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The Distinguish Method of Severe Aortic Stenosis Treatment Geriatric High Mortality Risk Patients

Aim	To improve quality of treatment for senile patients with pronounced aortic stenosis (AS).
Material and methods	Aortic valve stenosis (AS) is the most common valve pathology in cardiosurgical patients. Surgical correction of aortic valve (AV) stenosis accounts for 10 to 22% of open-heart operations. 125 patients with pronounced AS were treated in the N.N. Burdenko Main Military Clinical Hospital between 2010 and 2017. This study was based on the implementation of new, minimally invasive methods in our clinic in 2013: balloon aortic valvuloplasty (BAVP) of the aortic valve and transcatheter aortic valve prosthesis (TCAVP).
Results	In the group of patients receiving the drug therapy alone, the in-hospital mortality was 2%. At the time of maximum follow-up duration (3 years), the survival rate was 50.5%. In the group of patients who underwent the AV replacement with extracorporeal circulation, the 3-year postoperative mortality was 16.6%. There was no 3-year mortality in the group of patients who underwent TCAVP. The short-term beneficial effect of BAVP was confirmed.
Conclusion	An algorithm was developed for medical care of patients older than 75 with pronounced AS; the place of BAVP in the step-by-step management of these patients was determined. Using the developed approach in the management of these patients provided a 32% ($p<0.05$) increase in the number of cases of radical surgical care.
Keywords	Aortic stenosis; aortic valve replacement; balloon aortic valvuloplasty
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Cardiovascular diseases (CVDs) rank among the top causes of death in the global, adult population [1]. Valve disease is one of the most common indications for surgery in patients with CVDs [2]. The most common acquired valve defect is aortic valve (AV) stenosis (AS) [3]. Before the introduction of antibacterial therapy into clinical practice, acute rheumatic fever (ARF) was the primary cause of AS. In the 1965–1980 retrospective study at Mayo Clinic, ARF was the cause of AS in 56%, bicuspid aortic valve (BAV) in 24%, and senile AV stenosis in 20% of cases. Since the 1950s, an effective approach to the treatment and prevention of cardiac complications of ARF began to change the profile of AS causes. In developed countries by 1985, ARF as the cause of AV stenosis was already reduced to 5–15% [4]. The decreasing incidence of ARF had naturally led to the fact that by 1990, degenerative stenosis of bicuspid and tricuspid AVs had become a leading cause of AS. In the 21st century, senile degeneration of the tricuspid AV is the most common cause of AS. Degeneration of the bicuspid AV and rheumatic stenosis are the second and third most common causes of AS [5]. Other causes do not exceed 1% and include active infectious endocarditis, homozygous lipoproteinemia type 2, systemic lupus erythematosus, mucopolysaccharidosis syndrome (MPS I-S), Fabry's disease, and ochronosis [6–10].

Despite the development of immunological and genetic testing methods, the molecular cause of AS has not been identified. Deep sequencing and immunohistochemistry of the AV cusps revealed faster development of AV degeneration in the presence of NOTCH1 and GATA-5 proteins. The presence of the rs10455872 allele is associated with a 1.5–2.0-fold increased risk of developing AS [11, 12]. Despite these studies, it is not currently possible to break the pathogenetic chain of AV degeneration and subsequent decompensation of cardiac activity using therapeutic methods. At present, replacement of AV is the only effective method for correcting severe AS.

The mortality of senile patients who underwent AV replacement remains high and reaches 15%. Due to severe

concomitant pathology and an increased perioperative risk of death, 30% of patients refuse to have AV replacement under cardiopulmonary bypass (CPB). The search for alternative methods of AV replacement in the open heart resulted in the development of balloon aortic valvuloplasty (BAV). Only the short-term efficacy of this surgery was shown [13]. Restenosis of the AV [14] occurred in 1–1.5 mos. The next stage in the development of minimally invasive AV surgery was the construction of a stent prosthesis.

The objective of this study was to improve the treatment results of senile patients with severe AS.

Material and Methods

From 2010 to 2017, 643 patients with AS were treated in the Cardiovascular Surgical Center of the Burdenko Main Military Clinical Hospital. The inclusion criteria for the current study were severe AS confirmed by echocardiography (aortic valve area <1 cm^2, mean AV pressure gradient >40 mmHg, blood flow velocity >4.0 m/s), and the age of patients greater than 75 yrs. Of the 643 patients, 125 patients were eligible for inclusion (Table 1).

Due to high surgical risk, 89 patients received conservative therapy, 13 patients had AV replacement under CPB, 8 patients underwent BAV, and later 7 of them underwent transcatheter aortic valve replacement (TAVR). Twenty patients underwent TAVR. The study was performed according to the principles of the Helsinki Declaration.

Table 1. Clinical characteristics of the patients

Parameter	Value
Male	101
Female	24
Mean age, yrs	81.7±2.7
Body mass index, kg/m^2	25±2.4
Manifestations of CHF at the time of the surgery (NYHA FC), %	
• II	24
• III	60
• IV	16
Echocardiogram	
LVEDD, cm	5.5±0.5
LVESD, cm	3.6±0.7
EF, %	60.3±10.3
AV area, cm2	0.8±0.2
AV mean systolic gradient, mmHg	53.4±13.3
Peak blood flow velocity across AV, m/s	5.1±0.6
DVI	0.18±0.03
VTI	0.19±0.02
PA systolic pressure, mmHg	36.7±11.6

CHF, chronic heart failure;
FC, functional class: EDD, end-diastolic dimension;
LV, left ventricle; ESD, end-systolic dimension;
EF, ejection fraction; AV, aortic valve; DVI, Doppler velocity index;
VTI, velocity time integral; PA, pulmonary artery.

Results

Of the 89 patients treated only with drug therapy, hospital mortality was 2%, and 6-mo mortality was 15.7%. Within the maximum follow-up period of 3 yrs, the survival rate for this group was 50.5%. AV replacement under CPB was performed in 12 patients. 17% of these patients had chronic heart failure (CHF) of functional class (FC) IV (NYHA), 67% had FC III, and 17% FC II. The EuroSCORE I was 22.2±1.6%, EuroSCORE II was 6.0±0.5%. The Charlson Comorbidity Index (CCI) was 10±2 points, and the Cumulative Illness Rating Scale-Geriatric (CIRS-G) was 19±2. There were no fatal outcomes during the intra-operative and 12-mo follow-up periods. In the early postoperative period, there were no cases of myocardial infarction and strokes. Transient heart rhythm disorders that required temporary cardiac pacing were observed in 49% of these patients for up to seven days. Biological valve prostheses were implanted in all patients. The duration of CPB was 121±30.3 min with aortic cross-clamping for79.3±15.2 min. The 3-yr postoperative mortality was 16.6%.

Patients who underwent AV BAV (n=8) had CHF FC IV. Their mean age was 84.6±3.25 yrs, CCI was 18±5.4 points, and CIRS-G was 28±3. The EuroSCORE I and EuroSCORE II risk scores were 69.5±1.6% and 42.3±0.5%, respectively. The duration of the BAV procedure was 50.2±8.5 min. Fluoroscopy time was 12.4±4.2 min, and 8 of the 10 procedures were performed without contrast enhancement. Atlas Gold LD 20x40; Maxi LD 18x40, 16x40, 14x40, Nucleus 22x40 balloons were used. The puncture site was closed using a Proglide device. No complications during the procedure were reported.

In the pre-operative period, all patients needed inotropic support with dopamine (7.6±2.2 μg/kg/min). Hemodynamics stabilized after the surgery. Changes in intracardiac hemodynamics are presented in Table 2. In the next stage, seven patients underwent TAVR, and two patients had the BAV procedure performed twice, since, at the time of the surgery, they had absolute contraindications to radical correction of the AV defect. One 88-yr old patient with an extremely high CCI, i.e., 50% probability of death during hospitalization and 94% probability of death within a year, died of progressive heart failure on Day 4 following the second BAV procedure. The postmortem examination found no macroscopic signs of cusp rupture, which can be explained by splitting the AV cusps along commissures using BAV The AV diameter was 13 mm, indicating that the AV BAV procedure was effective.

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TAVR was performed on 20 patients. The EuroSCORE I and EuroSCORE II scores of surgical risk were 46.4±5.3% and 5.0±0.8%, respectively. The CCI and CIRS-G were 23±2 and 25±2, respectively. The mean duration of the TAVR intervention was 84±11 min, and fluoroscopy lasted for 12 min. The mean amount of iodine contrast for the procedure was 300 ml. All patients had a CoreValve Transcatheter Aortic Valve, size 23–31, implanted (Figure 1). Permanent pacemakers were implanted in four patients. There were no fatal outcomes during the maximum follow-up period of 3 yr.

The mean ICU stay and duration of hospitalization of patients who underwent TAVR were less than in patients after AV replacement under CPB (2.3±1.4 days vs. 3.6±1.2 days and 4.6±1.7 days vs. 12.8±3.7 days, respectively; $p<0.05$). After AV replacement, all patients had CHF FC II.

Discussion

Since 2013, endovascular techniques for aortic stenosis, AV BAV and TAVR, has been adopted in the Cardiovascular Surgical Center of the Burdenko Main Military Clinical Hospital. These new treatment methods made it necessary to review the treatment algorithm for severe AS.

In 2010–2013, 60 patients over 75 yrs with severe AS were treated at our center. A multidisciplinary advisory team examined all the patients. Until 2013, there had been two treatments available for such patients, conservative therapy and AV replacement under CPB. In more than 50% of cases, the possibility of radical correction was associated with extremely high risk to the patient. The leading monocausal reasons for canceling surgical correction of the AV defect were cancer recurrence (25%) and the patient's refusal of treatment (25%; see Figure 1).

At the same time, only 33% of patients had absolute contraindications to surgery, These included blood disorders, severe chronic obstructive disease, acute exacerbation of systemic disease (rheumatoid arthritis, multiple myeloma), and acute gastric ulcer. Of the 60 patients who had indications for AV replacement, only 10% underwent radical surgery for valvar defects.

In 2013, a new algorithm for the treatment of such patients was developed when the BAV and TAVR methods were introduced into clinical practice (Figure 2). Results are presented according to the developed algorithm in Table 3.

Transcatheter AV replacement is now widely used worldwide. Several Russian cardiosurgical centers have performed hundreds of such surgeries. The study carried out at the Sverdlovsk Regional Clinical Hospital No. 1 (Yekaterinburg) in 2012–2018 included 251 patients. A random number table was used for the simple randomization of patients, according to which 128 patients underwent transcatheter AV replacement, and 123 patients had AV replacement under CPB. The mean age of the patients

Table 2. Echocardiographic findings in patients before and after AVBAV

Parameter	Before surgery	First 24 hours after surgery
AV peak systolic pressure gradient, mmHg	108±15	88.3±12.6
AV mean systolic pressure gradient, mmHg	50±12	43.3±7.5
AV peak stenotic jet velocity across AV, m/s	5.0±0.3	4.05±0.3
DVI	0.18±0.01	0.22±0.04
VTI	0.19±0.02	0.26±0.03

Figure 1. Reasons for conservative therapy in the presence of severe aortic stenosis in patients over 75 yrs with high surgical risk

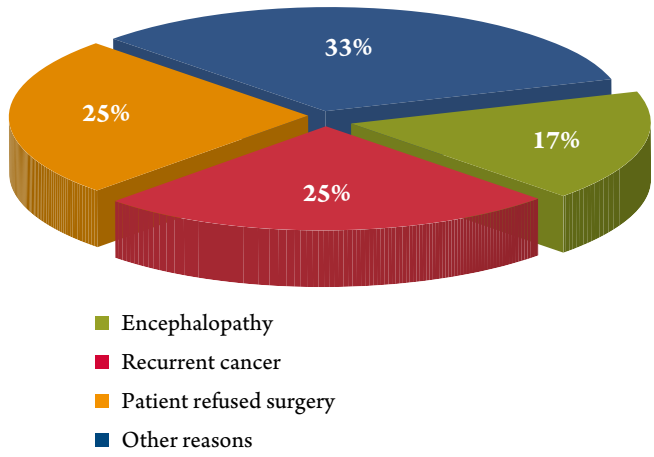


Table 3. Efficacy of the new treatment algorithm for senile patients with severe aortic stenosis and high surgical risk

Parameter	Before the new algorithm is implemented	After the new algorithm is implemented
Number of patients with severe AS over 75 yrs	60	65
Number of AV replacements using CPB	6	7
Number of BAV procedures	0	10
Number of TAVR procedures	0	20
Patients with radical AV correction, %	10	41.53

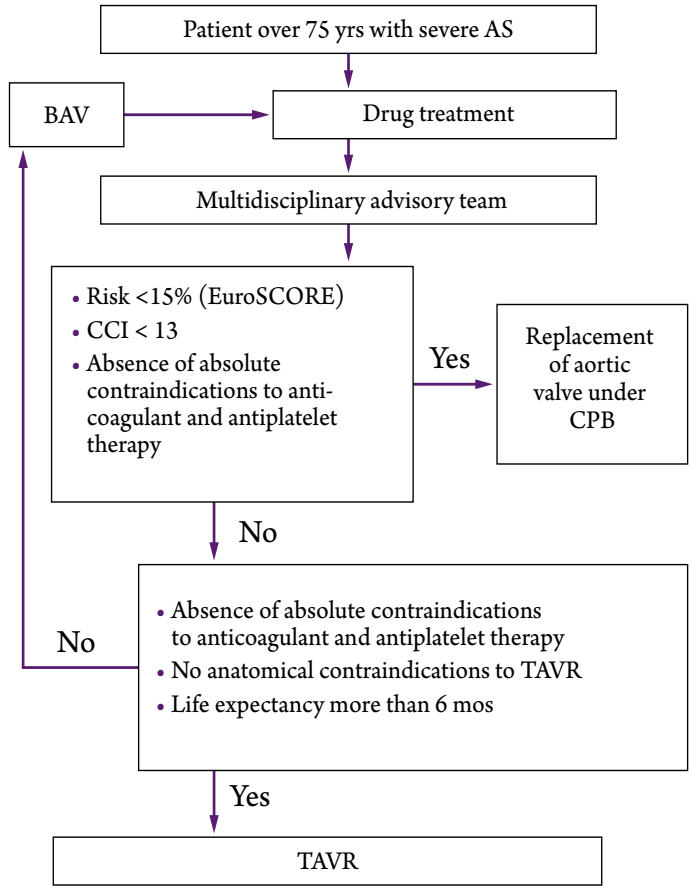
AS, aortic stenosis; AV, aortic valve; CPB, cardiopulmonary bypass; BAV, balloon aortic valvuloplasty; TAVR, transcatheter aortic valve replacement.

was 67.2±9.94 yrs. The rate of postoperative complications was 10.7% in patients who underwent endovascular AV correction and 30.9% in patients who had valve replacement was performed under CPB [15].

In the Meshalkin National Medical Research Center, a prospective study was carried out in patients with high surgical risk. That study included an analysis of the treatment of 140 patients who underwent the TAVR procedure. The maximum follow-up period was 12 mos. The 1-yr mortality was 9%. Interestingly, CCI greater than 5 and initially poor quality of life were identified as predictors of postoperative complications [16].

Despite the comprehensive coverage of the methods of AS correction in both Russian and foreign literature, the patient selection criteria for endovascular or CPB interventions are not yet finally determined. Several recent extensive foreign studies (Evolut, Partner 3) were carried out to determine indications for TAVR in patients with low surgical risk. The Evolut study, carried out from March 2016 to November 2018, involved 1468 patients in whom radical AS correction was performed. The mean age of the patients was 74 yrs. Patients were randomized into two groups, and TAVR was performed in 725 patients, and AV replacement under CPB in 678 patients. All patients had low surgical risks (STS 1.9%). The maximum follow-up period was 24 wks. The 2-yr mortality and the number of disabling strokes in the TAVR and CPB groups were 5.3% and 6.7%, respectively. Patient mortality (4.5%) did not differ between the groups. The rate of postoperative complications (bleeding, heart rhythm disorders, cardiovascular and renal failure) was significantly lower in the group of patients who underwent TAVR [17].

Figure 2. Algorithm of the differentiated approach to the selection of treatment methods for senile patients with high surgical risk and severe AS



AS, aortic stenosis; BAV, balloon aortic valvuloplasty; TAVR, transcatheter aortic valve replacement; CPB, cardiopulmonary bypass.

Conclusion

Our work resulted in the creation of an algorithm for the differentiated approach to the selection of treatment for patients over 75 yrs with severe aortic stenosis. The use of this approach at our center increased the number of radical surgeries for patients with high surgical risk by 32% ($p<0.05$). The 3-yr survival rate in the patients who underwent transcatheter aortic valve replacement was 100%. Balloon aortic valvuloplasty is an independent method of treatment for patients with severe aortic stenosis. The short-term effect of this procedure was shown. Thus, additional studies of transcatheter aortic valve replacement or aortic valve replacement are required in the future [18].

No conflict of interest is reported.

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