

## OPINION

for

**the dissertation on the topic of**

**"ENDOVASCULAR TREATMENT OF TYPE "A" AND TYPE "B" DISSECTION OF THE AORTA"**

for the awarding of educational and scientific degree "Doctor" in the scientific specialty "cardiology" with cipher. 03.01.47 of Dr. Zoran Stankov, with scientific director Prof. Dr. Ivo Petrov, PhD, University of Sofia

Introduction. The thesis sent for review is written on 179 standard typewriter pages, bibliographical reference, and applications. It is properly structured, contains all mandatory parts and meets the requirements.

Dissecting aneurysms of the aorta and aortic diseases are socially significant diseases, leading to relatively high mortality or disability of patients. In recent years, due to the accumulated experience and the application of new diagnostic and therapeutic methods, some success has been achieved in the diagnosis and treatment of this disease. However, there are still uncertainties both in terms of the etiology and pathogenesis of this disease, and with regard to the choice of therapy – surgical, endovascular or medicated. The application of endovascular treatment of dissecting aneurysms in high-risk patients of type A and in type B dissections, as well as the application of hybrid therapeutic methods changes both therapeutic approach and long-term results. However, there are no protocols for therapeutic behavior, including all variants of the disease.

In Bulgaria there are scientific studies on the surgical treatment of type A dissections, but no scientific studies have been conducted on endovascular treatment of dissecting aneurysms type A and B. The study of this problem, with the development of diagnostic and therapeutic models of behavior for the great application of endovascular treatment, as well as taking into account its effectiveness, has scientific value both for Bulgaria and global medical science and practice. Any additional information in this area would be useful in managing this severe vascular disease.

Dr. Stankov's thesis is focused precisely in this field, which makes it up-to-date and timely.

Literary review. The literary review is written in 69 pages and is supported by 187 literary references, of which 3 in Cyrillic and the rest in English.

The literary overview presents comprehensive information about the state of scientific knowledge of the diagnosis and endovascular treatment of dissections type A and B. The thorough information shows knowledge in depth of the problem, the ability to analyze the open information and creative arrangement in its most essential elements. The complex study of the problem by presenting the most modern achievements in every important aspect shows

an excellent knowledge of both literature and matter. There is a definite ability for analytical and synthetic thinking. Each problem is addressed both comprehensively and critically, highlighting the results achieved so far and identifying all the under-explored aspects, indicating the way for the results. There is nothing superfluous or unrelated to the problem studied.

The literary review discusses the following more important scientific issues:

Aortic syndrome, its pathophysiology and the importance of some of the known risk factors are discussed.

DeBakey and Stanford's classifications of dissecting aneurysms of the aorta are presented.

The more important clinical symptoms and more important diagnostic methods – CT scan, MRI, Echocardiography, angiography, in the dissections of the aorta are described.

The main therapeutic methods are discussed – surgical, endovascular, hybrid, in the case of dissecting aneurysms, their results and complications.

Different types of hybrid techniques are discussed in the treatment of dissections – chimney technique, de-branching technique, in dissections type A and B.

The good results from the surgical treatment of type A dissections and excellent results in endovascular treatment of dissections high-risk patients as an alternative to surgery.

Very good results are presented in endovascular treatment of type B dissections.

Surgical treatment of dissecting aneurysms type B is poorly effective and with high mortality. According to many authors, Malperfusion syndromom, developing in dissecting aneurysms of the aorta, leads to severe, fatal complications if not treated in a timely manner.

In 10-30% of cases with the treatment of dissecting aneurysms of the aorta, at the second stage, re-intervention is required.

The recommendations of the European and American associations for the treatment of dissecting aneurysms and the administration of TEVAR are presented.

By analyzing the data from the literary review, the author makes the following more important conclusions:

There are no reliable data on the indications and results of endovascular treatment of dissecting type A aneurysms as an alternative to surgical treatment.

There are no clear criteria for indications and methods of endovascular or hybrid treatment in type B dissections as an alternative to drug treatment.

There are no developed behavior algorithms in patients with acute aortic syndrome, complicated by malperfusion syndrome.

There are no developed behavior algorithms in patients with persistent dissection and an increase in false lumen after the conducted "proximal" treatment - surgical or endovascular.

The role of uncovered stents of the aorta and its branches has not been established, to improve blood flow in the real lumen and reduction of blood flow and thrombosis in the false lumen.

## 2.Objective, tasks, material and methods.

The purpose of the dissertation work is to establish the effectiveness of endovascular treatment in type A and type B dissection of the aorta.

In order to achieve the formulated objective, the author sets himself 6 main tasks:

They are generally worded as:

Perform an imaging and invasive diagnostics of dissecting aneurysms,

Perform an endovascular treatment and report early and late healing effect.

To identify and analyze complications.

To monitor the effect of treatment within a one-year period and in indications – to perform repeated endovascular interventions.

To design a diagnostic and therapeutic model of treatment of patients with dissection type A and type B.

These tasks can achieve the objective set and contributing to increasing knowledge in the field under study.

The material used to perform the formulated tasks covers a total of 70 patients, who are divided into 2 groups, respectively 14 in the Stanford type A aortic dissection group and 56 in the group with aortic dissection type B.

The risk factors for dissecting aneurysms for the two studied groups are described – hypertension, dyslipidemia, diabetes mellitus, smoking, family history, ischemic heart disease. No statistically significant difference in the incidence of risk factors was found for the two groups studied.

The clinical material used is sufficient to realize the tasks assigned and allows reliable results to be obtained.

The methods used are clinical, laboratory, imaging and statistical. State-of-the-art methodologies have been applied, which are in order to fulfill the assigned tasks and achieve the main objective. The most important diagnostic methods are: computer tomography with contrast, aorto and angiography, echocardiography with TEE and TTE, MRI.

An appropriate set of a variety of statistical methods has been used to obtain reliable results.

Numerous protocols are described - the stent-graft implant protocol used, a Manta closure device closure protocol and a Proglide closure device, a "preclose technique".

The materials, methods and order of the studies carried out are clearly described as allowing an understanding of their nature.

3. Analysis of the results obtained. The results of the studies conducted are correctly presented, richly illustrated with evidence and include 41 tables and 68 figures. The results are described in 74 pages, including analysis of the results.

The overall result of endovascular treatment of dissecting aneurysms type A and B was positive in 97% of cases, with relatively low mortality – 2.8%.

The results of endovascular treatment in type A dissections are shown and analyzed:

In 11 out of 14 patients in this group, primary surgical treatment of dissection was performed in patients, followed by endovascular, and in the other three, due to high operational risk, endovascular treatment was carried out independently.

The frequency of risk factors for dissection in this group is presented.

Malperfusion syndrome is found in the arteries of the aortic arch, visceral, renal and peripheral arteries, which has required endovascular treatment to improve perfusion.

A high rate of engagement of truncus brachiocephalicus -71.4% was found - requiring its stenting at 21%, a. subclavia sinistra.- at 71% - required stenting and at 37%, affecting the visceral arteries at 57% - required stenting at 14% of a. mesenteric sup., affecting renal and arteries in 64% - requiring stenting in 14%, affecting the common iliac arteries in 57% of cases, necessitating stenting in some of the cases.

In 78% of cases, there was more than one entry.

Overall, the procedural success of endovascular treatment of type A dissections was very good – 92.9% , in 7.1% failure and zero early mortality. At 28% it was necessary to perform balloon dilation of a stent – graft. When monitoring patients over time, in 31% of cases reintervention was required due to re-dissection or endoleak.

In a total of 56 patients in this group, endovascular treatment of the dissecting aneurysm of the aorta was performed.

The results of endovascular treatment in type B dissections have been given and analysed:

Malperfusion syndrome is found in truncus brachiocephalics, carotid and subclavian arteries, visceral, renal and peripheral arteries.

Involvement of truncus brachiocephalics occurred in 5% of cases, of which the left subclavian artery – in 57% of cases, of visceral arteries – in 57% of cases – of which in 25% truncus celiac disease was affected, and in 12% mesenteric superior, affecting renal arteries – 69% of cases, of iliac arteries 71% of cases.

In 80% of cases, there was more than one entry.

Early procedural success from endovascular treatment of type B dissections is very good – 98.2 % successful procedure, early mortality is in only one patient. By the 30th day after the procedure, the mortality rate was 14%. Or overall – successful procedure – in 82.1%, early mortality – 3.5%, mortality up to 30 days – 14.3%.

At 12.5% a hybrid procedure was performed – debranching, by-pass, or chimney technique.

Postdilation of endoprosthesis was conducted in 23% of the cases, endoleak after postdilation was evident at 12% of the cases.

Need for more than one stent graft – at 63%.

In 16% of cases, a single stenting of the femoral arteries was performed to gain good access.

In 25% of cases, reintervention was required due to endoleak dissection progression or re-dissection (most commonly retrograde).

The discussion presented three clinical cases – two with type A dissection and one with type B dissection, successfully treated endovascularly.

#### **4. Discussion**

The discussion analyses again the alleged risk factors for the development of dissecting aneurysms of the aorta – arterial hypertension, dyslipidemia, smoking, diabetes mellitus, family history, renal failure and ischemic heart disease. Comparison is done with the results of other authors.

Data from the literature regarding the involvement of truncus brachiocephalic, carotid and subclavia arteries are cited. The data are contradictory, and the frequency of involvement of these vessels in aortic dissections is significantly lower than the data found in the dissertation work. The same phenomenon was found when comparing the results of other studies in terms of the frequency of involvement of visceral arteries, with scarce data on the frequency of involvement of iliac arteries, while this study found a relatively high incidence of peripheral arteries involvement.

The same applies to the frequency of Malperfusion syndrome, which has a significantly higher frequency in dissections type A and B compared to literary data.

In the literature, no definitive data are found on the frequency of acute renal failure due to malperfusion syndrome, as well as the frequency of involvement of the renal arteries by AD.

The excellent procedural success of endovascular treatment of dissecting aneurysms type A and B, with a low mortality rate, which is established in the dissertation work is completely comparable to the world results in this field.

Particularly valuable are the excellent results found in high-risk patients from type A dissections.

The application of hybrid procedures, simultaneous vascular stenting and reinterventions with implantation of an additional aortic stent graft for the treatment of endoleaks, or re-dissection, make the scientific work original and at a high scientific level.

Completely original are also the data presented in the discussion about examining the dimensions of the real and false lumen in each patient before intervention and six months after the procedure. The results showed a statistically significant change in the dimensions of the real and false lumen in the direction of positive aortic modeling.

Of course, a number of other data have been exported and compared, but the main results are sufficient to draw the scientific conclusions of this dissertation.

**5. Conclusions** drawn are a logical consequence of the results obtained. They are a synthesis of all significant results and clearly and accurately formulate their qualities, importance for theory and practice.

The conclusions summarize the most important results from the dissertation work. They are as follows:

Endovascular treatment of dissections type A and B is an effective treatment method with a low incidence of complications.

It successfully combines with hybrid treatment and is a real alternative to the surgical treatment of type A dissections in high-risk patients.

Concomitant dissection malperfusion syndrome has a high frequency, affects the arch of the aorta, visceral, renal and peripheral arteries and untreated, is associated with severe complications and high mortality, which requires additional vascular interventions.

Successful endovascular treatment in AD type A and type B leads to a significant increase in the size of the true lumen and reduction of the false lumen, which leads to a decrease in the risk of aneurysm and rupture and improvement in perfusion. With decompression of the maximum dissected segment using uncovered stents, the re-intervention frequency is significantly reduced.

Endovascular methods of treatment of AD type A and type B are a modern alternative to surgical correction and drug treatment.

Treatment of aorta dissection is most often complex, involving both endovascular and surgical treatment. It is not a one-time act, but requires periodic diagnostic control and, if necessary, operational and/or endovascular corrections of the complications that have arisen.

## **6. Evaluation of the dissertation work**

The thesis under consideration is dedicated to an extremely important field of modern medicine and cardiology. Properly set and constructed, the scientific study realizes the goal set. The results obtained are clear, supported by statistical credibility, comparable and extremely important are theory and practice.

The dissertation work proves the effectiveness of endovascular treatment of dissecting aneurysms of the aorta type A and B, as well as the great importance of malperfusion syndrome requiring the application of complex therapeutic options– endovascular, hybrid and surgical.

For the first time in Bulgaria, a large study is carried out on the endovascular treatment of dissections of the aorta type A and B and the therapeutic possibilities are explored.

It is established that endovascular treatment is a method of choice in dissections type B. Dissections type A and B lead not only to aneurysms and ruptures, but also to malperfusion syndrome, requiring secondary endovascular, or hybrid revascularization. This conclusion is especially valuable for both theory and clinical practice.

Endovascular therapy in type A and B dissections has been found to significantly increase the true lumen, which leads to an improvement in perfusion.

It is proven that the modern treatment of dissecting aneurysms of the aorta is complex and/ or hybrid.

These are important and original theoretical contributions of the dissertation work.

The other contributions shall be of a confirmatory nature and may be formulated in such a way:

Endovascular treatment of dissections type A and B is effective and safe.

The frequency and endovascular treatment of malperfusion syndrome has been studied.

Endovascular treatment of aortic dissection type A is an alternative to a surgery or hybrid one in patients with very high perioperative risk.

Endoleak is a major cause of reinterventions, and balloon dilation is an effective method of its treatment.

Dissecting aneurysms type, A and B require periodic diagnostic control and, if necessary, endovascular corrections.

In general, the dissertation work has many qualities. It has a number of original and confirmatory contributions.

## **7.Critical notes.**

On the literature review:

In the literary overview on the problem, only three Bulgarian publications are quoted, which seems insufficient to me.

There are a number of things that have no direct connection to the research problem. For example, the overview looked at pathophysiology, epidemiology, risk factors and symptoms of dissecting aneurysm of the aorta.

With regard to the material:

Data on suspected risk factors were presented in patients in both groups, but due to the relatively small number of patients studied, especially in type A-14 and the lack of a control group, the results had no scientific value both as standalone values in the group and as a comparison between the two groups.

The discussion again discusses the risk factors for dissecting aneurysms, which due to small groups and the lack of a control group has no real scientific value. The exception is the results for a high incidence of renal failure, established in dissecting aneurysms.

Some of the data exported, the place of which is in "results", are presented in the "discussion". For example, the implantation of an additional aortic stretch and the change in the real and false lumen after endovascular treatment. The discussion analyzes already exported data and compares it with those of other authors.

Unfortunately, the task is not accomplished: To design a diagnostic and therapeutic model of treatment of patients with dissection type A and type B. This task is of course extremely difficult, and although there are some ideas for such a model in the work, in general it is not implemented and can be the subject of further studies.

The problem of malperfusion syndrome in the arteries of the lower extremities, clinically manifested as PAB – peripheral arterial disease, has not been thoroughly studied.

Although it has been established, the fact that there is a very high percentage of malperfusion syndrome with an affecting the aorta arches, visceral aorta and arteries of upper and lower extremities in type A dissections, which syndrome practically persists after surgical treatment of dissection, and requires subsequent diagnosis and endovascular treatment.

These shortcomings do not significantly reduce the contributions of the dissertation work.

## **8. Contributions.**

The following original and confirmatory contributions of the dissertation work should be recognised.

Original theoretical contributions may be indicated: No1,2,6,7,8,9,12

1. For the first time in Bulgaria, a large study is conducted on the endovascular treatment of aortic dissection type A and type B.



2. For the first time in Bulgaria, the endovascular therapeutic treatment options for AD type A and type B are explored.
3. Endovascular treatment in type B aortic dissection is necessary as a method of choice and is a real alternative to surgical and medical treatment.
4. It is established that dissection of the aorta type A and B cause not only severe pathological damage of the aorta, leading to an aneurysm and rupture, but also a high incidence of malperfusion syndrome caused by stenosis/thrombosis of the carotid, subclavian, visceral and peripheral arteries, which necessitates secondary endovascular or hybrid revascularization.
5. A high percentage of residual vascular stenosis of truncus brachiocephalicus, a.carotis , a.subclavia and visceral arteries is found in patients operated on type A dissection, which necessitates secondary endovascular or hybrid revascularization.
6. It is proven that successful endovascular treatment in AD type A and type B leads to a significant increase in the size of the true lumen and reduction of the false lumen, which leads to an improvement in perfusion and reduces the risk of developing an aneurysm and rupture.
7. It is proven that the modern treatment of dissecting aneurysms of the aorta type A and B is complex - includes both self-endovascular treatment and combined primary or secondary hybrid treatment – combined surgical and endovascular therapy.

As confirmatory contributions, we may accept No 3,4,5,10,11,13

- 1.It is proven that endovascular treatment of AD type A and type B is effective and safe and improves the prognosis in these patients.
- 2.For the first time in Bulgaria, the frequency and methods of endovascular treatment of malperfusion syndrome are studied.
- 3.All endovascular treatment of aortic dissection type A is an alternative to a surgery or hybrid one in patients at very high perioperative risk.
- 4.It is proven that the presence of endoleak and persistent communication between the false and the real lumen are the most common causes of re-intervention.
- 5.Balloon post-dilation is an effective method of treating type I and type III endoleaks
- 6.It is proven that the treatment of dissecting aneurysms of the aorta type A and B is not a one-time act, but requires periodic diagnostic control and, if necessary, endovascular corrections of the complications that have arisen.

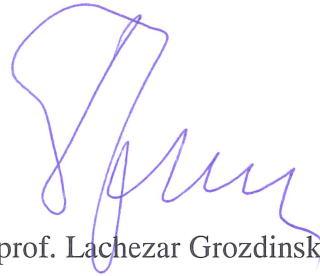
**Audience activity.** Dr. Stankov has published 12 publications in our and foreign scientific journals, of which 8 in foreign magazines and 4 in Cyrillic, as well as 10 participations in Bulgarian and international forums.

#### Conclusion

The dissertation is met with all the conditions for the award of the educational and scientific degree "Doctor".

12.05.2022

Sofia

A handwritten signature in blue ink, consisting of a large, stylized initial 'L' followed by several loops and a long horizontal stroke.

prof. Lachezar Grozdinski, PhD