

GEORGE EMIL PALADE UNIVERSITY OF MEDICINE, PHARMACY, SCIENCE, AND
TECHNOLOGY OF TÂRGU MUREȘ (UMPHST)
DOCTORAL SCHOOL OF MEDICINE

ABSTRACT OF DOCTORAL THESIS

Acut aortic syndrome. Medical-surgical considerations.

PhD student: **Bănceu Cosmin Marian**

PhD supervisor: **Prof. Dr. Deac Radu**

TARGU MURES 2024



UNIVERSITATEA DE MEDICINĂ,
FARMACIE, ȘTIINȚE ȘI TEHNOLOGIE
„GEORGE EMIL PALADE”
DIN TÂRGU MUREȘ

1. Background

Acute conditions of the thoracoabdominal aorta are grouped under the entity of acute aortic syndrome (AAS), which is still considered part of the spectrum of high-mortality conditions, even though the medical field has seen progressive development in all aspects, technologically or in acquired experience. Under the umbrella of this syndrome are aortic dissection (AD), intramural hematoma (IMH), atherosclerotic penetrating ulcer (APU), and traumatic aortic dissection (TAD). Understanding the spectrum of pathologies within AAS helps clarify the aetiology and prognosis of aortic injury. Acute ascending aortic dissection represents the most prevalent medical condition among all the components of AAS, requiring urgent diagnosis and treatment. Among the high-prevalence risk factors for triggering AD are uncontrolled essential hypertension, aortic coarctation, bicuspid aortic valve, ascending aortic and/or aortic root aneurysm, collagen dysfunction, pregnancy, inflammatory aortic disease, or surgical history in the cardiac sphere.

2. Objective

This paper presents the analysis results conducted on the medico-surgical aspects of cases diagnosed with AAS at the Emergency Institute for Cardiovascular Diseases and Transplants in Târgu Mureș. The argument underlying this thesis is that various known risk factors of this syndrome require constant re-evaluation in the context of technological progress, increasing levels of medical personnel experience, and improved patient access to medical services. Specialized literature mentions that the sex of patients with AAS represents a risk factor, specifically male sex, with higher mortality among men being considered. Recent studies, albeit few, have highlighted that this aspect is no longer unanimously accepted and that the sex of patients with AAS is beginning to lose the same importance among the risk factors of this syndrome. Considering that AD treatment focuses on surgical replacement of the ascending aorta through specific surgical techniques and that postoperatively the remaining native segments of the aorta remain vulnerable to various risk factors, the survival perspective or postoperative mortality of these patients may be significantly influenced. In this context, it is important to establish whether histopathological changes can be used as predictive factors of an evolving pathological process at the level of the aortic wall or are merely represented by isolated histopathological changes. Another aspect to consider is the timing presentation of patients with AAS to the medical unit, whether during the weekend or on weekdays. The organisation of the surgical service, preoperative patient preparation stages, identification, exclusion, prevention of intraoperative risk factors, and ensuring surgical treatment in optimal time are aspects that may show significant variability depending on the timing of patient presentation, weekends, or weekdays. This aspect may influence intraoperative or postoperative mortality in some surgical services.

3. General methodology

This paper presents the approval of the Ethics Committees of the University of Medicine, Pharmacy, Science, and Technology "G.E. Palade" and of the Emergency Institute for Cardiovascular Diseases and Transplants Targu Mures (decisions no. 7225/07.10.2019, no. 878/23.04.2020, no. 1359/10.05.2021). The study cohort consists of cases diagnosed and hospitalised with AAS at the Emergency Institute for Cardiovascular Diseases and Transplants Targu Mures during the period January 2019 – December 2022. The study includes the analysis of general and specific surgical factors, macroscopic and microscopic changes of the aortic tissue highlighted through specific colorations, and in addition to the analysis, the evaluation of mortality rates was conducted. Preoperatively, statistical differences regarding acute renal failure, administered inotropic treatment, and the sex of hospitalized and surgically treated patients were analyzed, as well as an age-decade analysis of the two cohorts. Intraoperatively, the administered inotropic treatment, extracorporeal circulation time, and ischemia time were considered and correlated with the patient's sex. Subsequently, postoperatively, an analysis was conducted based on sex, administered inotropic treatment, duration of respiratory support, and length of stay in the intensive care unit. This study also analyzes the mortality recorded during hospitalisation and six months after patient discharge. The data obtained from the processing and examination of intraoperatively collected aortic tissue fragments from patients surgically treated for acute ascending aortic dissection were analyzed. The data obtained from these analyses and the analysis of cohort

characteristics in the preoperative and postoperative periods allowed the evaluation of their impact on mortality recorded during the hospitalization stage and after discharge, up to 6 months. An analysis was also conducted on two cohorts of patients diagnosed and treated for acute ascending aortic dissection, considering patients who underwent surgical intervention during the weekend as one group, and a control group comprising patients who underwent surgical intervention during weekdays. Characteristics of the cohorts were analyzed before and after treatment, their mortality rates before intervention, intraoperatively, and postoperatively at 6 months.

4. Results

Study 1. Heterogeneity study in Acute Aortic Syndrome. In this prospective study, we analyzed whether gender is a predictive factor of mortality recorded in patients with acute aortic syndrome.

Our study highlighted that males tend to have a higher tendency to develop pericardial effusion or pulmonary hypertension, while females are predisposed to essential hypertension. Preoperative dobutamine administration is associated with a higher risk of death, whereas intraoperative or postoperative noradrenaline administration is associated with lower mortality, all without being influenced by heterogeneity. Risk factors such as age, administered inotropic support, and acute renal dysfunction, viewed in the context of gender, can guide the medico-surgical management of patients with aortic dissection and can influence postoperative prognosis. Concerns regarding postoperative mortality observed in patients with aortic dissection are a current topic. In this context, our analysis does not highlight relevant differences between male and female patients, and consequently, heterogeneity does not play a significant role when considering mortality recorded during the hospitalization period or after discharge.

Study 2. Histopathological gap in Acute Aortic Syndrome. This prospective study analyses whether the degree of medial degeneration of intraoperatively harvested aortic tissue influences the mortality of cohorts and whether it can be considered a predictive factor for the mortality of patients with AAS.

The complex analysis conducted reveals significant differences between the two groups when MEMA-i changes occur, discussing moderate media degeneration in the AA patient group and severe media degeneration in patients with AD Stanford A. MEMA-t changes were observed in the AA group in the forms of mild or moderate degeneration and severe in the DA patients. Fragmentation and/or loss of elastic fibers were observed in the AA group in cases of mild or severe degeneration, while in the DA group, it was observed in cases of moderate degeneration. Loss of smooth muscle cell nuclei was found in samples with mild degeneration in AA patients and those with DA. The lamellar medial collapse was encountered in mild degeneration in AA cases and in moderate or severe degeneration in DA cases. The data obtained from the analysis show that the histopathological changes observed in intraoperatively harvested specimens were significantly correlated with the mortality of the examined cohort, indicating that in-hospital mortality and after-discharge mortality significantly correlate and increase according to the degree of aortic media degeneration. This can be considered an important risk factor that needs to be known when establishing prevention and monitoring plans for these patients. Such studies need to be complemented for implementation in medical practice.

Study 3. The "weekend effect" in medical-surgical management of acute AD Stanford A. This prospective study evaluates the weekend effect on patients hospitalized and surgically treated for AAS, analyzing the predictive nature of this aspect regarding the recorded mortality.

Our results did not highlight major differences between the two cohorts regarding preoperative mortality. Through subjecting the data to a comprehensive analysis, which involved conducting three statistical tests—log-rank (Mantel-Cox), Breslow (generalized Wilcoxon), and Tarone-W—it was observed that the

percentage of deceased cases leans towards the group of patients treated during the week, but without reaching the predetermined level of statistical significance compared to those treated during the weekend. Our data do not show a significant correlation between the mortality rate during the hospitalization period and the day of the week when the patient was admitted, and the same response was obtained regarding the death rate after surgical treatment and follow-up for 6 months thereafter.

5. Originality of the thesis

The originality of the work is highlighted by the subject of each study, which formed the basis of the elaboration of the present thesis, as follows: **a)** Although there are studies regarding the heterogeneity of patients developing one of the forms of acute aortic syndrome, they do not address the subject of gender but provide results extrapolated from other studies. Heterogeneity in our study is the main subject of analysis, thus providing pertinent information with clinical applicability. **b)** Another subject emphasizing the originality of the work is the correlation of histopathological diagnosis of medial degeneration with the mortality recorded in patients who underwent surgical procedures for aortic wall conditions. The present work is the first of its kind in the specialized literature; the recent classifications developed by the European Association of Cardiovascular Pathology and the Cardiovascular Pathology Society regarding the histopathological diagnosis of aortic fragments have not been used in similar studies to ours. This approach may offer very important practical information for establishing monitoring and prevention strategies for other similar pathological events at the level of native aortic segments. **c)** The next element of originality is represented in the final chapter presented. It analyzes the weekend effect as a risk factor in aortic dissection. The subject is sporadically discussed in medical literature, with discordant results, and in our specialized literature, that of cardiac surgery, the approach is almost absent. The subject is analyzed by very few centers dedicated to aortic surgery, without reaching a consensus. At the national level, the theme is unique and further accentuates the originality of this work.