To

Members of the Scientific Jury

Order No. RD- 26-683/03.04.2023

of the Executive Director of the University Hospital "N.I. Pirogov EAD competition for the acquisition of educational and scientific degree "DOCTOR" in the scientific specialty "Pediatric Surgery".

I submit a Review

Professional field : 7.1 Medicine

Doctoral programme: Paediatric surgery

Free PhD student: Dr. Nikola Kostadinov Kartulev

to the Primary Scientific Unit of Pediatric Surgery of the University Hospital "N.I. Pirogov EAD - Sofia.

Scientific supervisor: prof. dr. Hristo Ivanov Shivachev, PhD

Prof. Dr. Alexander Chervenyakov, PhD, DsC

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R E C E N T I O N S

From

Prof. Dr. Alexander Chervenyakov, PhD - SofiaMed University Hospital - Medical Faculty of Sofia University "St. Kl. Ohridski" - Sofia, Clinic of Thoracic Surgery

of dissertation work

BRONCHOSCOPIC OBTURATION FOR PERSISTENT AIR LEAK AFTER VIDEO-ASSISTED THORACOSCOPIC ABSCESSOTOMY IN CHILDHOOD

of Dr. Nikola Kostadinov Kartulev

For the award of the doctoral degree

1. General presentation of the procedure and the PhD student

The submitted set of materials on paper and electronic media is in accordance with the requirements of the Law on the Development of Academic Staff of the Republic of Bulgaria, the Regulations for its implementation and the Regulations for the Development of Academic Staff of the University Hospital "N.I. Pirogov" EAD - Sofia. The set of documents is complete and containsДисертационен труд;

1. Abstract;
2. Autobiography;
3. Diplomas and certificates;
4. List of publications and participation in scientific forums;
5. Reference for fulfillment of the scientific-metric criteria;
6. Administrative documents in accordance with the Regulations for the Development of the Academic Staff of "UMHATEM N.I. Pirogov" EAD - Sofia - orders for enrolment, dismissal, scientific jury, declarations of conflict of interest and authenticity of the data presented;

The doctoral candidate has applied 4 publications in connection with the dissertation. In two of them he is the first author.

2. Short biographical data about the PhD student

Dr. Nikola Kostadinov Kartulev graduated in medicine at the Medical University - Sofia. He graduated from the University of Sofia in 2014. He obtained his medical specialty "Pediatric Surgery" in 2020. He is currently specializing in Thoracic Surgery. He received additional professional qualification in the field of laparoscopic surgery with trainings such as Advanced Course

Laparoscopic Neonatal Surgery, Naples, Italy /07.2016/, Fresh-up Laparoscopische hirurgie, Bochum, Germany /03.2017/, Endoscopy Summer School, Sheffield, United Kingdom /06.2022/, 2021. Certificate - Conventional Gastrointestinal Endoscopy, 2022 Certificate - Interventional Gastrointestinal Endoscopy, 2023 Certificate - Bronchology Level I, 2024 Certificate - Bronchology Level II.

He is a member of the Society of Paediatric Surgery and SCIOP EUROPE.

After graduating as a physician, Dr. Kartulev started as an attending at the Pediatric Surgery Clinic in 2015 for a period of five months. After obtaining his specialty in 2020, he remained working in the same structure until the present moment.

He is fluent in written and spoken English.

3. Relevance of the topic and appropriateness of the aims and objectives

The dissertation work is extremely topical due to the significant problems with the treatment of purulent lung diseases with the development of destruction and bronchial fistula. He developed and applied video-assisted thoracoscopic surgery (VATS) in 2004 as a routine intervention in children with PPU and PPPU at the Pediatric Surgery Clinic of the N.I. Pirogov University Hospital. It described the possibilities of minimally invasive management and faster recovery in these patients, replacing completely open surgical techniques as the primary choice in this nosological entity.

4. Knowledge of the problem.

Dr. Kartulev is a specialist with established experience in minimally invasive bronchoscopic obturation. Already in the literature review of the dissertation, the author's professional erudition makes an impression. For the period 01.2015 to 12.2023 in the Department of Pediatric Thoracic Surgery at the Clinic of Pediatric Surgery of the University Hospital "N.I. Pirogov" were treated 120 children with PPU. Only patients aged up to 18 years in whom the inflammatory process occurred in a normally developed lung were included in the clinical material. Patients in whom PPPU developed with concomitant pathology such as:

- congenital anomalies (CPAM)
- parasitic cysts
- specific inflammatory process

5. Research methodology

For the purpose of the clinical material, a wide range of diagnostic and therapeutic methods were used to create a comprehensive management algorithm for children with PPU.

1. History - onset of complaints and course of the disease, outpatient and/or hospital treatment, concomitant diseases and allergies.

2. Physical status - general condition, inspection, palpation and percussion of the chest and auscultation of the lung. The presence and severity of DN is assessed.

3. Laboratory tests:

a. standard panel of blood tests - Complete blood count, biochemistry, CPR, coagulogram, blood group.

b. Biochemical examination of pleural exudate - pH, LDH, protein, glucose

c. Microbiological testing

- Nose secret
- Throat swab
- Anal discharge
- Haemoculture
- Pleural exudate secretion
- Material from necrotic lung parenchyma
- Tracheobronchial secretion
- Broncho-alveolar swab

4. Histological study:

a. Cytological examination of pleural exudate

b. Pleural schwarts

c. Lung parenchyma

5. Imaging:

a. Chest and lung roentgenography/roentgenoscopy - the presence and size of pleural effusion, its mobility, the presence of encapsulated collections or intraparenchymal cavities are assessed.

b. Ultrasound as a routine investigation is the method of choice due to its easy accessibility and lack of radiation exposure for patients. It can assess not only the volume of pleural effusion but also its consistency as well as changes in the lung parenchyma.

6. Characteristics and evaluation of the thesis

Structure, scope; aim; objectives; subject; main thesis; scientific literature used.

The dissertation contains 118 pages and a 10 page Bibliography. It is illustrated with 62 figures and 19 tables. The bibliography contains 124 references.

1) Contents, abbreviations and introduction - 6 page
2) Literature review - 34 pages
3) Aims and Objectives - 1 page
4) Clinical material - 6 pages
5) Methods - 11 pages

6) Results - 18 pages

7) Comparative analysis - 9 pages

8) Discussion - 10 pages

9) Discussion - 41 pages

10) Conclusions and conclusion - 2 pages

11) Contributions - 1 page

12) Bibliography - 9 pages

The literature review is well structured and of sufficient length. It reflects the problem in a multifaceted and comprehensive way. Indicates in a separate section basic definitions of different types of pneumonia and pleuro-pulmonary complications, gives a classification in tabular form of seven classes of pleural effusion. A separate section is devoted to PAL with historical data, definitions, classification, clinical presentation, pathogenesis, treatment methods, bronchial valves, silicone blockers, chemical pleurodesis, etc.

The aim and objectives are clearly and concretely defined, being fully in line with the scientific topic of the thesis. The aim is consistent with the complex treatment and adequate evacuating of the pleural and abscess cavity and the elimination of persistent air loss due to lack of airtightness, with the advantages of minimally invasive methods. The 5 naturally derived tasks show an in-depth knowledge of the problem. Through them, the efficacy of minimally invasive bronchoscopic obturation with a synthetic blocker is evaluated. Specific indications for the development of a diagnostic and therapeutic algorithm for the application of the method are determined. Early and late results are evaluated and the results of the method are compared with others used in practice. Development and implementation of this technique as a routine procedure in the practice of the Pediatric Surgery Clinic.

Material and methods

Our own results are structured according to the presented five tasks and the data obtained in them, as 120 children with PPU treated in the Department of Pediatric Thoracic Surgery at the Clinic of Pediatric Surgery of the University Hospital "N.I. Pirogov" were followed up for a period of nine years.

For the purpose of the study, the patients were divided into three groups according to the course of the disease and the treatment methods used:

Group A - patients aged up to 18 years with lung abscess, in whom VATS abscessotomy was performed and air leak was spontaneously discontinued within 48-72 hours. In this group, no additional surgical or interventional manipulations were needed.

Group B - Patients aged up to 18 years with lung abscess in whom VATS abscessotomy and subsequent TT with resection of lung parenchyma due to PAL was performed.

Group B - patients aged up to 18 years with lung abscess who underwent VATS abscessotomy followed by bronchoscopic obturation due to persistent air leak.

Detailed demographic characteristics of the patients studied are given.

Much of the clinical material and characteristics are presented and illustrated in tabular form. Clinical and diagnostic methods used for the purpose of clinical material are described in detail - history, physical status, laboratory tests, histological examination, imaging. The statistical methods used for processing the obtained data are descriptive (quantitative and categorical), Kolmogorov-Smirnov test, Chi-square test, Kruskal-Wallis nonparametric test

The obtained results are presented in three groups according to the course of the disease and the different methods of treatment:

Group A - 57 patients aged up to 18 years with lung abscess who underwent VATS abscessotomy in whom air leak was spontaneously discontinued within 48-72 hours. No further surgical or interventional manipulations were required in this group.

Group B - 10 patients aged up to 18 years with pulmonary abscess who underwent VATS abscessotomy followed by TT with resection of lung parenchyma due to persistent air leak.

Group C - 50 patients aged up to 18 years with lung abscess who underwent VATS abscessotomy and subsequent bronchoscopic obturation for persistent air leak. Outside of the patient groups presented, bronchoscopic obturation was performed in 3 children with lung abscess with minimal pleural reaction and 1 child with PAL due to traumatic lung injury. These patients were not included in the comparative outcome analysis because of their small numbers and different disease course. Their results are presented separately from the other patients and illustrate the broader application of the methodology.

In the chapter "Comparative analysis" on demographic and clinical parameters a detailed presentation of the results is made as a transition to the next chapter "Discussion". It provides a detailed analysis of the data describing the construction of the overall management and follow-up algorithm not only for children with persistent air-liquids, but also further building on the previously validated treatment algorithm for PPU in the Pediatric Surgery Clinic.

Nine conclusions are formulated , based on the results of the presented work and derived from the study, and are a logical summary of the scientific work.

7. Contributions and Significance of the Development for Science and Practice

The following contributions of the dissertation are outlined:

1. A detailed literature review on the possibilities offered by minimally invasive methods in the treatment of patients with persistent air leak.

2. The advantages of bronchoscopic obturation over conventional surgical methods are demonstrated. The time of prolonged drainage was reduced by an average of 3.7 days and the hospital stay by an average of 5.66 days. Success rate of bronchoscopic obturation was achieved in 94% of cases. Operative intervention was required in three children (6%) after failed obturation. Only atypical resections were performed in the area of one lung segment. In contrast, in the group in which TT with resection was performed, the loss of lung parenchyma was in 100% of cases and in different volumes - from atypical resection to lobectomy.

3. Introduce manipulation as a routine procedure in practice and build on the existing management algorithm for patients with PPU.

4. The learning curve established criteria for the timing and duration of bronchoscopic obturation.

5. The methodology achieved success not only in patients after VATS-abscessotomy. This allows for the application in other diseases progressing with air leak for which further study of the effect of the procedure is necessary

8. Assessment of publications on the thesis

Dr. Kartulev has submitted a list of 39 publications, participation in scientific forums with papers and posters as related to the dissertation work are four of them, one publication with IF 2,9.

9.Personal participation of the PhD student

The dissertation is the personal work of the PhD student, under the supervision of his supervisor, showing very good theoretical knowledge and practical skills to carry out independent research.

10. Abstract

The abstract is prepared according to all requirements and adequately presents the scientific work. It reflects the content and the main results of the dissertation.

CONCLUSION

I have known Dr. Kartulev since he joined the Pediatric Surgery Clinic at UMHATEM. "I have witnessed his improvement and development as an established and sought-after specialist with a concern for patients and constant professional improvement. The dissertation work of the free doctoral student Dr. Nikola Kostadinov Kartulev "Bronchoscopic obturation in persistent air-leak after video-assisted thoracoscopic abscessotomy in childhood" is devoted to a topical problem in modern pediatric surgery. It contains scientific and applied results that represent an original contribution to science and fully meet the criteria for the award of the

degree of Doctor of Education and Science. The scientific work complies with the requirements of , the Implementing Regulations and the relevant Regulations of the University Hospital "Pirogov".

This gives me reason to give my positive evaluation of the conducted research, dissertation, abstract, achieved results, conclusions and contributions, proposing to the esteemed Scientific Jury to award the educational and scientific degree "Doctor" in the scientific specialty "Pediatric Surgery" to Dr. Nikola Kostadinov Kartulev.

22.05.2024 Reviewer: ……ATchervenyakov

Sofia / Prof. Dr. Al. Chervenyakov, Ph.D/.