THORACIC AORTIC DISEASE - AORTIC DISSECTION
Experiences of the University Clinic for Cardiology

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Abstract:

The term Thoracic Aortic Disease (TAD), covers a wide range of degenerative, structural, acquired, genetically based and traumatic diseases, conditions and presentations of the thoracic aorta. In 2010 several professional associations published joint Recommendations for diagnosis and treatment of TAD, and last year ESC published new Guidelines for diagnosis and treatment of Aortic Disease. Interesting enough is the fact that, 2010 Guidelines were the first recommendations accompanied by a campaign designed for the general population, with a purpose to increase awareness of the existence and importance of these conditions. It was explained by the fact that dissection of the thoracic aorta, the most distinguished acute clinical manifestation of TAD, is recognized as one of the twenty most common causes of death.

This is a condition that is diagnosed mainly based on data obtained by a detailed history and clinical examination, for the existence of high-risk situations, high-risk features of the chest pain and high risk clinical findings. Unfortunately, yet, there isn't sensitive and specific biomarker that could help in the diagnosis of this acute condition. The definitive confirmation of the disease is made by imaging of the aorta with one of the imaging modalities such as transoesophageal echocardiography (TOE), computed tomography (CT) or magnetic resonance (MRI). And in terms of rapid diagnosis, this condition is still characterized with high mortality.

This paper is an attempt to give an overview of the situation with TAD in our country, through a retrospective analysis of the medical database at the University Clinic of Cardiology of all patients hospitalized during the year 2009 with a working diagnosis of AoD.

Key words: ***thoracic aortic disease (TAD), thoracic aortic dissection (AoD), morbidity, mortality***

INTRODUCTION

The term THORACIC AORTIC DISEASE (TAD) covers a wide range of degenerative, structural, acquired, genetically based and traumatic diseases, conditions and presentations covering the thoracic aorta. In the year 2014 ESC published Guidelines - recommendations for diagnosis and treatment of these conditions. This description covers wide range of clinical situations that according to their clinical presentation are divided into:

Chronic aortic syndromes: atherosclerosis and calcification, dilatation and aneurysm, vasculitis and inflammatory diseases, genetic syndromes associated with TAD: *Marfan, Loeys-Dietz, Ehlers-Danlos, Turner Syndrome*, bicuspid aortic valve, inflammatory diseases associated with TAD: *Takayasu Arteritis and Giant Cell Arteritis,* Ankylosing Spondylitis Infective Thoracic Aortic Aneurysm, and

Acute aortic syndromes: aortic dissection (AoD), intramural hematoma, (IMH), penetrating atherosclerotic ulcer (PAU), pseudo aneurism, traumatic rupture of thoracic aorta (TRA).

Acute aortic dissection is the most important clinical presentation of TAD, because of the distinguish clinical presentation and high mortality even when diagnosis is made, which imposes the urgency of diagnosis and treatment of this condition.

The population-based studies point to an incidence of 2 to 3.5 / 100 000 inhabitants, while Sweden's author Olsson even refers to an incidence of 16/ 100000, but for men. There is a trend of increasing not only of the incidence, but of the prevalence of this condition also. Unfortunately, we have no data on the approximate frequency of TAD in the Macedonian population, but we tried to make a comparative analysis of the prevalence of it in the subpopulation of hospitalized patients due CVD at the University Clinic for Cardiology during the year 2009, compared with data from a group of academic medical centers (UHC-University Health system Consortium), which together with the connected hospitals, covers about 100 hospitals in the United States.

MATERIAL AND METHODS

Single center retrospective analyze was performed, on all comers in ICCU (Intensive Cardiac Care Unit) at University Clinic of Cardiology during the 2009. Medical files were analyzed, from which data for patients' history, physical findings, results from clinical examinations, and therapeutic treatment were analyzed. Only patients with confirmed diagnosis were included in our study.

RESULTS AND DISCUSSION

At our clinic, from a total of 3000 patients hospitalized in the ICCU in the year 2009, 2% were diagnosed with TAD, or from a total of 6500 hospitalizations annually, for the all hospitalizations at our University Clinic (utility with the highest volume of treatment of patients with cardiac conditions), 0.9% hospitalized patients were diagnosed with TAD. Compared with

the data from the UHC database (Table 1), it correlates with the frequency of hospitalizations due to some of the clinical forms of TAD in US, which in the period from 2002 to 2007 shows an increasing trend from 0.8% in 2002, over 0.9% in 2004, to 0.99 in 2006 and 0.9% in 2007. This growing trend is explained by the increase in the average span of life, but also with the rising influence of known risk factors for TAD.

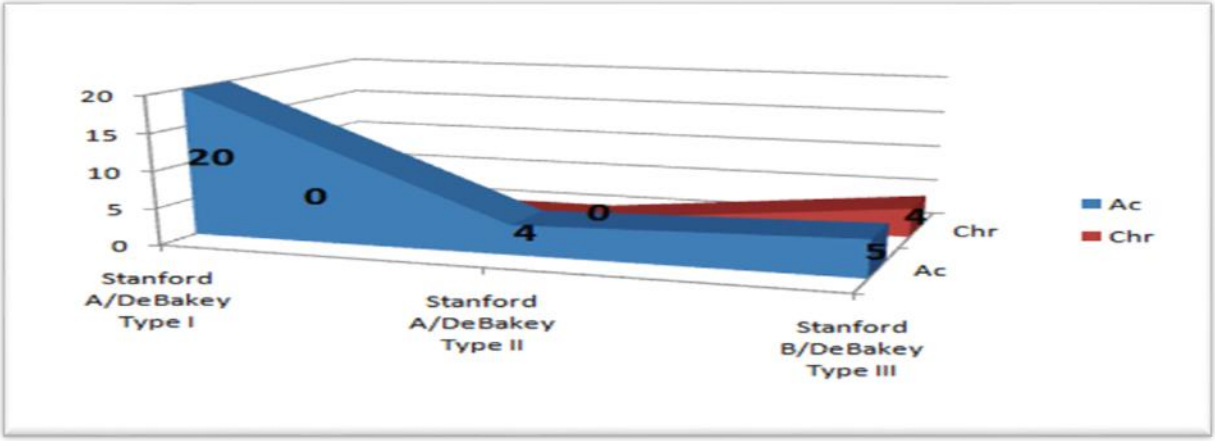
Table 1. Prevalence of hospitalizations due to TAD, according to the UHC database

Total No. of cases	**20 525**	**23 098**	**27 651**	**31 201**	**32 797**
Total No. of inpatient discharges	2679334	2777880	3018141	3222542	3297834
%	0,8	0,9	0,9	0,99	0,9

Type of dissection

Of the 33 patients analyzed, 29 (87.9%) were with an acute dissection, defined when the symptoms were present two weeks of the initial presentation, versus 4 (12.1%) patients with chronic dissection. According to the standard classification, predominating were patients with Stanford type a dissection 72.7%, all with acute dissection, 60.6% of type I and 12,1% of type II after DeBakey. Only 15.5% of the patients had Stanford type B dissection, or type III DeBakey. (Chart 1) Statistically significant difference in distribution was observed for the acute clinical presentation vs. DeBakey classification (p = 0,002), as well as vs. Stanford classification (p = 0,003) with OR 3,2 (CI 0,9 -10,8; p = 0,009) for type A in patients with acute dissection.

Chart 1. Distribution of the patients according to the type of dissection



Although it is known that dissection can occur in the absence of pre-dilatation of the dissected segment, in our population only one patient's dissection was registered in the absence of dilatation of the corresponding segment of the aorta. (Table 2)

Table 2.Correlation of dissection and the concomitant dilatation of the aorta

TAD	*Acute*	*Chronic*	*total*	*Sig (p)*
Without dilatation	1 (3,0%)	0 (0%)	1 (3,0%)	
With dilatation	28 (84,8%)	4 (12,1%)	32 (97,0%)	ns

total	29 (87,8%)	4 (12,1%)	33 (100%)

Risk factors for TAD

Three groups of risk factors are important for TAD development. They are:

- **Conditions associated with increased wall stress**: hypertension (especially uncontrolled), pheochromocytoma, use of cocaine or other stimulants, lifting weight or other Valsalva maneuvers, trauma, deceleration or torsical injuries, coarctation of the aorta.

- **Conditions associated with abnormalities of the aortic media**: **Genetic**: Marfan syndrome, Ehlers-Danlos syndrome (vascular form), Turner syndrome, Loeys-Dietz syndrome, Bicuspid aortic valve (including prior aortic valve replacement), anuloaortic ecstasy, familial thoracic aneurysm and dissection; **Inflammatory**-vacuities: Takayasu arteritis, Giant cell arteritis, Becket arteritis

- **Other**: Pregnancy, autosomal dominant polycystic kidney, chronic corticosteroid or immunosuppressive therapy, infections of the aortic wall due to bacteriemia or spread of local infection, iatrogenic causes (cardiac catheterization), syphilis, metabolic disorders (dislipidemias).

The presence of risk factors in our patients was as follows: uncontrolled arterial hypertension was by far the most common risk factor, present in 76% of the patients with TAD, which correlates with the data from the literature. It was followed with cigarette smoking 33,3% and dyslipidemia 18,2%.

Only 18,2% of analyzed patients had previously known condition associated with an increased risk of aortic dissection. (Table 3) In addition, one patient with a Marfan syndrome, and one with bicuspid aortic valve. Three of the patients were previously operated from aortic aneurism (one with replacement of aortic valve and aortic root, while two with previous operation of the abdominal Aorta, one with known chronic dissection. In three of the patients during the interrogation data for a family burden were obtained.

This is especially emphasized because of the fact that in none of these patients were implemented the recommendations for monitoring patients with genetic syndromes associated with TAD, a family outbreak of TAD and patients operated or with known TAD.

Table 3. Distribution of patient according to known previous condition

Previous condition	*frequency*	*Percentage (%)*
Without previous condition	27	81,8
Bicuspid aortic valve	1	3,0
Ao valve implantation + aortic root repair	1	3,0
Marfan syndrome	1	3,0
Chronic dissection	1	3,0

Abdominal Ao operation	1	3,0
Chronic dissection +Abdominal Ao operation	1	3,0
Total	6	18,0

Initial diagnostic evaluation of patients with suspected acute TAD

The initial assessment of a patient who presents with symptoms that make the possible diagnosis of TAD is based on the so-called pretest probability for TAD. (Table 4)

Table 4. Clinical data useful to assess the a priori probability of acute aortic syndrome

High-risk conditions	High-risk pain features	High-risk examination features
• Marfan syndrome (or other connective tissue diseases) • Family history of aortic disease • Known aortic valve disease • Known thoracic aortic aneurysm • Previous aortic manipulation (including cardiac surgery)	• Chest, back, or abdominal pain described as any of the following: - abrupt onset - severe intensity - ripping or tearing	• Evidence of perfusion deficit: - pulse deficit - systolic blood pressure difference - focal neurological deficit (in conjunction with pain) • Aortic diastolic murmur (new and with pain) • Hypotension or shock

Adopted from 2014 ESC Guidelines on Diagnosis and Treatment of aortic disease

This evaluation was made based on the data we got from the detailed history, especially the features of chest pain (as a dominant symptom), other symptoms of the disease, medical and family history, as well as detailed and focused clinical examination (Class I, le B). The list of high-risk features that define risk of TAD is presented in Table 4.

Based on the presence of any of these symptoms or signs, patients belong to one of the three risk categories that determine further diagnostic algorithm:

1. Patients with a low risk of TAD: patients who do not have any of the above high risk features.

2. Patients with an intermediate risk of TAD: patients who have one of high risk features; and

3. Patients with a high risk of TAD: patients who have at least two of the high risk features.

Clinical findings in patients with TAD

The blood pressure level is one of the specifics of TAD. According to Hiratzka and co-workers, about half of the patients with acute TAD are hypertensive at the time of presentation, 71% of patients with type B, and 36% of patients with Stanford type a dissection. About 20% of patients with acute TAD are hypotensive or in shock at the time of presentation. The hypotension in these patients may be due to cardiac tamponade, severe aortic valve insufficiency, compression of the false lumen on the right, intraabdominal complications or aortic hemorrhage. Patients that are hypotensive at the moment of presentation, often have neurological complications, myocardial, mesenterial or limb ischemia.

In our study population, only 27% of patients were normotensive at the moment of clinical examination. Hypertensive patients predominated (39%), while 18% were hypotensive,

and an additional 15% were in cardiogenic shock at the time of first examination. As it can be seen from Table 5, there are no significant differences in this respect with patients from the IRAD registry.

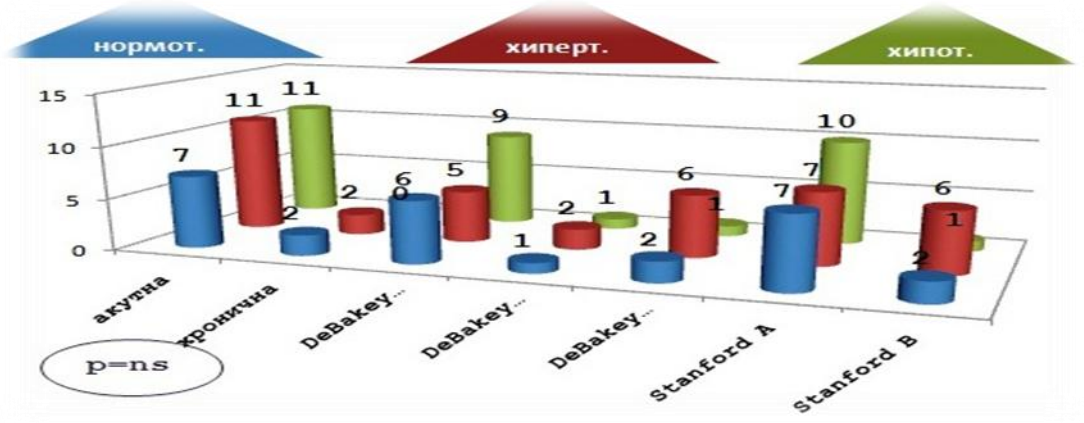
Table 5. Physical findings in patients with acute TAD

Physical findings	Referred (%)	Our study (%)
Normal blood pressure	45	27,3
Hypertension	32	39,4
Hypotension	14	18,2
Shock	13	15,1
Cardiac tamponade	5	3
Aortic regurgitation	45	54,5
Pulse deficit	26	27,3
Pericardial friction edge	2	0
CVI	8	3
Ischemic peripheral neuropathy	3	3
Ischemic spinal damage	2	3
Lower limbs ischemia	10	9,1
Comma	12	6,2
Congestive heart failure	5	0

**Referred according to International Registry of Acute Aortic Dissection (IRAD)*

When we tried to assess what is the linkage between blood pressure and the type of dissection, we found domination of the hypotension in patients with acute, Stanford tip A, DeBakey type I dissection *(Chart 4)*, while hypertension was present in patients with chronic, Stanford type B, DeBakey type III dissection, however recorded differences were without statistical significance.

Chart 4. Distribution of patients by type of dissection and value of BP



When it comes to target organ damage, cardiovascular complications were predominant. In 54% of the patients murmur indicating aortic insufficiency was registered, although we are not entirely sure whether it was always newly created. Although pericardial effusion was common finding (27% of patients), only in one patient we confirmed cardiac tamponade. The literature refers the incidence of syncope as clinical presentation in 13%, while in our series it was

registered in only one patient. We are not shore that there weren't cases of "misdiagnosis", so that some of these patients were 'wrong' estimated as CVI and diverted to other facilities that may have waste valuable time for such patients. 15% of patients at the time of presentation in our institution were already in a shock condition, a figure which is significantly higher than referred in the literature. If we want to speculate, that may be due to the fact that patients reach too late our institution, loosing time. Renal complications were predominant clinical manifestations other that cardiovascular. Renal failure was present in 15% of patients. Pulse deficit, limb ischemia, neurological deficit, are conditions that should always focus our attention to this condition. *(Table 6)* Only 24.2% of our patients were without signs of target organ involvement at the time of presentation.

Table 6. Target organ damage as a consequence of acute TAD

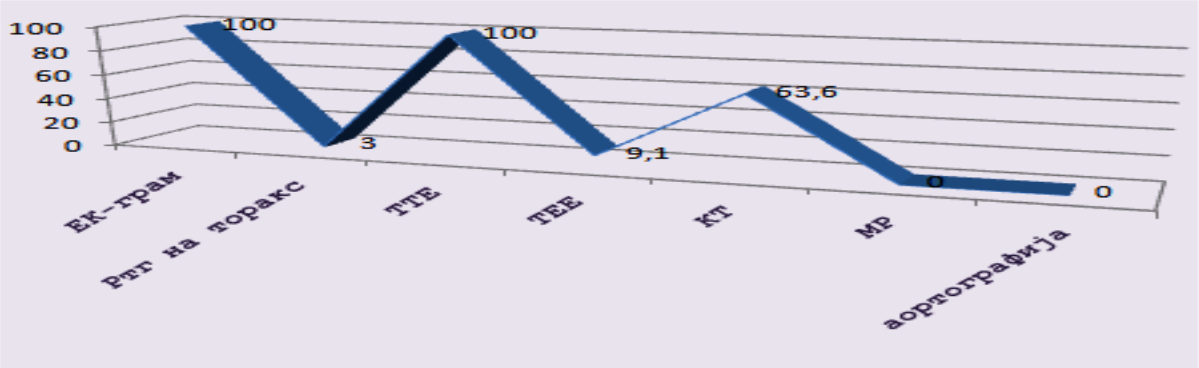
Type	***manifestation***	***referred****	***found***
CV complications	*Aortic valve insufficiently*	*41-76%*	*18(54,5%)*
	Syncope	*13%*	*1(3%)*
	Pericardial effusion/tamponade	*30 (8-10)*	*9(27,3%)*
	Myocardial ischemia/infarction	*7-19%*	*3(9,1%)*
	Heart failure/Shock	*6%*	*5(15,1%)*
Neurological	*CVI/TIA*	*17-21%*	*1(3%)*
	Peripheral neuropathy	*околу 12%*	*1(3%)*
	Paraparesys	*1-3%*	*1(3%)*
Pulmonal	*Aorto-pulmonary fistula*	*3%*	*1(3%)*
	Pleural effusion	*16%*	*0*
GIT complications	*Mesenterial ischemia/ infarction*		*0*
	Aorto-enteric fistula		*1(3%)*
Renal	*Renal failure*	*7%*	*5(15,1%)*
	Ischemia/infarction		*0*
Extremities	*Ischemia*	*10%*	*1(3%)*

** referred frequency according to the International Registry of Acute Aortic Dissection (IRAD)*

Diagnostic modalities that we utilized

ECG - done on all patients with symptoms of suspected acute TAD. Biomarkers (D-dimer test as a rule out procedure, if negative). Rtg of the chest that according to the Guidelines is recommended for the patients with low clinical probability was performed in only 3% of our patients. TTE is the first imaging modality in all patients with suspicion for TAD, and it was performed in all of our patients. Emergent and definitive diagnosis is made with TOE (Class IIa, Loe C), CT or MRI in patients with high risk for acute TAD *(Class I,le C).* The choice of the imaging modality depends on the patient's characteristics, the institutional capacities, including the immediate availability. Due to the existence of high clinical suspicion of dissection in terms of negative results from the first imaging, second imaging modality should be performed. *(Class I, le C)* In our patients only 9.1% were subjected to TOE while in most of the cases, 63.6%, definitive diagnosis was made with a computerized tomography. *(Chart 5)*

Chart 5. Screening tests applied in our patients



Legend: ЕК-грам-ECG; Рtг на торакс- chest radiogram; TTE- TT echocardiography; TEE- TOE; KT- CT; MP- MRI; аортографија-aortography

Features of TAD by sex and age

What are the data in the literature in terms of gender distribution? According to the IRAD database, the gender significantly affects the presentation of acute TAD. Only 32% of patients included in this database were female, at higher age than males, asking for medical help in the later hours of clinical presentation (not in the first six hours), rarely had an abrupt beginning of the symptoms, and more often first signs were heart failure and alterations of the mental status. This all leads to delay in the diagnosis of acute TAD, that is rarely confirmed in the first 24 hours, and consequently leads to higher hospital mortality compared with men (30% vs. 21%, p = 0,001).

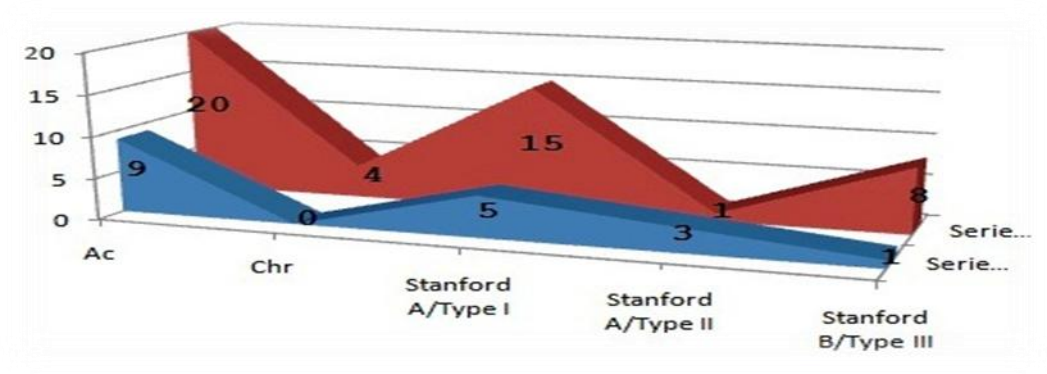
Same distribution by sex (3:1) at the expense of males was found in our population also. Female patients were at higher mean age, although statistically insignificant. In the male population, males at age 40-60 predominated, while among women the same was with the age 50-70 years. Females had significantly lower number of risk factors. *(Table 7)*

Table 7. Distribution of patients according to sex and age

variable	*gender*	*N*	*Mean*	*SD*	*Sig (p)*
age	*female*	*9*	*60,22*	*13,81*	*ns*
	male	*24*	*54,92*	*10,18*	
Nr of risk factors	*female*	*9*	*1,11*	*0,60*	*<0,05*
	male	*24*	*1,92*	*1,17*	

Regarding the type of dissection, no statistical significance was found between genders, although female patients had statistically insignificant increased risk for development of acute dissection (OR = 1,7; p = ns), as well as triple higher risk of developing Stenford type A dissection (p = 0,054; OR = 3,0; p = ns), while in terms of classification according to DeBakey, no statistically significant difference was found (p = ns). *(Chart 6)*

Chart 6. Distribution of patients by sex and type of dissection



The comparison of patients of the opposite sexes in our study in terms of clinical presentation of the disease showed, contrary to findings from the literature, that women were the ones that asked for medical help earlier, and had significantly shorter time to the definitive diagnosis. *(Table 7)*

Table 7. Comparative characteristics of clinical presentation by gender

	females	*males*				
	Mean±SD	***Mean±SD***	***Min-max***	***Mediane***	***Mode***	***Sig (p)***
Time to first medical contact (h)	*43±110*	*139±305*	*2-336-f* *1-1440-m*	*3* *5,5*	*2*	*0,002*
Time from first medical contact to definitive diagnosis(h)	*15±23*	*16±24*	*2-72-f* *1-72-m*	*4* *2*	*2*	*<0,000*

Table 8. Comparative characteristics of clinical course by gender

variable		***females***	***males***	***Sig (p)***	***OR females***	***Sig (p)***
Target organ damage	***no***	*3*	*5*	*ns*	*1,6*	*ns*
	y	*6*	*19*			
In-hospital mortality	***no***	*8*	*19*	*ns*	*1,8*	*ns*
	y	*1*	*5*			

Although women had slightly greater risk of target organ damage (OR 1.6), and hospital mortality (OR 1,8), these differences were without statistical significance.

RECOMMENDATIONS FOR A DEFINITE TREATMENT OF ACUTE TAD

1. **Urgent surgical consultation** was done for all of the patients with acute TAD, regardless of the anatomical localization (ascending / descending), right after setting a definitive diagnosis. *(Class I, le C)*
2. **Acute dissection which involved the ascending aorta was immediately reported for immediate surgical correction** because of the high risk of associated life threatening complications such as rupture. *(Class I, leB)*

3. **Acute dissection which involved the descendant thoracic aorta was treated with medications**, unless there was a development of life threatening complications: organ malperfusion syndrome, progression of dissection, aneurysm growing, and pure control of blood pressure and / or symptoms despite optimal drug treatment. *(Class I, le B)*

Why urgency in the treatment of patients with acute TAD?

Urgency of treatment results from the fact that it is a life threatening condition which is characterized by a 40% immediate mortality, while mortality of 1% follows with each passing hour from the time of onset of symptoms. If the patient reaches the operation room he carries a risk of 5-20% for the peri- and immediate post-operative mortality, while the five-year survival is 50%.

The hospital mortality of our patients was 18.2%. Of those who survived, 63.6% were reported and treated surgically, while in 24.2% of the patients after cardio surgical consultation an intensive drug treatment was undertaken. Worth noting is the fact that the total time from the point of the beginning of the symptoms to the point of setting a definite diagnosis was significantly shorter in patients in whom the outcome was hospital death. The time passed since the onset of symptoms until the moment of hospitalization in patients with fatal hospital outcome was about 3,7 ± 1,6 h, compared to 137,8 ± 291,6 h in surviving patients (p = 0,024). The time from the first contact with a physician in our institution to the moment of setting a definitive diagnosis was also significantly shorter in patients with hospital death 2 ± 1 h versus 19,1 ± 25,1 h (p = 0,002). This leads us to the conclusion that patients, who early after the initial presentation seek for medical help, are exactly those with worse clinical outcome and a higher risk of fatal outcome.

Trying to define which high-risk features overlook the fatal outcome in our patients, we made a multivariable logistic regression analysis in which we included the following risk characteristics: *Stanford type of dissection, DeBakey type of dissection, presence of newly showed aortic insufficiency, presence of pericardial effusion, a reaction of blood pressure (hypotensive), the presence of target-organ involvement*, we created a model with a regression coefficient: Chi square = 24,702; p = 0,001, accuracy of prediction of 93.9%, in which none of these features was identified as independent risk factor for in-hospital mortality. Our opinion is that it is due to the small study group.

CONCLUSION:

Acute thoracic aortic disease continuous to be one of the major conditions presenting predominantly with chest pain, together with acute coronary syndrome, but as opposite of the first one is characterized with lower capacity for rapid diagnosis and treatment, and by far worse clinical outcome.

That is the reason, why we are urged to think of this condition and actively source for it in patients presenting with chest pain and other typical and less typical signs and symptoms associative for acute TAD.

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