

Disfunkcija umjetnoga srčanog zalistka; etiologija, strategije i ishodi liječenja: opisno-analička studija

Prosthetic Valve Malfunction; Etiologies, Treatment Strategies and Treatment Outcomes: A Descriptive-analytic Study

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SAŽETAK: Uvod: Bolesti srčanih zalistaka rasprostranjene su diljem cijeloga svijeta te povezane s velikom stopom pobola i smrtnosti. Kirurška zamjena zalistaka najvažniji je način liječenja bolesti srčanih zalistaka. Jedna od najvažnijih komplikacija liječenja jest disfunkcija umjetnoga srčanog zalistka, što zahtijeva brzu dijagnozu i liječenje. U ovoj smo studiji istraživali etiologiju, strategije i ishode liječenja u seriji bolesnika s disfunkcijom umjetnoga srčanog zalistka.

Bolesnici i metode: Ova je presječna, analitičko-opisno studija uključivala 63 slučaja u 52 bolesnika s disfunkcijom umjetnoga srčanog zalistka. Upitnikom su prikupljeni podaci o koagulacijskom statusu te demografski, klinički podaci. Zabilježeni su i podaci o liječenju, ishodima liječenja te o učestalosti ponovne hospitalizacije. Podatci su analizirani primjenom programa SPSS 20.

Rezultati: U ovoj je populacijskoj studiji prosječna dob bila $49,98 \pm 14,31$, a 53,9 % bolesnika bile su žene. Od ukupno 63 slučaja, 57 ih je imalo disfunkciju mehaničkog zalistka, a 6 bolesnika disfunkciju na biološkom zalistku. Svi slučajevi disfunkcije bili su uzrokovani trombozom. Kirurški su zahvati bili najčešća metoda i bili su povezani s odličnim ishodima u usporedbi s drugim strategijama liječenja ($p = 0,002$). U ovoj smo studiji proučavali prihvatljive ishode za trombolitičku terapiju.

Zaključak: Tromboza je bila najčešći uzrok disfunkcije umjetnoga srčanog zalistka, najvjerojatnije uzrokovana neadekvatnim antikoagulantnim liječenjem. Može se zaključiti da je za smanjenje disfunkcije nužna edukacija i praćenje bolesnika radi točnog utvrđivanja koagulacijskog statusa. Također smo zamijetili da su kirurški zahvati bili mnogo uspješniji od drugih oblika liječenja.

SUMMARY: Background: Valvular heart diseases are common worldwide and are associated with a high rate of mortality and morbidity. Surgical valve replacement is the most important treatment for valvular diseases. One of the most important complications of this treatment is prosthetic valve malfunction which requires rapid diagnosis and treatment. In this study, we examined the etiologies, treatment strategies, and treatment outcomes in a series of patients with prosthetic valve malfunction.

Patients and Methods: In this cross-sectional, analytic-descriptive study, 63 cases in 52 patients with prosthetic valve malfunction were included. Their coagulation status, demographic, and clinical information was collected in a questionnaire. Patients treatment and their outcomes or rehospitalization rate was recorded as well. Data were analyzed using SPSS 20 software.

Results: In our study population, average age was 49.98 ± 14.31 , and 53.9% of patients were women. Among 63 cases, 57 of them had mechanical valve malfunction and 6 of them had biological valve malfunction. All cases of mechanical valve malfunction were caused by thrombosis. Surgery was the most common treatment strategy and was associated with excellent outcomes compared with other strategies ($p=0.002$). In this study, we observed acceptable outcomes for thrombolytic therapy.

Conclusion: Thrombosis was the most frequent cause of prosthetic valve malfunction in this study, which seems to be due to inadequate anticoagulant therapy. It can be concluded that educating and following patients for their accurate coagulation status is necessary for decreasing prosthetic valve malfunction. We also found surgical treatment to be significantly better than other treatments.

KLJUČNE RIJEČI: umjetni zalistak, kirurški zalistak, tromboza, trombolitička terapija, bolest srčanih zalistaka.

KEYWORDS: valve prosthesis, surgical valve, thrombosis, thrombolytic therapy, heart valve diseases.

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Uvod

Bolesti srčanih zalistaka pogađaju više od 100 000 000 ljudi u svijetu s prevalencijom od 2,5 % u SAD-u te se povezuju s visokom stopom pobola i smrtnosti. Kirurška zamjena zalistaka jedna je od najvažnijih strategija liječenja bolesti srčanih zalistaka te je praćena odličnim dugoročnim ishodima¹.

Kirurška zamjena srčanog zalistka može uzrokovati kratkoročne komplikacije koje vode do invaliditeta ili smrti. Malfunkcija umjetnog zalistka jedna je od najvažnijih komplikacija koja može biti opasna i smrtonosna u bolesnika pa stoga zahtijeva brzu dijagnozu i liječenje².

Malfunkcije umjetnoga srčanog zalistka dijele se na opstruktivne i insuficijentne³. Među opstruktivnim uzrocima, tromboza umjetnoga srčanog zalistka zahtijeva brzu dijagnozu i liječenje te se uglavnom povezuje s akutnim simptomima poput zaduhe, akutnoga plućnog edema, bolova u prsnoj koži, moždanim udarom ili perifernom embolijom⁴. Na transtorakalnoj ehokardiografiji (TTE) može biti detektirana povišenjem gradijenta tlaka i izostankom ili oštećenjem pokretnosti zalistka⁵. Prva linija liječenja uključuje ponovni kirurški zahvat, trombolitičku ili intenzivnu antikoagulantnu terapiju, što ovisi o lokaciji i opsegu tromboze, funkcijskom stupnju zaduhe, riziku od kirurškog zahvata, iskustvu liječnika itd.⁶.

S obzirom na opasnost od komplikacija, odlučili smo istražiti seriju bolesnika s malfunkcijom umjetnih srčanih zalistaka te utvrditi njihovo zdravstveno stanje, uzroke, primijenjene strategije liječenja i njihove ishode u Afshar Heart Center tijekom razdoblja od 3 godine.

Bolesnici i metode

Odlučili smo provesti presječnu, opisno-analitičku studiju u svih bolesnika s dijagnozom malfunkcije umjetnoga srčanog zalistka putem TTE-a ili fluoroskopije upućenih u Afshar Heart Center od 2015. do 2017. godine. Svi su bolesnici potpisali informirani pristanak da se njihovi medicinski i demografski podatci mogu iskoristiti u istraživačke svrhe. Studiju smo oblikovali i proveli na temelju odredaba postojeće Helsinške deklaracije.

Uključili smo sve bolesnike s malfunkcijom umjetnih srčanih zalistaka koji su bili upućeni u Afshar Heart Center (Yazd, Iran) od 2015. do 2017.; bolesnici s malfunkcijom umjetnog zalistka zbog endokarditisa, tehničkih grešaka poput neusklađenosti i oporavkom tlaka bili su isključeni iz studije.

U istraživanje su uključena 52 bolesnika (63 slučaja) te su prikupljeni podatci o njihovu koagulacijskom statusu te demografske, kliničke informacije. Podatci o dobi, spolu, vremenu proteklom od kirurške zamjene srčanog zalistka, anamnestičkim podacima o prethodnoj malfunkciji umjetnoga srčanog zalistka, podacima o preboljenom moždanom udaru, kliničkoj slici, funkcijskom stupnju zaduhe, srčanom ritmu, vrijednosti INR-a (engl. *international normalized ratio*), ejekcijskoj frakciji lijeve klijetke (LVEF; prema engl. *left ventricular ejection fraction*), abnormalnim ehokardiografskim ili fluoroskopskim nalazima, provedenim postupcima i ishodima liječenja prikupljeni su s pomoću upitnika te su analizirani u programu SPSS 20.

Metodama deskriptivne statistike prikazani su srednja vrijednost \pm standardna devijacija, postotak i frekvencija. U ovoj su istraživanju sve ispitivane vrijednosti bile nominalne i kategorijske te je stoga χ^2 -test primijenjen za sve slučajeve. De-

Introduction

Valvular heart diseases involve more than 100 000 000 people around the world with a prevalence of 2.5% in the USA and is associated with high rate of mortality and morbidity. Surgical valve replacement is the most important treatment strategy for valvular diseases, resulting in excellent long term outcomes¹.

Surgical valve replacement can lead to short-term complications causing disability or death. Prosthetic valve malfunction is one of the most important complications which can be dangerous and lethal in patients and requires rapid diagnosis and treatment².

Prosthetic valve malfunctions can be categorized as obstructive or insufficiency malfunctions³. Among obstructive malfunctions, prosthetic valve thrombosis requires rapid diagnosis and treatment and is usually associated with acute presentations such as dyspnea, acute pulmonary edema, chest pain, stroke, or peripheral emboli⁴. In transthoracic echocardiography (TTE) it can be associated with elevated pressure gradient and no or impaired leaflet movement⁵. First-line treatment options include repeated surgery, thrombolytic therapy, or intensive anticoagulant therapy which depends on location and size of the thrombosis, patients functional class of dyspnea, surgical risk, or physicians experience, etc.⁶.

Given the dangerous complications of impaired prosthetic valve function and efficacy and outcomes of the abovementioned treatments, we decided to investigate a series of patients with prosthetic valve malfunction for patient condition, the cause of malfunction, applied treatment strategies, and outcomes of treatment in the Afshar Heart Center during a 3-year period.

Patients and Methods

We decided to perform a cross-sectional, descriptive-analytic study on all patients diagnosed with prosthetic valve malfunction via TTE or fluoroscopy referred to the Afshar Heart Center between 2015 and 2017. All patients signed an informed consent form allowing their medical and demographic information to be used for research purposes. We designed and carried out this study based on the latest Helsinki declaration.

We included all patients with prosthetic valve malfunction between 2015 and 2017 referred to the Afshar Heart Center, Yazd, Iran; patients with prosthetic valve malfunction due to endocarditis, technical errors such as mismatch, and pressure recovery were excluded.

Finally, 52 patients (63 cases) were enrolled and their coagulation status and demographic, clinical, and para-clinical information was collected. Data including age, gender, time passed after surgical valve replacement, previous history of prosthetic valve malfunction, history of stroke, clinical manifestations, patients dyspnea functional class, cardiac rhythm, international normalized ratio (INR), left ventricular ejection fraction (LVEF), abnormal echocardiography of fluoroscopy findings, performed treatments, and treatment outcomes were collected using a questionnaire and data were analyzed using SPSS 20 software.

Descriptive statistics are reported as mean \pm SD, percentage, and frequency. In this study, all analyzed variables were nominal and categorical and thus the Chi-square test was used

skriptivni rezultati prikazani su u obliku tablica, a analitički su rezultati prikazani kao P-vrijednosti; u svim se slučajevima dvosmjerna P-vrijednost <0,05 smatrala statistički značajnom.

U ovom smo radu samo analizirali i izložili glavne rezultate s naglaskom na strategije liječenja i njihove ishode. Ostale detaljne informacije uvijek su dostupne te će zainteresiranim istraživačima ili čitateljima biti stavljene na raspolaganje ako kontaktiraju autora za dopisivanje.

Rezultati

Istraživanje je uključilo 63 slučaja u 52 bolesnika s malfunkcijom umjetnoga srčanog zalistka, koji su primljeni u Afshar Heart Center u razdoblju od 2015. do 2017. Dva su bolesnika isključena zbog neusklađenosti. Prosječna je dob uključenih bolesnika bila $49,98 \pm 14,31$. Detaljni deskriptivni statistički podatci prikazani su u **tablici 1**.

Od ukupna 63 slučaja, 57 (90,4 %) ih je imalo malfunkciju mehaničkoga srčanog zalistka, a njih 6 (9,6 %) malfunkciju biološkoga zalistka. Prosječno vrijeme koje je proteklo od zamjene umjetnoga srčanog zalistka bilo je $5,65 \pm 4,89$ godina, a vrhunac za razvoj malfunkcije mehaničkoga umjetnog zalistka bio je u prve 3 godine nakon ugradnje, kao što je vidljivo na **slici 1**.

in all cases. Descriptive results are presented in the form of descriptive and frequency tables, while analytic results are reported as P-values; in all cases, a 2-tailed P-value <0.05 was considered to be statistically significant.

In this paper we only analyzed and report main findings focused on treatment strategies and their outcomes. Other detailed information is always available and will be made available to interested researchers or readers contacting the corresponding author.

Results

This study included 63 cases in 52 patients with prosthetic valve malfunction admitted to the Afshar Heart Center during 2015 and 2017. Two patients were excluded because of mismatch. The average age was 49.98 ± 14.31 in our population. Detailed descriptive statistical information of our study population is summed up in **Table 1**.

Of the total 63 cases, 57 (90.4%) had mechanical valve malfunction and 6 (9.6%) had biological valve malfunction. Average time since surgical valve replacement was 5.65 ± 4.89 years, and the peak for mechanical valve malfunction was in the first 3 years after surgery as seen in **Figure 1**.

TABLE 1. Descriptive statistics associated with study population.

Studied variables	Number	Percentage
Age	49.98±14.31	
Gender	Women=34	Women=53.9%
	Men=29	Men=46.1%
Type of prosthetic valve	Mechanical	57
	Biological	6
AF rhythm	21	33.3%
LVEF <40%	8	12.7%
Suboptimal INR	47	74.6%

AF – atrial fibrillation; LVEF – left ventricular ejection fraction; INR – international normalized ratio

Etiologija malfunkcije u svim slučajevima mehaničkog zalistka bila je tromboza, koja je u 12 bolesnika bila povezana s formiranjem panusa. Među slučajevima s trombozom mehaničkog zalistka, 42 bolesnika (73,6 %) imala su opstrukciju zalistka, a 15 slučajeva (26,4 %) bilo je bez opstrukcije. Među slučajevima s malfunkcijom biološkoga zalistka uočena su 4 slučaja s degenerativnim promjenama, koje su u dvaju bolesnika bile povezane s trombozom. U 42 slučaja s opstruktivnom trombozom, 14 (33,3 %) bolesnika primilo je trombolitičku terapiju, a 28 (66,7 %) ih je na kraju bilo podvrgnuto kirurškom liječenju. Među bolesnicima odabranima za kirurških zahvat, on je proveden u 21 bolesnika, među kojima se njih 20 potpuno oporavilo, a zabilježen je jedan smrtni slučaj. Od 14 slučajeva koji su primili trombolitičku terapiju, 10 (71,4 %) ih se potpuno oporavilo, 2 (14,3 %) su se djelomično oporavila, a u 2 bolesnika (14,3 %) razvilo se intrakrani-

The malfunction etiology responsible for all cases with mechanical valve was thrombosis, which associated with pannus formation in 12 cases. Among cases with mechanical valve thrombosis, 42 patients (73.6%) had valvular obstruction and 15 cases (26.4%) were non-obstructive. Among patients with biological valve malfunction, 4 cases with degenerative changes were observed, which were associated with thrombosis in 2 cases. In 42 cases with obstructive thrombosis, 14 (33.3%) cases received thrombolytic therapy and 28 (66.7%) of them were selected for surgical treatment. Among selected patients, 21 of them eventually underwent surgery, of which 20 patients had complete recovery and 1 mortality was recorded. Among 14 cases who received thrombolytic therapy, 10 (71.4%) had complete recovery, 2 cases (14.3%) had partial recovery, and 2 patients (14.3%) developed intracranial hem-

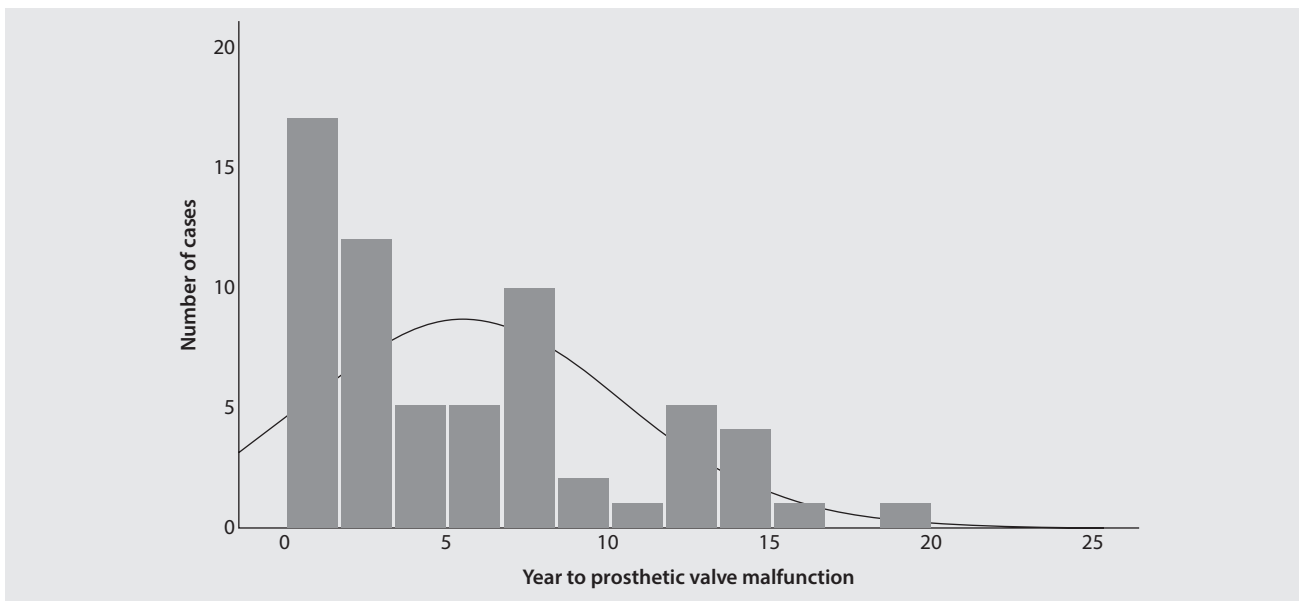


FIGURE 1. Average time after surgical valve replacement before prosthetic valve malfunction, 5.65±4.89.

jalno krvarenje (ICH; prema engl. *intracranial hemorrhage*) kao posljedica liječenja. Nije zabilježen nijedan embolijski cerebrovaskularni inzult (CVA; prema engl. *embolic cerebrovascular accidents*) ili smrt kao posljedica trombolitičke terapije.

U ovom istraživanju 21 bolesnik je bio podvrgnut kirurškom zahvatu, 14 ih je primilo trombolitičko liječenje, a 28 bolesnika primilo je intenzivnu antikoagulantnu terapiju. Među bolesnicima koji su primili antikoagulantnu terapiju, 17 ih je imalo neopstruktivnu trombozu, a 11 je bolesnika bilo odabrano za kirurški zahvat koji nije bio proveden zbog različitih razloga kao što su visoka rizičnost zahvata, komorbiditeti itd. Učestalosti strategija liječenja prikazane su u **tablici 2**.

orrhage (ICH) due to treatment. No embolic cerebrovascular accidents (CVA) or deaths were recorded following thrombolytic therapy.

In this study population, 21 patients underwent surgery, 14 patients received thrombolytic treatment, and 28 patients received intensive anticoagulant therapy. Among cases who received anticoagulant therapy, 17 cases had non-obstructive thrombosis and 11 cases were selected for surgery but did not undergo surgery for various reasons such as high risk of surgery, comorbidity, etc. The frequency of treatment strategies is shown in **Table 2**.

TABLE 2. Distribution of different treatment strategies in the study sample.

Treatment	Frequency	Percentage
Surgery	21	33.3%
Thrombolytic therapy	14	22.2%
Intensive anticoagulant therapy	28	44.5%
Total	63	100%

Ako usporedimo odgovor i ishode liječenja, kirurško je liječenje bilo mnogo bolje od drugih strategija. Na temelju provedenih postupaka, 44 bolesnika postigla su potpuni oporavak, 16 ih se djelomično oporavilo ili su bili predloženi za drugi elektivni kirurški zahvat, a liječenje nije bilo uspješno u 3 bolesnika zbog komplikacija uzrokovanih liječenjem. U jednom slučaju neuspjelog liječenja u bolesnika se razvio respiratorni distres nakon trombolitičke terapije te je podvrgnut kirurškom postupku tijekom tog bolničkog liječenja, dok su u druga

When comparing response to treatment and treatment outcomes, surgical treatment was significantly better than other treatment strategies. Based on performed treatments, 44 cases had complete recovery, 16 cases had partial recovery or were suggested for another elective surgery, and our treatment failed in 3 patients due to treatment complications. In one of the failed treatments, the patient developed respiratory distress following thrombolytic therapy and underwent surgical treatment during the same hospitalization, while patients in the other two

2 neuspjela slučaja liječenja zabilježena u bolesnika u kojih se razvio ICH zbog trombolitičke terapije, zbog čega je na 1 bolesniku proveden kirurški zahvat, a 1 je liječen konzervativno. Ishodi liječenja prikazani su u **tablici 3**. Bazirano na χ^2 -testu, postojala je statistički značajna razlika ($p = 0,002$) u ishodima liječenja na temelju različitih strategija liječenja.

failed cases developed ICH because of thrombolytic therapy, for which 1 underwent surgery and 1 received conservative treatment. Treatment outcomes are summed up in **Table 3**. Based on the Chi-square test, there was a statistically significant difference ($p=0.002$) in treatment outcomes based on different treatment strategies.

TABLE 3. Treatment outcomes in different treatment groups.

Treatment	Complete recovery	Partial recovery/ selected for surgery	Failure of treatment	Total
Surgery	20 (31.7%)	0	1 (1.6%)	21 (33.33%)
Thrombolytic therapy	10 (15.9%)	2 (3.17%)	2 (3.17%)	14 (22.24%)
Intensive anticoagulant therapy	15 (23.8%)	13 (20.63%)	0	28 (44.43%)
Total	45 (71.4%)	15 (23.8%)	3 (4.8%)	63 (100%)

Surgical treatment was followed by significantly better outcomes (P -Value=0.002)

U ovoj studiji u 9 bolesnika zabilježeno je 11 slučajeva rehospitalizacije, pri čemu je 1 bolesnik imao 3 epizode bolničkog liječenja zbog malfunkcije zalistka. U trima slučajevima rehospitalizacije zahvaćeni se zalistak razlikovao od onog iz prethodne hospitalizacije. Prosječno vrijeme do rehospitalizacije bilo je $1,82 \pm 3,82$ mjeseca nakon prethodne hospitalizacije, kao što je vidljivo na **slici 2**.

Učestalost rehospitalizacija prikazana je u **tablici 4**. Na temelju rezultata χ^2 -testa, nije bilo statistički značajne razlike u broju rehospitalizacija na temelju primljenog liječenja ($p = 0,825$).

In the present study, 11 cases of rehospitalization were recorded in 9 patients, with 1 patient who had 3 hospitalization episodes because of valvular malfunction. In 3 cases, the involved valve was different from the previous hospitalization. Average time to rehospitalization was 1.82 ± 3.82 months after previous hospitalization as seen in **Figure 2**.

The frequency of rehospitalization cases is presented in **Table 4** below. Based on the Chi-square test, there was no statistically significant difference in number of rehospitalizations based on received treatment ($p=0.825$).

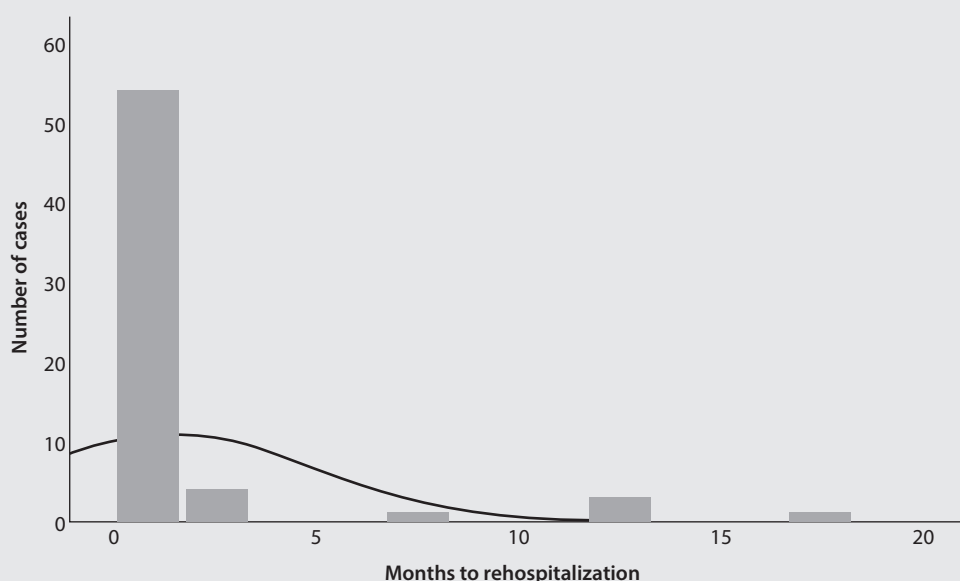


FIGURE 2. Average time before rehospitalization, $1,82 \pm 3,82$.

TABLE 4. Number of rehospitalization cases in different treatment groups.

Treatment	Number	Percentage
Surgery	4	36.4%
Thrombolytic therapy	3	27.2%
Intensive anticoagulant therapy	4	36.4%
Total	11	100%

There was no statistically significant association between different treatment strategies and number of rehospitalization cases (P-Value=0.825).

Rasprava

U ovo smo istraživanje uključili i istražili 63 slučaja malfunkcije umjetnoga srčanog zalistka u 52 bolesnika u razdoblju od 3 godine. U drugim sličnim istraživanjima broj je sudionika bio mnogo manji unatoč duljem razdoblju istraživanja^{7,8}, primjerice u studijama koje su proveli Dürrleman *i sur.* koji su pratili samo 39 slučajeva tromboze umjetnoga srčanog zalistka tijekom 20 godina⁹ i Wei-Guo Ma *i sur.* koji su prikazali 48 bolesnika s malfunkcijom umjetnoga srčanog zalistka u razdoblju od 15 godina¹⁰. Mogući razlozi za ovakve razlike jesu: 1) istraživački je centar referentni centar koji prikuplja bolesnike iz drugih centara; 2) neke su studije isključivale bolesnike s biološkim zalisticima; 3) viša učestalost neopstruktivnih tromboza u ovoj studiji u usporedbi sa sličnim istraživanjima; 4) niža učestalost suradljivosti u ovom istraživanju pri uporabi propisanih antikoagulantnih lijekova; 5) nedostatak dobrog registra i sustava praćenja bolesnika.

U ovoj je studiji prosječna dob bolesnika bila $49,98 \pm 14,31$ godina, a 53,9 % bolesnika bile su žene. U drugim sličnim istraživanjima također je bilo više žena nego muškaraca (ali s većom razlikom), a prosječna dob nije se mnogo razlikovala^{8,11,12}.

Prosječno vrijeme proteklo od kirurške zamjene srčanog zalistka do njegove malfunkcije bilo je $5,65 \pm 4,89$ godina s vrhuncem u 3. godini. Vrijednost te varijable bila je različita u drugim sličnim istraživanjima. Primjerice, u studiji koju je proveo Fidel Manuel Cáceres-Lóriga to je prosječno vrijeme bilo 6,8 godina⁷. Ta razlika može biti uzrokovana okolišnim i genetskim razlikama u skupinama koje su istraživane.

Tromboza je u ovom istraživanju nađena u 59 slučajeva (93,6 %) te je bila opstruktivna u 70,2 % slučajeva. U studijskoj populaciji, 18,97 % slučajeva tromboze bilo je povezano sa formiranjem panusa, a u 2 slučaja (3,7 %) bila je povezana s degenerativnim promjenama u biološkim srčanim zalisticima. U drugim je sličnim istraživanjima najčešća etiologija malfunkcije umjetnoga srčanog zalistka također bila tromboza, a ostale etiologije poput formacije panusa većinom su bile prisutne zajedno s postojećom trombozom^{13,14}. To je potvrđeno i u ovom istraživanju, a čini se da je glavni razlog neadekvatna antitrombotska terapija u bolesnika nakon kirurške zamjene srčanog zalistka. Primjerice, u studiji koju su proveli Ahmad Separham *i sur.* tromboza je primijećena u svih bolesnika te je u 88,3 % slučajeva navedena kao opstruktivna, a u 26,7 % slučajeva bila je povezana s formiranjem panusa¹⁵.

Među bolesnicima s opstruktivnom trombozom u ovoj studiji, njih 28 (66,7 %) bilo je odabrano za ponovni kirurški za-

Discussion

During this study, we included and examined 63 cases of prosthetic valve malfunction in 52 patients over a period of 3 years. In other similar studies, this number was significantly lower despite a longer study period^{7,8}, for example in a study performed by Dürrleman *et al.* that examined only 39 cases of prosthetic valve thrombosis over a period of 20 years⁹ and Wei-Guo Ma *et al.* who only reported on 48 patients with prosthetic valve malfunction over a period of 15 years¹⁰. Different reasons can be suggested for such a difference including: 1) our study center is a referral center that gathers patients from other centers; 2) some studies excluded patients with biological valves; 3) higher rate of non-obstructive thrombosis in our study compared to similar studies; 4) less compliance of our study population in using prescribed anticoagulant agents; 5) lack of a good registry and follow-up system for patients.

In our study, the average age of patients was $49,98 \pm 14,31$, and 53.9% of our cases were women. In other similar studies, women were also more numerous than men (but with a bigger difference) and the average age was not very different, being both lower and higher in some studies^{8,11,12}.

The average time since surgical valve replacement before valvular malfunction in our study was 5.65 ± 4.89 years with a peak at 3 years. This variable was different in different similar studies. For example, Fidel Manuel Cáceres-Lóriga reported this average time to be 6.8 years⁷. This difference can be due to environmental and genetic differences in the studied populations.

We observed thrombosis in 59 cases (93.6%), which was obstructive in 70.2% of cases. In our study population, 18.97% of thrombosis cases were associated with pannus formation, whereas in 2 cases (3.7%) thrombosis was associated with degenerative changes in biological valves. In other similar studies, thrombosis was also reported to be the most common etiology for prosthetic valve malfunction and other etiologies such as pannus formation were mostly observed together with underlying thrombosis^{13,14}. These findings are confirmed by our study, and the principal reason seems to be inadequate antithrombotic therapy in patients after surgical valve replacement. For example, in a study by Ahmad Separham *et al.*, thrombosis was observed in all patients and reported as obstructive in 88.3% of cases, and was associated with pannus formation in 26.7% of cases¹⁵.

Among patients with obstructive thrombosis in our study, 28 patients (66.7%) were selected for repeated surgery, of which

hvat, koji je proveden u 21 bolesnika, a ostalih 7 primilo je jaku antikoagulantnu terapiju. Od 21 kirurškog slučaja, u 20 njih postignut je potpun oporavak, a zabilježen je jedan smrtni ishod uzrokovan akutnim respiratornim distresom. U sličnim su studijama kirurški zahvati izabrani češće nego drugi načini liječenja, što je slično našim rezultatima (60 % bolesnika bilo je podvrgnuto kirurškom zahvatu)^{16,17}.

U većini prijašnjih istraživanja^{18,19} stopa je uspješnosti kirurških zahvata bila viša od stope uspješnosti trombolitičkog liječenja, iako smo ostvarili prihvatljivu stopu uspjeha i trombolitičkom terapijom, slično kao i u istraživanju Fidel Manuel Cáceres-Lóriga²⁰. Na temelju toga može se zaključiti da trombolitička terapija može biti važna strategija liječenja te dobra alternativa kirurškom zahvatu kod malfunkcije umjetnoga srčanog zalistka, uz smanjen rizik embolije.

Zaključak

U ovom istraživanju, kao u drugim sličnim studijama, otkrili smo da je tromboza najčešći uzročnik malfunkcije umjetnoga srčanog zalistka, koji je najčešće uzrokovan neadekvatnom antikoagulantnom terapijom. Možemo zaključiti da smanjenje pojavnosti malfunkcije umjetnoga srčanog zalistka edukacijom i poticanjem bolesnika na kontrolu i bilježenje svojega koagulacijskog statusa može spriječiti teret liječenja malfunkcije umjetnih srčanih zalistaka.

21 underwent surgery whereas the other 7 patients received intensive anticoagulant therapy. Among 21 surgical cases, 20 achieved complete recovery and 1 mortality was recorded due to acute respiratory distress. In similar studies, surgery was selected more than other treatment strategies, which is similar to our findings (60% of patients underwent surgery)^{16,17}.

In most previous studies^{18,19}, success rate of surgery was higher than the success rate of thrombolytic treatment, although we also achieved an acceptable success rate using thrombolytic therapy, similar to the study by Fidel Manuel Cáceres-Lóriga's²⁰. This can lead to the conclusion that thrombolytic treatment can be an important treatment strategy and a good alternative for surgery in prosthetic valve malfunction with lower risk of emboli.

Conclusion

In our study, as in other similar studies, we found thrombosis to be the most common etiology for prosthetic valve malfunction, which is mainly due to inadequate anticoagulant therapy. We can conclude that to decrease incidence of prosthetic valve malfunction, educating patients and encouraging them to control and record their coagulation status can remove a considerable burden of treatment of prosthetic valve malfunction.

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