

REVIEW

By prof. Krasimir Antonov Antonov, MD, PhD

Clinic of Gastroenterology, University Hospital "Sv. Ivan Rilski",

Department of Internal Diseases, Ministry of Finance, MU-Sofia

About the dissertation of dr. Krasen Zdravkov Ivanov, PhD student in "Internal Diseases" at "Acibadem City Clinic, University Hospital Tokuda" on the topic "MALIGNANT ASCITES AND PLACE OF PERITONEAL TUNNEL CATHETERS IN THEIR TREATMENT" with supervisors prof. Simeon Stoynov, MD, PhD for awarding educational and scientific degree "Doctor" in the field of higher education 7. Health and sports, professional field 7.1. Medicine, Ph.D. program "Internal Medicine".

The dissertation work of Dr. Krasen Ivanov is dedicated to a topical problem in modern gastroenterology-oncology, namely the place of peritoneal tunnel catheters in the treatment of malignant ascites. The role of tunnel peritoneal catheters has not been sufficiently studied. Worldwide, there is a lack of sufficient data and studies on many aspects related to the pre- and post-procedural period. The study of these aspects could contribute to the creation of a selection algorithm for patients suitable for this procedure.

The dissertation work is presented in a fully finished form. It is structured correctly and consistent with the generally accepted requirements – introduction, literary review, goals and tasks, materials and methods, results and discussion, main conclusions and contributions, bibliography. It is written in clear scientific Bulgarian on 112 pages.

The introduction is in a volume of 2 pages and in concentrated form overlaps the literature review.

The literature review, written on 28 pages (25% of the volume of the dissertation) is fully up to date. The bibliography contains 136 literary sources, of which 4 are in Cyrillic and 132 – in English. There have been a total of 12 publications from the last 5 years.

The aim is clear – to study the causes, characteristics and features of the course of ascites associated with malignancies in order to determine the role, location and results of the application of tunnel peritoneal catheters.

The seven tasks are adequately selected and their implementation ensures the achievement of the set goal.

The chapter "Material and Methods" covers 15 pages. It describes in detail the experimental models, the persons examined and the applied research methods, as well as the statistical analyses used, which are modern and correspond to the nature of the object under study.

The study included 124 patients who underwent the tunnel peritoneal catheter induction procedure in the period 2016 – 2023. The study was retrospective in nature and included patients who had passed through the Department of Gastroenterology of Acibadem City Clinic UMHAT Tokuda

EAD, with whom a tunnel peritoneal catheter was placed. The source of the information is the history of disease, medical history, protocol of procedures and data from patient follow-up.

The results obtained are original and are reflected on 40 pages. The more significant of these are:

In the study group of patients over 70% have ascites fluid with characteristics of exudate and are about 4 times more than patients in whom the characteristics of ascites are as transudate, which in turn shows us that patients in whom the pathogenetic mechanism for the occurrence of ascites is portal hypertension are much less than those in which the leading mechanism is peritoneal carcinomatosis.

In 53 patients (42.7%) the cause of ascites is peritoneal carcinomatosis, in 33 patients (26.6%) portal hypertension caused by massive liver metastases or liver cancer was found. In 38 patients (30.6%) a combination of peritoneal carcinomatosis and portal hypertension was observed.

Among the examined patients, 4 types of ascites were macroscopically found – serous, fibrinous, hemorrhagic and chylotic. There is no statistically reliable relationship between the macroscopic appearance of the ascites fluid and the pathogenetic mechanism that led to its occurrence ($p=0.673$).

A statistically significant relationship ($p=0.007$) was found between the mean neutrophil values and the macroscopic appearance of the ascites fluid.

The introduction of a tunnel peritoneal catheter in patients receiving active chemotherapy, radiotherapy or immunotherapy for the underlying cancer leads to lasting relief of ascites-related symptoms and improves patients' ability to treat their underlying disease.

In patients who are on palliative type of treatment, there is a lasting relief of symptoms after insertion of a tunnel catheter and a reduction in the need for hospitalizations and travel to hospitals for the occasion of ascites syndrome. These palliative patients have an improvement in the quality of their lives.

A statistically significant relationship ($p=0.001$) is found between the ECOG status of patients and the life expectancy and operation of the device (catheter days).

A statistically significant relationship ($p=0.001$) was found between the ECOG status of the patients in the study and the complications that occurred.

T-test results showed that patients with complications were more likely to have lower INR values ($p=0.042$).

In the majority of patients, catheter days were also consistent with life expectancy, with only 9 patients requiring catheter removal due to severe complications, and 5 patients had the catheter removed due to a good response to chemotherapy and stopping ascites accumulation.

About 26% of patients survive up to 100 days after insertion of a tunnel catheter, and up to 200 days survive only 8%.

Spearman's correlation analysis showed a significant correlation between catheter days and hemoglobin values ($R=0.217$, $P=0.015$).

The average number of visits to hospital after insertion of a catheter was significantly lower than the number of visits before insertion of a catheter ($p<0.001$).

On the 30th day after the introduction of a tunnel catheter, a statistically significant relationship was found in a positive plan in 8 symptoms ($p=0.001$). These are the symptoms pain, general weakness, nausea, drowsiness, appetite, shortness of breath, bloating and impaired mobility.

Presence of worsening of some of the symptoms, such as depression, anxiety, where a statistically significant relationship is found in negative terms ($p = 0.001$).

The discussion of the results is in-depth, based on the available world scientific information concerning the topic under consideration and is on page 9.

The 13 conclusions drawn correspond to the results obtained.

The contributions are 7 of a scientifically applied and methodical nature. From them I would distinguish:

A new for the country methodology is presented - tunnel peritoneal catheter for the treatment of refractory malignant ascites. The study is the first of its kind in the country on its own series of patients, assessing the effectiveness and safety of these devices, and the results obtained are in line with those of international centers and authors. Its own algorithm for selection of the appropriate patients and indications for performing the procedure itself is presented.

The causes and laboratory characteristics of ascites fluid in patients with malignant ascites were analyzed and the diagnostic value of the serum-ascites albumin gradient was evaluated to specify the etiology and pathogenesis of ascites. The quality of life and survival of patients with advanced oncological diseases and malignant ascites was also assessed.

I fully accept the conclusions and contributions of the dissertation pointed out by the author.

In summary, the results of the dissertation Dr. Krasen Ivanov are original and are the work of the dissertant himself. They have a scientifically applied significance and lead to the expansion of our knowledge in the field of treatment of malignant ascites.

Dr. Krasen Ivanov presents a list of 8 publications and participations in national and international scientific forums related to the topic of the dissertation.

Based on the above, I believe that Dr. Krasen Ivanov's dissertation fully meets the requirements of the Law on the Development of Academic Staff in Bulgaria and the terms and conditions for acquiring academic degrees, which is why I give my positive assessment with conviction.

I call on the honorable members of the scientific jury to vote "Yes" for the award of NSA "Doctor" to Dr. Krasen Zdravkov Ivanov

18.12.2023

/Prof. Dr. K. Antonov, MD, PhD/

