The pathogenesis and drug treatment of aortic dissection

Xuanmin Tian *

Beijing Luhe International Academy, Beijing, China

* Corresponding Author Email: xuanmin0330@gmail.com

Abstract. Aortic coarctation belongs to a life-threatening condition in which the walls of the true and false aorta separate. There are two classifications: type A and type B. Current treatments include surgery and taking medications. This research analyzes the results of previous literature on drugs for aortic coarctation treatment to summaries effective drug treatments from previous studies. The main topics in the article include pharmacological induction of endothelial dysfunction in mice and studying the therapeutic effects of pitavastatin for aortic coarctation, comparing the possible associations between antihypertensive medications, antithrombotic drugs, anticoagulant medications, and statins, and long-term survival. In addition, this research focuses on the therapeutic effects of statins, antihypertensive drugs, antithrombotic drugs, and anticoagulant drugs in aortic coarctation and their association with long-term survival, to provide a cross-sectional comparison of drugs and the advantages and disadvantages of different modes of nonsurgical treatment for aortic coarctation. The advantages and disadvantages of different therapeutic modalities.

Keywords: aortic dissection, pharmacotherapy, antihypertensive drugs.

1. Introduction

Aortic dissection (AD) can be caused by tears in the innermost portion of the aortic wall, which permit blood to enter the aorta and form a new blood channel known as a "false lumen", leading to a life-threatening disease that results in the formation of separation of the true and false aortic walls. The age group of 65 to 75 years old is the most prevalent for aortic dissection, with 35 instances per 100,000 individuals annually in this cohort. Additional risk factors include connective tissue-related genetic diseases such Marfan syndrome, hypertension, and dyslipidemia. While severe abdomen pain may be the presenting symptom of type B dissection, abrupt onset ripping chest pain is the characteristic and most common manifestation of type A AD. Hypertension is common; however, low blood pressure can also occur when acute AD ruptures. There are different physical manifestations such as insufficient pulse and differences in blood pressure [1].

Currently, the only treatment options are antihypertensive medications and surgery. Surgical treatment consisted mainly of surgical resection of the intimal tear and isolation with a coated stent. Medication is one form of non-surgical treatment that lowers heart rate, controls blood pressure, and relieves pain. Operation is always the first line of treatment for acute type A AD, and it frequently entails replacing the dissected ascending aorta with a graft, either with or without aortic valve replacement or repair. The most effective medical management of type B AD involves the use of anti-impulse and hypertension medications. When emergent surgery is not needed, current therapeutic recommendations support medicinal therapy with aggressive blood pressure lowering for individuals with acute aortic dissection. Patients with Stanford type B AD—that is, those without involvement of the ascending aorta—are specifically treated medically. Consequently, individuals with complex type B aortic dissection are advised to undergo thoracic endovascular aortic repair, according to current guidelines. However, even after receiving treatment with thoracic endovascular aortic repair, individuals with visceral ischemia still have a dismal prognosis.

The AD is a high-risk operation, which is prone to a series of surgical complications. Drug therapy is the first choice of treatment for chronic aortic clamp, and it is also an important means of preoperative and postoperative management [2-6]. Drug treatment is non-invasive, and it is a very good treatment option for middle-aged and elderly patients to avoid the risk of surgery. The current literature focuses on the outcomes of a single or small number of drugs for aortic dissection, but no systematic comparison has been made to date. Therefore, the therapeutic effect of each drug is

compared horizontally with the different clinical symptoms targeted, and effective drug treatment methods are obtained from previous studies.

In order to provide a summary of the most successful pharmacological interventions for aortic coarctation, this research summarizes the findings of earlier research on the subject. In order to provide a cross-sectional comparison of drugs and the benefits and drawbacks of the various therapeutic modalities for the nonsurgical management of aortic coarctation, this research focuses on the therapeutic effects of statins, antihypertensive drugs, antithrombotic drugs, and anticoagulants for the management of aortic coarctation, as well as their association with long-term survival. The benefits and drawbacks of various treatment approaches.

2. Analysis of drug therapy for AD

For AD treatment, a new AD mouse model was developed [2]. In this work, the researchers took advantage of pharmacologically induced endothelial dysfunction by administering the nitric oxide synthase inhibitor Nv-nitro-L-arginine methyl ester to C57BL/6 mice. The used mice can be injected with angiotensin II (Ang II) and the lysine oxidase inhibitor b-aminopropionitrile (BAPN) using a micro-osmotic pump. A novel mouse aortic coarctation model was established. Compared to the Ang II and BAPN (AB) groups, the Nv-nitro-L-arginine methyl ester, Ang II, and BAPN (LAB) groups had significantly greater rates of aortic coarctation and aneurysm rupture mortality. Oral pitavastatin administration was conducted in LAB mice. It obviously decreased the risk of entrapment and rupture, as well as medial degeneration and inflammation, which were both worse in the LAB group. The results imply that acute aortic coarctation may develop only in the presence of endothelial dysfunction. 3-hydroxy-3-methylglutaryl-CoA reductase inhibitors are commonly used as lipid-lowering medications that slow the development of aortic aneurysms and are useful in preventing cardiovascular disease [7]. Statin use was found to dramatically lower the incidence of aortic coarctation. In LAB mice, pitavastatin inhibits aortic coarctation. We examined the impact of pitavastatin on aortic coarctation in order to determine whether LAB-induced aortic coarctation in mice adds to the evaluation of medication efficacy. Therefore, by lowering blood pressure, pitavastatin may not be able to diminish the incidence of aortic clamping. According to the study's findings, pitavastatin aids in preventing aortic coarctation, which is linked to endothelial dysfunction.

The possible associations between antihypertensive, antithrombotic, anticoagulant and statin drugs and long-term survival has been analyzed [3]. As shown in Fig. 1, the Swedish Medical Register was searched for every patient diagnosed with aortic coarctation between 2006 and 2015 who got out and survived within 30 days. Using Cox proportional hazards models, the study's methodology examined the relationship between medication treatment and long-term survival. The study's findings showed that individuals receiving surgical treatment tended to be younger than those receiving simply medicine. During the same time period, the number of patients receiving treatment with ACE inhibitors declined, and the number receiving treatment with receptor blockers for angiotensin II (ARBs), calcium channel blockers (CCBs), and diuretics grew. Treatment with four or more antihypertensive medications and statins is becoming more common. Long-term survival is higher with treatment with antihypertensive drugs compared with no antihypertensive drugs. Therapy with beta-blockers and ARBs was linked to improved long-term survival in surgical patients. Treatment with statins, ACE inhibitors, diuretics, or CCBs, on the other hand, was not linked to long-term survival following surgical repair. When CCBs and ACE inhibitors were used in patients receiving medical care, their long-term survival rates increased. Nevertheless, there was no correlation found between the patients' long-term survival and the use of diuretics, beta-blockers, or antiretroviral inhibitors. Consequently, the present study confirms that β-blockers were used in 90% of the cases, most often in combination with other medications. It is concluded that statin therapy was associated with prolonged prognosis in drug-treated AD patients, while beta-blocker therapy was only associated with improved survival in surgically treated AD patients.

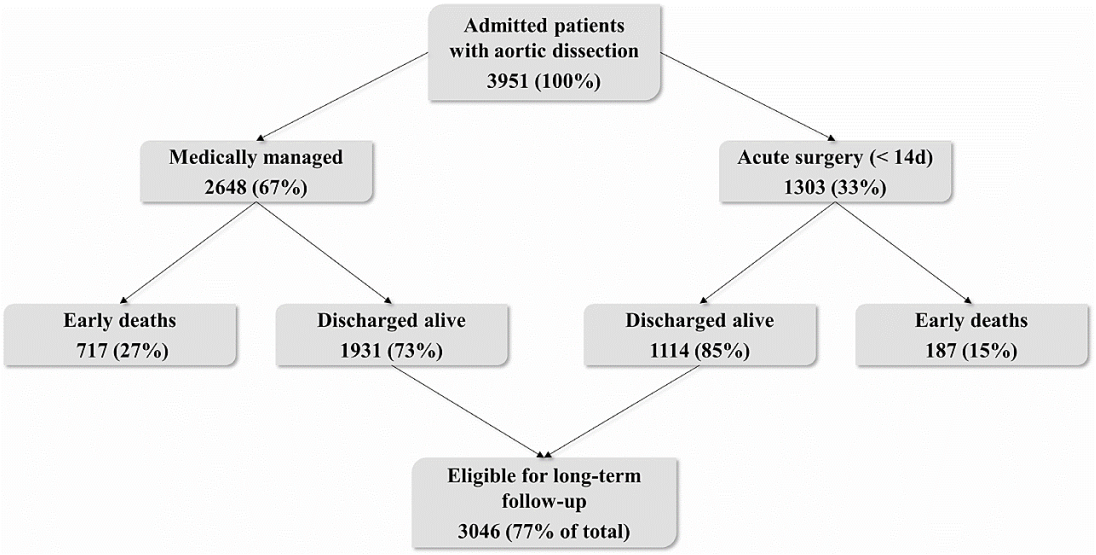


Figure 1. Incorporate the patient's flow chart [3].

The existing research compares efficacy of beta-blockers, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), or other antihypertensive medications in patients with aortic coarctation after prolonged use of these medications (control group) [4]. The study's findings showed that the prevalence of drug-treated hypertension was highest in the ACEI or ARB group, lowest in the β-blocker group, and neither group's outcomes differed significantly from the other. The ACEI or ARB group was followed by the control group. Nevertheless, the β-blocker and ACEI or ARB groups show a lower risk of all-cause death, and the ARB group shows a lower risk of all-cause mortality than the ACEI group. Also, this paper confirms that the rate of beta-blocker use, ACEI or ARB combined versus ARB assessed alone, increased over the timeframe of the study, while the rate of ACEI assessed alone decreased over the years. The application of ARB or ACEI beta-blockers was significantly related with a lower risk of all-cause mortality as compared to the CCBs, according to sensitivity analysis and other analyses. Thus, it can be said that the long-term therapy of aortic coarctation benefits from the application of β-blockers, ACEIs, or ARBs.

The efficacy of first-line beta-blockers versus other first-line antihypertensive drug classes was evaluated for the treatment of chronic type B aortic coarctation [5]. Because chronic type B aortic coarctation is now usually treated medically to reduce pressure in the aorta, and because current practice guidelines recommend β-blockers as the first-line therapeutic agent, it is important to consider the use of α-blockers for the treatment of chronic type B aortic coarctation as a first-line therapy. Pharmacological therapy is an effective means of controlling uncomplicated type B aortic coarctation. Aortic wall shear stress is lowered by antihypertensive medicine used as an initial treatment for aortic coarctation. Ventricular contraction velocity, rate, and blood pressure all affect this. Furthermore, compared to treatment with other antihypertensive drugs, long-term beta-blocker use appears to be linked to a decrease in the requirement for surgery related to aortic coarctation and aortic dilatation progression. However, compared to other antihypertensive drugs, beta-blockers are less successful in managing hypertension when used as first-line therapy. As a first-line therapeutic intervention, beta-blockers do not currently appear to be superior to other antihypertensive drugs based on available data. In order to identify the best course of action for treating chronic type B aortic coarctation, this research does a randomized controlled experiment. In this work, when it came to treating chronic type B TAD, there was no RCT that compared first-line β-blockers with other first-line antihypertensive medication classes.

Patients with AD who did not undergo surgery were divided into five groups based on the number of antihypertensive drug classes [6]. The first group consisted of patients taking other antihypertensive medications, the second group consisted of patients taking RAS medications in combination with other medications, and the third group consisted of patients taking a triple combination of medications (CCBs, RASs, and other medications), which served as a reference

control group. According to the study's findings, CCBs were the most often recommended antihypertensive medications, followed by ARBs and beta blockers. Compared to conventional antihypertensive medications, patients in group 1 had a substantially lower chance of an adverse event when taking RAS medicines. Compared to patients taking RAS medications with other treatments, patients in group 2 who used β-blockers+CCBs or CCBs+RAS drugs had a decreased risk of the combined result. In order to lower the risk of complications connected to AD, it is recommended that patients with non-operated AD utilize alternative combination strategies for RAS medications, beta-blockers, or CCBs than for other treatments.

It can be to examines the effect of blocker medications on aortic coarctation case fatality by analyzing the International Registry for Acute Aortic Dissection (IRAD) global registry database [7]. All aortic coarctation patients included in IRAD between December 26, 1995, and May 5, 1997, were the subject of an analysis that focused on follow-up data including medication use and survival patients who were discharged with medication. This study showed that, although survival declined with age, the use of blockers improved overall prognosis and prognosis for surgical treatment in all patients, even type A patients. On the other hand, only type B patients' use of CCBs was linked to better survival. There was no correlation seen between the usage of angiotensin-converting enzyme medications and death.

The efficaciousness and prescribing patterns of several antihypertensive medication classes in patients having aortic coarctation surgery can be also investigated [8]. The renin-angiotensin system, beta-blockers, CCBs, and other antihypertensive medications were the antihypertensive medications. Based on the number of classes of antihypertensive drugs prescribed, patients were categorized into five groups: 1) Class 0, which includes no antihypertensive drugs; 2) Class 1, which includes the same class of drugs; 3) Class 2, which includes two classes of drugs; 4) Class 3, which includes three classes of drugs; and 5) Class 4, which includes four classes of drugs. As a result, two or three antihypertensive drugs were prescribed for the majority of patients. Within the class of antihypertensive medications, beta-blockers were the most often recommended medication, while the most often prescribed pharmacological combinations were beta-blockers+CCBs and CCBs+RAS. No particular kind of antihypertensive drug was linked to a better prognosis in patients with type A aortic coarctation undergoing surgery, but the use of β-blockers and CCBs was linked to a significant reduction in the risk of a combined prognosis in patients with type B aortic coarctation.

3. Conclusion

The primary findings of this study are that statin therapy is linked to a longer-term prognosis in patients with AD receiving pharmaceutical treatment, and that endothelial dysfunction is linked to the development of aortic constriction, while pitavastatin aids in its prevention. The long-term therapy of aortic constriction benefits from the use of beta-blockers, ACEIs, or ARBs; among antihypertensive drugs, beta-blockers are most frequently utilized. The use of blockers improves overall prognosis and prognosis for surgical treatment in all patients and in type A. No particular kind of antihypertensive drug is linked to a better outcome in individuals with type A aortic coarctation having surgery. The usage of CCBs and β-blockers was linked to a considerably decreased composite prognosis risk in individuals with type B aortic coarctation. A distinct combination approach for RAS medications, beta-blockers, or CCBs should be employed in individuals with non-operated AD in comparison to other medications.

References

[1] Criado F J. Aortic dissection: a 250-year perspective. Texas Heart Institute Journal, 2011, 38 (6): 694.

[2] Izawa-Ishizawa Y, Imanishi M, Zamami Y, et al. Development of a novel aortic dissection mouse model and evaluation of drug efficacy using in-vivo assays and database analyses. Journal of Hypertension, 2019, 37 (1): 73 - 83.

[3] Smedberg C, Hultgren R, Leander K, et al. Pharmacological treatment in patients with aortic dissection. Open Heart, 2022, 9 (2): e002082.

[4] Chen S W, Chan Y H, Lin C P, et al. Association of long-term use of antihypertensive medications with late outcomes among patients with aortic dissection. JAMA Network Open, 2021, 4 (3): e210469 - e210469.

[5] Chan K K, Lai P, Wright J M. First-line beta-blockers versus other antihypertensive medications for chronic type B aortic dissection. Cochrane Database of Systematic Reviews, 2014 (2): CD010426.

[6] Huang Y H, Chiu K L, Shen C W, et al. Evaluating Prescription Pattern and Effectiveness of Antihypertensive Drugs in Non-Operated Aortic Dissection Patients. Journal of Clinical Medicine, 2023, 12 (5): 1962.

[7] Suzuki T, Isselbacher E M, Nienaber C A, et al. Type-selective benefits of medications in treatment of acute aortic dissection (from the International Registry of Acute Aortic Dissection [IRAD]). The American journal of cardiology, 2012, 109 (1): 122 - 127.

[8] Laio K M, Shen C W, Huang Y H, et al. Prescription pattern and effectiveness of antihypertensive drugs in patients with aortic dissection who underwent surgery. Frontiers in Pharmacology, 2023, 14: 1291900.