

Single-center experience in the surgical treatment of combined lung Echinococcosis

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ABSTRACT

الأهداف: مقارنة نتائج ومضاعفات العلاج الجراحي للمرضى الذين يعانون من داء المكورات المشوكية من جانب صدري أو كلا الجانبين.

الطريقة: أجريت هذه الدراسة المستعرضة لدراسة مستقبلية في قسم جراحة الصدر وجراحة الأطفال، المركز الجراحي الطبي، أستانا، كازاخستان واشتملت على 598 مريض مصابين بداء المكورات المشوكية، وخضعوا للعلاج الجراحي بأساليب جراحية مختلفة، اعتماداً على انتشار بداء المكورات المشوكية وهي على النحو التالي: الرئة اليمنى 357 مريض (59.5%)، والرئة اليسرى مريض 243 (40.5%)، وكلا الجانبين 95 مريض (15.8%)، ومضاعفات داء المكورات المشوكية 317 (52.8%) مريض. قلت مدة الإقامة في المستشفى ($p < 0.0001$) عند استئصال المكورات المشوكية باستخدام الليزر بالطاقة العالية للكيس بالمقارنة مع استئصال المكورات المشوكية وعلاج الكيس باستخدام بوفيدون اليود. بينما سجل العلاج بالفورمالين أطول مدة إقامة في المستشفى ($p < 0.0001$).

النتائج: أوضحت تحليل مقارنة المرضى الذين يعانون من داء المكورات المشوكية المعقد وغير المعقد زيادة حدة المضاعفات ما بعد الجراحة والمرتبطة بداء المكورات المشوكية المعقد ($OR = 2.2, p < 0.0001$).

الخاتمة: بالرغم من نجاح العلاج الجراحي لداء المكورات المشوكية إلا أنه يوجد مشاكل في السلامة والإنتثار أثناء العملية ومن الممكن تطوير معدل نجاح العلاج، حيث أن هذه العوامل تتطلب دراسات استباقية متعددة المراكز

Objectives: To compare results of surgical treatment and complications of patients with unilateral or bilateral thoracic and combined pulmonary echinococcosis.

Methods: This cross-sectional analysis of a prospective study was conducted in the Department of Thoracic and Pediatric Surgery, Scientific Center

of Surgery, Almaty, Kazakhstan among 598 patients with pulmonary echinococcosis, who had surgical treatment with various surgical methods, depending on the prevalence of echinococcosis, as follows: right lung in 357 (59.5%) patients, left lung in 243 (40.5%) patients, bilateral in 95 (15.8%) patients, and complicated echinococcosis in 317 (52.8%) patients. Length of stay per hospital stay has been decreased ($p < 0.0001$) by video-thoroscopic echinococcectomy with the high-energy laser (HEL) treatment of cyst, than after echinococcectomy by cyst treatment with povidone-iodine. Treatment with formalin presented the most longest hospital stay ($p < 0.0001$).

Results: Comparative analysis of patients with uncomplicated and complicated pulmonary echinococcosis showed a high frequency of postoperative complications associated with complicated echinococcosis ($OR = 2.2, p < 0.0001$).

Conclusion: Despite the success of surgical treatment of pulmonary echinococcosis, issues of intraoperative dissemination and safety remain, and treatment success rates can be improved. These factors require further prospective multicenter studies.

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Echinococcosis is a widespread parasitic disease representing serious medical and social problems.^{1,2} Pulmonary cystic echinococcosis has no clinical presentation and may cause impassable cough, colored sputum, hemoptysis, and fever. Radiographs can detect lung abscess, bronchoscopy can detect cystic lesion, and serological testing can detect antibody titer to *Echinococcus granulosus*.³⁻⁵ Cystic echinococcosis is the most common type, and represents 95% of the cases. Estimated cases worldwide was 2 to 6 million, and the mortality rate was 2% to 4% per 100,000 world population.⁶ Endemic cystic echinococcosis primarily occurs in Mediterranean countries, Central Asia, North and East Africa, Australia, and South America.^{7,8} Despite of development of new oral anti-parasitic medicines; only surgical approaches were able to prove its effectiveness in the treatment of cystic echinococcosis. Other important challenges that are deserving to study are postoperative complications and recurrent echinococcosis.^{9,10} The purpose of this study is to explore the number of postoperative complications associated with various surgical treatments of complicated and uncomplicated pulmonary echinococcosis.

Methods. This cross-sectional analysis of a prospective study was conducted in the Department of Thoracic and Pediatric Surgery, Scientific Center of Surgery, Almaty, Kazakhstan from 2010 to 2017. Ultrasound or CT and other complete data available obtained from the patients with primary pulmonary echinococcosis were included in this review. Adult age ≥ 18 and < 70 years old were also included. Patients referred from any out-patients department or hospitals throughout Kazakhstan were also included. Presence of hydatid cysts, any size on the US or CT, were the indications for echinococectomy. Exclusion criteria were pregnant women, patients with fever and active pulmonary tuberculosis, HIV positive with HIV symptoms, as well as with primary or secondary lung or liver cancer.

We analyzed treatment results of 598 patients with pulmonary echinococcosis who were hospitalized in the department of thoracic surgery. Two hundred eighty-three patients had uncomplicated echinococcosis, and 317 patients had complicated echinococcosis, due to festering echinococcosis cysts in the bronchus.

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Patients ranged in age from 32 to 67 years and included 74 (12.4%) women and 524 (87.6%) men. Data were collected prospectively from the Institutional Echinococcosis Registry. The study protocol was approved by our Institutional Local Research Ethics Committee (06/26/2016), and the study protocol was developed to conform to the ethical standards of the Declaration of Helsinki. We received informed consent from all participants in the study.

Analysis were conducted with SPSS software version 18.0 and MedCalc; a Z-statistic for analysis of main characteristics surgical patients, complications and deaths, Chi-square test for analysis of surgery methods, the odds ratio (OR) for analysis of complications; and deaths in 95% confidence interval (CI). A $p < 0.05$ was used to determine significance. Continuous data (hospital stay, days) are presented as mean standard deviation (SD) or median, and categorical data are presented as frequency in percentage. Comparisons of patients' characteristics and outcomes were conducted in the 2 patient groups with uncomplicated and complicated cases of pulmonary echinococcosis.

Results. Study population. Combined lesions on lungs and liver was seen in 136 (22.7%) patients, lungs and other organs in 40 (6.7%) patients, 22 (3.7%) of them in the lesser sac, 8 (1.3%) of them in the spleen, 6 (1%) of them in the abdomen, and 4 (0.7%) in the greater omentum (Table 1). Unilateral common lesion of the lung with echinococcosis is statistically important, followed by bilateral lesion ($p \leq 0.0001$), and combined lesion of the lung, liver, and other abdominal organs, ($p \leq 0.0001$).

Operative procedures. Organ-preserving surgery was performed, which is more statistically significant ($p \leq 0.0001$) than frequency of lung resection (Table 2). Lung resection was carried out in 23 (3.8%) cases of festering cysts; in 18 (3%) cases of echinococcosis occupying the volume of almost the entire fraction (2 lobes) with irreversible coarse perifocal changes and fibrosis in the surrounding pulmonary tissue; and in 13 (2.2%) cases of echinococcosis with excessive multiplicity lesion of one or 2 lobes. Organ-preserving surgery consisted of closed echinococectomy by methods Delbe's, echinococectomy or lung resection by Bobrov-Spasocucotsky's or Vishnevsky's methods.

The treatment of fibrous pulmonary echinococcosis cyst capsule cavity was performed using a high-energy laser beam or using low-frequency ultrasound. The effectiveness of these methods has been compared to the result of antiparasitic treatment with formalin or povidone-iodine. Filling a cyst of fibrous capsule with

vertical half purse-string suture by Kulakeev's method was carried out in 176 cases, 50% of them with pulmonary echinococcosis complications. Capitonage was carried out through a combination of horizontal and vertical sutures in 21 patients with complicated cysts (12 suppuration, 4 chitin membrane detachment, 2 rupture of cyst into bronchus, one rupture of cyst into the pleural cavity, and 2 pulmonary hemorrhage). In patients with bilateral echinococcosis adhered to tactics, 2-stage bilateral thoracotomy was performed with an interval of 3, 6, or 8 weeks between them, depending on the severity.

In patients with right pulmonary echinococcosis and upper segment liver right lobe, simultaneous

one-stage thoracotomy with diaphragmotomy and echinococcectomy of the lung and liver were performed. In 44 (7.4%) patients with bilateral lesion of the lungs and spleen and liver echinococcosis, after phased thoracotomy with lung echinococcectomy (with an interval of 1 to 2 months between them), next-stage laparotomy was carried out to excise echinococcosis cysts of the abdominal parenchymatous organs. Of these, 27 patients had one-stage surgery; the others had 2-stage surgery with an interval of 4 to 8 weeks between them. In 40 (6.7%) patients with combined pulmonary echinococcosis and abdominal organs, after thoracotomy and lung echinococcectomy, they received second-stage laparotomy and echinococcectomy from

Table 1 - Comparison between patients with unilateral, bilateral, and combined lungs and extrathoracic involvement.

Variables	Unilateral involvement n (%)	Bilateral involvement n (%)	Combined lungs and extrathoracic involvement n %	Confidence interval	Chi-square	P-value
Patients	327 ^{ac} (54.7)	95 ^{ab} (15.9)	176 ^{bc} (29.4)	28.3; 47.5 ^a 2.4; 23.4 ^b 16.1; 33.9 ^c	44.5* 6.0 29.4*	0.0001 - 0.0001
Right lung	195 (59.6)	- -	88 (14.7)	33.2; 54.52	49.1*	0.0001
Left lung	132 (40.4)	- -	32 (5.3)	18.6; 45.2	14.1*	0.0002
Both lungs	- -	- -	12 (2.0)	-	-	-

*Statistical significant difference $p \leq 0.05$. ^acomparison between patients with unilateral and bilateral involvement; ^bbilateral involvement and combined lungs and extrathoracic involvement; ^cunilateral involvement and combined lungs and extrathoracic involvement

Table 2 - Organ-preserving surgery consisted of closed echinococcectomy by methods Delbe's, echinococcectomy or lung resection by Bobrov-Spasocucotsky's or Vishnevsky's methods.

Methods	Organ-preserving surgery n (%)	Lung resection n (%)	95% confidence interval	Chi-square
<i>Methods of surgery</i>	536 (89.6)	62 (10.4)	68.4; 85.9	229.7*
Delbe's	281 (47.0)	- -	-	-
Bobrov-Spasocucotsky's	11 (1.8)	37 (6.2)	17.6; 25.6	0.3
Vishnevsky's	7 (1.0)	25 (4.2)	17.6; 25.6	0.3
One-stage bilateral thoracotomy with echinococcectomy	23 (3.8)	- -	-	-
One-stage bilateral video-assisted thoracoscopic echinococcectomy	30 (5.0)	- -	-	-
One-stage bilateral thoracotomy with echinococcectomy through transmediastinal access	9 (1.5)	- -	-	-
Two-stage bilateral thoracotomy with echinococcectomy	33 (5.5)	- -	-	-
One-stage thoracotomy with laparotomy	59 (9.9)	- -	-	-
Two-stage thoracotomy with laparotomy	84 (14.1)	- -	-	-
<i>Cyst-closing methods</i>				
Kulakeev's	176 (2.3)	- -	-	-
Capitonage	43 (7.2)	- -	-	-
<i>Treatment pathways of fibrous capsule cyst cavity</i>				
High-energy laser	109 (18.2)	- -	-	-
Low-frequency ultrasound	97 (16.2)	- -	-	-
Formalin	180 (30.1)	- -	-	-
Povidone-iodine	200 (33.4)	- -	-	-

*Statistical significant difference $p \leq 0.05$

the lesser sac in 22 (3.7%) patients, from the abdomen in 6 (1%) patients, from the greater omentum in 4 (0.7%) patients, and with a splenectomy in 8 (1.3%) patients. One-stage bilateral video-assisted thoracoscopic echinococcectomy was performed in 30 (5%) patients with pulmonary echinococcosis. Organ-preserving video-assisted thoracoscopic echinococcectomy is performed under general anesthesia with separate intubation of the bronchi, which allows the surgeon to shut down the lung in the vents on the operative side. The cyst is covered with povidone-iodine wet napkins to prevent inadvertent implantation of scolices or daughter cysts. The pipe tool punctures the cyst through a thoracoport with hydatidic fluid aspirates; without removing the needle, 10% solution of povidone-iodine as scolicidal agent injected (nearly the same amount of the fluid aspirated) for 3 minutes. The fibrous capsule is opened and the chitin membrane is removed. The fibrous capsule cavity is eliminated depending on the size of the application clips or suturing.

A method of removing bilateral echinococcosis cysts of the lungs through transmediastinal access, was developed by our center. In bilateral lung echinococcosis when hydatid cysts located in the upper lobe, and in any part of the other lung, we carry out a one-sided lateral thoracotomy, hydatid cyst removed from one lung, and then performed resection of retrosternal mediastinal pleura, cyst of the upper lobe of the other lung moved to retrosternal mediastinal approach and then performed echinococcectomy. Then 2 pleural cavities drained by 2 drainage tubes, one tube in the pleural cavity on the side of the thoracotomy, and second drain tube going through mediastinal approach to other pleural cavity, outputting the end of the tube through the chest wall on the side of thoracotomy. The advantages of this method is that the one-stage bilateral echinococcectomy using transmediastinal approach reduces the cosmetic defect

and reduces pain. This method was used in 9 (1.5%) patients, who had no postoperative complications.

Postoperative outcomes. A comparative study of the postoperative period features and the long-term results of treatment with a high-energy laser (HEL) was carried out in comparison with the treatment of cyst by formalin or povidone-iodine solutions (Table 3).

The worst results were after treatment of fibrous capsule with formalin solution ($p < 0.0417$). The frequency of complications after cyst treatment with HEL and povidone-iodine did not reach a statistically significant difference ($p \geq 0.05$). The treatment method for echinococcosis cyst with 10% povidone-iodine is the most simple, safe, and effective method. Presently in our center, HEL or a 3-time treatment with 10% povidone-iodine results in the cyst drying up; if a patient has an allergy to iodine, we treat the cyst with 70% alcohol.

Length of stay per hospital stay has been decreased ($p < 0.0001$) by video-thoracoscopic echinococcectomy with the HEL treatment of cyst, than after echinococcectomy by cyst treatment with povidone-iodine; finally, treatment with formalin presented the most longest hospital stay ($p < 0.0001$).

Complications. We noted postoperative complications in 139 (23.2%) of 598 operated patients. Complications resulted in death in 4 (0.6%) patients. In 45 (16%) of 281 patients with uncomplicated pulmonary echinococcosis, postoperative complications occurred, including one death from cyst removal with formalin. Complications from pulmonary echinococcosis occurred in 94 (29.7%) patients of 317 (53%); 3 of these resulted in death. Comparative analysis of patients with uncomplicated and complicated pulmonary echinococcosis showed a high frequency of postoperative complications associated with complicated echinococcosis (OR = 2.2, $p < 0.0001$). Mortality

Table 3 - Comparative characteristic of the postoperative period.

Comparative characteristic	Treatment methods of fibrous capsule							
	High-energy laser		Povidone-iodine		Formalin	95% confidence interval	Z statistic	P-value
	n	(%)	n	(%)	n (%)			
Complications	12 ^{a,b}	2.0	44 ^{a,c}	15.5	94 ^{b,c} (29.7)	15.6; 27.7 ^a 1.4; 38.2 ^b 2.5; 27.9 ^c	1.5 4.1* 3.2	- 0.0417 -
Hospital stay (days)	5.5±0.8 ^{a,b}		16.3±2.0 ^{a,c}		19.4±2.1 ^{b,c}	9.6; 11.9 ^a 12.7; 15.1 ^b 2.3; 3.8 ^c	18.2* 22.6* 8.2*	0.0001 0.0001 0.0001

*Statistical significant difference $p \leq 0.05$, ^acomparison results between high-energy laser and povidone-iodine, ^bbilateral involvement and Combined lungs and extrathoracic involvement, ^cunilateral involvement and combined lungs and extrathoracic involvement

Table 4 - Surgical complication frequency

Surgical complication	The course of pulmonary echinococcosis					
	Complicated n (%)	Uncomplicated n (%)	95% confidence interval	Odds ratio	Z statistic	P-value
Complications	94 (29.7)	45 (16.0)	1.5; 3.3	2.2	3.9*	0.0001
Deaths	3 (0.5)	1 (0.2)	0.2; 25.8	2.7	0.8	-

*Statistical significant difference $p \leq 0.05$

frequency has a direct relationship with complicated echinococcosis, but this relationship was not statistically significant (Table 4). Complications included reactive pleurisy in 47 (7.9%) patients, suppuration of the postoperative wound in 37 (6.2%) patients, bronchial fistula in 15 (2.5%) patients, and pneumonia in 14 (2.3%) patients. Less common complications were pleural empyema in 8 (1.3%) patients, residual cavities in the lung in 8 (1.3%) patients, pulmonary heart disease in 6 (1.0%) patients, and hemorrhage in 1 (0.2%) patient. Postoperative complications occurred in 17.6% of patients when applying the method by Delbe and in 18.6% when applying the method by Bobrov-Spasocucotsky. Postoperative complications occurred in 40% of the patients when applying the method by A.A. Vishnevsky. For patients with uncomplicated pulmonary echinococcosis, filling a cyst of fibrous capsule with vertical half purse-string Kulakeev suture resulted in postoperative complications in 22.7% of 176 (29.4%) patients. In the method of liquidation of the fibrous capsule, with capitonage carried out through a combination of horizontal and vertical sutures, no postoperative complications occurred during the 1 to 9 months after surgery.

There were no complications in the postoperative period in 9 (1.5%) patients after echinococcectomy via transmediastinal access, despite the extent of the surgical intervention: right-sided lateral thoracotomy, removal of the upper lobe of the right lung echinococcosis cyst, and subsequent removal of the echinococcosis cyst from the liver.

Discussion. Surgical intervention is the only radical method of pulmonary echinococcosis treatment.^{9,10} Important elements of surgical intervention are the technique of antiparasitic cavity treatment of the fibrous capsule and the elimination of the pulmonary cystic echinococcosis. The means used in antiparasitic treatment of the cavity must be effective while preserving the surrounding tissues. The elimination of an echinococcosis cyst cavity of the lung should be simple, non-traumatic, and effective, regardless of the

cyst size and the disease complications.¹¹ The prevention of intraoperative dissemination can be achieved by placing gauze with hypertonic saline solution (20%) or a povidone-iodine solution.¹² That's why the search for new, effective and safe methods of the echinococcal cyst cavity treatment of the lung remains relevant.¹³ Surgery is compulsory for large cysts that are superficial, infected cysts, and cysts located in vital anatomical sites.² The surgery by A.A. Vishnevsky's method is applied in medium, large, and giant cysts when two-thirds of the cyst are above the lung surface and only one third of the cyst volume is in lung parenchyma. Whereas, small bronchiolar fistulas are treated thorough suturing by necessity, but postoperative complications often develop.^{14,15}

Capitonage cystostomy is the preferred method of echinococcosis hydatid treatment. Cystostomy includes aspiration of cyst fluid and eliminating of growing membrane (Barrett's techniques).¹⁶ Capitonage is complete closing of the cyst by suturing the cyst's wall. The method provides extra strength of lung parenchyma and prevents subsequent dissemination through air and formation of empyema.^{17,18}

The primary criteria for lobectomy are cysts involving more than 50% lung lobe; festering cysts that are unresponsive to antibiotic therapy; multiple cysts that are located inside one lobe; and echinococcosis with the bronchiectasis, pulmonary fibrosis, or severe hemorrhage. The method of choice for small and medium cysts, which are located intraparenchymally, and are mostly uncomplicated and cylindrical and conical type, is a method of closed echinococcectomy, according to Delbe.⁶

In the case of multiple cysts, priority should be given to cysts that are more likely to rupture, are of larger size, and may possibly disseminate. Large cysts require certain management of the residual space to avoid postoperative dissemination through air and formation of empyema.^{19,20}

With combined pulmonary echinococcosis with involvement of abdominal organs, surgery should start from pulmonary echinococcosis, considering

the possibility of high risk for developing pulmonary complications.²¹ An echinococcosis cyst from the opposite lung should be eliminated with bilateral pulmonary echinococcosis, which allows a one-stage bilateral echinococcectomy of an upper lobe right liver cyst with subsequent elimination of echinococcosis cysts from the liver. The patients with combined bilateral pulmonary lesion and liver and spleen damage are good candidates for cystectomy laparotomy after bilateral phased thoracotomy and echinococcectomy of the lungs.²² In cases of one-stage bilateral echinococcectomy thoracotomy, surgery should be started on the side of the largest cyst or with the largest threat of complications. However, this method is traumatic, and can lead to respiratory failure and increased risks of postoperative wounds in the early postoperative period. Video-assisted thoracoscopic surgery is a useful method for elimination of surface and small or moderate-sized hydatid cysts, with less morbidity compared with the usual surgery method.²³ To reduce surgery-related trauma, reducing the duration of the operation and the postoperative period using a bilateral one-stage sequential video-assisted thoracoscopic echinococcectomy from both lungs is effective.^{24,25} The method of one-stage surgical treatment and 2-stage pulmonary echinococcosis via transmediastinal access to the eliminated right pulmonary echinococcosis and liver, through one skin incision with the use of video-assisted thoracoscopic techniques allows the reduction of trauma and the length of treatment, and patients are relieved to avoid the next-stage operations and repeated anesthesia.

This study has revealed significant proportion of complications within patients with complicated course of pulmonary echinococcosis. One of the limitations of this prospective study is the distance, because patients, with echinococcosis are pretty much about rural population, its make difficult to patients recruiting, early disease detection and monitoring of them. However, the findings highlighted the common tactic that may guide reduce of postoperative complications level and substantiate the need for further prospective studies.

In conclusion, despite the surgical treatment success of pulmonary echinococcosis, issues of intraoperative dissemination, safety, and treatment success are still a problem. Through detailed multi-center studies the researchers will be able to best define the complications risk and relapse, choice of optimal strategies for effective surgical treatment.

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