بیمارستان قلب شهید رجایی

ماندگاری دریچه های بیولوژیک قلبی در بیمارانی که در طی سال های ۹۸-۸۲ در بیمارستان قلب و عروق شهید رجایی تحت درمان قرار گرفته اند

شناسنامه طرح

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عنوان طرح:	ماندگاری دریچه های بیولوژیک قلبی در بیمارانی که در طی سال های ۹۸-۸۲ در بیمارستان قلب و عروق شهید رجایی تحت درمان قرار گرفته اند
عنوان لاتین طرح:	The durability of biologic heart valves in patients undergoing treatment in Rajaie CMRC between ۱۳۸۲ and ۱۳۹۸
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نام و نام‌خانوادگی	سمت در طرح	نوع همکاری	توضیحات
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قویدل			
سعید حسینی	همکار طرح	ارزیابی بالینی بیماران	
غلامرضا عمرانی	همکار طرح	ارزیابی بالینی بیماران	
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پرهام صادقی پور	ناظر	نظارت بر اجرای طرح	

دانشکده/مرکز مربوطه

رده	نوع ارتباط با مرکز
مرکز تحقیقات بیماری های دریچه ای قلب	وارد کننده

متون پیشنهاد

آیتم اطلاعات تفضیلی	متن
جدول متغیرها	
جدول زمان بندی	
بیان مسئله	With the increasing use of bioprosthetic valves in last decade, about 75% of implantations have been biologic valve (1). The main reasons for growing use of bioprosthetic valves include (1) the high rate of implantations in elderly patients who might benefit more from biologic valves, (2) the lack of risk for thromboembolic and bleeding events compared to mechanical valves, and (3) an improved design of biologic valves in last decades compared to mechanical valves leading to higher durability than previous generations (2, 3). Two main features of tissue valves are used for the evaluation of routine use in practice, including durability and hemodynamic performance. The improvement of durability of new-generation tissue valves results in more use of such prosthesis, so that it has contributed to the growing use of tissue valves for aortic valve replacement (AVR) (independently of age, with the use of mechanical valves becoming almost negligible (4). There are three types of biologic valve with regard to its origin, including autograft, homograft, and xenograft. A human heart valve that is harvested from the same person is called an autograft, such as in the Ross procedure, during which the pulmonic valve is transferred to the aortic position. A homograft is a human heart valve that has been cryopreserved and treated with antibiotics. Xenograft prostheses are made of porcine aortic valves or bovine pericardium (5). In

addition, xenograft valves are categorized into three major classes including stented (mounted on metal), stentless (mounted on Dacron cloth support), or sutureless (6). Stented biologic valves derived from pericardium have a comparable or slightly lower degeneration rate: 77% of surviving patients still have a properly functioning prosthesis 15 years after aortic valve implantation. Fewer than 10% of patients over age 65 need a second valve replacement procedure (7). Moreover, stentless bioprosthetic valves have also been implemented and their durability has been evaluated in short- to mid-term follow-up period. It has been found that the Sorin Freedom Solo stentless bioprosthesis is as safe as the stented Carpentier Edwards's bioprosthesis, and provides better short- and mid-term haemodynamic performance than the Carpentier Edwards bioprosthesis (8); however, other reports have shown that stentless bioprosthesis are associated with structural valve .(deterioration at longer follow-up (9, 10

Probably the greatest barrier to understanding which bioprostheses offer the best durability, is the fact that most comparative studies are observational rather than randomized, and the wide variability in baseline patient characteristics, perioperative technique, management and follow-up precludes direct comparison of data for specific models of bioprosthesis (11). An additional obstacle to interpreting the available data stems from differences in the definition of durability. Several authors of most recent studies use the definition of structural valve deterioration (SVD) used in the 2008 Guidelines (i.e., dysfunction or deterioration involving the operated valve (exclusive of infection and thrombosis), as determined by reoperation, autopsy or clinical investigation (12), and some other authors use different definitions, including the narrower 1996 guideline definition (i.e., a decrease of one New York Heart Association functional class or more of an operated valve resulting from an intrinsic abnormality of the valve that causes stenosis or regurgitation) (13). The lifetime risk of reoperation for a patient 50 years of age undergoing bioprosthetic valve replacement is approximately 45%, which decreases by approximately 10% for every additional 5 years in patient age at the time of implantation. There is no strong evidence that choosing any individual second- or third-generation bioprosthesis has a significant impact on freedom from reoperation, although available data suggest that there may be a continued trend .(towards improved durability with third generation biologic valve models (2

Hence, in this retrospective cohort study, we sought to evaluate the durability of bioprosthetic valves in our population and to find that which features are associated with the durability of .biologic valves in patients undergoing valvular surgery in Rajaie CMRC between 1382 and 1398

ضرورت اجرا

With the increasing use of bioprosthetic valves in last decade, about 75% of implantations have been biologic valve. The main reasons for growing use of bioprosthetic valves include (1) the high rate of implantations in elderly patients who might benefit more from biologic valves, (2) the lack of risk for thromboembolic and bleeding events compared to mechanical valves, and (3) an improved design of biologic valves in last decades compared to mechanical valves leading to higher durability than previous generations. The lifetime risk of reoperation for a patient 50 years

of age undergoing bioprosthetic valve replacement is approximately 45%, which decreases by approximately 10% for every additional 5 years in patient age at the time of implantation. There is no strong evidence that choosing any individual second- or third-generation bioprosthesis has a significant impact on freedom from reoperation; although available data suggest that there may be a continued trend towards improved durability with third generation biologic valve models. Hence, in this retrospective cohort study, we sought to evaluate the durability of bioprosthetic valves in our population and to find that which features are associated with the durability of biologic valves in patients undergoing valvular surgery in Rajaie CMRC between 1382 and 1398.

بررسی متون

Brennan et al (14) evaluated long-term data comparing biological versus mechanical aortic valve prostheses in older individuals from the Society of Thoracic Surgeons Adult Cardiac Surgery National Database. They performed follow-up of patients aged 65 to 80 years undergoing AVR with a biological (n=24,410) or mechanical (n=14,789) prosthesis from 1991 to 1999 at 605 centers within the Society of Thoracic Surgeons Adult Cardiac Surgery Database using Medicare inpatient claims (mean, 12.6 years; maximum, 17 years; minimum, 8 years), and outcomes AVR valve replacement (mean age, 73 years), both reoperation (4.0%) and endocarditis (1.9%) were uncommon to 12 years; however, the risk for other adverse outcomes was high, including death (66.5%), stroke (14.1%), and bleeding (17.9%). Compared with those receiving a mechanical valve, patients given a bioprosthesis had a similar adjusted risk for death (hazard ratio, 1.04; 95% confidence interval, 1.01–1.07), higher risks for reoperation (hazard ratio, 2.55; 95% confidence interval, 2.14–3.03) and endocarditis (hazard ratio, 1.60; 95% confidence interval, 1.31–1.94), and lower risks for stroke (hazard ratio, 0.87; 95% confidence interval, 0.82–0.93) and bleeding (hazard ratio, 0.66; 95% confidence interval, 0.62–0.70). Although these results were generally consistent among patient subgroups, bioprosthesis patients aged 65 to 69 years had a substantially elevated 12-year absolute risk of reoperation (10.5%). They finally concluded that the comparative safety and effectiveness of prosthetic heart valves are highly dependent on patient age and underlying comorbidities, and the choice of an appropriate prosthesis remains complex. Ultimately, the most appropriate prosthesis for a given patient can only be determined through careful discussion between patients and their healthcare providers.

The durability of mitral bioprostheses has long been known to be inferior to aortic bioprostheses. Mitral valve reconstruction/repair is currently recommended for most mitral valve procedures. The choice of prostheses for non-reparable or failed mitral valve repairs has been evaluated by Jamieson et al (15), in which the Carpentier-Edwards supra-annular (CE-SAV) porcine bioprosthesis was implanted in 1135 patients (1175 operations) for mitral valve replacement (MVR) from 1982 to 2000. The mean age was 65.0 ± 12.1 years (range 13–86 years). The mean follow-up was 6.4 ± 4.5 years, 7555.9 patient-years and 98.3% complete. The evaluation considered freedom from SVD and freedom from composites of complications, as well as risk assessment. For the 51–60 year age group, the actual and actuarial freedom from SVD was, at 18 years, 56.0 ± 4.1% and 14.7 ± 5.8%; for the 61–70 year age group was, at 18 years, 69.6 ± 2.6% and 26.5 ± 5.9%, respectively. For the >70 group, at 15 years was 92.2 ± 2.0% and 69.0 ± 9.7%, respectively. There were a total of 256 SVD events with 31 fatalities and 226 reoperations with 10 fatalities (4.42%). The predictors of SVD were age (hazard ratio [HR] 0.98, p = 0.0002), concomitant coronary artery bypass graft surgery (HR 0.66, p = 0.020) and valve size (HR 1.08, p = 0.034). The overall actual freedom, at 15–18 years, for >70 age group was, for valve-related reoperation, 94.3 ± 1.5%; and for valve-related mortality was 87.8 ± 2.3%. Based on their findings, the CE-SAV mitral porcine bioprosthesis cannot be recommended as representative of prosthesis-type of choice for non-reparable or failed repair of native mitral valves for age ≤70 years. The CE-SAV mitral porcine bioprosthesis is satisfactory for implantation >70 years of age. The clinical performance of the CE-SAV is similar to other mitral bioprostheses.

Gao et al (16) compared the long-term performance of the Carpentier-Edwards (CE) porcine bioprosthesis and the CE pericardial bioprosthesis for AVR. They reviewed 518 AVR with CE porcine valves from 1974 to 1996 and 1,021 AVR with CE pericardial valves from 1991 to 2002. The age distribution and clinical profiles were similar for both groups. The mean follow-up time was 6.4 years for porcine and 2.5 years for pericardial. Long-term mortality was similar (p = 0.29) for porcine and pericardial, with 10-year survival rates of 34 ± 2% and 38 ± 6%, respectively. Ten-year freedom from major adverse cardiac events was also similar for both (respectively): thromboembolism (80 ± 2% and 87 ± 2%; p = 0.24); endocarditis (98 ± 1% and 99 ± 1%; p = 0.30). However, 10-year freedom from explant was lower for porcine (90 ± 2%) than for pericardial (97 ± 1%, p = 0.04). Reasons for explant for porcine were structural valve deterioration (SVD) (n = 25), endocarditis (n = 4), and peri-prosthetic leak (n = 2). The reasons for explant for pericardial were SVD (n = 4), endocarditis (n = 4) and peri-prosthetic leak (n = 1). Accordingly, they concluded that the current CE pericardial valve offers better midterm durability than the traditional CE porcine valve. Its freedom from SVD and reoperation makes it our current bioprosthesis of choice for AVR in appropriately selected patients.

The durability of bioprosthetic valves in the pulmonary position is not well defined. Lee et al (17) examined the durability of bioprosthetic valves in the pulmonary position and risk factors associated with bioprosthetic pulmonary valve failure. Between 1993 and 2004, 181 patients underwent pulmonary valve replacement using bioprostheses. Patients who underwent valved conduit or homograft implantation were excluded. Mean age was 14.2 ± 9.8 years and median valve size was 23 mm (range, 19–27 mm). Types of bioprosthesis used were Hancock II (n = 83), Perimount (n = 53), Freestyle (n = 23), Carpentier–Edwards porcine valve (n = 18), and others (n = 4). There were 3 early and 7 late deaths. Follow-up completeness was 88.6% and mean follow-up duration was 7.3 ± 2.9 years. Forty-three patients underwent redo pulmonary valve replacement. Overall freedom from redo pulmonary valve replacement at 5 and 10 years was 93.9 ± 1.9% and 51.7 ± 8.6%, respectively. Overall freedom from both valve failure and valve dysfunction at 5 and 10 years was 92.2 ± 2.1% and 20.2 ± 6.7%, respectively. In multivariable analysis, younger age at operation, diagnosis of pulmonary atresia with ventricular septal defect, and use of stentless valve were identified as risk factors for redo pulmonary valve replacement. Based on their findings, the durability of bioprosthetic valves in the pulmonary position was suboptimal. Valve function was maintained stable until 5 years after operation. By 10 years, however, about 80% will require reoperation or manifest valve dysfunction.

Johnston et al (18) tried to find risk factors for reoperation of biologic valves in young patients. They evaluated risk factors associated with explantation for SVD in a long-term series of CE PERIMOUNT aortic valve. From June 1982 to January 2011, 12,569 patients underwent AVR with CE PERIMOUNT stented bovine pericardial prostheses, models 2700PM (n = 310) or 2700 (n = 12,259). Mean age was 71 ± 11 years (range, 18 to 98 years). 93% had native aortic valve disease, 48% underwent concomitant coronary artery bypass grafting, and 26% had additional

valve surgery. There were 81,706 patient-years of systematic follow-up data available for analysis. Three hundred fifty-four explants were performed, with 41% related to endocarditis and 44% to SVD. Actuarial estimates of explant for SVD at 10 and 20 years were 1.9% and 15% overall, respectively, and in patients younger than 60 years, 5.6% and 46%, respectively. Younger age (p <0.001), lipid-lowering drugs (p = 0.002), prosthesis-patient mismatch (p = 0.001), and higher postoperative peak and mean aortic valve gradients were associated with explant for SVD (p <0.001). The effect of gradient on SVD was greatest in patients younger than 60 years. They finally concluded that durability of the CE PERIMOUNT aortic valve is excellent even in younger patients. Strategies to reduce early postoperative AV gradients, such as root enlargement or more efficient prostheses should be considered.

In recent years, an increasing number of patients undergoing tricuspid valve replacement have received bioprostheses due to the great durability in the tricuspid position and to the advantage of freeing patients from anticoagulant medication. However, bioprostheses inevitably calcify and get stenotic, which may cause valve dysfunction. Hirata et al (19) followed-up thirty-one patients with bioprosthetic tricuspid valve replacement (mean age: 60.5 ± 16.6 years, male/female: 11/20) for 79.5 ± 49.1 months (14–188 months). Eleven patients developed bioprosthetic tricuspid valve stenosis (mean tricuspid gradient >5 mmHg) at a median interval of 96 months (interquartile range: 61–114 months). The mean tricuspid gradient at the time of tricuspid valve stenosis diagnosis was 10.9 ± 3.9 mmHg. Although the mid-term tricuspid valve stenosis-free survival was favorable (92.4% at 60 and 78.7% at 84 months), it had declined steeply to 31.5% by 120 months. Ten out of 11 tricuspid valve stenosis patients showed signs of right heart failure as manifested by edema and elevated jugular venous pressure, requiring moderate-to-high doses of diuretics. Diastolic rumble was audible in 10 patients. Five of the 11 tricuspid valve stenosis patients required redo tricuspid valve replacement as a result of refractory heart failure. Examination of the five excised bioprostheses showed pannus in four, fusion of the commissure in three, native valve attachment in two, and sclerosis in one. Detailed clinical pictures and pathology of the explanted valves in three cases that underwent surgery are presented in this case series. Bioprosthetic tricuspid valve stenosis is not uncommon after 8 years. Tricuspid valve replacement performed at the second surgery was associated with a higher incidence of bioprosthetic tricuspid valve stenosis.

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اهداف: هدف اصلی، اهداف اختصاصی، هدف کاربردی

اهداف (خروجی ها) اصلی طرح[8]:

To evaluate mid- to long-term durability of bioprosthetic valves in patients undergoing valve replacement

اهداف (خروجی ها) اختصاصی طرح[9] :

۱. Determining the predictors of bioprosthetic valves' durability in patients undergoing valve replacement

۲. Determining the durability of bioprosthetic valves by valve position in patients undergoing valve replacement

۳. Determining the durability of bioprosthetic valves by age groups in patients undergoing valve replacement

۴. Determining the durability of bioprosthetic valves by valve size in patients undergoing valve replacement

اهدف کاربردی طرح[10]:

۱. To identify the durability of bioprosthetic valves in our population

۲. To identify the predictors of bioprosthetic valves' durability in our population

فرضیات یا سوالات پژوهشی

۱. Which variables can predict the durability of bioprosthetic valves in patients undergoing valve replacement?

۲. What is the difference between valve positions with regard to the durability of bioprosthetic valves in patients undergoing valve replacement?

۳. What is the difference between age groups with regard to the durability of bioprosthetic valves in patients undergoing valve replacement? ۴. What is the difference between valve sizes with regard to the durability of bioprosthetic valves in patients undergoing valve replacement?	
In a retrospective manner, we will review the electronic database of Rajaie CMRC for finding data related to patients underwent valve replacement using bioprosthetic valves between 1382 and 1398. Data will comprise of baseline demographics, data on details of surgical techniques, and echocardiographic examinations of patients during visit to echocardiographic laboratory before surgery and during follow-up period. Inclusion criteria include adult patients who underwent bioprosthetic valvular replacement in Rajaie CMRC. Exclusion criteria include patients without complete data on surgical modalities and echocardiographic examinations as well as the lack of data on echocardiographic examinations during follow-up period after valvular replacement. Statistical analysis will be as follows: Comparing continuous variables between subgroups by an independent t-test or Mann-Whitney U test for two groups as well as ANOVA or Kruskal-Wallis test for more than two groups Comparing categorical variables by chi-squared test Logistic regression analysis for identifying predictors of outcomes Kaplan-Meier curve for identifying survival and freedom from re-operation and bioprosthetic valvular dysfunction at follow-up period	روش اجرا

مشخصات ابزار جمع آوری اطلاعات و نحوه جمع آوری آن	All required data will be gathered via electronic database of Rajaie CMRC. All data will be entered into the Excel datasheets after extraction from hospital database, and then those will be transferred into statistical software.
روش محاسبه حجم نمونه و تعدادآن	All available data in the hospital database will be evaluated and patients who underwent bioprosthetic valvular replacement associated with sufficient and reliable data will be entered in this study. Based on recent experience of similar surgeries in our center, approximately 3000 patients will be entered into study.
ملاحظات اخلاقی	The study protocol will be reviewed by the local ethics committee of Rajaie CMRC Confidentiality and anonymity of information will be considered by researchers
محدودیتهای اجرایی طرح وروش کاهش آنها	The major limitation of this study will be the lack of data on surgical report and echocardiographic evaluations in our database. In cases with insufficient data, those will be excluded from final analysis. In addition, due to being retrospective study, we will not be able to provide any complications at follow-up period; therefore, we will only collect data on some selected complications which can be available in our databases.
معیارهای ورود (فقط مربوط به طرحهای کارآزمایی بالینی)	
معیارهای خروج (فقط مربوط به طرحهای کارآزمایی بالینی)	
چگونگی تصادفی سازی و Concealment (فقط مربوط به طرحهای کارآزمایی بالینی)	
تعریف گروه مداخله (فقط مربوط به طرحهای کارآزمایی بالینی)	
تعریف گروه شاهدیامقایسه (فقط مربوط به طرحهای کارآزمایی بالینی)	
چگونگی کورسازی (Blinding) (فقط مربوط به طرحهای کارآزمایی بالینی)	
پیامدها اولیه (primary) ثانویه (secondary) ایمنی (Safety) (فقط مربوط به طرحهای کارآزمایی بالینی)	

پیگیری (follow up) (فقط مربوط به طرحهای کارآزمایی بالینی)	

جدول متغیرها

نام متغیر	نقش متغیر	نوع متغیر	نوع متغیر کمی – پیوسته است؟	نوع متغیر کمی – گسسته است؟	نوع متغیر کیفی – رتبه ای است؟	نوع متغیر کیفی – اسمی است؟	واحد اندازه گیری	تعریف کاربردی	نحوه اندازه گیری
Age	مستقل	کمی	☑	☐	☐	☐	Year	The years of life	Examination
Sex	مستقل	کیفی	☐	☐	☐	☑	Male/Female	Phenotype	Examination
Weight	مستقل	کمی	☑	☐	☐	☐	Kg	Weight of body	Examination
Height	مستقل	کمی	☑	☐	☐	☐	Meter	Height of body	Examination
Body mass index	مستقل	کمی	☑	☐	☐	☐	Kg/m۲	Body mass index	Examination
Valvular pathology	مستقل	کیفی	☐	☐	☐	☑	Yes/No	The pathology of valves that is mentioned in echocardiographic report and diagnosis of patient, including primary or secondary insufficiency, valvular stenosis, congenital involvement of valves	Echocardiography report
Grading of valvular pathology	مستقل	کیفی	☐	☐	☑	☐	Yes/No	The grading of valvular pathology defined as mild, moderate, or severe at preoperative echocardiography and follow-up period	Echocardiography report
Concomitant surgery	مستقل	کیفی	☐	☐	☐	☑	Yes/No	Any surgeries performed concomitant with TV repair	Database
Re-operation	مستقل	کیفی	☐	☐	☐	☑	Yes/No	The re-operation of patients during follow-up period due to bioprosthetic valve dysfunction	Examination

Bioprosthetic valve dysfunction	مستقل	کیفی	☐	☐	☐	☑	Yes/No	Bioprosthetic valve dysfunction based on definition developed by “Guidelines for reporting mortality and morbidity after cardiac valve interventions at ۲۰۰۸”	Database
Death	مستقل	کیفی	☐	☐	☐	☑	Yes/No	Mortality of patients during follow-up period as in-hospital or late mortality	Database
Concomitant surgery	مستقل	کیفی	☐	☐	☐	☑	Yes/No	Any surgeries performed concomitant with TV repair	Database

زمانبندی و مراحل اجرا

شرح مختصر مرحله	درصد مرحله	مدت اجرا – ماه	از تاریخ	تا تاریخ
Database review and data collection		۲		
Data cleaning and data handling		۶		
Report		۴		

ملاحظات اخلاقی

شما اجازه مشاهده این فرم را ندارید

هزینه وسایل و مواد مورد نیاز

نوع	نام دستگاه/ وسیله/ مواد	تعداد مورد نیاز	قیمت دستگاه/ وسیله/ مواد – ریال	کشور سازنده	شرکت سازنده	شرکت فروشنده	محل تامین اعتبار	جمع کل هزینه به ریال

هزینه پرسنلی

نام و نام خانوادگی	توصیف دقیق فعالیتی که فرد در این تحقیق باید انجام دهد	کل حق‌الزحمه – ریال
رکوردی یافت نشد		

هزینه ازمایشات و خدمات تخصصی

نام خدمت	نام مؤسسه ارائه کننده	تعداد یا مقدار لازم	قیمت واحد – ریال	قیمت کل – ریال
رکوردی یافت نشد				

هزینه مسافرت

مقصد	تعداد مسافرت در مدت اجرای طرح و منظور آن	نوع وسیله نقلیه	تعداد مسافرت	مبلغ
رکوردی یافت نشد				

هزینه کتب، نشریات و مقالات

نوع هزینه	توضیحات	مبلغ – ریال
رکوردی یافت نشد		

سایر هزینه ها

نوع هزینه	مبلغ – ریال
جمع آوری دیتا(افرادی که توسط مجری طرح و معاونت پژوهشی معرفی می شوند)، آنالیز،نوشتن مقاله.(هزینه طرح طبق صحبتی که از طرف مجری انجام شده توسط شرکت جهان گسترش تجارت تامین خواهد شد، که تا الان ۲۴۰۰۰۰۰۰ ریال از کل مبلغ قرارداد توسط شرکت پرداخت شده است)	۶۰۰,۰۰۰,۰۰۰

جمع کل – ریال : ۶۰۰,۰۰۰,۰۰۰

کل اعتبار درخواست شده

هزینه پرسنلی (هیات علمی و غیر هیات علمی)	هزینه مواد مصرفی	هزینه مواد غیر مصرفی	هزینه تجهیزات،موادوخدمات موجوددر مرکز	هزینه مسافرت	هزینه چاپ و تکثیر	سایر هزینه ها	جمع کل هزینه – ریال
۰						۶۰۰,۰۰۰,۰۰۰	۶۰۰,۰۰۰,۰۰۰