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專題報導

Non-pharmacologic Management of Structural Heart Disease

Ying-Hsiang Lee[1,5], Po-Lin Lin[3], Wei-Ru Chiou[4], Feng-Ching Liao[1], Sheng-Hsiung Chang[1,5], Jen-Yuan Kuo[1,5], and Charles Jia-Yin Hou[1,2,6]

[1]Division of Cardiac Arrhythmia and Electrophysiology, Division of Cardiology, Cardiovascular Center/Departments of Internal Medicine, MacKay Memorial Hospital Taipei;
[2]Division of Critical Care Medicine, MacKay Memorial Hospital, Taipei, Taiwan;
[3]Hsinchu Mackay Memorial Hospital;
[4]Taitung MacKay Memorial Hospital;
[5]Department of Medicine, Mackay Medical College, New Taipei City, Taiwan;
[6]Mackay Junior College of Medicine, Nursing and Management, New Taipei City, Taiwan

Abstract

Structural heart disease is defined as malfunction of heart valves, chambers, and contractility strongly associated with prognosis, life expectancy, and quality of life. It also refers to non-coronary cardiovascular disease processes and related interventions. The last twenty years, the percutaneous therapeutic modalities and processes has seen tremendous advances. In addition, the emerging evidence via clinical trials are helping to accomplish patient or therapy selection properly. Inherent challenges exist in training physicians, supportive medical affairs and paramedical systems. Ultimately, credentialing societies and training programmes will emerge to help assure expertise within the cardiovascular community. This review focuses on the update of left atrial appendage occluder, transcatheter mitral valve repair, and transcatheter aortic valve replacement. At the end, the challenges unique to structural heart disease would be introduced for future directions. (J Intern Med Taiwan 2017; 28: 218-222)

Key Words: Structural heart disease, LAAO, TMVR, TAVI

Introduction

'Structural heart disease' is a term first introduced at the 1999 Transcatheter Cardiovascular Therapeutics meeting to provide a term encompassing non-coronary disease processes and developing interventional techniques.[1] Catheter-based interventions aiming to alleviate conditions related to heart structure have existed for over half a century, however, several new technologies have started being widely used in past few years. The article is aimed to introduce the indications and evolving application of micro-invasive procedures.

Left Atrial Appendage Closure

Stroke prevention is the main treatment goal in patients with atrial fibrillation (AF). Anticoagulation therapy is recommended to reduce the risk

Reprint requests and correspondence：Dr. Jen-Yuan Kuo
Address：Division of Cardiology, Cardiovascular Center/Department of Internal Medicine, Mackay Memorial Hospital, No. 92, Chung-Shan North Road, 2nd Section, Taipei, Taiwan

of systemic embolization; however, varying risk of bleeding should be counted individually. Nonpharmacologic strategies are necessary for those not suitable for long-term anticoagulants. Left atrial appendage (LAA) is the site of thrombus formation in more than 90% of cases based on autopsy studies and echocardiography.[2] The importance of the LAA in thromboembolic risk provides the rationale for ligation, amputation, or occlusion of the LAA, so some patients would receive LAA exclusion at the time of cardiac surgery. For those intolerant of log-term anticoagulant but not indicated for cardiac surgery, percutaneous LAA occlusion (LAAO) is an alternative.

The occlusion devices include the Watchman (Boston Scientific, Plymouth, MN), followed by the Amplatzer Cardiac Plug (St Jude Medical, MN). In a randomized trial comparing the Watchman device vs. anticoagulation in 707 patients, the efficacy of percutaneous closure of the LAA with this device was non-inferior to that of anticoagulation therapy.[3] Although there was a higher rate of periprocedural complications in the beginning, the incidence has decreased from 9% to 2% in the following clinical trials.[3] But complications in the control group were mainly due to bleeding related to long-term anticoagulation and consequently continued to occur during follow-up. In another prospective study of 64 patients with paroxysmal or permanent atrial fibrillation receiving a different device, the annualized stroke/transient ischemic attack rate was 3.8%. This was less than the rate predicted by the CHADS2 scoring system (6.6%/year) after up to 5 years of follow-up.[4] Based on these studies, percutaneous left atrial appendage closure may provide an alternative to anticoagulation in properly selected patients with non-valvular AF. It is recommended that anticoagulation for at least six weeks after implantation of the Watchman device, as was done in the randomized studies.

The device was evaluated in two major studies (PROTECT AF and PREVAIL) in patients with nonvalvular AF eligible for oral anticoagulation. PROTECT AF was a noninferiority trial in which 707 patients were randomly assigned in a 2:1 ratio to either the device or to long-term warfarin (international normalized ratio 2 to 3).[3] Inclusion criteria allowed for patients with AF and a CHADS2 score ≥1. Device implantation was successful in 91 percent of all patients in whom it was attempted. Post-implantation, patients were continued on warfarin and aspirin for 45 days, followed by switching warfarin to clopidogrel plus aspirin to six months, followed by aspirin alone indefinitely. The composite primary efficacy end point included stroke, systemic embolism, and cardiovascular death; the primary safety end point was a composite of major bleeding, pericardial effusion, procedure-related stroke, and device embolization.

According to label of percutaneous LAAO in Taiwan: 1) Intolerant of long-term anticoagulation and 2) Cerebral infarction under anticoagulation, the indications could be thrombocytopenia or known coagulation defect, recurrent gastrointestinal bleeding, prior severe bleeding, including intracranial hemorrhage, poor adherence to anticoagulants, and unprotective anticoagulation therapy.

Transcatheter Mitral Valve Repair

Severe mitral regurgitation (MR) is associated with increased mortality regardless of symptoms.[5] A defect at any level of mitral apparatus may result in regurgitation of blood from the left ventricle to left atrium. The complex structure consists of the mitral valve leaflets, the annulus, chordae, papillary muscles, and ventricle. Surgical therapy is the preferred method,[6] however, it is seldom feasible in the elderly or subjects with failing left ventricle.

Percutaneous approach by transcatheter device are currently under varying stages of development. Coronary sinus annuloplasty are supposed to reduce the antero-posterior diameter of the mitral annulus

like the surgical results.[7] Method of Alferi edge-to-edge repair is an alternative, by which anterior and posterior leaflets are sutured to reduce the regurgitant orifice and decrease the severity of mitral regurgitation.[8] Based on the idea, the MitraClip (Abbott Vascular, CA, USA) is operated via transeptal route, transcatheter mitral valve repair (TMVR), which grasps the mitral valve leaflets together and thereby could also create a "double orifice" mitral valve. Because of the need for transesophageal echocardiography guidance and careful device manipulation, the procedure is usually performed under general anesthesia. In investigational studies of the device, aspirin 325 mg was administered for 6 to 12 months, along with clopidogrel 75 mg daily for one month.[9] These recommendations are based on extrapolation from prior studies of device endothelialization.

The EVEREST II randomized trial compared the outcomes of TMVR to surgical mitral repair or replacement among 279 patients with moderate-to-severe or severe (grade 3+ or 4+) MR who were candidates for either procedure.[10] The primary composite endpoint, freedom from death, from surgery for mitral valve dysfunction, and from grade 3+ or 4+ MR at 12 months, was more frequent in the surgery group (73% versus 55%). It was due to the higher rate of subsequent surgery for mitral valve dysfunction in the TMVR group (20% versus 2%). All-cause mortality (6% versus 6%) and grade 3+ or 4+ MR (21% versus 20%) were similar in at one year. Major adverse event rates at 30 days were lower in the TMVR group (15% versus 48%), majorly due to higher rate of transfusion in the surgery group. Regarding left ventricular reverse remodeling, reduction in both left ventricular end-diastolic volume and left atrial volume was noted in a cohort study; in the EVEREST II trial, surgical repair was also associated with a greater reduction in left ventricular volumes.[10,11]

The Indication of TMVR with the MitraClip device: 1) heart failure (New York Heart Association Class III or IV) despite medical therapy, 2) chronic moderate to severe or severe (3 to 4+) primary MR, 3) favorable anatomy for the repair procedure, 4) reasonable life expectancy, and 5) prohibitive surgical risk due to comorbidities[12]

Transcatheter Aortic Valve Implantation

While surgical treatment of severe aortic stenosis (AS) was the gold standard, significant number of patients were not ideal candidates for surgical aortic valve replacement (SAVR) due to high operative risk. However, high-risk patients are able to be improved significantly if the valve can be replaced via less invasive means. For these patients, transcatheter aortic valve implantation (TAVI) is evolving to be an important alternative since it was first performed in 2002.[13] Some of the well-designed percutaneous devices (Sapien, Edwards Lifesciences, CA, USA and CoreValve, Medtronic, MN, USA) has been widely used in Taiwan, which are balloon-expandable and self-expandable, respectively. Clinical trials investigating these devices in patients with extreme-, high-, and intermediate risk for surgery has proved effectiveness and even superiority of TAVI as compared with SAVR. In low-risk symptomatic patients, limited data are available.

A meta-analysis included four trials (one with 2032 intermediate-risk patients, two with 699 and 795 high-risk patients, and one with 280 low-risk patients) to assess outcomes at two years.[14] Mortality was reduced with TAVI as compared with SAVR (hazard ratio [HR] 0.87, 95% CI 0.76 to 0.99) with homogeneity across the trials. In high-risk symptomatic patients, the meta-analysis included a randomized trial comparing balloon-expandable TAVI and SAVR in high-risk patients with AS reported similar mortality rates at five years.[15] In contrast, another included randomized trial that compared self-expanding TAVI and SAVR in high-risk

patients with AS reported a significantly lower mortality rates of mortality or stroke at three years.[16]

In intermediate risk patients, a meta-analysis of four randomized trials with 3179 patients with severe AS, transfemoral TAVI compared with SAVR resulted in reduced mortality (HR 0.79, 95% CI 0.88-0.94) and reduced acute kidney injury (relative risk [RR] 0.38, 95% CI 0.27-0.53, 53).[17] In contrast, TAVI compared with SAVR resulted in more frequent worsened symptoms of heart failure (one point worse on New York Heart Association scale; odds ratio 1.29, 95% CI 1.08-1.55, 59 more per 1000 patients), aortic valve re-intervention (RR 3.25; 95% CI 1.29-8.14, 7 more per 1000 patients), permanent pacemaker insertion (RR 2.45, 95% CI 1.17-5.14, 134 more per 1000 patients) , and moderate or severe aortic valve regurgitation (RR 12.22, 95% CI 5.17-28.88, 80 more per 1000 patients). The rate of death from any cause or disabling stroke was similar (19.3% versus 21.1%) in the TAVI and SAVR groups at two years.

According to label of TAVI for symptomatic severe AS in Taiwan, patients with any one the following is suitable for TAVI: 1) STS score >10% or logistic EuroSCORE >20%, 2) >80 years of age, 3) prior cardiac surgery, 4) porcelain aorta, 5) subsequent thoracic burn, 6) prior radiotherapy, 7) severe connective tissue diseases, 8) liver cirrhosis at Child A or B, and 9) poor pulmonary test, FEV <1 L

Challenges Unique to Structural Heart Disease

Over the last 10 years, the term 'structural heart disease' has become generally accepted as a category of disease by the medical community.[1] As most of these procedures are based on catheter and wire manipulation skills, it stands to reason that interventional cardiologists can also treat structural disease, however, there are a number of issues unique to structural disease. The first issue is the role of adjunctive imaging and preprocedural assessment in treating structural heart disease. A second issue relates to patient and procedural volume. A third challenge relates to the wide spectrum of structural heart disease and subtle variability within each disease process. Additionally, availability of bail-out modalities and professions depends on a well-organized medical system

Conclusions

As a field, structural heart disease has seen tremendous advances over the past 20 years, the indication and application of percutaneous intervention is emerging. Patient selection and multidisciplinary programming is mandatory to promise the effectiveness.

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以非藥物的方式治療結構性心臟病

李應湘[1,5] 林柏霖[3] 邱威儒[4] 廖峰慶[1] 張盛雄[1,5] 郭任遠[1,5] 侯嘉殷[1,2,6]

台北馬偕紀念醫院 [1]心律不整暨電生理檢查科/內科部 心臟內科 [2]重症醫學科
[3]新竹馬偕紀念醫院
[4]台東馬偕紀念醫院
[5]馬偕醫學院 醫學部
[6]馬偕醫護管理專科學校

摘 要

結構性心臟病一詞通常被用來泛指心臟瓣膜，心腔室和收縮異常相關之心臟疾病；其預後與壽命和生活品質高度密切。它也常被當作非冠狀動脈心臟病介入治療的標的疾病。在過去二十年間，經皮介入治療方式有了長足進步，也經由臨床試驗得到新證據，幫助醫師做治療上的選擇，但仍需相關的認證機構和培訓計劃來確保結構性心臟病的專業知識。如何有效完成人員培訓，技術支援和非臨床系統整合，將扮演具足輕重的角色。本綜述重點在介紹左心耳封堵術，經導管二尖瓣修復手術和經導管心臟主動脈瓣膜置換手術的最新資料。