patient, in both surgeries (28,5%), complained about decreased sensation, sited around the scar; the mean of severity, in term of VAS, was 3.5 during the first month, but in nobody paresthesia disturbed social life or school performance; after 3 months no one complained anymore about discomfort. *Table 12* resumes the incidence and characteristics of paresthesia on patients.

Scar*:* in a scale from 0 = "*terrible, it's too visible*" to 10= "*perfect, I can't see it*" in two surgeries the scars were very satisfying with a score of 9/10 for both; these scars were 2 cm long. Three patients had a mild satisfaction (score from 4 to 7) and two patients gave a score of severe discontent (from 0 to 3). No patients treated the scar to improve the aesthetic appearance and, right now, no one has pain or paresthesia in the scar anymore.

Parameter	n. of patients	%
Presence of paresthesia during the 1st month	6/7	86%
Characteristic		
Pins and needles	1	14%
Electric shock	1	14%
Heat	0	-
Swelling of chest wall	1	14%
Hyperesthesia	1	14%
Decreased sensation/numbness	5	71%
Itchiness	1	14%
Side		
Anterior thorax	3	43%
Posterior thorax	0	-
Around the scar	4	57%
Arm	1	14%
Contralateral thorax	0	-
Exacerbating factors		
Exercise	2	28%
Touch	1	14%
Rest	1	14%
Change of weather	0	-
None	4	57%
Severity (VAS)		
Mild (1-3)	3	43%
Moderate (4-7)	3	43%
Severe (8-10)	0	-
Functional disturbance		
No effects	4	57%
Sleep disturbance	2	28%
Affected school performance	0	-
Decreased exercise tolerance	0	-
Affected social life	0	-

Table 12. *Paresthesia during the 1st month following U-VATS for PSP: incidence, characteristic and effects on 5 patients (7 surgeries) of cohort A; some patients reported more characteristics.*

Were asked also to the U-Team surgeons to give a score to the scars, and their answers were compared to the patient's one. Finally, they were questioned about "what they think it was the score that the patients had given to their scar" and all of them increased the score, thinking that the patients could have a better perception of their scar; they were right only in 58% of cases.

There has been not agreement in the final judgement of the scar by the surgeons, and only in 1 case they agreed between them and also with the score given by the patient.

Fig.40 shows the comparison of the scar score between patients and U-Team surgeon.

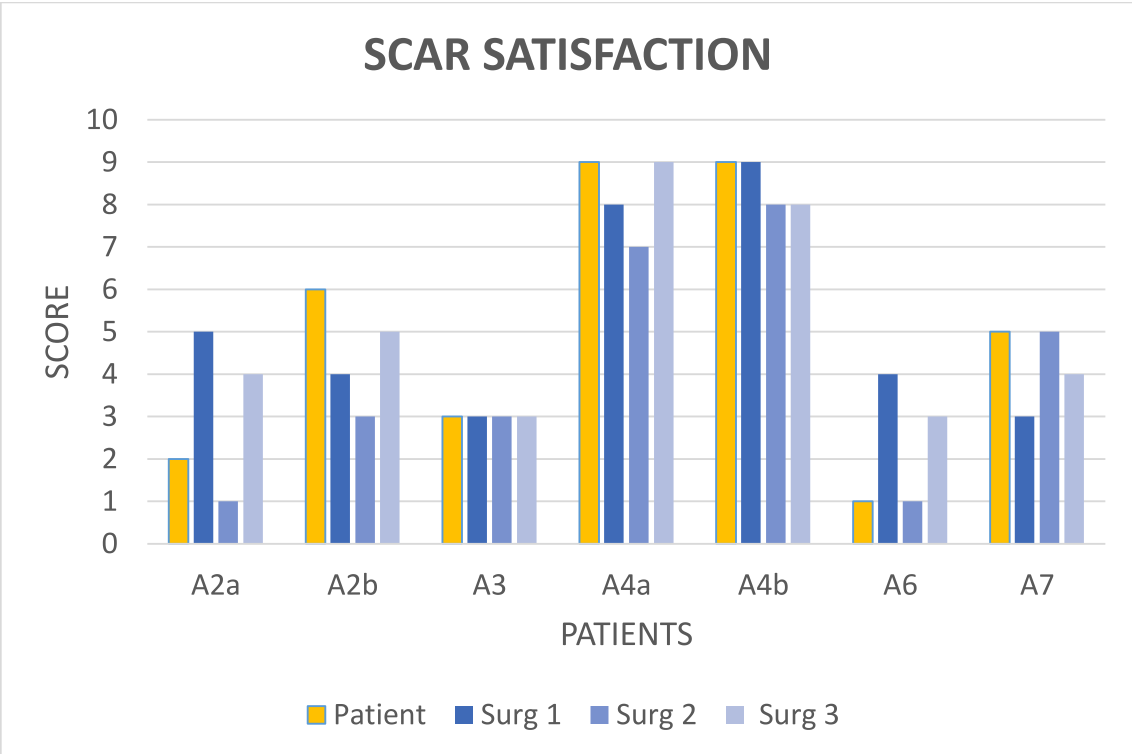


Fig.40 *Comparison of the scar-score between patients and U-Team surgeon.*

PART IV

DISCUSSION

Children and adolescents have a higher likelihood to develop PSP than adults, and an early surgical treatment can be proposed.[14]

Historically, the first-line of management of PSP in children has been conservative, since traditional thoracotomy was invasive and painful. Thoracoscopy in paediatric patients was first described in 1971 by Klimkovich and al. who performed diagnostic procedures for mediastinal and lung lesions; Rothenberg et al. reported the first thoracoscopic lung lobectomy[3] in 1994–1995, and the first thoracoscopic pure esophageal atresia repair was performed in Berlin in 1999.[3]

The advent of VATS, guaranteed a less invasive surgical approach, with a shortened hospital stay. These improvements produced a shift toward an earlier surgical management for PSP to prevent recurrences.[9]

The size of the infants may hinder proper exposure and increase the risk of complications, this limits the use of minimally invasive approaches, including robotic surgery, to specific weights.[3]

The goals of surgical treatment in PSP are the prevention of air leakage and recurrence of the disease.

Prolonged post-operative air leakage is, in fact, a risk factor for PSP recurrence, therefore, during surgery, every attention must be paid to minimizing these losses during the lysis of any adhesions and the use of mechanical staplers.[10]

We found, in Cohort B, 23% of re-do surgeries for new bullae, and 15,3% of recurrences: some authors suggested that a resection of the apical segment of the lower lobe should be systematically performed because bullae, at that level, can be a potential risk for PSP recurrence after VATS, but neither of the two cohorts followed this advice.[26] Also the coverage of the suture line with sealants has been proposed to prevent the formation of new bullae on the weak pulmonary tissue and decrease the recurrence rate. [27,28]

In fact, the formation of bullae in children and adolescents is a dynamic process caused by a weakness of visceral pleural and a lower elastic capacity of connective tissue, that can be further compromised by the tension created around the staples after parenchymal resection. On the basis of intraoperative findings during redo surgery, new bullae were observed arising from the staple line.[45,46]

In our study the time interval for surgical indication in both cohorts was similar, 11.2 *vs* 14.1 days, but far from current Italian clinical practice for adult, that considered 3-5 days of unsolved PNX a right time range for a surgical indication.[10]

Most of the thoracoscopic procedures described in literature, for children, are performed using multiple incision for the scope and the instruments.[47] Long term follow-up, however, has revealed that the minimally invasive approach is not without complications, as up to one half of patients complained of chest wall paresthesias and one third of patients experienced chronic thoracic wall pain.[48,49]
While initially slow to catch on, the traditional multi-port approach has evolved into a uniportal approach, that mimics open surgical vantage points, while utilizing a non-rib-spreading single small incision.

U-VATS was introduced as a minimally invasive approach by pioneers such as Marcello Migliore in 2003 and Gaetano Rocco in 2004.[19] The early period of U-VATS development was focused on minor procedures for adult; it has since been developed to encompass also major lung resections, most famously by Diego Gonzalez Rivas in 2014:[50] during a double port technique surgery, he realized that he could have a better direct view putting the camera through the utility incision, so he started the first thoracic "single-port" surgery with success, first used only for lower lobes.[50]
This evolution in the approach, from three port to single port technique, required a new learning curve: different lung exposure and learning how to coordinate the instruments and the camera with no interference during surgery. He suggests to pass through a double port technique (removing the posterior port) for learning uniportal VATS, and to start with female and thin patients.[50] Furthermore, for learning from open approach to uniportal, because uniportal mimics the open manoeuvres, is useful add the thoracoscope to thoracotomy (use monitor view and open direct view during surgery) and reduce progressively the size of incision after gained experience.

Apicoectomy is considered a minor procedure and requires a low level of expertise to be conducted with U-VATS technique.[51] In literature reported conversion rate and complications are quite low.[51] Our data show a very low complications rate (with zero major complications) and no conversion, reflecting adult papers.

Despite technical safety and feasibility were advocated by many authors, U-VATS is still little used in paediatric surgery, especially for major surgeries in young children < 5 years old.[1,2,3,4] Potential obstacles for the use of U-VATS in small children concern space limitations within the paediatric chest.[12,2,52]
Therefore, bullectomy, being mostly performed in adolescents or children of more than 30 kg, can represent a good springboard to acquire skills, to subsequently apply also to major surgeries or smaller thoraxes.

Obviously, as reported by Halexerogly et al.[2] and by Ugolini et al.[51] in some conditions the length of instruments, like the stapler, can make a two-portal conversion necessary emphasizing the importance of dedicated paediatric surgical instruments, to facilitate the diffusion of this technique.
It has also been suggested that parallel positioning of the instruments in U-VATS could be even more useful in children where there is limited working space.[21] Moreover, due to the well-known geometrical advantages, a lower rate of competition among instruments, could be associated with a reduced incidence of neuralgia/paresthesia due to lower angle rib stress and nerve compression, in fact pain could be explained by trocar compression over the intercostal nerve during camera movement.[51,19] In our cohort there were an incidence of paresthesia of 20% during hospitalization , according to medical records.

The main feature of the U-VATS approach consists of targeting, through a caudo-cranial (sagittal) plane, any area of surgical interest inside the chest (*Fig.41*).[53] Two advantages result from such a perspective: the procedure allows for a similar approach as is used for open surgery and the reacquisition of the depth of visualization lost with conventional three-port VATS.[3] The latter is based on the development of a transversal latero-lateral (or anteroposterior) plane, along which the operative instruments are deployed to address the target area.

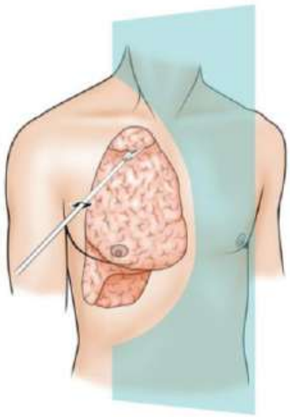


Fig.41 *Caudo-cranial approach (i.e sagittal plane) for U-VATS.*

Luca Bertolaccini made a physical and mathematical demonstration with equations of why uniportal technique (through one incision) was better than other techniques with multiple ports.[19] The advantage of using the camera in coordination with the instruments is that the vision is directed to the target tissue, bringing the instruments to address the target lesion from a straight perspective, thus we can obtain similar angle of view as for open surgery (*Fig.42*).

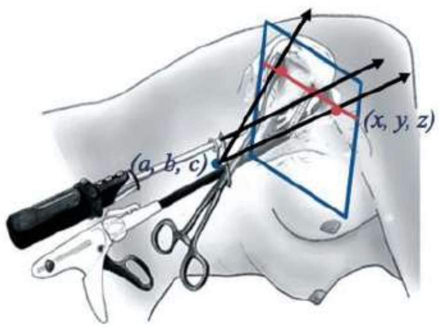


Fig.42 *Geometric concept of uniportal VATS.*

Conventional three port triangulation makes a forward motion of camera to the vanishing point. This triangulation creates a new optical plane with genesis of dihedral or torsional angle that is not favourable with standard two-dimension monitors and demands an extent of hand-eye coordination to overcome the geometrical obstacle originating from this torsion angle (*Fig.43a*).[53] This hand-eye coordination represents an added difficulty.

Conversely, in the uniportal approach, the eye "accompanies" in depth the stems of the instruments, which are deployed parallel to each other along the sagittal plane, and effectively represents an extension of the surgeon's hands (*Fig.43b*).[53]

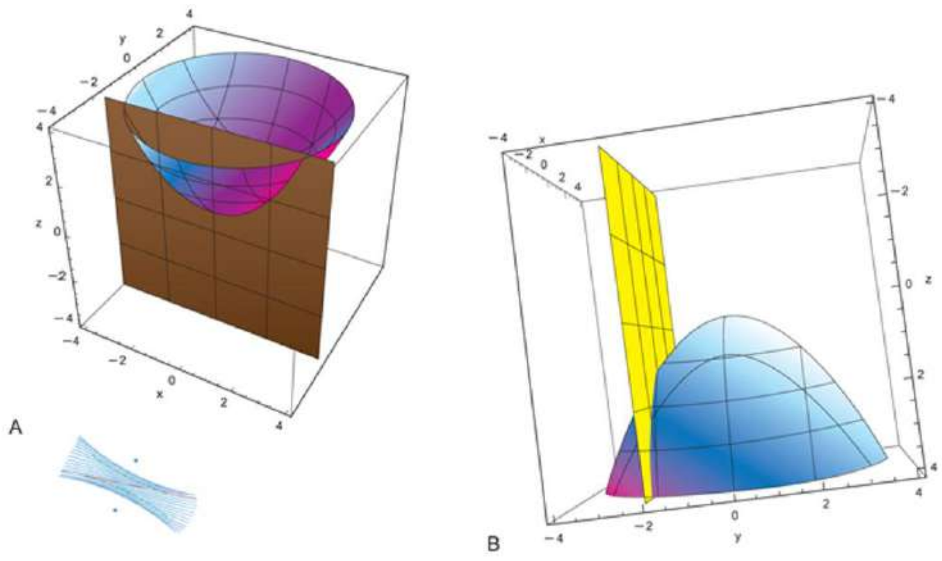


Fig.43 A. *The torsion angle resulting from instrument interaction along a transversal plane obstructing in depth visualization through 2-D imaged conventional three-port VATS;* ***B.*** *2-D imaged U-VATS enabling improved in-depth visualization of the surgical field.*

This theory of easy reproducibility of the technique fully agrees with our U-Team experience, where surgical times improved in general, as the surgeries were performed, by any U-Team member; we will elaborate on this aspect in the "*Learning curve*" paragraph.

Furthermore, the fulcrum of the operative instruments is inside the chest, at a short distance from the actual lesion. This characteristic assimilates uniportal VATS to robotic surgery; indeed, robotic surgery is considered to be the minimally invasive surgical approach that most closely duplicates the technical features of open thoracotomy.[50]

The U-VATS technique is a practical method to perform bullectomy for the treatment of PSP, in association with pleurodesis with a reduction, according to the literature, in the postoperative stay, initial postoperative pain scales, and chronic pain;[54,55]
Qin et al in 2015[56] and Yang in 2018[57] conducted a meta-analysis comparing Uniportal with three-port VATS for spontaneous pneumothorax in adult. The uniportal VATS technique neither increased mortality or recurrence rate nor prolonged the operative time, length of postoperative drainage or postoperative hospital stay. However, this new technique could reduce patients' postoperative pain and paresthesia, and improve patients' satisfaction. This meta-analysis indicates that the uniportal VATS is a safe, feasible and effective treatment for PSP.

Scott et al.[58] demonstrated a significantly less post-operative narcotic usage in patients undergoing uniportal VATS, when compared to traditional VATS; for Jutley and al. in patients undergoing thoracoscopy for PNX, uniportal technique was associated with decreased postoperative pain.[54]
According to these data our U-VATS cohort had a similar surgical time, compared to VATS group, and , even if we couldn't demonstrate a significant difference in post-operative stay, a trend towards less hospitalization is present in the U-VATS group; in addition we confirmed the reduction of post-operative pain , especially in the first post-operative day and, above all, an important difference in the use of Opioid and Benzodiazepines during the first three days after surgery, as evidence of intense pain resulting from the multiportal technique.
Finally, no patient of group A had uncontrolled pain or went to ICU, the latter element has also economic and arranging implications.

Chronic pain or discomfort after VATS has been reported in a large variety of ways: 'sharp and piercing', 'deep and penetrating', 'burning', 'cramping', or 'dull and unspecific'. The site of the discomfort has also been variable, with patients describing it 'at the scar', 'segmental', 'diffuse', or 'in the arm'.[38]

Even if U-VATS, according to literature and to our data, is considered less painful than VATS, looking at the score results of pain at home, reported in the telephonic questionnaire, probably it could be useful to prescribe a therapy for the first few days at home, to limit the pain arising when patients start moving more.

The uniportal approach confers the least invasiveness with only one single incision and has shown to be safe and efficient, not only for pulmonary resections and biopsies but also for lobectomy, and not only for adults.[19,1,59]
Over time the size of our incisions has been reduced, this change translated into a greater appreciation of the scar by the patients, in fact in the last two surgeries the score for "appreciation of the scar" was of 9, where 0 = "*terrible, it's too visible*" to 10= "*perfect, I can't see it*".
We aim for a further reduction of incision size with time to improve the scar appreciation.

Another interesting proposition could be a protocol for the topical treatment of the scar after surgery, to further improve the aesthetic result.

Additionally, the uniportal VATS had surgical costs like three port VATS with lower postoperative stay costs, expecially because of the no-use of ICU. The procedures in our series were performed with some dedicated instruments and other instruments for traditional multiple-incision thoracoscopy, furthermore, the use of a simple scratch pad and a normal grasper to perform pleural abrasion further reduced costs; the occupancy time of operating theatre was similar in both group.

We had a significant difference in residual PNX at discharge between the two groups, but this datum is probably related to the 100% performing of pleurodesis in Cohort A that facilitates the adhesion of lung to the chest wall.

Salati et al.[55] found that the uniportal approach did not increase the risk of recurrence of PNX (10% uniport *vs* 13% three-port) and allowed almost all patients to resume complete working and physical activities as before the operation. Our patients of U-VATS group had no recurrences, with a median follow-up of 13 months, and 43% were back to their activities in less than 2months, the others in 6 months. Curious the case of a patient that started for the first time to practice sport just 1 month after the surgery.

Excessive PNX creation may lead to decreased cardiac preload resulting in significant hypotension and reflex tachycardia.[37]

With adolescents, an optimal selective intubation is easy to obtain. Exclusion of ventilation of the affected lung is a crucial aspect for U-VATS feasibility, since there is open-air communication with the pleural cavity through the retractor.

Nonetheless, well-established one-lung ventilation could allowed gas-free VATS procedures, especially in a small child where CO2 brain absorption is associated with a higher risk of sequelae[51] and , furthermore, avoid the risk of excessive intrathoracic pressure; surprisingly there are not study in literature focused on this aspect of U-VATS technique and, because of the retrospective aspect of our study, unfortunately we have incomplete data about PO2 and PCO2 during surgeries; therefore we think that this aspect deserves a deepening with a prospective analysis.

Learning curve

Uniportal VATS is performed in many centers around the world. The learning curve for the application of this technique in children is higher than in adults, due to the lower incidence of thoracic pathology and the size of the thoracic cavity of the children, but several factors influence the length of the learning curve.[46]

An advantages of the technique, over conventional VATS, include the coaxial position of the instruments, which mimics an open thoracotomy, but not the coaxial movement of camera and instruments,[47] that can be difficult in one trocar surgery, with a more rapid learning curve and greater accessibility to most of the centers.

The conditions for those surgeons' learning curves are better with the possibility of learning under supervision by an experienced VATS surgeon; for this reason, during the first period of our U-MIS program, we invited an experienced U-VATS surgeon, from a high volume Thoracic Center for Adult, to perform surgeries being supervised and mentored, learning important tips and tricks from him, during operation.

The experience of the surgeon in training is another important factor, as understanding the anatomy of the lung with the many anatomical variations makes the learning curve shorter.

Experience with other VATS procedures is an advantage, as the surgeon will get familiar with the port placement and working with the VATS tools in a monitor based setting.[60]

Once overcome the initial feeling of moving things around all the time, this approach is the easiest and the one that offers the least amount of conflict between instruments initially you are tempting to move.

It was also extremely important standardizing the technique, above all during the learning curve, and operating always in two consultant surgeons. This approach, like also suggested by other authors[61], allowed to overcome technical difficulties, reduce surgical stress and ease the management of complications that could have required a conversion in inexperienced hands. Another recommendation is to resist the temptation of inserting more instruments than necessary through the wound, in the attempt to achieve a good visualisation.

During our surgeries the camera was almost always in the upper part of the incision, instruments in the middle and stapler in the bottom; to facilitate this arrangement we use a little trick, suggested by our supervisor: a silk thread, passed from part to part in the upper third of incision, after Alexis positioning, to keep camera in suspension (*Fig.44*).

Fig. 44 *Silk thread (arrow) to support the camera.*

The learning curve for Surgeon 1 (senior surgeon, skilled in VATS) was quite rapid, 5 surgeries to reach the surgical time plateau and the awareness of the technique; but surprisingly also the first apicoectomy made by Surgeon 2 (surgeon in training for VATS) and Surgeon 3 (surgeon not trained for VATS) was in line with the last surgical time of the Surgeon 1, to underline the easiness of reproducibility of this technique and the "in-line" movements of the instrument *(Fig.45-46).*

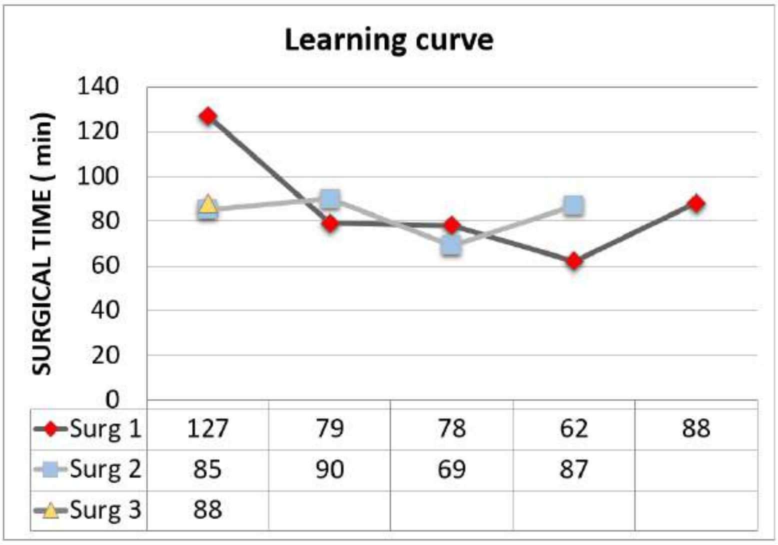


Fig.45 *Learning curve of the surgeons of U-Team.*

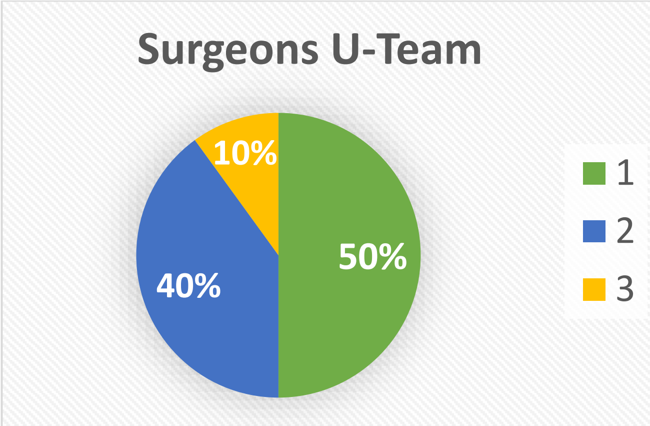


Fig.46 *Percentage of operation made by the three surgeons of U-Team (Cohort A).*

Study limitations

This study has several limitations: first of all, the study is limited from the small sample size, as often happens in paediatric population;
Second, the retrospective nature of the data lends themselves to inherent bias.
Third, the not standardized nature of the care that the patients received in two separate hospitals can create a bias, in term of medication and hospitalization: for example, although post-operative pain based on VAS data can be useful, it is a highly subjective marker, and subject to tremendous bias both from patients and nurse.
Another limit is the lack of data about outpatient visit for Cohort B: we couldn't compare pain at home, paresthesia and scar satisfaction.
Important also the need to a prospective randomized study with hemogasanalysis during surgery, to compare hemodynamic and metabolic changes and see if there are any differences for the effect of CO_2 absorption and insufflation.

About our telephonic questionnaire, probably it would be more reliable if it was filled in during outpatient visit at 1, 3 and 6 months after surgery, rather than many months later.
Finally, we were not able to determine the exact impact of the technique on chest wall function or to see any chest deformities, which would require years of follow-up.

CONCLUSIONS

Thoracoscopy is the minimally invasive technique applied in the vast majority of thoracic surgical interventions. One of the main disadvantages of thoracoscopy in paediatric surgery is the lack of space within the thoracic cavity. This, together with the low volume of thoracic pathology at this age, generates a longer learning curve and reduces the application of this technique to highly complex surgical procedures.

U-VATS technique offers a similar vision to open surgery because of direct thoracic access, unlike thoracoscopy that offers an angular vision.[19] In addition, in uniportal VATS, all surgeons are looking at the same screen in front of them, this position improves the surgical posture and facilitates manual movements because of better hand-eye coordination.[19] The direct vision (anatomic visualization) makes manual movements similar to open surgery and learning curve is shorter than in multiportal approach.[5]

In our experience, as confirmed from previously published cases, U-VATS could be a feasible and safe surgical option for the treatment of PSP in children/adolescent, with a rapid learning curve, offering advantages of a minimally invasive approach and allowing, if necessary, easiness to conversion or utility thoracotomy; furthermore, without the insufflation of CO2, prevents that intraoperative venous bleeding may be covered when intrathoracic pressure exceeds venous pressure.

Despite very few paediatric publications on the subject, U-VATS has no morbidity related to the technique. Potential extra advantages over conventional VATS are multiple: first of all, a better postoperative outcome in terms of pain; in fact, according to literature, [6;12;54;58;62] the single incision approach has generated, also in our study, less post-operative pain than conventional multiport access, due to the avoidance of intercostal nerve stress;[5] this allowed a fast return (1-2 months) to physical activity in almost half of the patients.

Second: a significantly less post-operative narcotic usage; the decrease of postoperative pain accelerates extubation, allowing to introduce fast track protocols in thoracic paediatric surgery, with extubation in the O.R, without the need to stay in ICU, resulting in economic and organizational feedback.[63,64]

Third: the uniportal VATS technique neither increased recurrence rate nor prolonged the operative time, length of postoperative drainage or postoperative hospital stay.
Therefore, bullectomy, being mostly performed in adolescents or children of more than 30 kg, can represent a good springboard to acquire skills, to subsequently apply also to major surgeries or smaller thoraxes.

Finally, it has a greater accessibility for every centers, without additional costs for instruments and it can provide a scar appreciated by patients, especially when size incision is inferior to 2.5 cm.

With this encouraging data we will continue the U-VATS program and we will try to expand it also to other thoracic diseases, as is already done for adult population,
because the future of the thoracic surgery is to reduce the surgical and anaesthetic trauma and we firmly believe that Uniportal-VATS can make to achieve this goal possible.

PART V

REFERENCES

1. Shaqqura B, Rumman N, Gonzalez Rivas D, Abu Akar F. Uniportal video-assisted thoracoscopic lobectomy in a 9- week-old patient. Interact CardioVasc Thorac Surg 2020; 30:327.
2. Halezerogˇlu S, Okur E, Ergene G. Single-incision videoassisted thoracic surgery for an extralobar sequestration in a child. Innovations (Phila) 2016;11:64–66.
3. Osama A Bawazir. Thoracoscopy in pediatrics: Surgical perspectives. Annals of Thoracic Medicine A : 2019 | Vol: 14 | Issue : 4 | Page : 239—247.
4. Osama A Bawazir. Thoracoscopy in pediatrics: Surgical perspectives. Annals of Thoracic Medicine A : 2019 | Vol: 14 | Issue : 4 | Page : 239—247.
5. I. Casal-Beloy, L. Míguez Fortes, M. A. Gómez Tellado, D. González-Rivas . Thinking uniportal in pediatric thoracic surgery. Pediatr Med 2019;2:13.
6. Gonzalez-Rivas D. Uniportal thoracoscopic surgery: From medical thoracoscopy to non-intubated uniportal videoassisted major pulmonary resections. Ann Cardiothorac Surg 2016;5:85–91.
7. Rocco G, Martin-Ucar A, Passera E. Uniportal VATS wedge pulmonary resections. Ann Thorac Surg 2004;77:726-8.
8. Reinersman JM, Passera E, Gaetano Rocco G. Overview of uniportal video-assisted thoracic surgery (VATS): past and present. Ann Cardiothorac Surg 2016;5:112-7.
9. Miscia et al. Management of Spontaneous Pneuothorax in Children: a Systematic Review and meta-Analysis; Eur J Pediatr Surg 2020 Feb;30(1):2-12.
10. Pneumotorace spontaneo primitivo Linee guida della Società Italiana di Chirurgia Toracica; Linea guida pubblicata nel Sistema Nazionale Linee Guida- Roma, 18 maggio 2022.
11. Gupta D, Hansell A, Nichols T, et al. Epidemiology of pneumothorax in England. Thorax 2000;55:666–671.

12. Fernandez-Pineda I, Seims AD, VanHouwelingen L, et al. Modified uniportal video-assisted thoracic surgery versus three-port approach for lung nodule biopsy in pediatric cancer patients. J Laparoendosc Adv Surg Tech A 2019;29: 409–414.
13. E. Matuszczak, W. Dębek, A. Hermanowicz, M. Tylicka. Spontaneous pneumothorax in children – management, results, and review of the literature; Kardiochirurgia i Torakochirurgia Polska 2015; 12 (4): 322-327.
14. S. Furia, C. Breda. Primary spontaneous pneumothorax in children and adolescents: a systematic review; Pediatr Med 2019;2:12.
15. Fujino S, Inoue S, Tezuka N, et al. Physical development of surgically treated patients with primary spontaneous pneumothorax. Chest 1999;116:899–902.
16. Imperatori A, Rotolo N, Spagnoletti M, Festi L, Berizzi F, etal. Risk factors for postoperative recurrence of spontaneous pneumothorax treated by video-assisted thoracoscopic surgery. Interact Cardiovasc Thorac Surg. 2015;20(5):647- 652. doi: 10.1093/icvts/ivv022.
17. K. Poulikidis, L. Gerson, J. Costello, W.T. Vigneswaran. Video-Assisted Thoracoscopy in the Management of Primary and Secondary Pneumothorax. Pneumothorax (chapter) 2019.
18. Soccorso G, Anbarasan R, Singh M, Lindley RM, Marven SS, Parikh DH.Management of large primary spontaneous pneumothorax in children: radiological guidance, surgical intervention and proposed guideline. Pediatr Surg Int 2015;31(12):1139–1144.
19. L. Bertolaccini , a. Pardolesi, J. Brandolini, P.Solli; Uniportal video-assisted thoracic surgery for pneumothorax and blebs/bullae. Journal of Visualized Surgery. 2017; 3-107.
20. Gaetano Rocco MD. Single-Port Video-Assisted Thoracic Surgery (Uniportal) in the Routine General Thoracic Surgical Practice; Operative Techniques in thoracic and cardiovascular surgery. A 2009.
21. Katz MS, Schwartz MZ, Moront ML, et al. Single-incision thoracoscopic surgery in children: Equivalent results with fewer scars when compared with traditional multipleincision thoracoscopy. J Laparoendosc Adv Surg Tech A 2012; vol 22:180–183.

22. Takahashi R. Evaluation of Spontaneous Pneumothorax Surgeries: A 16-Year Experience in Japan. Surg Res Pract 2016;2016:7025793.
23. Torre M, Grassi M, Nerli FP, et al. Nd-YAG laser pleurodesis via thoracoscopy. Endoscopic therapy in spontaneous pneumothorax Nd-YAG laser pleurodesis. Chest 1994;106:338-41.
24. Li Z, Chen L, Wang J, et al. A single institution experience using the LigaSure vessel sealing system in video-assisted thoracoscopic surgery for primary spon-taneous pneumothorax. J Biomed Res 2014;28:494-7.
25. Linchevskyy O, Makarov A, Getman V. Lung sealing using the tissue-welding technology in spontaneous pneumothorax. Eur J Cardiothorac Surg 2010;37:1126-8.
26. Obuchi T, Yoshida Y, Wakahara JI, et al. Pneumothorax in teenagers: reducing recurrence through resection of superior segment of lower lobe. J Thorac Dis 2018;10:3507-11.
27. Lee S, Kim HR, Cho S, et al; Korean Pneumothorax Study Group.Staple line coverage after bullectomy for primary spontaneous pneumothorax: a randomized trial. Ann Thorac Surg 2014;98:2005-11.
28. Haraguchi S, Koizumi K, Mikami I, et al. Staple line coverage with a polyglycolic acid sheet plus pleural abrasion by thoracoscopic surgery for primary spontaneous pneumothorax in young patients. J Nippon Med Sch 2012;79:139-42.
29. Mukhtar, Ahmed M. MD; Obayah, Gihan M. MD; Elmasry, Ashraf MD; Dessouky, Nabil M. MD. The Therapeutic Potential of Intraoperative Hypercapnia During Video-Assisted Thoracoscopy in Pediatric Patients; Anesthesia & Analgesia: January 2008 - Volume 106 - Issue 1 - p 84-88.
30. Brock H, Rieger R, Gabriel C, Polz W, Moosbauer W, Necek S. Haemodynamic changes during thoracoscopic surgery. The effects of one-lung ventilation compared with carbon dioxide insufflation. Anaesthesia 2000;55:10 – 6.
31. Dong Kyu Lee, Heezoo Kim, Hyun Koo Kim, Dong Ik Chung, Kook Nam Han, Young Ho Choi**.** CO_2 during single incisional thoracoscopic bleb resection with two-lung ventilation. *J Thorac Dis* 2018;10(8):5057-5065.
32. Jones DR, Graeber GM, Tanguilig GG, Hobbs G, Murray GF. Effects of insufflation on hemodynamics during thoracoscopy. Ann Thorac Surg 1993;55:1379 – 82.

33. Yunqin Ren, Xing Zhu, Hong Yan, Liyong Chen & Qingxiang Mao. Cardiorespiratory impact of intrathoracic pressure overshoot during artificial carbon dioxide pneumothorax: a randomized controlled study; BMC Anesthesiology (2022) 22:76.
34. Suarez-Pierre A, Terasaki Y, Magruder JT, et al. Complications of CO2 insufflation during endoscopic vein harvesting. J Card Surg 2017;32:783-9.
35. Wolfer RS, Krasna MJ, Hasnain JU, McLaughlin JS. Hemodynamic effects of carbon dioxide insufflation during thoracoscopy. Annals of Thoracic Surgery 1994; 58: 404–8.
36. A. Gentili, M. Lima, R. De Rose, A. Pigna, V. Codeluppi, S. Baroncini. Thoracoscopy in children: anaesthesiological implications and case reports. MINERVA ANESTESIOLOGICA Vol. 73 - No. 3.
37. Stefaan H. A. J. Tytgat; Maud Y. A. van Herwaarden; Lisanne J. Stolwijk; Kristin Keunen; Manon J. N. L. Benders; Jurgen C. de Graaff; Dan M. J. Milstein; David C. van der Zee; Petra M. A. Lemmers. Neonatal brain oxygenation during thoracoscopic correction of esophageal atresia. Surg Endosc (2016) 30:2811–2817.
38. A.D.L. Sihoe et al. Incidence of chest wall paresthesia after video-assisted thoracic surgery for primary spontaneous pneumothorax ; European Journal of Cardio-thoracic Surgery 25 (2004) 1054–1058.
39. Ohnhaus EE, Adler R. Methodological problems in the measurement of pain: Acomparison between the verbal rating scale and the visual analogue scale. Pain 1975;1:379–384.
40. Delgado DA, Lambert BS, Boutris N, McCulloch PC, Robbins AB, Moreno MR, Harris JD. Validation of digital visual analog scale pain scoring with a traditional paper-based visual analog scale in adults. Journal of the American Academy of Orthopaedic Surgeons. Global research & reviews. 2018 Mar;2(3).
41. D. Gould et al. Visual Analogue Scale (VAS). Journal of Clinical Nursing 2001; 10:697-706.
42. Weigl K, Forstner T. Design of paper-based visual analogue scale items. Educational and psychological measurement. 2021 Jun;81(3):595-611.
43. https://www.physio-pedia.com/Visual_Analogue_Scale.

44. Serlin RC, Mendoza TR, Nakamura Y, Edwards KR, Cleeland CS. When is cancer pain mild, moderate or severe? Grading pain severity by its interference with function. PAIN_ 1995;61:277–84.
45. Cho S, Jheon S, Kim D, et al. Results of repeated video-assisted thoracic surgery for recurrent pneumothorax after primary spontaneous pneumothorax. Eur J Cardiothorac Surg 2018;53:857-61.
46. Ota H, Kawai H, Kuriyama S. The Presence of a Reticulated Trabecula-Like Structure Increases the Risk for the Recurrence of Primary Spontaneous Pneumothorax after Thoracoscopic Bullectomy. Ann Thorac Cardiovasc Surg 2016;22:139-45.
47. Cobellis G, Torino G, Noviello C, Cruccetti A., Mastroianni L. Amici G. Martino A. Versatility of onetrocar surgery in children. J Laparoendosc Adv Surg Tech A 2011;21:549–54.
48. Sihoe AD, Au SS, Cheung ML, Chow IK, Chu KM, Law CY, Wan M, Yim AP. Incidence of chest wall paresthesia after video-assisted thoracic surgery for primary spontaneous pneumothorax. Eur J Cardiothorac Surg 2004;25:1054–1058.
49. Passlick B, Born C, Sienel W, Thetter O. Incidence of chronic pain after minimal-invasive surgery for spontaneous pneumothorax. Eur J Cardiothorac Surg 2001;19:355–358.
50. D.Gonzalez-Rivas , e. Fieira, M. Delgado, L. Mendez, R. Fernandez, M. De la Torre; Evolving from conventional video-assisted thoracoscopic lobectomy to uniportal: the story behind the evolution. J.*Thorac Dis* 2014;6(S6):S599-S603.
51. S.Ugolini, R.Coletta,A. Morabito et al. Uniportal Video-Assisted Thoracic Surgery in a Pediatric Hospital: Early Results and Review of the Literature. J Laparoendosc Adv Surg Tech A 2022; 32, Number 6.
52. Fernandez-Pineda I, Seims AD. Modified uniportal videoassisted thoracic surgery in children. J Minim Access Surg 2016;12:373–374.
53. G. Rocco. Uniportal video-assisted thoracoscopic surgery (VATS); https://thoracickey.com/uniportal-video-assisted-thoracoscopic-surgery-vats/.
54. Jutley RS, Khalil MW, Rocco G. Uniportal vs. standard threeport VATS technique for spontaneous pneumothorax: comparison of post-operative pain and residual paresthesia. Eur J Cardiothorac Surg 2005;28:43–46.

55. M. Salati , A. Brunelli, F. Xiumè, M, Refai, V. Sciarra, A. Soccetti, A. Sabbatini. Institutional report - Thoracic general Uniportal video-assisted thoracic surgery for primary spontaneous pneumothorax: clinical and economic analysis in comparison to the traditional approach Interactive CardioVascular and Thoracic Surgery 7 (2008) 63–66.
56. S.L. Qin, J.B Huang, Y.L Yang, L. Xian. Unportal vs. three-port VATS for spontaneous pneumothorax. J Thorac Dis 2015;7(12):2274-2287.
57. Yang X, Li M, Yang X, Zhao M, Huang Y, Dai X, et al. Uniport versus multiport video-assisted thoracoscopic surgery in the perioperative treatment of patients with T1–3N0M0 non-small cell lung cancer: a systematic review and meta-analysis. J Thorac Dis 2018;10:2186–95.
58. Scott Gregory Louis, William James Gibson, Chase Lynn King, Nirmal Kumar Veeramachaneni. Uniportal video-assisted thoracoscopic surgery (VATS) technique is associated with decreased narcotic usage over traditional VATS lobectomy. J Vis Surg 2017;3:117.
59. Gonzalez-Rivas D, Marin JC, Granados JP, et al. Uniportal video-assisted thoracoscopic right upper sleeve lobectomy and tracheoplasty in a 10-year-old patient. J Thorac Dis 2016;8:E966-9.
60. McKenna RJ., Jr Complications and learning curves for video-assisted thoracic surgery lobectomy. Thorac Surg Clin 2008;18: 275-80. 10.1016/j.thorsurg. 2008.04.004.
61. D. Nachira, E, Meacci, V. Porziella, M.L. Vita , M.T. Congedo, M. Chiappetta, L. Petracca Ciavarella, M. Ismail, E. Gualtieri, A. Cesario, S. Margaritora; Learning curve of uniportal video-assisted lobectomy: analysis of 15-month experience in a single center. Journal of Thoracic Disease; Nov 2018; Vol10, supplement 31.
62. Sihoe AD. Reasons not to perform uniportal VATS lobectomy. J Thorac Dis 2016;8:S333-43.
63. Kugler C. Minimal-invasive thoracic surgery in pediatric patients. J Vis Surg 2018;4:10.
64. Clermidi P, Bellon M, Skhiri A, et al. Fast track pediatric thoracic surgery: Toward day-case surgery? J Pediatr Surg 2017;52:1800-5.