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Journal of Taiwan Society of Cardiovascular Interventions

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Review Articles, Original Articles, Brief Articles including images, Case Reports, Letters to the Editor, Editorial Comments. Please look into each category for specific requirements and manuscript preparation.

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1. Xu J, Cui G, Esmailian F, et al. Atrial extracellular matrix remodeling and the maintenance of atrial fibrillation. *Circulation* 2004;109:363–8.
2. Boos CJ, Lip GY. Targeting the renin-angiotensin-aldosterone system in atrial fibrillation: from pathophysiology to clinical trials. *J Hum Hypertens* 2005;19:855-9.

Books

1. Gotto AJ, Farmer JA. Risk factors for coronary artery disease. In: Braunwald E, Ed. *Heart Disease: A Textbook of Cardiovascular Medicine*. 3rd ed. Philadelphia: Saunders, 1988:1153-90.
2. Levinsky NG. Fluid and electrolytes. In: Thorn GW, Adams RD, Braunwald E, et al, Eds. *Harrison's Principles of Internal Medicine*. 8th ed. New York: McGraw-Hill, 1977:364-75.

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CONTENTS

ORIGINAL ARTICLE

REVIEW ARTICLE

CASE REPORT

Gender Differences in Management and Clinical Outcomes after Acute Myocardial Infarction among Older Patients – A 10-year Population-based Study in Taiwan

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Abstract

Background: Previous studies on gender differences in the outcome of acute myocardial infarction (AMI) patients are mostly from Western countries. The objective of our study of Taiwanese patients is to assess the influence of gender on the management and clinical outcomes after AMI between 1999 and 2008.

Methods: We used the Taiwan National Health Insurance Research Database (1999-2008) to identify hospitalized patients ≧70 years of age presenting with AMI. We obtained information on each patient's demographic data, in-hospital medications, and the use of AMI-related procedures (percutaneous transcoronary angioplasty or coronary artery bypass graft). We used a logistic regression model to quantify the effects on in-hospital mortality.

Results: We enrolled 50,110 AMI patients (women: 37.6%). Women were older (79.0 yrs ± 6.0 yrs vs. 77.6 yrs ± 5.5 yrs; P < 0.001), and had more diabetes mellitus (49.8% vs. 36.0%; P < 0.001) and hypertension (81.0% vs. 72.7%; P < 0.001) than men. During the index hospitalization, women received lower percentages of dual antiplatelet therapy (60.0% vs. 61.6%; p < 0.001), but higher percentages of beta blockers (55.2% vs. 52.5%; p < 0.001), statin (28.0% vs. 24.3%; p < 0.001), and ACEi/ARB (72.6% vs.71.9%; p = 0.066). However, women received lower rates of coronary revascularization including percutaneous coronary interventions (35.9% vs. 41.7%; p < 0.001) and coronary artery bypass grafts (4.7% vs. 7.1%; p < 0.001). The mean mortality rate in women was 24.0% versus 21.8% in men (P < 0.001). Multivariable logistic regression analysis revealed that the determinants of in-hospital death in AMI patients in Taiwan included old age, female gender, diabetes mellitus, old MI, and old stroke.

Conclusion: Women have higher rates of mortality after AMI compared to men because of greater age, higher baseline risk profiles, and underutilized coronary revascularization.

Keywords: acute myocardial infarction, gender difference, population-based study

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Introduction

Previous studies have shown higher crude hospital mortality rates for acute myocardial infarction (AMI) in women than in men. The major difference may be attributed to the greater age and higher prevalence of comorbidities in women.[1] Less frequent use of revascularization procedures in women may also account for some of the excess mortality. Indeed, findings from large database studies have indicated that women with acute myocardial infarction tend to undergo less aggressive hospital management than men.[2-6] Women develop AMI about a decade later in life than men do.[7] Besides, age itself is an important predictor of short- and long-term mortality in AMI.[8] The American National Registry of Myocardial Infarction reported a progressive decrease in the difference (higher mortality in females) with increasing age until the age of 75 years.[9] Study results for gender differences in the outcome for AMI among elderly patients over 70 years of age have rarely been described as well as they have for middle-aged patients. Both female gender and advanced age have been considered risk factors for atypical AMI symptoms and a less aggressive treatment including coronary revascularization.[10] Therefore, it is of interest to compare clinical features and outcomes between elderly women and men with AMI. Since the implementation of National Health Insurance (NHI) in Taiwan in 1995, more than 98% of Taiwan's 23 million people have received health care coverage through this system.[11] NHI data provides us an opportunity to evaluate AMI care in older Taiwanese patients. In the present study, we assess the influence of gender on management and clinical outcomes after AMI in the period from 1999 to 2008.

METHODS

The Database

This study used claims data from the 1999 to 2008 National Health Insurance Research Database (NHIRD) provided by the National Health Research Institute in Taiwan. The NHIRD includes data on every inpatient admission, with nearly 99% of the Taiwanese population (23 million residents) enrolled. The databases used in this study contained all inpatient and outpatient medical claims made between January 1, 1999 and December 31, 2008. From the databases, we retrieved medical information including disease diagnosis, prescription drugs, procedures, and surgery conducted during a hospitalization or an outpatient visit. All health care providers are requested to submit the diagnosis information using International Classification of Disease-Clinical Modification, ninth revision, (ICD-9-CM) together with service claims during the study period. The study was approved by the Institutional Review Board of National Cheng Kung University Hospital, Tainan, Taiwan.

Study Patients

We selected all adult patients (≧70 years) who were admitted to hospitals for AMI from January 1, 1999 to December 31, 2008. AMI admission was defined as a hospitalization with a primary or secondary discharge diagnosis code of ICD9-CM 410.x. We retained only those patients who were admitted at an acute care hospital. We excluded patients who were coded as AMI and survived but were hospitalized for less than 2 days. For each patient, the comorbidities were retrieved from both the inpatient and outpatient claim databases for the 12 months up to the index date. We obtained information on each patient's age at time of index AMI admission, gender, days of hospitalization, and the use of AMI-related interventional procedures, including percutaneous coronary interventions (PCI) and coronary artery bypass graft (CABG). We specifically looked at the following four performance measures during hospitalization, according to the current guideline[12,13]: (1) use of dual antiplatelet therapy (DAPT), (2) use of angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), (3)

use of beta blockers, (4) use of statins. We also evaluated whether patients received other invasive procedures including ventilator support, intra-aortic balloon pump (IABP), and extracorporeal membrane oxygenation (ECMO) during the same hospitalization. We obtained data on in-hospital medication use for several comorbidities using the anatomic therapeutic chemical (ATC) classification system.

Comorbid Diseases

For each patient, the comorbidities related to AMI were retrieved from both the inpatient and outpatient claims databases for one year up to and during the index AMI hospitalization. Several diseases proven to predispose patients to AMI and other comorbidities were based on ICD-9-CM codes. (Table 1)

Statistical Analysis

Categorical data are presented as percentages with absolute numbers. We used a logistic regression model to quantify the effects on in-hospital mortality of age, gender, co-morbidity (respiratory disease, diabetes, cancer, cerebrovascular disease, peripheral arterial disease, hypertension, heart failure, atrial fibrillation, and renal failure), revascularization procedures (PCI or CABG), and use of ventilator, IABP, and ECMO. Men and women are considered separately in the models because gender was a significant predictor of outcome and because of an interaction previously seen between age and gender in the outcome after an AMI. Odds ratios are reported, and Wald tests and 95% confidence intervals (CIs) are provided to check for the significance of differences between proportions. All variables were entered

Table 1. World Health Organization International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] used for present analysis

Disease or procedure	ICD-9-CM or procedure codes
Acute myocardial infarction	410.xx
Hypertension	401.0-405.9
Heart failure	428.0-428.9
Ischemic heart disease	411-414
Renal insufficiency	580-589
Chronic lung disease	490-496
Diabetes mellitus	250.00-250.90
Ischemic stroke and intracerebral hemorrhage	434.0-434.9, 436, 430-432.9
Atrial fibrillation	427.31
Cancer	140-208
Dyslipidemia	272.X
Peptic ulcer	531-534
Peripheral artery disease	443.9
Intra-aortic balloon counterpulsation	37.61
Extracorporeal membrane oxygenation	39.65
Percutaneous coronary intervention	36.0
Coronary artery bypass graft	36.1X, 36.2
Ventilator	96.7

simultaneously into the models. All of the tests were 2-tailed, and a p value of less than 0.05 was considered statistically significant. We used SAS statistical software (version 9.1, SAS Institute, Cary, NC) for data collection and all statistical analyses.

RESULTS

Baseline Characteristics

The study included 50,110 patients (31,278 male, 62.4%) enrolled from January 1, 1999 to December 31, 2008. The clinical characteristics and in-hospital treatment of AMI for male and female patients are shown in Table 2. Compared with male patients, females were older and had a higher prevalence of hypertension, diabetes mellitus, and hyperlipidemia. Female patients also had more comorbidities, including heart failure, atrial fibrillation, peripheral artery disease, but less chronic lung disease. Besides, female patients received significantly less AMI standard therapies, including dual antiplatelet therapy and revascularization including PCI and CABG. We found that female patients received more beta blockers and statins than males.

Temporal Trends of Care Quality and Clinical Outcome

Of the four performance measures during hospitalization according to the current guideline, only the use of DAPT and statin increased significantly. There were no significant changes for the use of ACE inhibitor or ARB (Table 3). From 1999 to 2008, DAPT increased from 29.3% in 1999 to 83.1% in 2008 ($P < 0.001$). ACE inhibitors or ARB were used in 69.5% in 1999 and 70.7% in 2008 (P = NS) and beta blocker was used in 49.8% in 1999 and 54.8% in 2008 ($P < 0.001$). Statin use increased from 8.6% to 41.0% from 1999 to 2008 ($P < 0.001$). The proportion of patients who received "four-combined care" increased from 1999 to 2008 (Figure 1). For in-hospital procedures or surgery, there was significantly increased use of PCI for AMI during hospitalization in Taiwan, but the CABG rate did not change significantly (Figure 2). In addition, more AMI patients received the support of a ventilator, IABP, or ECMO during hospitalization (Table 3).

The overall in-hospital mortality rate has markedly decreased from 25.2% in 1999 to 14.9 in 2008 ($P<0.0001$) (Figure 3). However, the mortality of female patients always remained significantly higher than male patients over the 10-year study period. In 2008, the in-hospital mortality was 14.8% for males and 15.1% for females. Multivariable logistic regression analysis demonstrated that the determinants of in-hospital death in AMI patients in Taiwan included old age, female gender, diabetes mellitus, old MI, and old stroke (Table 4). We also found that in-hospital use of DAPT (OR 0.686, 95% CI, 0.653-0.721), ACE inhibitor/ARB (OR 0.550, 95% CI, 0.524-0.578), beta blocker (OR 0.752, 95% CI, 0.717-0.789), statin (OR 0.584, 95% CI, 0.549-0.622), and PCI (OR 0.492, 95% CI, 0.464-0.521) were associated with significantly lower in-hospital mortality.

DISCUSSION

Our findings showed that, among AMI patients, women were older and had a higher prevalence of hypertension, diabetes mellitus, and hyperlipidemia. Female patients also had more comorbidities, including heart failure, atrial fibrillation and peripheral artery disease. In addition, females were less likely to receive DAPT and coronary revascularization, including PCI and CABG, while they received a higher rate of beta-blockers, statins, and four-combined care, as compared to men. Furthermore, elderly women experienced a higher in-hospital mortality rate than men during the period. Our study results are consistent with those of previous investigators who have reported that, compared with men, women with acute coronary syndrome are generally older, have more comorbidities at the time of presentation, and undergo fewer

Table 2. Clinical Characteristics and Treatment of AMI in Taiwan from 1999 to 2008

	Overall N=50,110	Male N=31,278	Female N=18,832	P value
Age, years (SD)	78.1 (5.7)	77.6 (5.5)	79.0 (6.0)	<0.001
Risk factors (%)				
Hypertension	75.8	72.7	81.0	<0.001
Diabetes mellitus	41.2	36.0	49.8	<0.001
Dyslipidemia	29.7	26.8	34.5	<0.001
Cardiovascular history (%)				
Old MI	12.4	12.9	11.5	<0.001
Atrial fibrillation	4.6	4.1	5.5	<0.001
Peripheral artery disease	4.4	4.0	4.9	<0.001
Ischemic stroke	16.9	16.7	17.2	0.168
Heart failure	49.4	46.6	54.0	<0.001
Comorbidity (%)				
Chronic lung disease	42.5	45.8	36.9	<0.001
Chronic renal disease	19.6	19.3	20.0	0.083
Cancer	16.8	14.5	18.1	<0.001
Peptic ulcers	28.2	28.3	28.1	0.652
In-hospital drug use (%)				
Aspirin	93.2	93.6	92.6	<0.001
Clopidogrel	58.6	58.0	59.4	0.003
Ticlopidine	10.4	11.2	9.1	<0.001
GP IIbIIa inhibitor	11.0	12.0	9.4	<0.001
DAPT	61.0	61.6	60.0	<0.001
Beta blocker	53.5	52.5	55.2	<0.001
ACEI or ARB	72.2	71.9	72.6	0.066
Statin	25.7	24.3	28.0	<0.001
In-hospital procedure or surgery (%)				
Ventilator support	12.5	12.0	13.5	<0.001
IABP	5.0	5.5	4.3	<0.001
ECMO	0.4	0.4	0.2	<0.001
PCI	39.5	41.7	35.9	<0.001
CABG	6.2	7.1	4.7	<0.001

Data are presented as percentages or mean values ± SD.
P value compared between male and female groups using a Student's t test or χ^2 test.
DAPT indicates dual antiplatelet therapy; IABP, intra-aortic balloon pumping; ECMO, extracorporeal membrane oxygenation; PCI, percutanous coronary intervention; CABG, coronary artery bypass graft.

Table 3. Temporal trends of treatments for AMI patients from 1999 to 2008

	Period 1 (1999~2002) N=14041	Period 2 (2003~2005) N=16122	Period 3 (2006~2008) N=19947
In-hospital drug use (%)			
Aspirin	96.9	91.7	91.7
Clopidogrel	10.4	65.8	86.5
Ticlopidine	27.9	5.5	2.1
GP IIbIIIa inhibitor	7.4	13.6	11.4
DAPT	34.4	61.5	79.5
Beta blocker	52.0	54.2	54.0
ACEI or ARB	73.2	73.5	70.3
Statin	12.3	24.3	36.2
Four-combined care	3.6	11.2	18.6
In-hospital procedures			
Ventilator support	6.8	14.7	14.8
IABP	3.6	4.7	6.4
ECMO	0.1	0.3	0.6
PCI	31.9	38.1	46.0
CABG	6.0	6.5	6.2

Data are presented as percentages.
DAPT indicates dual antiplatelet therapy; IABP, intra-aortic balloon pumping; ECMO, extracorporeal membrane oxygenation; PCI, percutanous coronary intervention; CABG, coronary artery bypass graft.

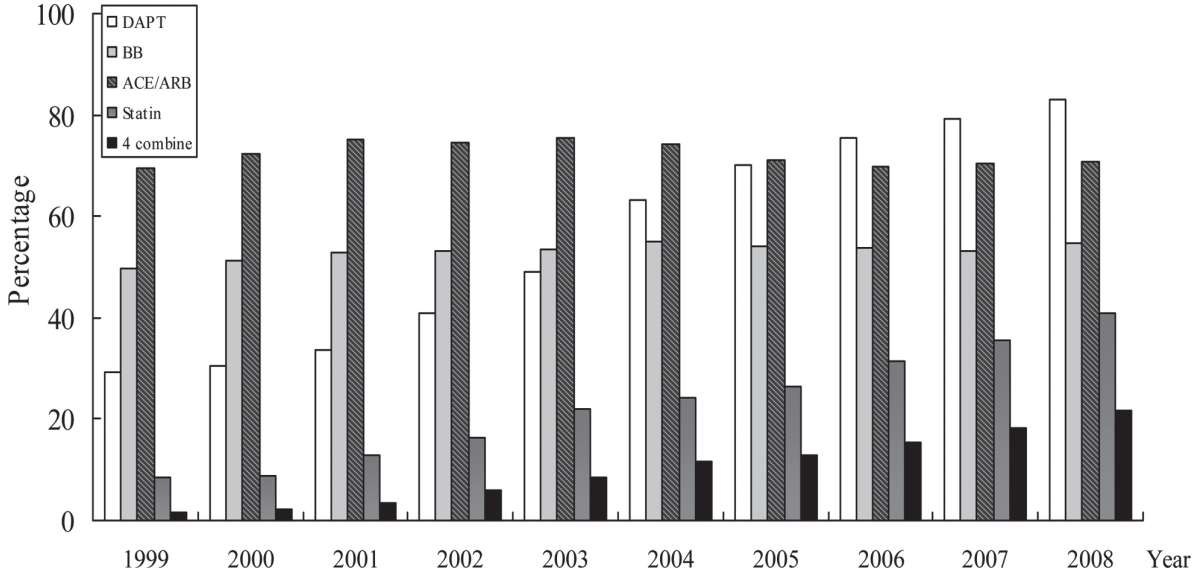

Figure 1. Serial changes in the use of guideline-based medications for acute myocardial infarction from 1999 to 2008.

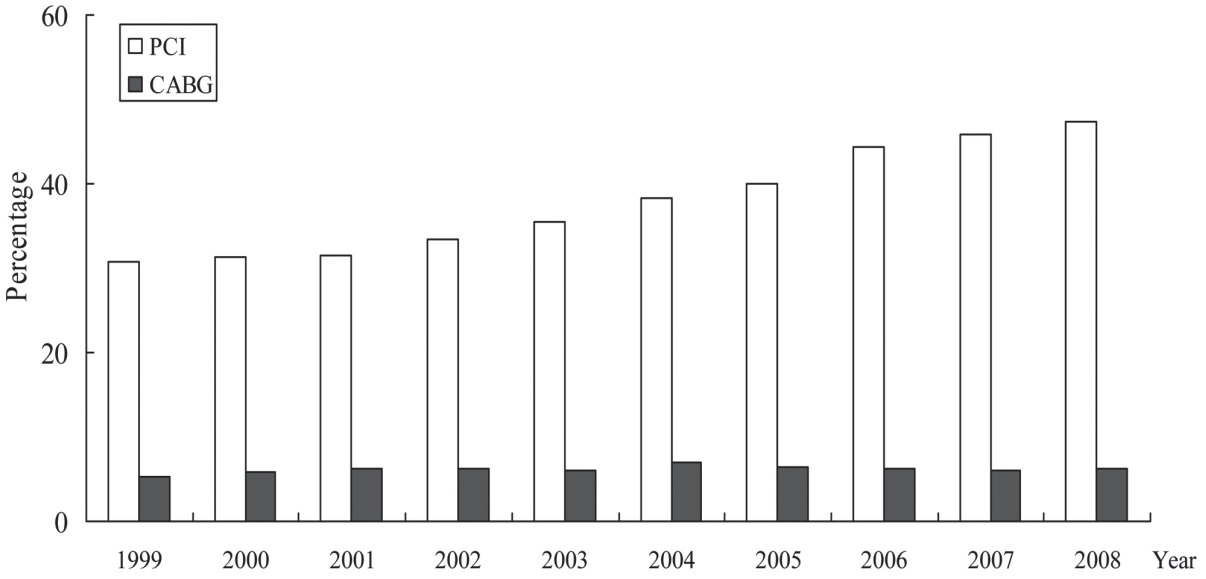

Figure 2. Serial changes in the use of coronary revascularization for acute myocardial infarction from 1999 to 2008.

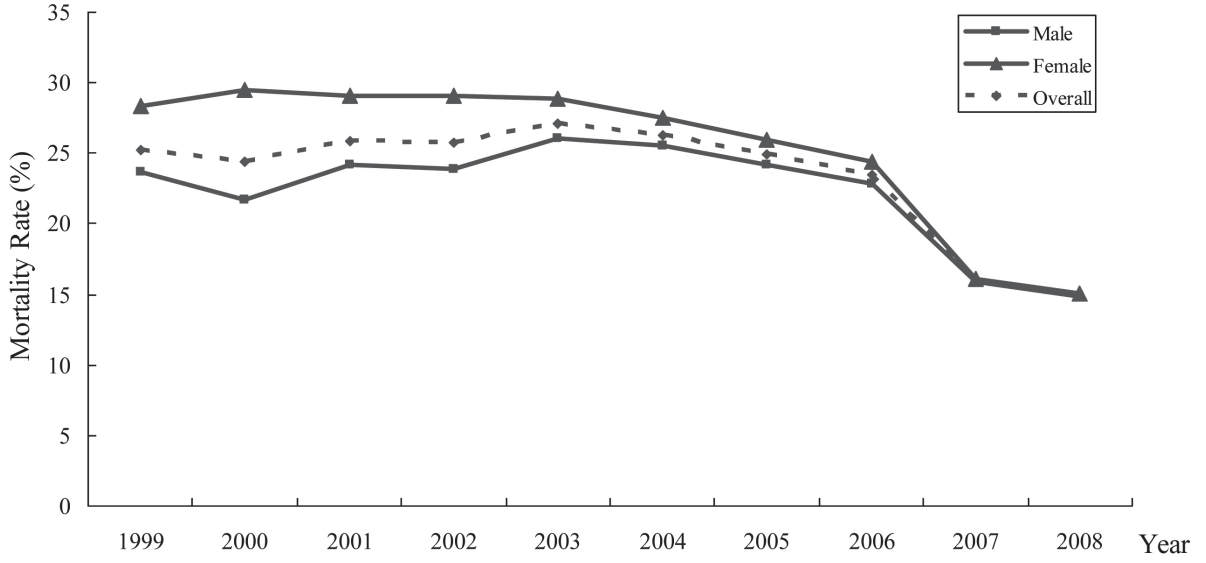

Figure 3. The trend in in-hospital mortality between men and women from 1999 to 2008.

coronary interventions.[1-6] However, several studies have reported that the lower rate of invasive cardiac procedures could not be associated with differences in prognosis after the acute coronary episode, nor has it been linked to any systematic biases.[14-17] There are many possible explanations for the differences in the rates of coronary revascularization between women and men, including atypical presentation of AMI, patient preferences towards invasive cardiac procedures, and physicians' practices in the referral of men for cardiac catheterization.[18,19]

Table 4. Multivariable logistic regression analysis of variables associated with in-hospital mortality

Clinical characteristics	Odds ratio (95% CI)
Male	0.941 (0.897 – 0.987)
Age	1.036 (1.032-1.040)
Diabetes mellitus	1.188 (1.133 – 1.245)
Old myocardial infarction	1.201 (1.116 – 1.293)
Old Stroke	1.178 (1.111 – 1.250)
In-hospital medical therapy	
Dual antiplatelet use	0.686 (0.653 – 0.721)
ACEI/ARB	0.550 (0.524 – 0.789)
Beta blocker	0.752 (0.717 – 0.789)
Statin	0.584 (0.549 – 0.622)
In-hospital procedures	
Ventilator	4.167 (3.922 – 4.425)
Intra-aortic balloon pumping	3.509 (3.185 – 3.846)
Extracorporeal membrane oxygenation	6.369 (4.566 – 8.929)
Percutaneous coronary intervention	0.492 (0.464 – 0.521)
Coronary artery bypass graft	1.185 (1.080 – 1.302)

The epidemiological characteristics and real-world practice in regard to AMI have not been well studied in Asian countries despite their importance for public health. Most of the available information comes from data in highly selective medical centers or from AMI treatment networks rather than from an unselective nationwide database.[20-22] Our study is a 10-year nationwide population-based cohort study that clearly demonstrates the temporal trends of epidemiological features and management of AMI in Taiwan. Concerning guideline-based medications for AMI, our previous AMI epidemiological study showed that there has been continued improvement in the temporal use of DAPT and statins from 1999 to 2008 in Taiwan, but there has been no further improvement in the use of ACE inhibitors or ARB and beta blockers.[23] In this study, we also observed a similar trend of inadequate guideline-based medications for elderly AMI populations. In 2008, DAPT was used in 83.1% of cases, ACEI/ARBs in 70.7%, beta blockers in 54.8%, and statins in 41%. Overall, the guideline-based medications for AMI were significantly underused in Taiwan, especially among elderly populations when compared with the data reported from the United States. In 2006, data from the National Registry of Myocardial Infarction (NRMI) in the United States demonstrated that 92% of patients received beta blockers and 88% received lipid-lowering agents.[24] The very low rate of statin use in Taiwan should be related to the Taiwan National Health Insurance regulation before August 2013, which allowed statins prescription only for AMI patients with serum LDL level higher than 130 mg/dl or total cholesterol higher than 200 mg/dl. The Taiwan Acute Coronary Syndrome (ACS) registry study from October 2008 to January 2010 also reported underused guideline-based medications for AMI after 2008. Only 77.2% of ACS patients

received DAPT, 64.7% received ACEI/ARBs, 55.2% received beta blockers, and 62.5% received statins during hospitalization.[25] Our study clearly demonstrated the benefit of using guideline-based medications and PCI to reduce the in-hospital mortality rate with AMI in Taiwan. To improve the prescription rate of guideline-based medications, it is necessary to enhance adherence to the guidelines for the treatment of AMI in Taiwan through quality improvement programs and revision of the regulations regarding statins use.

Overall, our analysis has some strengths, including the following: its inclusion of a nationwide population, inclusive of all regions of Taiwan; its comprehensive evaluation of multiple care processes and clinical data; and the robustness and consistency of our findings. Our database utilized carefully defined data entries, standardized diagnostic criteria, and regular quality assessment. According to our internal validation of the ICD9-CM coding in our study, the positive predictive value of AMI cases was 0.88 and the percentage of consistency in comorbidity diagnoses was 95.9%[26-28]. This is an important distinction from other national databases that enroll patients with suspected AMI at presentation, many of whom are later determined to have been misdiagnosed. On the other hand, the major limitation of our study is that we could not clearly and accurately differentiate ST-segment elevation and non-ST-segment elevation MI in our database. Therefore, the differences of guideline-based therapies between ST-segment elevation and non-ST-segment elevation MI in Taiwan warrant further studies. From our database, we could not understand the details of the procedures including procedure time and procedure complications, therefore, there was no detailed information of door-to-balloon time for primary percutaneous coronary intervention (PCI) and TIMI flow after PCI.

Conclusions

Underutilization of the guideline-based medications and coronary revascularization for AMI, especially in elderly women is a major issue in Taiwan. Enhancing adherence to the AMI guideline should be an important objective in Taiwan.

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Disclosures

The authors declare no conflict of interest.

Authorships

CH Lee initiated and designed the study, prepared the data, conducted the analysis and interpretation, and wrote the first draft of the paper. YH Li coordinated the execution of the study. CL Cheng and YH Kao Yang established the strategy of data processing of the claims data, and participated in the manuscript preparation.

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Closure of the Left Atrial Appendage by Watchman Device for Stroke Prevention in Patients with Atrial Fibrillation: The Initial Taiwan Experience

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Abstract

Background: In patients with non-valvular atrial fibrillation (NVAF), the left atrial appendage (LAA) is the main source of thrombus that causes thromboembolic events. Our study reports the initial safety, feasibility, and clinical outcomes following Watchman device implantation in Taiwan.

Methods: Twenty patients with NVAF (12 males, age 72.7 ± 11.7 years) with mean CHA_2DS_2-VASc scores 3.2 and contraindications to warfarin or novel anticoagulant use received Watchman device implants from Nov. 2014 to Sep. 2017. All patients received general anesthesia and the procedures were guided by fluoroscopy and transesophageal echocardiography (TEE). The patients received clinical follow-up at 45 days and then every 3 months after implantation, and a follow-up TEE was scheduled at 2 months upon completion of warfarin therapy.

Results: The LAA occluder was successfully implanted in all of the 20 patients. The procedure was completed without major complication or mortality. The mean size of implant was 26.2 ± 4.0 mm. The average hospital stay was 4 days. Follow-up TEE showed all the LAA orifices were sealed without device-related thrombus formation or significant peri-device leak (>5 mm). No stroke event or death had been recorded at a mean follow-up of 13.1 ± 9.8 months.

Conclusions: Our data showed that percutaneous closure of LAA by Watchman is a safe, and technically feasible procedure with satisfactory clinical outcomes in Taiwan.

Keywords: left atrial appendage occluder, Watchman, Taiwan

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INTRODUCTION

Patients with atrial fibrillation (AF) have a higher risk of thromboembolic events.[1,2] Usage of warfarin or novel anticoagulants (NOAC) is now a routine clinical practice for patients with non-valvular AF (NVAF) and high $CHADS_2VASc$ (more than 1 or 2 according to different clinical guidelines).[3,4] However, patients frequently suffer from bleeding complications of warfarin or NOAC and thus some have contraindications to these drugs. The mortality rate has been reported high for anti-coagulant related intracranial hemorrhage.[5] Moreover, patients may still experience stroke or cardioembolic events even with adequate therapy using these drugs. It has been well proven that in more than 90% of patients with NVAF most thrombi originate in the left atrial appendage (LAA)[6] and occlusion of the LAA by devices may prevent thrombus formation in the LAA and thereby reduce the risk of stroke.[6] The PROTECT-AF study has shown that percutaneous closure of the LAA orifice with the WATCHMAN device (Atritech, Plymouth, MN, USA) is not inferior to warfarin in patients with NVAF for the prevention of stroke, systemic embolization, and cardiovascular death.[7] Furthermore, a 4-year follow-up study for patients in the PROTECT AF trial showed a 60% reduction of cardiovascular mortality and nearly 40% reduction of total mortality compared to warfarin use.[8]

Although clinical data are adequate in Caucasian populations, the safety and efficacy of the Watchman device has not been reported in Taiwan. Like patients generally in the Asia Pacific region, Taiwanese patients generally have a smaller body size and more labile INR, as compared with those in Western populations,[9] and are generally more intolerant towards oral anti-coagulants. Our study for the first time reports the safety, feasibility, and clinical outcomes after Watchman device implantation for NVAF patients in a single center in Taiwan.

METHODS

Study Population

Twenty patients receiving LAA occlusion with the Watchman device by a single operator at National Taiwan University Hospital between Nov. 2014 and Sep. 2017 were prospectively enrolled. All patients had a diagnosis of paroxysmal or persistent AF and had CHA_2DS_2-VASc score more than 2, and had at least one contraindication to warfarin or NOAC therapy (presence of major bleeding, labile INR, or patient refusal) or recurrence of thromboembolic stroke even after taking warfarin or NOAC. The patients had received transthoracic echocardiography and transesophageal echocardiography (TEE) prior to the intervention. Oral anti-coagulant was not stopped before the procedure.

Implantation Procedure and Follow-Up

The patients underwent general anesthesia guided by the anesthesiologist. We conducted the procedure via the femoral venous approach and under fluoroscopic, angiographic, and continuous TEE guidance. Intravenous heparin (100 unit/kg) was given to patients to achieve activated clotting time (ACT) of at least 250 seconds after successful trans-septal puncture. The Watchman device was implanted with standardized techniques as reported.[10] Acute procedural success was defined as proper and stable Watchman device placement in LAA without significant peri-device leak (>5 mm) and impingement on surrounding cardiac structures.[7,10,11]

All patients were observed in the coronary care unit for one night after the procedure. All patients were prescribed aspirin 100 mg and warfarin (INR 2-3) for 45-60 days after the procedure. Clinical follow-up was arranged at 1 month and then every 3 months after device implantation to assess the clinical outcomes, whereas a follow-up TEE was scheduled at 2 months after the procedure.

Definition of Safety Endpoints

The safety end-points were defined as occurrence of events related to TEE (e.g., esophageal injury), heparin (e.g., intracranial or gastrointestinal bleeding, other major bleeding requiring transfusion), or procedure (e.g., catheter-related thrombus formation, air embolism, pericardial effusion, device embolization, procedural-related transient ischemic attack, or stroke). Serious pericardial effusion was defined as the presence of hemodynamically significant pericardial effusion requiring either pericardiocentesis or surgical drainage.[1] End-points assessed during TEE follow-up included the presence of visible thrombus on the surface of the Watchman device, significant peri-device leak (≥5 mm peri-device flow in vena contracta as detected by Doppler echocardiography), pulmonary venous obstruction, new-onset mitral regurgitation or delayed device embolization. The efficacy end-points were defined as the occurrence of ischemic stroke, transient ischemic attack, or systemic embolism.[1,12]

Statistics

The continuous variables are expressed as mean ± standard deviation (SD), and the categorical variables are expressed as number and percentage.

RESULTS

Baseline Characteristics

The LAA was successfully closed by the Watchman device in 20 of 20 patients (100%). The baseline characteristics, reasons for not taking warfarin/NOAC, and CHA_2DS_2-VASc scores are shown in Table 1. All the patients received general anesthesia during the procedure. The average angiographic maximal LAA diameter was 28.9 ± 5.3 mm, and mean implant size was 26.2 ± 4.0 mm. The average hospital stay was 4.2 ± 1.5 days.

Adverse Events During the Procedure

There was no event related to TEE or general anesthesia. There was also no event related to the procedure such as air embolism, device embolization, procedural-related transient ischemic attack, or stroke. There was one patient who experienced hemodynamically significant pericardial effusion requiring pericardiocentesis during observation in the coronary care unit.

Table 1. Baseline Characteristics of Patients

Variable	Patients (*n* = 20)
Age (yr)	72.7 ± 11.7
Men	12 (60%)
Reasons for not taking warfarin/NOAC	
History of severe bleeding	12 (60%)
Unstable INR	4 (20%)
Patient refusal	2 (10%)
Recurrent cerebrovascular event despite being on warfarin or NOAC	2 (10%)
CHA_2DS_2-VASc score components	
Diabetes mellitus	4 (20%)
Hypertension	16 (80%)
Congestive heart failure	2 (10%)
Age >75 yr	9 (45%)
Previous history of TIA/stroke	2 (10%)
Coronary artery disease	5 (25%)
Peripheral arterial occlusive disease	1 (5%)
Age between 65 and 75 yr	9 (45%)
Female sex	8 (40%)
$CHADS_2$ VASc score	3.2 ± 1.7
Left atrial appendage size	
Angiographic maximal orifice diameter range (mm)	21-38
Angiographic mean maximal orifice diameter (mm)	28.9 ± 5.3
Watchman implant (size range, mm)	21-33
Watchman implant (mean size, mm)	26.2 ± 4.0

INR, International normalized ratio; TIA, Transient ischemic attack; NOAC, novel oral anticoagulant

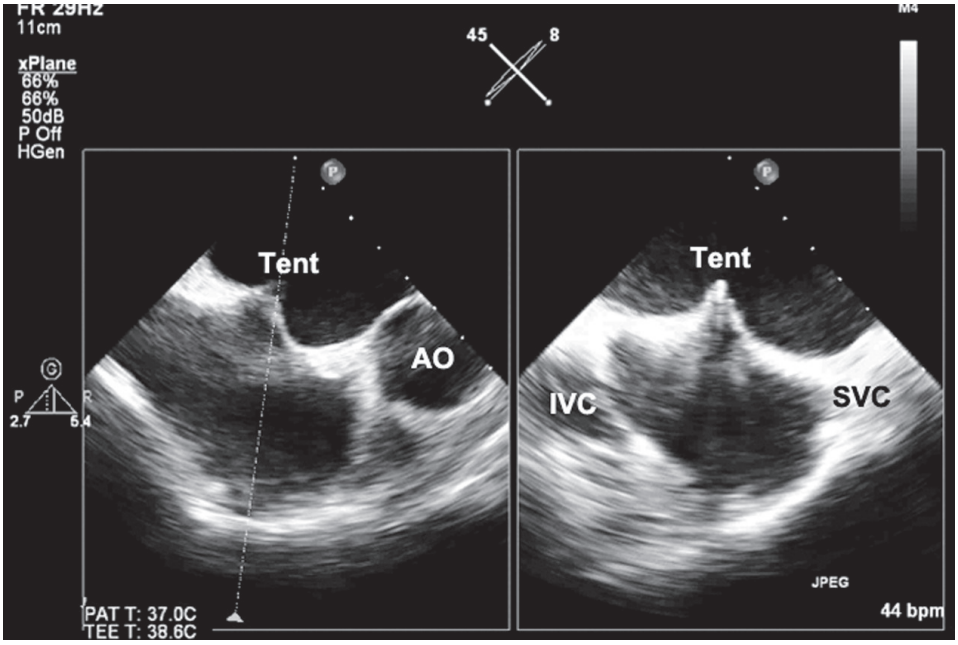

Figure 1. Position of the trans-septal puncture needle in trans-esophageal echocardiography images. Left panel, short axis view of the interatrial septum. The aorta is in the anterior aspect of the heart. When the trans-septal puncture needle is pushed against the interatrial septum, there is a "Tent" sign in the interatrial septum. The needle should be as far away from the aorta as possible (as posterior as possible). Right panel, bicaval view of the interatrial septum. The inferior vena cava (IVC) is in the inferior aspect of the heart; the superior vena cava (SVC) in the superior aspect of the heart. The needle should be as far away from SVC or as close to IVC as possible (as inferior as possible).

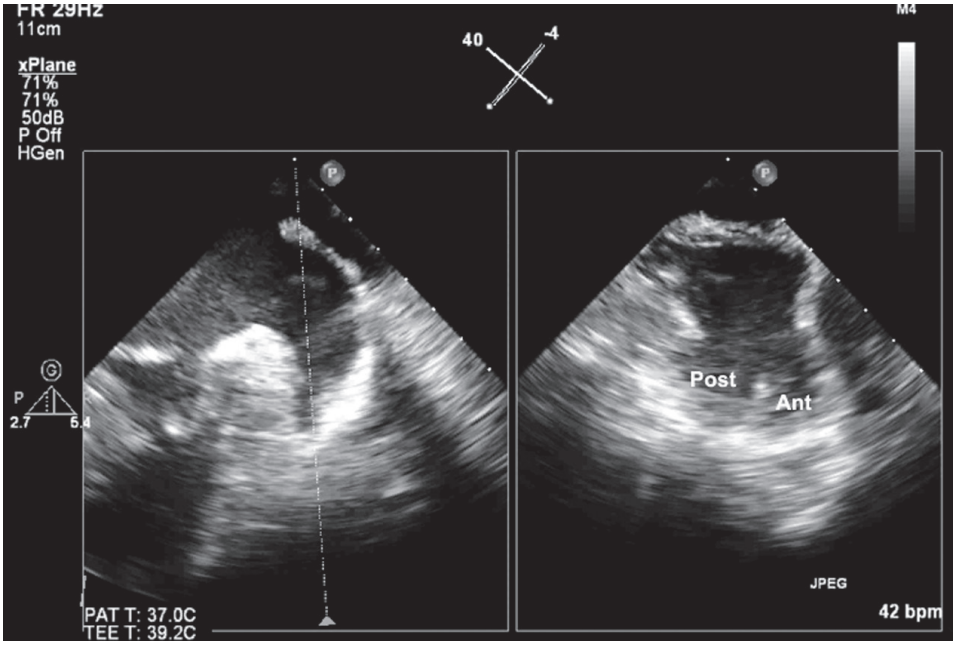

Figure 2. Morphology of the left atrial appendage in trans-esophageal echocardiography images. Left panel, long axis view of the left atrial appendage in 45-degree trans-esophageal echocardiography image. Right panel, short axis view of the left atrial appendage in 135-degree TEE image which shows the anterior (Ant) and posterior (Post) lobes of the left atrial appendage in this representative patient.

Follow-up Results

Follow-up TEE upon completion of aspirin showed no significant peri-device leakage, pulmonary venous obstruction, new-onset mitral regurgitation, thrombus formation on the implants, or delayed device embolization. No stroke, transient ischemic stroke, or systemic embolization had occurred in the patients at a mean follow-up of 13.1 ± 9.8 months.

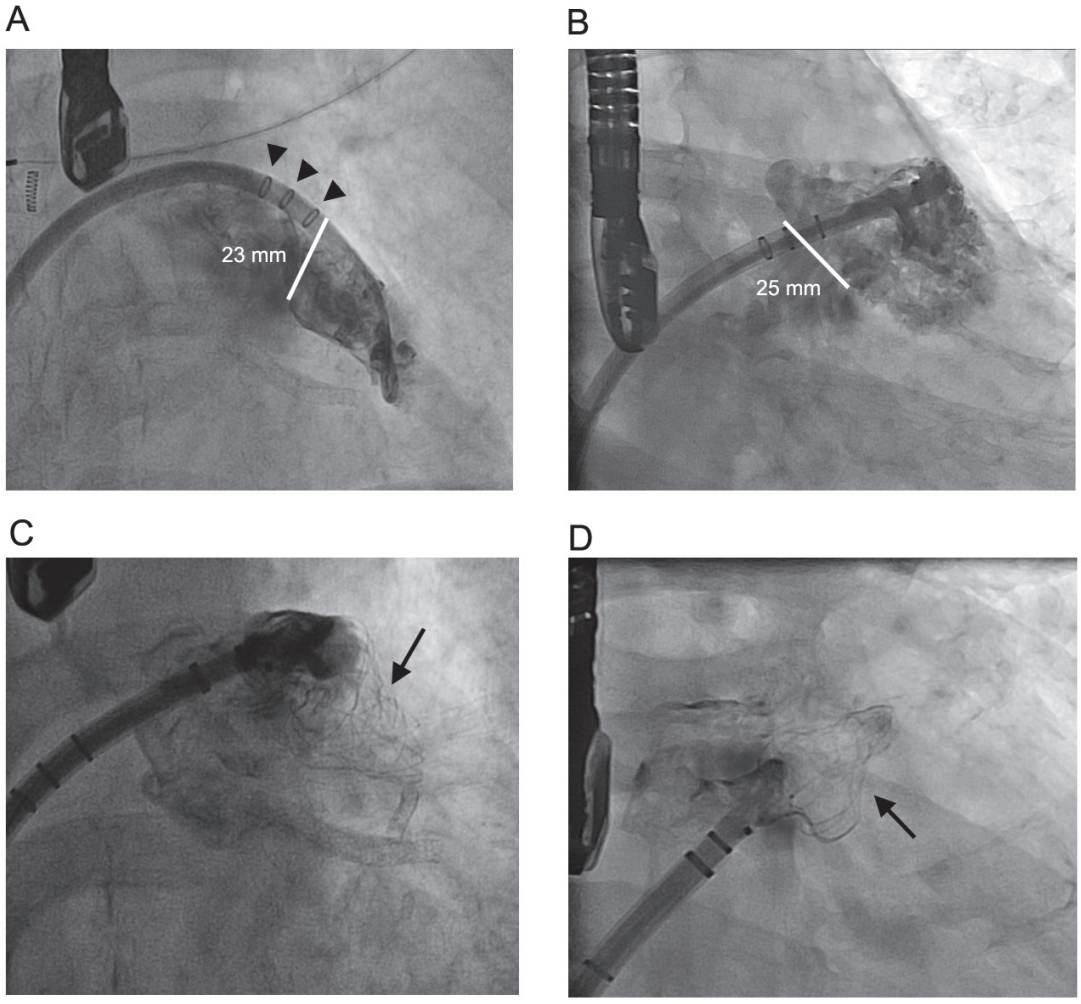

Figure 3. Angiography of the left atrial appendage before and after implantation of a 27 mm Watchman device. A, the RAO 20 degree and cranial 20 degree image shows the long axis of the left atrial appendage in this representative patient. The measured ostial size of the left atrial appendage is 23 mm. There are 3 marks (arrow heads) in the access sheath, which indicate the proximal screw positions of 3 expanded Watchman devices after implantation (21 mm, 27 mm and 33 mm, respectively). After implantation, the proximal part (screw) of the Watchman should be in alignment with the ostium of the atrial appendage. B, the RAO 20 degree and caudal 20 degree image shows the short axis of the left atrial appendage. The measured ostial size of the left atrial appendage is 25 mm. C, the RAO 20 degree and cranial 20 degree image shows the long axis of the left atrial appendage after successful implantation of a 27 mm Watchman device (arrow). The chosen size of Watchman should be 3-5 mm larger than the ostial size to allow compression of the device, which provides better stability of the device in the left atrial appendage. D, the RAO 20 degree and caudal 20 degree image shows the short axis of the left atrial appendage after successful implantation of a 27 mm Watchman device (arrow).

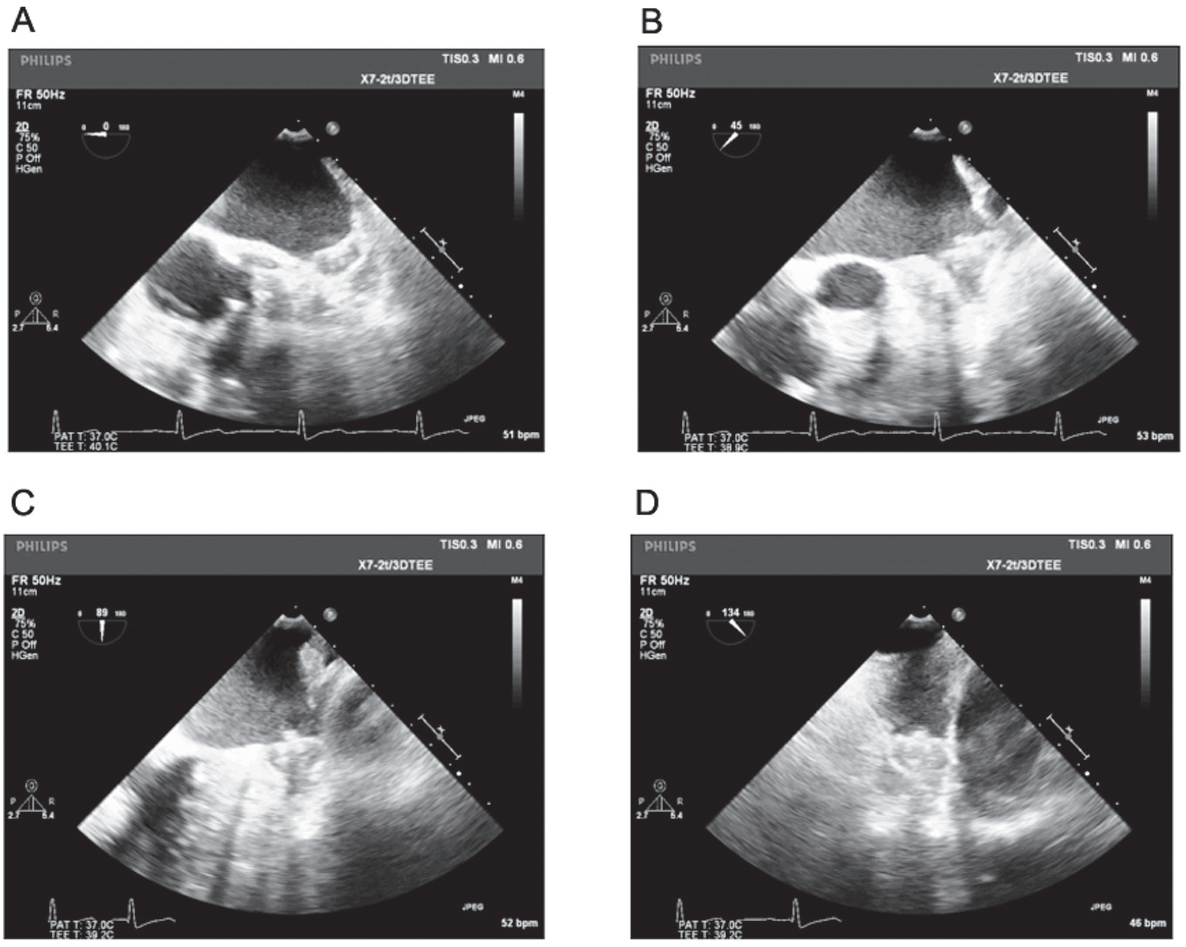

Figure 4. Trans-esophageal echocardiography images of an implanted 27 mm Watchman device in the left atrial appendage. After implantation of a Watchman device, multi-plane trans-esophageal echocardiography images should be obtained to ensure good positioning of the device and to detect any peri-device leak. A, 0-degree trans-esophageal echocardiography image. B, 45-degree trans-esophageal echocardiography image. C, 90-degree trans-esophageal echocardiography image. D, 135-degree trans-esophageal echocardiography image. This view shows the distal part of the Watchman device in the anterior lobe of the left atrial appendage.

DISCUSSION

We have shown that LAA closure with the Watchman device is a procedure with adequate safety, success rate and satisfactory clinical outcomes in a follow up period of 13.1 ± 9.8 months. This is the first report of experience with percutaneous LAA closure in Taiwan. Taiwan is one of the leading countries in the Asia-Pacific region in the implementation of percutaneous LAA closure, the first case having been done in Aug. of 2013 (Amplatzer cardiac plug).

Recent evidence has shown that closure of LAA by LAA occluder (Watchman device, Amplatzer cardiac plug, etc.) can be an alternative to warfarin therapy for stroke prevention in NVAF patients.[1,7,8,10,11,13,14] However, most of this evidence and the literature data has come from studies in Caucasian populations. It has been demonstrated that Asian patients, including Taiwanese, have a much smaller mean body size, more labile INR when on wafarin therapy

and higher bleeding rate when on NOAC, all of which increase the difficulty of applying clinical guidelines in practice.[9,15] Our data has shown for the first time that percutaneous LAA closure using the Watchman device in AF patients with contraindications to wafarin or NOAC, or self refusal, or experiencing embolic events even under adequate anticoagulant therapy is feasible, and may be a satisfactory alternative therapy with minimal complications and good clinical outcomes, for stroke prevention in patients with AF in Taiwan.

In the TEE follow-up study after the procedure, we found no significant peri-valvular leak, good impingement on the LAA orifice and no device-related thrombus. These good results are compatible with a recent large-scale Watchman registry study, EWOLUTION.[16] These findings also further strengthen the idea that no anticoagulant or anti-platelet therapy would be needed after Watchman implantation.[16] Other procedures to close LAA, such as surgical ligation or epicardial ligation are more invasive and technically challenging, which limits their application in general daily practice.[17,18]

There are limitations in the present study. First, this is a small clinical study with a short mean follow-up time. Second, the procedure was completed by a single operator in a single center.

In conclusion, closure of the LAA by Watchman device is a technically feasible and safe procedure, with a satisfactory one-year clinical outcome. Further larger scale clinical studies are warranted in the near future to prove the feasibility of percutanenous LAA closure in Taiwan and the Asia Pacific region.

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Management of Trapped Rotablator

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Abstract

Percutaneous coronary intervention (PCI) using intracoronary stents is widely applied in real world practice. Rotational atherectomy (RA) is sometimes needed to deal with undilatable fibrocalcific lesions. However, there are inherent risks in RA. A trapped rotablator during PCI is a real nightmare for cardiologists. Trapped rotablator can be a disastrous event and all intervention cardiologists who perform rotational atherectomy should be familiar with its management strategies. Good management strategies can help us wake up without being trapped in the nightmare. In this review article, we summarize the management strategies for trapped rotablator.

Keywords: calcification, complications, rotational atherectomy, entrapment

Introduction

Percutaneous coronary intervention (PCI) with intracoronary stents is the most common procedure for the invasive treatment of patients with coronary artery disease. Stent implantation and expansion are sometime infeasible because of severely calcified atherosclerotic plaque. Severely calcified coronary lesions can make balloon dilatation and stent placement extremely difficult and undilatable lesion is a common cause for PCI failure and procedural complications. For better stent apposition in order to improve clinical outcomes, debulking may be needed in calcified segments before stent implantation. Rotational atherectomy (RA) can be used for appropriate lesion preparation, the most important determinant of proper stent expansion in order to avoid stent thrombosis and restenosis in the era of the drug eluting stent.[1] RA can increase success rates of PCI in over 90% of cases with otherwise undilatable fibrocalcific lesions.[2,3]

However, there are inherent risks in RA. Severe complications such as no-reflow, coronary perforation and shock can occur in less than 2% of the procedures.[4] One of the rare but life-threatening complications is trapped rotablator, defined as "entrapment of the rotablation burr in a coronary lesion with the impossibility to rotate or retrieve the burr".[5,6] Trapped rotablator in a coronary lesion with the impossibility to rotate or retrieve by operator can lead to acute coronary occlusion and requires immediate management.[5] The aim of this review is to present our experience with rota-burr entrapment and discuss its management strategies. Current literature regarding stuck rotablator has been reviewed.

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Management of a trapped rota-burr

1. Intracoronary nitroglycerin (NTG) injection

Since rota-burr entrapment can be caused by severe coronary spasm, a first attempt with intracoronary injection of high dose NTG should be tried to relieve spasm, as nitroglycerin can sometimes alleviate the problem.[5,7]

2. Balloon dilatation at the site of the stuck burr

Parallel wiring of the stuck burr and subsequent passage of a balloon to release the burr can be tried next (Figure 1). Another polymer-coated or stiff wire can be advanced distally to the lesion with the trapped burr.[8,9] Sometimes, it can be extremely difficult to advance the wire and balloon through the narrow lumen of the guide catheter. It requires operators to cut off the RA system close to the advancer so another wire and rapid exchange balloon can be inserted.[8] If a conventional angioplasty balloon cannot be mobilized because of the poor residual lumen in the guiding catheter with the rotablator still in, a second vascular access using another artery for a second guiding catheter should be considered.[10]

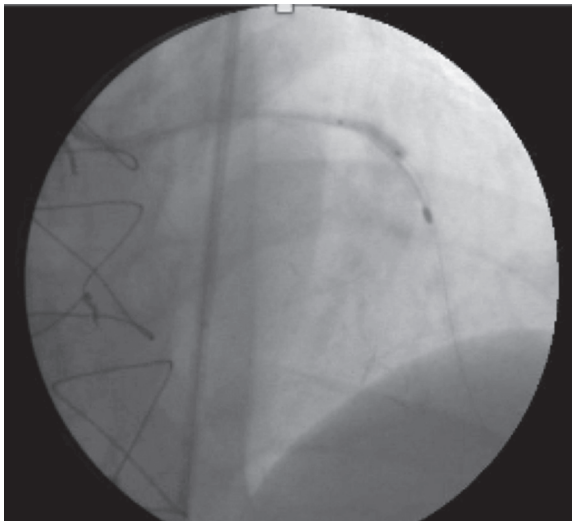

Figure 1. Second parallel wire was used and followed by balloon to loosen up the burr.

3. "Mother and Child" Technique with a 5 F guiding catheter or a Guideliner

A 5 Fr. "Mother and Child" catheter or a long 5 Fr. flexible straight guiding catheter can be inserted through the guiding catheter and over the rotational burr shaft after cutting away the advancer.[11] A 5 Fr. guiding catheter is introduced through the 6 or 7 Fr. guiding catheter down to the lesion and the trapped rotablator can be retrieved with the 5 Fr. guide catheter together. The "Mother and Child" technique provides support to enhance the pulling force. It is used to avoid extensive damage to the coronary artery. The "Mother and Child" technique requires operators to cut off the RA system close to the advancer as well. After removing the sheath and leaving only the driveshaft surrounding the rota-wire, the guiding catheter can be advanced along the rotablator remnants through the guiding catheter. Operators will aim to apply the force of retraction while the 5 Fr. catheter tip is pushed as close as possible to the proximal site of the stuck rotablator. An alternative method to the "Mother and Child" technique is to use a Guideliner instead of small size guide catheter.[12] The advantage of using a Guideliner is that the Guideliner is easier to advance along the rotablator remnants. A Guideliner is more flexible and can be intubated deeply into the coronary artery without traumatizing the vessel. (Figure 2). However, the disadvantage is that the guiding support is not as good as the standard 5 F guiding catheter.

4. Facilitated burr removal by deep guide catheter intubation

Deep intubation with original large size guide catheter and subsequent pullback of the stuck rotablator can provide even better support than the "Mother and Child" technique. The strong support helps operators to focus the pulling force on the trapped rotablator. The deep intubation technique can be facilitated by cutting off the system and pulling the burr shaft.[10] Usually the guiding catheter will follow the burr shaft into the stuck rotablator. Retrieval of the burr needs

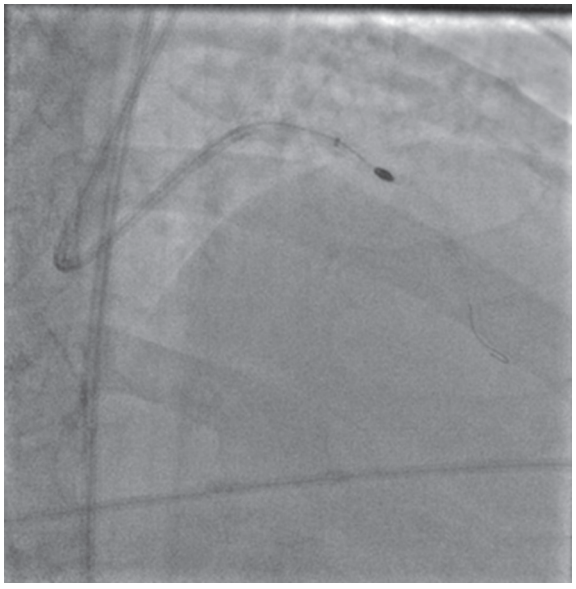

Figure 2. Use of a 5.5 F Guideliner to pull the stuck rotablator.

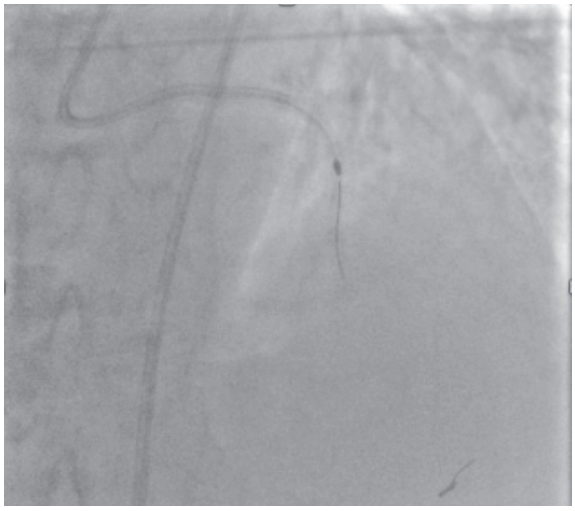

Figure 3. Deeply intubating 7F guiding catheter to pull the struck rotablator.

a lot of force, which can be safely done on the burr by pulling the deeply intubated catheter and burr shaft together (Figure 3). Extreme extracting force on the burr shaft without pulling the guiding catheter together may result in vessel dissection or perforation of the proximal segment. Previous disengagement of the guiding catheter from the vessel ostium to avoid deep seating of the guiding catheter during traction is recommended to prevent vessel injury.[10] However, from our experience, if the guiding catheter is deeply intubated following the burr shaft carefully into the vessel to the proximal half of the stuck rotablator, coronary dissection rarely occurs. Because a large force is needed for pulling the guiding catheter and the rota-burr together, applying the force of retraction as close to the site of entrapment as possible is really important.[10]

5. Surgical removal with subsequent coronary bypass grafting

If all the above techniques have failed, the stuck burr has to be retrieved surgically. Surgical removal with subsequent coronary artery bypass grafting is time consuming. Surgical mortality is usually high. Cardiac support with intra-aortic balloon pump and extracorporeal membrane oxygenation should be considered if the patient's hemodynamics start to deteriorate while waiting for surgery. While waiting for the cardiothoracic surgeon to arrive, another attempt to pull the stuck rotablator may be undertaken. We had a patient who had a trapped rotablator successfully retrieved after all the above interventional methods had been tried and had failed. While waiting for the consulted cardiothoracic surgeon, the trapped rotablator somehow got loose spontaneously. The trapped rotablator was pulled out easily without much force.

Conclusion

Trapped rotablator can be a disastrous event and all intervention cardiologists who perform rotational atherectomy should be familiar with its management strategies. It is a real nightmare to have a trapped rotablator during PCI. However, good management strategies can help us wake up without being trapped in the nightmare.

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Coronary Artery Disease and Heart Failure

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Abstract

Heart failure (HF) is a common clinical syndrome with high prevalence worldwide, which causes heavy economic burden in Taiwan. Coronary artery disease (CAD) is one of the most common etiologies of heart failure, regardless of the functional status of the left ventricle. Diagnosis of CAD in patients with HF is made by laboratory examination, noninvasive imaging tests, and coronary angiography. The selection of diagnostic tools is individualized, based on the clinical risks regarding signs or symptoms of myocardial ischemia. In addition to medical therapy, decisions regarding invasive management rely on the extent of ventricular dysfunction, clinical signs, and the existence of viable myocardium. In this review article, we update the current understanding of CAD in patients with HF and provide guideline-based treatment strategies for management of CAD in patients with HF.

Keywords: heart failure, coronary artery disease, myocardial ischemia, diagnosis

Introduction

The prevalence of heart failure (HF) is reportedly as high as 5.5%, causing over 22 thousand hospitalizations per year and up to a billion dollars' cost to the National health insurance and health budget.[1] As the aging of society in Taiwan is anticipated to continue to worsen, the future projected prevalence of HF is estimated to increase markedly.

Based on ventricular ejection fraction (EF), heart failure is currently categorized into HF with preserved ejection fraction (HFpEF) and HF with reduced ejection fraction (HFrEF). HFpEF is defined as the presence of clinical evidence of heart failure with ejection fraction over 50% without other identifiable causes (such as valvular heart disease, congenital heart disease or severely impaired renal function), whereas HFrEF has been traditionally defined as EF less than 40%.

Among numerous etiologies of HF, coronary artery disease (CAD) plays a key role for both HFpEF and HFrEF. CAD has been strongly established as a cause for the development of HFrEF. Cowie et al. analyzed the etiologies of 220 newly diagnosed HFrEF cases within a 20-month duration, and discovered that about one-third of cases had resulted from CAD.[2] Though

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not as conclusive as for HFrEF, slightly higher prevalence of CAD or prior myocardial infarction (MI) was also reported for HFpEF patients, when compared to the general population.[3,4] Overall, Framingham data has demonstrated that in general, over half of newly diagnosed HF cases were caused by CAD, making it the the most common etiology of HF development.[4] In Taiwan, ischemic heart disease has been reported in nearly 32% of heart failure cases.[5]

On the other hand, CAD is also considered a marker for poor prognosis in patients with heart failure. In the Survival and Ventricular Enlargement (SAVE) trial, patients with recent MI and EF less than 40% were enrolled for a 36-month frame study, which demonstrated that cases with prior MI history had an over 70% increase in cardiovascular death rate compared to those without.[6] In the Framingham study, participants with LVEF less than 45% who had had previous coronary heart disease showed significantly greater risk of mortality than other pathological disorders (HR 1.36, $p = 0.037$).[4] While there were few data examining the negative impact of CAD on patients with HFpEF, Coronary Artery Surgery Study (CASS) Registry data[7] showed a positive relationship between the number of diseased coronary arteries and mortality in heart failure patients with normal EF, indicating the potential impact on HFpEF outcomes derived from CAD.

The mechanism of CAD results in ventricular systolic or diastolic dysfunction

The pathogenesis of HF caused by CAD involves three mechanisms: LV remodeling, stunning/hibernating and mitral regurgitation (MR). Ischemia results in myocardial necrosis, apoptosis, and subsequent hypertrophy and fibrosis of the myocardium, which contribute to LV remodeling, and consequently causing LV dysfunction.[8] While HFrEF is mainly affected by myocardial remodeling, in HFpEF, numerous comorbidities, such as DM, contribute to ventricular and vascular stiffening, which ultimately result in LV diastolic dysfunction.[9] So-called viable myocardium refers to impaired myocardial contractility of the myocardium without irreversible damage or scarring. It includes two forms: myocardial stunning and hibernation, both of which are derived from myocardial ischemia, causing different degrees of contractility impairment. Ischemic MR is a complication of CAD, which may come from papillary muscle rupture in the acute-onset pattern and structural change of leaflet in the long-term pattern. The subsequent ventricular dysfunction may ultimately develop into HF.

Diagnosis of CAD in patients with HF

A thorough history taking and physical assessment should be performed when encountering a newly diagnosed HF patient to survey for potential atherosclerosis risk factors, and to evaluate any evidence of myocardial ischemia. However, clinicians must be wary of atypical symptoms that may manifest, and thus a high index of clinical suspicion needs to be maintained considering its high prevalence.

Biomarker-Troponin I

While Troponin I has been known as a distinct biomarker for the clinical diagnosis of acute coronary syndrome (ACS), elevated serum Troponin I or T level can frequently be detected in patients with HF, even in those without underlying CAD.[10] Considering the strong link between MI and the development of acute HF, the 2013 guidelines from the American College of Cardiology (ACC)/American Heart Association (AHA) on the management of HF placed the routine measurement of Troponin I or T in patients with acute decompensated HF in the Class I recommendations.[11] Abnormal troponin level in an acute HF patient should raise suspicion for MI, especially in those with typical symptoms, positive ischemia results on noninvasive imaging,

or the presence of newly onset compromised cardiac function.[10]

Noninvasive imaging

According to the ACC/AHA guideline,[11] noninvasive imaging to detect myocardial ischemia or viability is advised in patients with previously known CAD, who present with de novo HF but absence of angina unless unfeasible for coronary revascularization (Class IIa recommendation). Commonly used noninvasive imaging tests include stress/resting echocardiography, nuclear myocardial perfusion scan (such as SPECT); recently, innovative tools such as MRI/MRA and CTA have become alternative tests to provide more information, including the extent of calcification, myocardial scar burden, etc.[11,12]

Coronary angiography

Based on current guidelines (Class IIa recommendation), performing coronary angiography in order to diagnose CAD is reasonable when myocardial ischemia is suspected to be responsible for the development of HF.[11] Therefore, for HF patients at low to intermediate risk for ischemic heart disease, a conservative diagnostic strategy with noninvasive tests is advised, followed by coronary angiography if signs of ischemia are manifest. On the other hand, for those at high risk, such as presentation of overt angina, or sudden cardiac death, coronary angiography should be considered a first-line measure.[13]

Medical and device treatment

The medical and device treatments are summarized in Table 1 and Table 2. Generally speaking, the therapy for HFpEF depends on patients' co-morbidities. The treatments for patients with HFrEF are well documented depending on the severity of the clinical presentation.

Revascularization for CAD

While coronary revascularization is undoubtedly indicated in HF patients having ACS, this remains uncertain for those with stable ischemic heart disease. Following the current ACS guideline's suggestions, the invasive approach should be implemented in ACS patients with or without HF.[14] The European Society of Cardiology (ESC) guideline for HF also states that coronary revascularization is indicated for persistent angina refractory to medical therapy (Class I recommendation).[12] The selection of strategy depends on the risk stratification. Current evidence demonstrates better outcome with surgical revascularization in patients with LV systolic dysfunction; if the target vessel that causes a specific myocardial ischemia area can be identified then CPG (clinical practice guideline)-based percutaneous coronary intervention (PCI) strategy can be employed in

Table 1. Medical Treatment for HFpEF

Comorbidities	Recommendation
Hypertension	Beta blockers, ACEIs or ARBs Control blood pressure according to current practice guideline
AF	Rate control, anticoagulation, following AF practice guideline
CAD	OMT for CAD as per current guideline
DM	OAD or insulin replacement therapy as per current guideline
Signs of volume overload	Diuretics

ACEI = angiotensin-converting enzyme inhibitors, ARB = angiotensin receptor blockers, AF = atrial fibrillation, CAD = coronary artery disease, OMT = optimal medical therapy, DM = diabetes mellitus, OAD = oral anti-diabetic agents

Table 2. Medical and Device Treatment for HFrEF

Severity of clinical manifestations	Recommendation
Stage A	Control hypertension and serum lipid level according to current guideline Avoid co-morbidities that can cause HF
Stage B	All treatments of stage A ACEIs/ARBs, beta-blockers in all patients ICD in patients with asymptomatic ischemic cardiomyopathy, whose EF ≤ 30%
Stage C	All treatments of stage A Diuretics, ACEIs, ARBs, beta blockers, aldosterone receptor antagonists in all patients Hydralazine plus isosorbide dinitrate, Digoxin, anticoagulation, ICD and CRT in selected patients
Stage D	All treatments from stage A to stage C Inotropic agents, mechanical circulatory support, cardiac transplantation in selected patients

EF = ejection fraction, ACEI = angiotensin-converting enzyme inhibitors, ARB = angiotensin receptor blockers, ICD = implantable cardioverter-defibrillator, CRT = cardiac resynchronization therapy

patients ineligible for coronary artery bypass graft (CABG).[14]

Coronary revascularization is considered potentially beneficial for HFpEF patients with known CAD. The AHA/ACC HF guideline states that coronary revascularization is reasonable for patients with concurrent HFpEF and CAD, if myocardial ischemia is considered to have adverse effects on HF symptoms (Class IIa recommendation).[11] The CASS study,[15] conducted in the early 1970's, focused on CAD patients with HF symptoms whose EF was over 35% to compare the outcome between pure pharmacotherapy and pharmacotherapy plus coronary revascularization (CABG or PCI). Among those undergoing both medical and invasive therapy, there was a tendency toward improved 10-year survival rate (surgical group: 82%, medical group: 79%, $p = 0.25$), especially in the group with EF between 35 and 50% (surgical group: 79%, medical group: 61%, $p = 0.01$).[16] Thus, there is a rationale in saying HF patients whose EF is greater than 35% can benefit from coronary revascularization when myocardial ischemia is diagnosed.

Previous studies have failed to establish a clear correlation between coronary revascularization and superior outcome in severe LV dysfunction ($EF < 35\%$) HF patients. In a recent study, STICH (Surgical Treatment for Ischemic Heart Failure) trial, CABG and guideline-directed medical therapy (GDMT) yielded similar survival rates within a 5-year observation period in patients with EF less than 35%.[17] However, in terms of HF-related mortality, cardiovascular-associated mortality and hospitalization for HF/cardiovascular-associated causes, CABG produced superior results over GDMT. Given the potential benefit from CABG in HF patients with severe LV systolic dysfunction, and the ESC coronary revascularization guideline recommendation for HF patients with EF worse than 35%, CABG is recommended for those with LM stenosis, or proximal stenosis of both LAD and LCX, or significant LAD stenosis with concurrent multi-vessel disease (Class I recommendation).[18] Evidence from comparisons between PCI with pharmacotherapy and PCI with CABG is limited, and thus, the selection of strategy in patients with systolic dysfunction is individualized, based on co-morbidities, coronary anatomy, clinical

assessment and patients' preference.[19]

Myocardial viability assessment plays an essential role in predicting the effectiveness of coronary revascularization in patients with HF. Meta-analysis data has implied that the presence of viable myocardium could be an indicator for revascularization leading to lower mortality rate.[20] This, despite the fact that the STICH trial took an opposing position against the usefulness of myocardial viability testing,[21] but arguments have been raised over the trial's potential bias, which may have produced misleading results.[8,13] While the concept remains debated, according to current revascularization guidelines,[18] the performance of revascularization in patients with EF less than 35% with presence of viable myocardium is Class IIa recommendation, and PCI is to be considered in the same patient group if surgery is not feasible (Class IIb recommendation). The suggested algorithm of decision making for coronary revascularization in HF patients is demonstrated in Figure 1.

Take-home message on the latest guideline recommendation for HF medical treatment

According to the latest ESC guideline for the diagnosis and treatment of heart failure published in 2016, some innovative medical therapy concepts for HF patients with CAD have been integrated.[12] New medications, such as Ivabradine, Trimetazidine and Ranolazine are advised for anti-anginal treatment (Ivabradine, Class IIa recommendation; Trimetazidine, Class IIb recommendation) or alternatives despite the use of beta blockers (Ranolazine, Class IIb recommendation). Further, a combination of at least 2 anti-anginal medications could be an alternative strategy to revascularization (Class

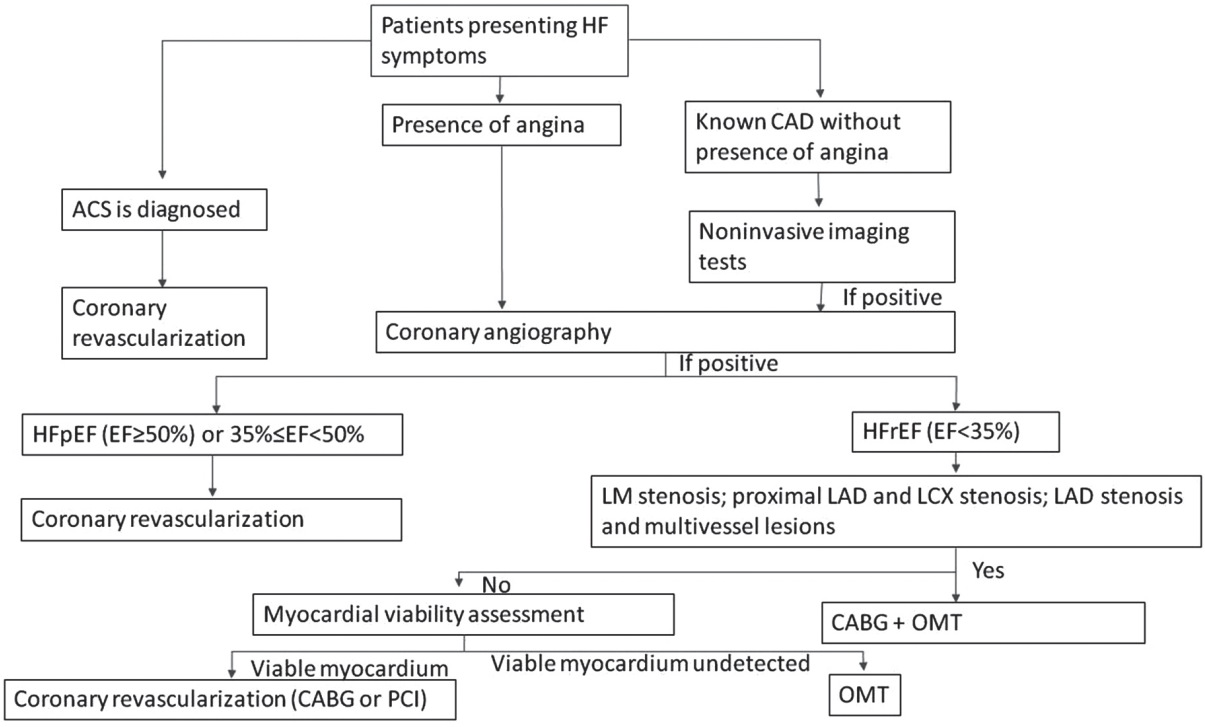

Figure 1. Suggested algorithm of decision making for coronary revascularization in heart failure patients. HF = heart failure, ACS = acute coronary syndrome, LM = left main, LAD = left anterior descending, LCX = left circumflex, CABG = coronary artery bypass grafting, OMT =o ptimal medical therapy, PCI=percutaneous cutaneous intervention

IIb recommendation), whereby the choice of medications is conditional.

Conclusion

In conclusion, CAD is one of the most common causes of developing HF, no matter with preservation of EF or not, and HF patients with CAD tend to have poorer prognosis. The selection of diagnostic tools for CAD in patients with HF, including serological test for troponin I, noninvasive imaging tests, and invasive angiography, is made based on clinical judgment. Once CAD is diagnosed, coronary revascularization is generally advised for HF patients with EF greater than 35%. As for those with severe LV systolic dysfunction (EF < 35%), the decision about coronary revascularization is made based on the lesions' features and the existence of viable myocardium. As the specific effects of several factors, such as the timing of revascularization and the detection of viable myocardium have yet to be determined, further large scale studies are warranted.

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Percutaneous Edge-to-Edge Transcatheter Mitral Valve Repair: The Tips and Tricks

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Abstract

The transcatheter mitral edge-to-edge repair, using MitraClip system, is a mini-invasive approach to treat patients with severe mitral regurgitation, who are deemed at high or prohibitive surgical risk. A randomized controlled study and numerous clinical registries have shown the feasibility and safety of MitraClip in treating patients with either primary or secondary mitral regurgitation. MitraClip demonstrates not only a low peri-procedure complication rate and an effective reduction of mitral regurgitation, but it also improves heart failure symptoms, functional capacity and quality of life. To date, more than 50,000 patients worldwide have undergone MitraClip procedures. Not surprisingly, the numbers continue to grow rapidly, and MitraClip has been available in Taiwan since 2016. The aim of this review is to illustrate who is the right patient for the trans-catheter therapy and how this procedure can be performed safely and effectively.

Keywords: mitral regurgitation; transcatheter mitral valve repair

Introduction

Mitral regurgitation (MR) affects more than 10% of the general population aged 75 years and older.[1] Open-heart surgery including mitral valve repair or replacement has been the gold standard and mainstay treatment for patients with severe MR.[2] Although surgical intervention is the curative treatment for MR, a certain portion of the patients, who are either too old or have multiple morbidities, would carry excessive surgical risks for peri-operative morbidities and mortality.[3] In fact, less than 15% of patients aged over 80 years receive mitral valve surgery for their severe MR. For those who are declined from surgery, _ENREF_2patients with symptomatic severe MR may experience deteriorating heart failure symptoms, and the 5-year mortality rate could be as high as 50%.[4] Given the significant extent of illness and the debilitating effect on quality of life, there is an unmet clinical need for a less invasive therapeutic option in patients who are deemed at high surgical risk.

The transcatheter edge-to-edge mitral valve repair, using MitraClip (Abbott Vascular, Menlo Park, CA, USA) is based on the double-orifice surgical repair technique. The Endovascular Valve Edge-to-Edge Repair Study (EVEREST II) was the first randomized trial to compare the safety and effectiveness of MitraClip to mitral valve

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surgery in surgery-eligible patients. In a total of 279 patients (184 MitraClip and 95 surgical control), MitraClip has demonstrated superior safety with regard to major adverse events (15% in MitraClip and 48% in surgery, p<0.001). Even though the recurrence of MR is more frequent in the MitraClip group, both groups have shown significant improvements in left ventricular size, New York Heart Association functional class and quality-of-life.[5] Moreover, comparably low rates of surgery for mitral valve dysfunction were recorded in both groups during the 5-year follow-up period. This long-term follow-up data may be seen to endorse the durability of both techniques.[6] In those ineligible for surgery, MitraClip has been proven a safe and feasible treatment by the EVEREST II high-risk registry[7] and in the real-world practice.[8]

Patient eligibility for MitraClip procedure

The first step in patient selection is to assess the etiology and severity of MR. MR could result from prolapsing leaflets or ruptured chordae (primary MR or degenerative MR, DMR), or be the consequence of annulus dilatation or abnormal left ventricular function (secondary MR or functional MR, FMR). The assessments to evaluate the severity of MR and treatment algorithms totally differ between these two etiologies of MR.[9] Severe FMR is classified with an effective orifice area (EOA) of ≥ 20 mm^2, whereas severe DMR is classified with an EOA value of ≥ 40 mm^2. In DMR cases, valvular reconstruction is the only therapy, while the reduction of FMR severity may be achieved by heart failure treatments,[10] revascularization,[11] or cardiac resynchronization therapy.[12] Hence, invasive valvular reconstruction by either surgery or transcatheter procedure could be an option to rescue medically refractory FMR patients.

Nowadays, both American and European guidelines recommend transcatheter mitral valve repair as a treatment option in patients with severe DMR and high surgical risk.[2,9] It remains debated whether MitraClip is indicated for subjects with FMR, given that valvular incompetence is the consequence of myocardial disease. However, patients with severe FMR are more fragile with regard to open-heart surgery. As a result, FMR patients constitute more than 60% of real-world applications of MitraClip.[16-18] Growing evidence has illustrated clinical and hemodynamic improvement after transcatheter correction of severe FMR[13-15], and MitraClip has been recommended in the European guideline for patients with severe FMR for whom revascularization is not indicated and who remain symptomatic even after optimal medical treatment.[9] However, the efficacy and long-term outcome can only be concluded when the results of the randomized-controlled trial (COAPT trial NCT01626079) are available.

Anatomical consideration for MitraClip

To date, the EVEREST II criteria have been acknowledged as the basis of an anatomical selection process. The eligible anatomy for the MitraClip procedure in the EVEREST II study included a primary regurgitation originating from the central A2/P2 region, coaptation length > 2 mm and coaptation depth < 11 mm in FMR, and flail gap <10 mm and width < 15 mm in DMR.[19] (Figure 1) The core concept of the EVEREST II criteria is to strictly define the "suitable" anatomy for MitraClip. By treating the most suitable pathology, the technical bias can be eliminated as much as possible in randomized controlled trial. However, only limited cases were available to fulfill the EVEREST II criteria for MitraClip procedure in real-world practice. In fact, Attizzani et al. have shown that with reasonably expanded criteria based on echocardiographic features, safety and efficacy are comparable to EVEREST II eligible patients.[20] Although some case reports have shown encouraging results in treating variable pathologies,[22-24] we should avoid using MitraClip to treat patients with cleft or perforated

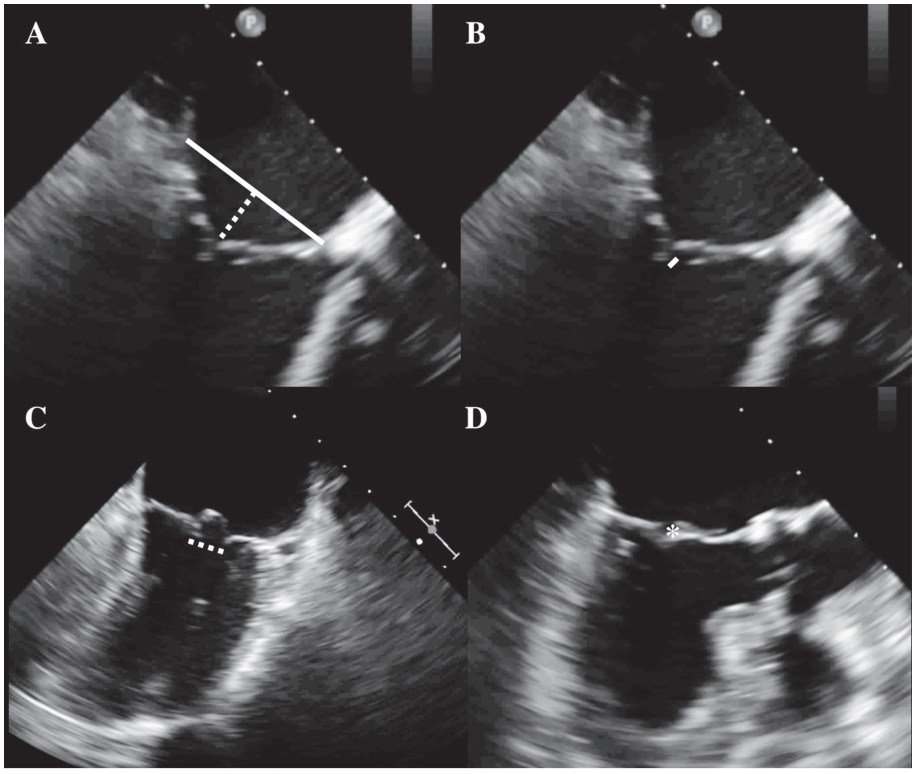

Figure 1. *(A)* Transesophageal echocardiography long axis view (130 degree): The mitral annulus line is drawn and the distance from the annulus line to the coaptation point (hatched line) represents tenting height. *(B)* Transesophageal echocardiography long axis view (130 degree): Coapation length is the distance of anterior and posterior mitral leaflet coapted (solid line). *(C)* Transesophageal echocardiography bi-commisure view (60 degree): Flail width (hatched line) is defined as largest width of flail segment and can be appreciated from bi-commisure view, 3-dimention en-face view, or mitral valve short axis view. *(D)* Transesophageal echocardiography long axis view (120 degree): Flail gap (asterisk) is defined as gap between flail and non-flail segment (default site for coaptation of anterior and posterior leaflet), which can be seen in long-axis view or 4-chamber view.

mitral valve, Barlow's mitral disease, co-existing infective endocarditis, length of posterior mitral leaflet less than 7 mm, or pre-existing mitral stenosis.[21]

The safety and efficacy of trans-catheter mitral valve repair have also been established in patients with advanced age,[25] LV systolic dysfunction,[25,26] frailty,[27] and extreme surgical risk, when surgery was usually declined.[28] Data from the German transcatheter mitral valve interventions (TRAMI) registry have shown impressive procedural safety and efficacy, and clinical improvement 1 year after MitraClip in patients with severely reduced or preserved LV function.[29] In patients with end-stage heart failure complicated by severe FMR, MitraClip could be a bridging therapy to preclude further clinical deterioration while awaiting a donor.[30]

The procedure: how to perform MitraClip

Before starting the MitraClip procedure, there are several important issues regarding pre-medication and nursing care, which have been addressed in detail by previous publication.[31] The procedure is conducted under general anaesthesia with the guidance of fluoroscopy and trans-esophageal echocardiogram (TEE) in a hybrid

operative room or catheterization room. Even though some experts have proposed a different approach to avoid intubation,[32] the majority of experienced centers still stick to the general anesthesia approach. At the same time, continuous pulmonary artery pressure and cardiac output monitoring by pulmonary artery catheter are suggested during the whole procedure. Not only are these hemodynamic parameters important indicators for procedural success,[33] but we can also identify acute afterload mismatch earlier[34].

The basic steps of MitraClip procedure are as follows: 1. transseptal puncture; 2. advancement of the steerable guide catheter and the clip delivery system into the left atrium; 3. diving the clip into the left ventricle; and 4. grasping the leaflets and assessing the result.

1. Transseptal puncture

The optimal puncture site is at the superior and posterior margin of the fossa ovalis. When the "tenting" of the atrial septum is identified (Figure 2A, 2B), we may check the height of the assumed puncture site relative to the mitral annulus. Because of the limitations of the steerable sleeve and the delivery shaft, the height of transeptal puncture is critically important in the MitraClip procedure. The optimal puncture height is 4 to 4.5 cm above the mitral annulus measured in the 4-chamber view of TEE. (Figure 2C) After a successful trans-septal puncture, a super-stiff guide wire is placed into the left upper pulmonary vein.

2. Advancement of the steerable guide and clip delivery system into the left atrium

The steerable guide catheter is gently advanced into the left atrium along with the super-stiff guide wire. The dilator is retrieved and the clip delivery system is advanced into the left atrium.

3. Diving the clip into the left ventricle

We use the "M" knob of the clip delivery system to steer the clip toward the mitral valve. Combined 2D and 3D enface view may facilitate the steering process and orientate the clip arms perpendicularly to the coaptation line (Figure 3). After advancing the clip into the left ventricle, we may re-check the perpendicularity by 3D enface view again.

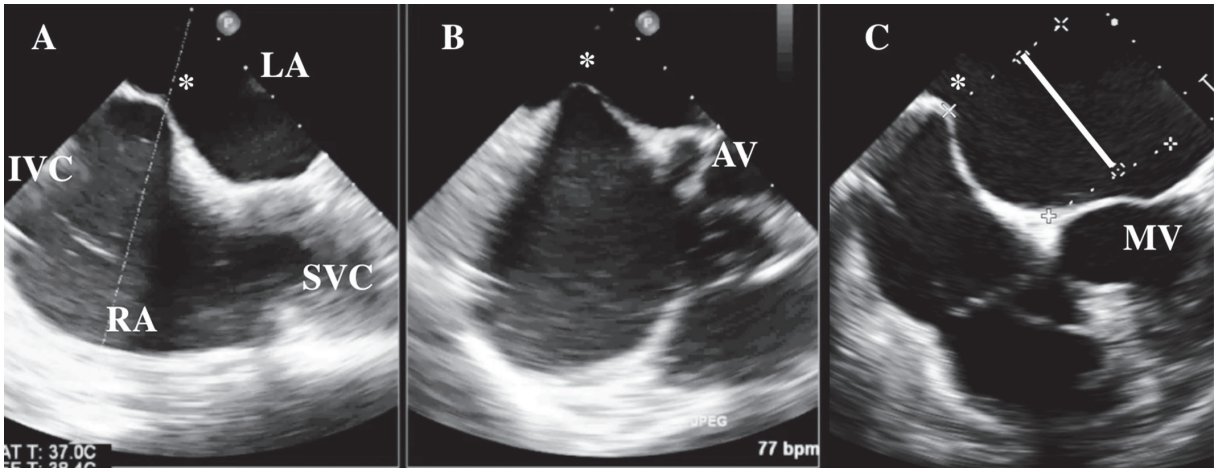

Figure 2. *(A)* Transesophageal echocardiography bi-caval view (110 degree): SVC: superior vena cava; IVC: inferior vena cava; RA: right atrium; LA: left atrium; asterisk marks the tenting site of the interatrial septum. *(B)* Transesophageal echocardiography short axis view (20 degree): AV: aortic valve. (C) Transesophageal echocardiography 4-chamber view (0 degree): height is measured from the tenting site to the mitral annulus plane (solid line).

4. Grasp the leaflets and assess the result:

We may retract the clip gently until both anterior and posterior leaflets are sitting steadily on the clip arm by the long-axis view (Figure 4), and then we can grasp the leaflets. Before the deployment of the clip, it is mandatory to evaluate the residual MR and the remaining mitral valve area to decide whether an additional clip is indicated. Neuss et al. have shown that patients experience significantly poorer long-term outcome when the mean trans-mitral pressure gradient is > 5 mmHg.[36] Since both residual MR[37] and worsened trans-mitral pressure gradient[36] have comparable impacts on the prognosis, there is always a trade-off between residual MR and remaining mitral valve area when using multiple clips.

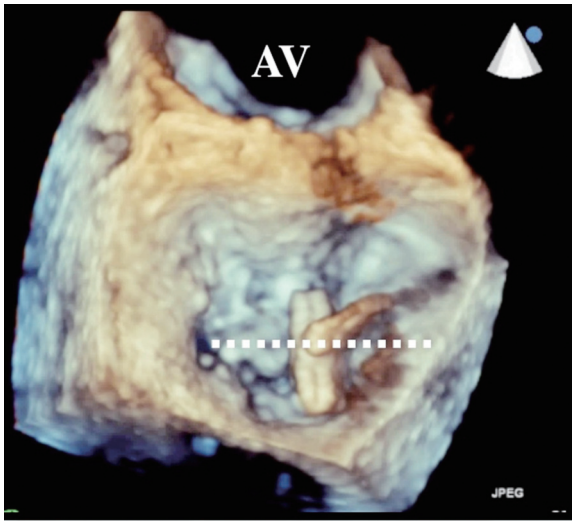

Figure 3. In the 3 dimensional en-face view, the clip should be perpendicular to the coaptation line (hatched line). AV: aortic valve

Conclusions

The transcatheter edge-to-edge repair is a safe and effective treatment in patients with severe MR who carry high or prohibitive surgical risk. The EVEREST II criteria have defined the most eligible mitral valve anatomy for this technology. TEE plays a major role in the diagnosis of MR,

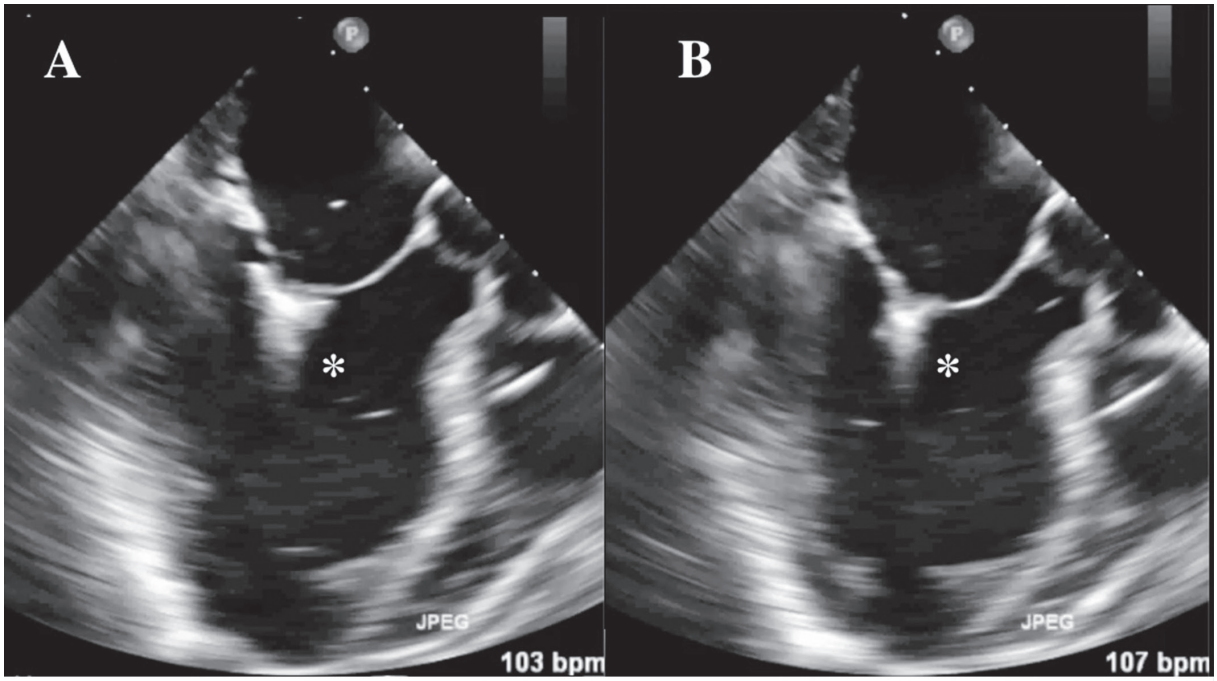

Figure 4. In the long-axis view, the process of leaflet grasping can be clearly appreciated. *(A)* MitraClip arm open with leaflets sitting steady on both clip arms. Asterisk marks the MitraClip. *(B)* Clip arms are fully closed.

the evaluation of eligibility for the procedure, and guidance during the procedure. To achieve not only the best procedural results and also clinical outcomes, a teamwork approach is mandatory.

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Acute Myocardial Infarction with Bifurcation Lesion in a Single Coronary Artery: A Case Report

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Abstract

Single coronary artery cases have already been reported over the years, but are still considered a topic worthy of discussion because of their significance. More often than not, such cases constitute an incidental diagnosis during an angiogram, however the risk of myocardial ischemia, other congenital anomalies or even sudden cardiac death should be taken seriously. Here, we present a 75-year-old female, who came to the emergency room due to chest tightness with cold clammy perspiration. Emergency cardiac catheterization was performed and an anomalous right coronary artery was found originating from the proximal portion of the left anterior descending artery. Culotte stenting technique was done on the bifurcation lesion. Hospital course was smooth and the patient was subsequently discharged with improved condition.

Keywords: acute myocardial infarction, anomaly, primary percutaneous coronary intervention

Introduction

Single coronary artery per se is no longer a rarity as more and more cases have been reported in the last decade. However, the point of origin of a single coronary artery offers a different perspective as to how extraordinary a given case may be, when encountered. Be it an incidental finding in the course of an angiogram, or as the culprit behind a disease condition, single coronary artery still poses an important challenge for accurate diagnosis and intervention with proper treatment. We report on a case of acute myocardial infarction with bifurcation lesion in a single coronary artery.

Case Report

A 75-year-old female with a history of diabetes mellitus type II, presented to our emergency department with chest tightness and cold clammy perspiration. The electrocardiogram showed ST-elevation over anterior and inferior leads. (Figure 1A) Tigacrelor 180 mg, acetylsalicylic acid 300 mg and heparin 100 IU/Kg IV bolus doses were administered and she was immediately referred to our cardiology service for emergency cardiac catheterization. A 6-French right Judkins diagnostic catheter failed to engage the right coronary artery. Contrast injection with 6-French left Judkins diagnostic catheter revealed total occlusion at the proximal portion of the left

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anterior descending artery. (Figure 1B) After crossing the lesion with a Fielder FC wire, a 2.5 x 15 mm Trek balloon was delivered across the lesion without inflation. We discovered that the right coronary artery originated from the proximal portion of the left anterior descending artery. (Figure 1C) Intravascular ultrasound was then used to assess the lumen size of both the right coronary artery and the left anterior descending artery. Two Orsiro stents (3.5 x 40 mm and 3.5 x 30 mm) were deployed to the bifurcation lesion using culotte stenting technique, and were post-dilated with non-compliance balloons. (Figure 1D) Recurrent ventricular tachycardia was noted

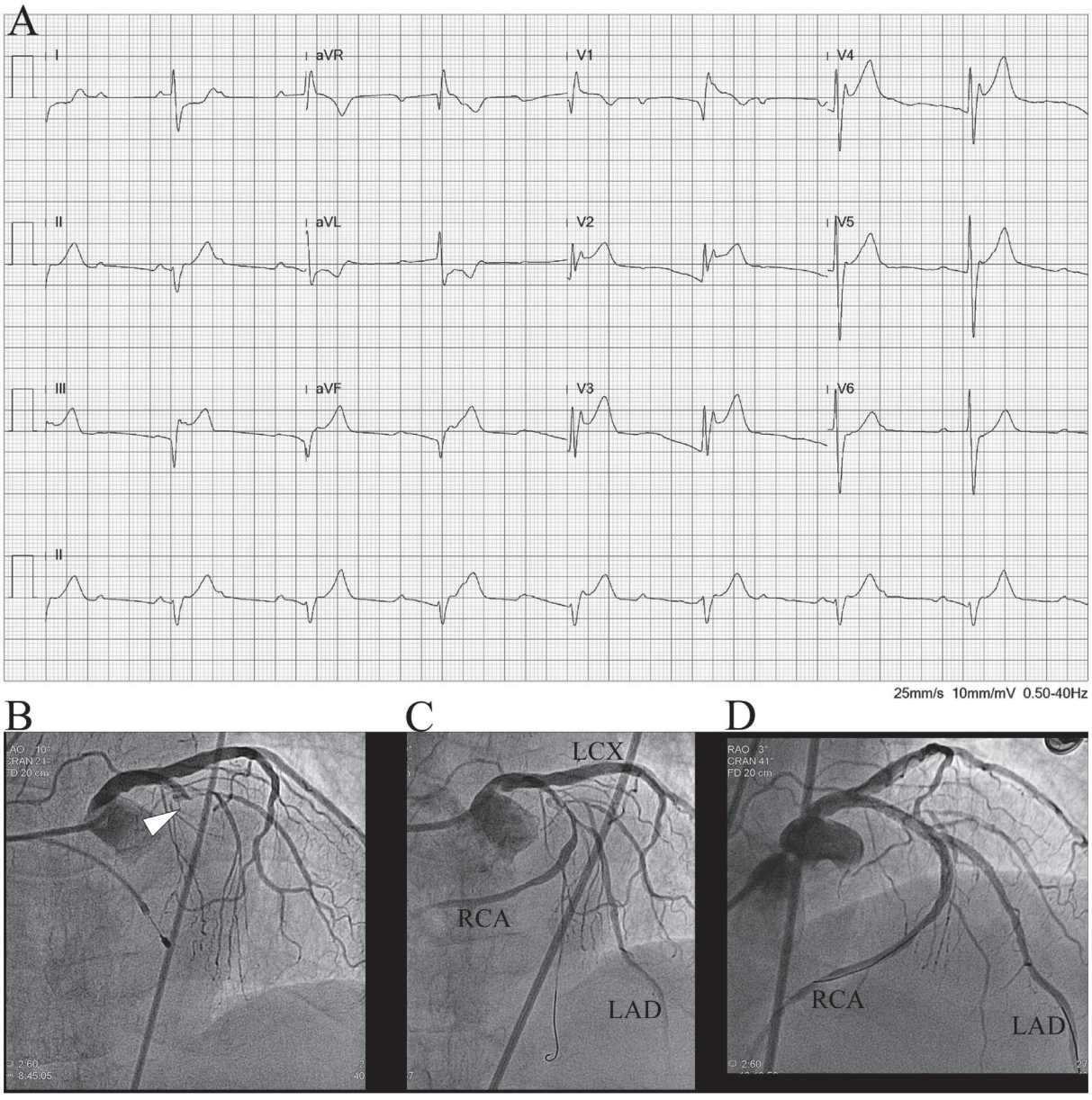

Figure 1. (A) The electrocardiogram showed ST-elevation over inferior and anterior leads, and complete atrio-ventricular block. (B) A total occlusion was noted at the proximal portion of the left anterior descending artery. (arrowhead) (C) The right coronary artery originated from the left anterior descending artery. (D) Two drug eluting stents were deployed to the bifurcation lesion with culotte stenting technique.
LAD: the left anterior descending artery; LCX: the left circumflex artery; RCA: the right coronary artery.

during the procedure, so electrical cardioversion was performed over 15 times. Intra-aortic balloon pump was inserted and IV inotropic agent was started. After the procedure, the patient was admitted to the intensive care unit for close monitoring and continued care. During the course of hospital treatment, clinical symptoms and hemodynamic status gradually improved, and hence the patient was discharged from the hospital on day 6 with improved medical condition. After 6 months of out-patient department follow-up, the patient's condition was stable and she was free from chest discomfort and complications.

Discussion

Aberrant coronary arteries occur in 1% of the general population and single coronary artery is a rare congenital anomaly of the coronary arteries that occurs in 0.02-0.07% of the population undergoing coronary angiography. Although these anomalies are mostly asymptomatic and are discovered as incidental findings during cardiac catheterization, they may cause angina, myocardial infarction, fatal cardiac arrhythmias, and sudden death. Single coronary artery is considered the rarest among coronary anomalies,[1-3] whereby the single left coronary ostium is rarer than the single right coronary ostium. Most frequently seen cases are aberrant right coronary artery originating from the left main coronary artery and crossing over anterior to the right ventricle, or passing between the pulmonary trunk and the ascending aorta. Another type of aberrant right coronary artery originates from the left circumflex artery. The right coronary artery originating as a branch of the left anterior descending artery is considered the rarest anomaly among the three mentioned,[4] and is the type we found in our patient during catheterization. A previously reported case, also with an unusual type of single coronary artery in which the right coronary artery originated from the middle portion of the left anterior descending artery closely resembled our case.[5] The only difference was that in our case the right coronary artery originated from the proximal portion of the left anterior descending artery, and an intravascular ultrasound was likewise used in assessing the lumen size of both right coronary artery and left anterior descending artery. Several mechanisms of myocardial ischemia in single coronary artery have been proposed, and include, to name just a few, entrapment of an anatomically ectopic artery between aorta and the pulmonary trunk, flap-like ostium closure, coronary spasm, slow controlled ischemia and atherosclerotic change in the coronary artery.[5] Our patient's culprit lesion was at the bifurcation of the right coronary artery and the left anterior descending artery, so culotte stenting technique was done, and the most probable mechanism of ischemia was the atherosclerotic change which brought about insufficient blood supply, leading to acute myocardial infarction. The exact correlation between coronary artery disease and single coronary artery is inconclusive, but there has been previously reported literature suggesting an aberrant coronary artery is more susceptible to atherosclerotic change due to its altered blood flow pattern. The incidence thereof, however, did not vary much when compared to a normally-originating coronary artery.[6-8]

Diagnostic methods used to evaluate aberrant coronary arteries are important because of the association with ischemia and sudden death. Multi-detector computed tomography (MDCT) has reduced the imaging time, the amount of contrast medium used, as well as the radiation exposure, and therefore can be used as a non-invasive means for diagnosing anomalous coronary artery, increasing the success rate of cannulation during coronary angiogram. MDCT also plays a vital role in the diagnostic process of coronary artery imaging that allows an ideal anatomic picture of the coronary artery course.

Multiple treatment alternatives also exist, depending on the varying clinical signs and symptoms, which can be from the most asymptomatic patient to a patient with sudden cardiac death condition. These include medical

treatment, percutaneous coronary intervention, or surgical procedures.[6] Potentials for serious complications are higher during percutaneous coronary intervention in a single coronary artery than in a normal coronary anatomy, which can be a challenging experience especially in an emergency setting, but must nevertheless be performed when deemed necessary.[3] In this case, we report on a 75-year-old patient with anomalous right coronary artery arising from the proximal portion of the left anterior descending artery, who underwent successful percutaneous coronary intervention utilizing the culotte stenting technique over the bifurcation lesion.

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CASE REPORT
Retrograde Revascularization of a Chronic Total Occlusion Obstructed by a Subintimal Stent: It is Never Too Late to Salvage a Vessel with an Inadvertently Subintimal Stent Deployed 10 Years Prior

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Abstract

We report the case of a 54-year-old man who presented as an acute non-ST elevated myocardial infarction (NSTEMI) complicated with cardiogenic shock. Coronary angiography revealed the middle segment of the right coronary artery (RCA) had critical stenosis with TIMI 2 flow and thrombus formation and chronic total occlusion of the proximal segment of the left anterior descending artery (LAD). RCA intervention was performed successfully but LAD CTO crossing failed. Instead, we cannulated the proximal LAD to the first diagonal branch (D1) and a 3.5x32mm BMS was deployed at LAD proximal to bifurcation. Four months later, follow-up angiography revealed LAD middle and distal vessel had emerged. However, we failed to advance the wire to the LAD middle segment because the stent in the proximal LAD had been deployed ten years earlier in subintimal space and had compressed the true lumen; only now had the patient developed severe angina. Finally, we revascularized the LAD by retrograde approach. Two new stents were deployed, crushing the subintimal stent that had been implanted 10 years prior.

Keywords: CTO, retrograde, subintimal stent, IVUS

Introduction

Chronic total occlusion of the left anterior descending (LAD) coronary artery is associated with long-term morbidity and mortality. Therefore, no effort should be spared to recanalize the CTO in order to improve symptoms and quality of life. Here, we describe an LAD CTO endovascular therapy complicated by inadvertent subintimal stenting in which we finally salvaged the vessel with a retrograde approach.

Case Report

A 54-year-old man, a heavy smoker with a medical history of hypertension presented to

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our emergency room with typical chest pain and diaphoresis for two hours. The initial electrocardiogram reported ST-segment depression over leads V4-6. Cardiac enzyme was elevated (CK = 153 IU/L, CKMB = 11.6 U/L, Troponin-I = 1.52 ng/mL). He was admitted to the intensive care unit and received low-molecular-weight heparin, aspirin and clopidogrel. His chest pain was still not resolved and blood pressure decreased, suggesting cardiogenic shock had developed; therefore, he was transferred to the coronary catheterization laboratory. Coronary angiography revealed the distal segment of the right coronary artery (RCA) had critical stenosis with a large burden of thrombus (Figure 1A), suggesting the RCA was the infarct-related artery, while the proximal segment of the left ascending artery (LAD) showed chronic total occlusion (CTO) (Figure 1B), and the left circumflex artery (LCX) had collateral vessels connected to the first diagonal branch (D1). Under intra-aortic ballon pump (IABP) support, we started the RCA treatment first. After applying an aspiration catheter, a bare-metal stent (BMS) was deployed at the distal RCA. By this point, Thrombolysis In Myocardial Infarction (TIMI) – grade 3 flow had been established. Post-stenting angiography also revealed the distal LAD filling from the posterior descending artery (PDA) of the RCA via collateral channels. Because the patient still suffered from cardiogenic shock, LAD revascularization was planned. We used 6 French 3.5 BackUP Left (BL 3.5) guiding catheter and Miracle 3 g (Asahi Intec) wire to try to cross the LAD CTO but failed. The wire could only reach the D1 branch (Figure 1C). We performed multiple inflations of a 1.5 x 20 mm balloon but the wire still could not advance to the LAD mid-vessel. A BMS 3.5 x 32 mm was then deployed at the LAD proximal to LAD-D1 bifurcation (Figure 1D) in order to preserve at least the proximal part of the LAD. The patient's condition improved after the procedure and he was discharged smoothly.

Four months later, a second attempt to recanalize the LAD CTO was scheduled. Coronary angiography surprisingly revealed the LAD middle and distal vessel was filling from antegrade TIMI grade 2 blood flow (Figure 1E). Percutaneous coronary intervention (PCI) was performed using radial approach with a 6 French BL 3.5 guiding catheter. A Runthrough NS wire (Terumo) was advanced into the stent and then to D1; a Fielder FC (Asahi Intec) wire was advanced to the LAD-D1 bifurcation site but we failed to manipulate it into the LAD middle vessel. In the spider view, we found the LAD proximal vessel emerged from the side of the proximal stent (Figure 1F), suggesting the stent had been implanted in the subintimal space. During previous PCI, the Miracle 3 g (Asahi Intec) wire had penetrated from the LAD proximal CTO cap through subintimal space to the D1 branch and had re-entered back to the true lumen of the D1. During the previous intervention, subintimal space had been created, extending from the proximal LAD to the LAD-D1 bifurcation, and the stent had then inadvertently been deployed in the subintimal space. The second-time intervention eventually failed to re-enter the wire to the LAD middle true lumen.

This patient received optimal medical treatment in the following ten years until he developed worsening effort angina. Myocardial perfusion scan revealed extensive ischemia at the anterior and apical wall. Coronary angiography revealed worsening antegrade flow in the LAD. RCA angiography revealed the LAD distal vessel filling from the PDA branch via collateral channels. We used transradial 6 French 3.5 Extra Back-up (XB 3.5, Cordis) guiding catheter to engage the left coronary artery (LCA). A 6 French XBRCA (Cordis) was engaged in the RCA via the right femoral artery. An Ultimate 3 g wire (Asahi Intec) with a Stride microcatheter (Asahi Intec) support could not be manipulated into the LAD middle vessel and was placed in the distal end of the stent, which was presumed to have been implanted in the subintimal space. Then a Fielder FC wire (Asahi Intec) with a FineCross microcatheter (Terumo) was advanced to the RCA-PDA using

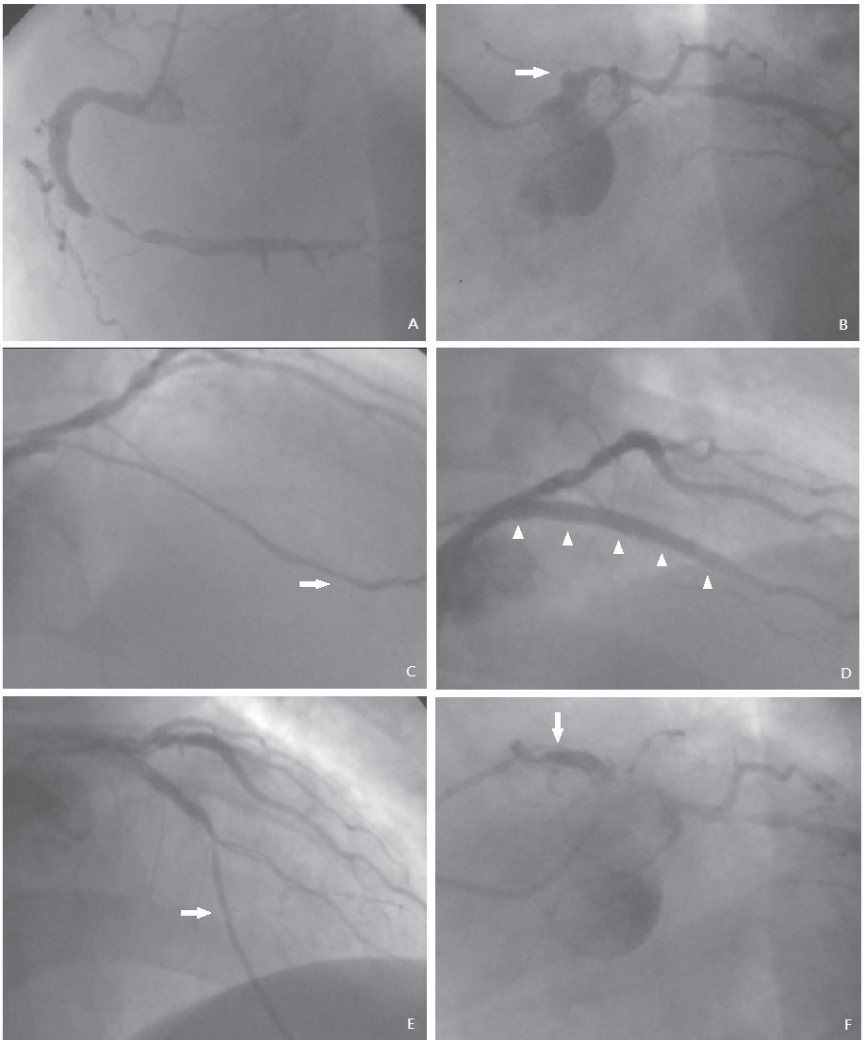

Figure 1. (A) RCA distal critical stenosis with large thrombus. (B) The spider view revealed the LAD proximal CTO stump (white arrow). (C) The wire advanced to D1 branch (white arrow). After multiple small balloon dilatations, the vessel from the proximal LAD to the D1 branch was filling by antegrade blood flow. (D) A BMS 3.5 x 32 mm was deployed in the proximal vessel of the LAD (white arrow heads). (E) Initial coronary angiography at the second attempt revealed that the middle segment of the LAD had emerged (white arrow). (E) The spider view revealed the true vessel of the LAD actually emerged from the side of the stent.

a retrograde approach. The wire was successfully advanced into the distal vessel of the LAD through a collateral channel from the PDA. However, the wire failed to penetrate into the lumen of the subintimal stent. After switching to a ProVia 9 g wire (Medtronic), it became possible for the wire to enter the true vessel lumen compressed by the subintimal stent, and then puncture into the strut of the stent itself. (Figure 2A). Then the wire was negotiated into the lumen of the XB 3.5 guiding catheter whereupon the FineCross microcather could be delivered into the lumen of the XB 3.5 guiding catheter as well. We achieved Rendezvous with a Runthrough NS wire entering the tip of the FineCross microcatheter antegradely. After the IVUS image (Volcano Corporation) confirmed the

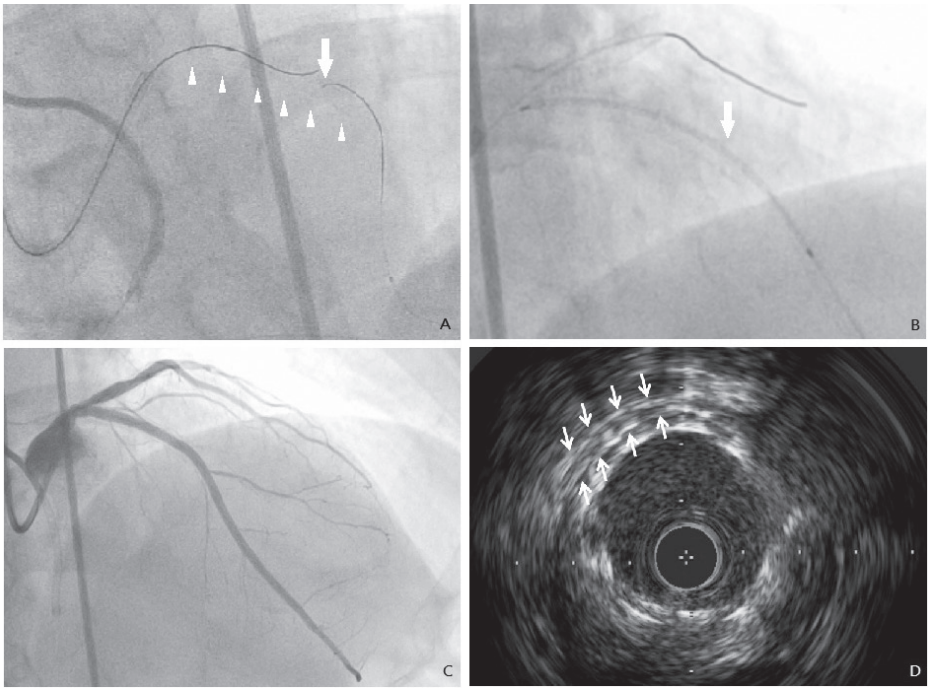

Figure 2. (A) The Provia 9g wire was manipulatde into the true vessel lumen space compressed by the subintimal stent (white arrow heads) and then punctured the strut of the stent (white arrow). (B) After Rendezvous and multiple dilatations of the Sapphire 2.0 x 15 mm balloon, a 2.75 x 48 mm Xience Xpedition stent was deployed across the subintimal stent strut (white arrow). (C) The final angiography after the new stents' deployment. Most of the LAD side branches were preserved. (D) The IVUS image revealed the crushed previous subintimal stent, which could be identified by the three metal layers of the stent struts (white arrows).

wire was in the true lumen of the LAD, multiple antegrade dilatation of the entire CTO segment with Sappire 2.0 x 15 mm balloon was performed. A 2.5 x 48 mm drug eluting stent (DES, Xience Xpedition) was deployed distally and then a 2.75 x 48 mm DES (Xience Xpedition) was deployed at the middle to proximal vessel of the LAD across the subintimal stent strut (Figure 2B), followed by high pressure post-dilatation with 2.75 x 15 mm and 3.25 x 15 mm NC Quantum (Boston Scientific) at the middle and proximal segment of LAD. Final angiography showed restoration of antegrade TIMI grade III flow in the LAD (Figure 2C). The IVUS image (Volcano Corporation) of the LAD demonstrated good expansion of the new stents and provided the image of the crushed subintimal stent (Figure 2D).

Discussion

In this case, we illustrate a subintimal stent deployment when treating a LAD CTO lesion. During antegrade crossing attempts of a CTO, it is not uncommon to penetrate a wire into the subintimal layer. It is very important to confirm that a wire is in the true lumen of the vessel before proceeding with balloon dilatation or stent deployment. There are several methods to avoid subintimal stenting, including dual site contrast injection, contrast injection through a microcatheter or IVUS evaluation.[1] Dual site contrast injection has been suggested for almost every CTO treatment. However, collateral vessels may not always clearly fill the distal vessel post CTO segment. In our case, we failed at crossing

the LAD CTO during the first attempt, only advancing the wire to LAD-D1; thus, it was not possible to confirm the wire position by dual site contrast injection. Besides, a wire advancing to a side branch is usually suggestive of a true lumen position;[2] however, as in our case, this may be misleading as the wire can advance subintimally into the side branch and re-enter the distal true lumen of the side branch. Thus, we recommend the IVUS evaluation, although advancing the imaging catheter distally is usually a challenge.

After the subintimal stent implantation in our case, the LAD true vessel lumen emerged from the side of the stent. This phenomenon probably contributes to increased antegrade blood flow in the LAD after LAD proximal stenosis has been resolved by the stent.[3] The salvaging of a CTO obstructed by a subintimal stent by antegrade and retrograde approach have both been reported before. In our case, if an antegrade approach had been chosen, a wire should have advanced into the stent and then out of the distal edge of the stent. Thereafter the wire should puncture back from subintimal space to the true lumen of the vessel, however, this is a difficult procedure because the wire tends to advance along a subintimal space due to lower resistance than a true vessel lumen.[4] During manipulation, a wire may create further dissection space, which may extend beyond a bifurcation site. If a wire re-enters the true lumen distal to a bifurcation, the major side branch, such as the D1 branch in our case, would have a high risk of occlusion. Thus, the challenge is to re-enter the true lumen before the bifurcation, in this case using an antegrade approach. An alternative way is to manipulate a wire through the stent strut to re-enter the true lumen. However, the wire manipulation through the stent strut to the compressed true lumen of the vessel is extremely difficult. Therefore, when a subintimal stent is close to a bifurcation, we recommend the retrograde approach, which can minimize further subintimal dissection and can preserve side branches. When a retrograde wire fails to penetrate the distal stent edge, an alternative method is to penetrate a wire through the stent strut into the subintimal space and then deploy a new stent across the stent strut, followed by high pressure balloon post-dilatation to avoid non-uniform expansion.[5] Final IVUS image post-stenting is very important to confirm the new stent is well expanded around the old stent strut remnant. A LAD CTO obstructed by a subintimal stent is a rare situation. Our case demonstrated a retrograde approach to salvage the CTO vessel successfully by deploying the new stent across the strut of the previous subintimal stent that had been implanted 10 years prior.

Conclusion

It is important to confirm that a wire is actually in the true lumen of the vessel before deploying a stent, especially when treating a CTO. Once a stent has been deployed in a subintimal space, the retrograde approach, crushing the previous stent is effective to revascularize the vessel and improve long-term outcomes.

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Premature Coronary Artery Disease with Severe Left Main Bifurcation Lesion Presenting with Unstable Angina as the Initial Clinical Manifestation of Systemic Lupus Erythematosus

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Abstract

Coronary artery disease (CAD) is common in patients with systemic lupus erythematosus (SLE) and is responsible for the high morbidity and mortality of SLE. The incidence of myocardial infarction among middle aged women with SLE is 50-times greater than that of the age matched general population. In this article, we report on a 38-year-old woman who is a chronic smoker presenting with unstable angina for weeks. Multi-slice computerized tomography scan revealed left main lesion and we performed percutaneous coronary intervention. Due to her young age for CAD, several immunological studies were arranged for her which revealed elevation of antibody titer and the diagnosis of SLE was confirmed by rheumatologist. Although CAD as an initial clinical manifestation of SLE is much rarer, a high level of suspicion and awareness of SLE is needed in a middle aged woman who has coronary artery disease despite the lack of rheumatological sign and symptoms.

Keywords: coronary artery disease, systemic lupus erythematosus

Introduction

Coronary artery disease (CAD) is frequent in patients with systemic lupus erythematosus (SLE). The three major coronary abnormalities related to myocardial injury in SLE include premature atherosclerosis, coronary arteritis and, less commonly, coronary aneurysms.[4,7] The incidence of atherosclerosis increases up to ≥30% in SLE, probably due to pro-inflammatory cytokine burden and SLE related treatments such as corticosteroids with a dose of >10 mg/day to promote atherogenesis.[5] The steroid may elevate not only serum cholesterol and triglyceride level but also elevate systolic blood pressure. CAD is usually uncommon in premenopausal women, but frequent in SLE patients with long-standing corticosteroid therapy. In this article, we report on a middle aged woman who presented with unstable angina as an initial clinical manifestation of systemic lupus erythematosus.

Case Report

A 38-year-old woman who is a chronic smoker (one pack per day for 18 years) and

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who denied any history of oral contraceptive use and other CAD risk factors (hypertension, diabetes mellitus and hypercholesterolemia) presented with unstable angina. She visited our cardiovascular outpatient department and multi-slice computerized tomography scan was arranged for her, which revealed a lesion from the left main coronary artery to the left anterior descending coronary artery (LAD). Coronary angiography was performed, which showed left main bifurcation lesion with 70% stenosis in the distal portion of the left main, 90% stenosis in the LAD ostium and 70% stenosis in the middle portion of the LAD. There was also a 50% stenotic lesion in the left circumflex coronary artery (LCx) and another 50% stenotic lesion in the proximal portion of the right coronary artery (RCA). First, we checked the size and characteristics of the lesion by intravascular ultrasound (IVUS). Percutaneous coronary intervention was performed by deploying a drug eluting stent (3.0 x 20 mm, Synergy) to the LAD middle lesion. We decided on provisional one stent technique for the left main bifurcation lesion and hence deployed another drug eluting stent (3.0 x 16 mm, Synergy) to the distal portion of the left main coronary to LAD ostial lesion. The left main distal lesion was post dilated with non-compliance balloon (NC Euphora, 4.0 x 8 mm). Follow up intravascular ultrasound revealed good expansion and apposition of the stent. After stent deployment, the plaque shifted to the left circumflex artery and jailing of the left circumflex ostium. We performed fractional flow reserve (FFR) test on the left circumflex ostial lesion. After intracoronary adenosine injection of 60 ug and 120 ug, FFR persisted at 0.89. Therefore, we decided not to perform further intervention on the left circumflex artery.

Due to the patient's young age for coronary artery disease, we consulted a rheumatologist and arranged for several immunological investigations. The results revealed high antinuclear antibodies >1:1280, high anti-RNP antibodies >240, high anti-SM antibodies >480 and low C3 and C4 levels. Diagnosis of SLE was confirmed by the rheumatologist and regular follow up at our cardiovascular and rheumatology outpatient department was started.

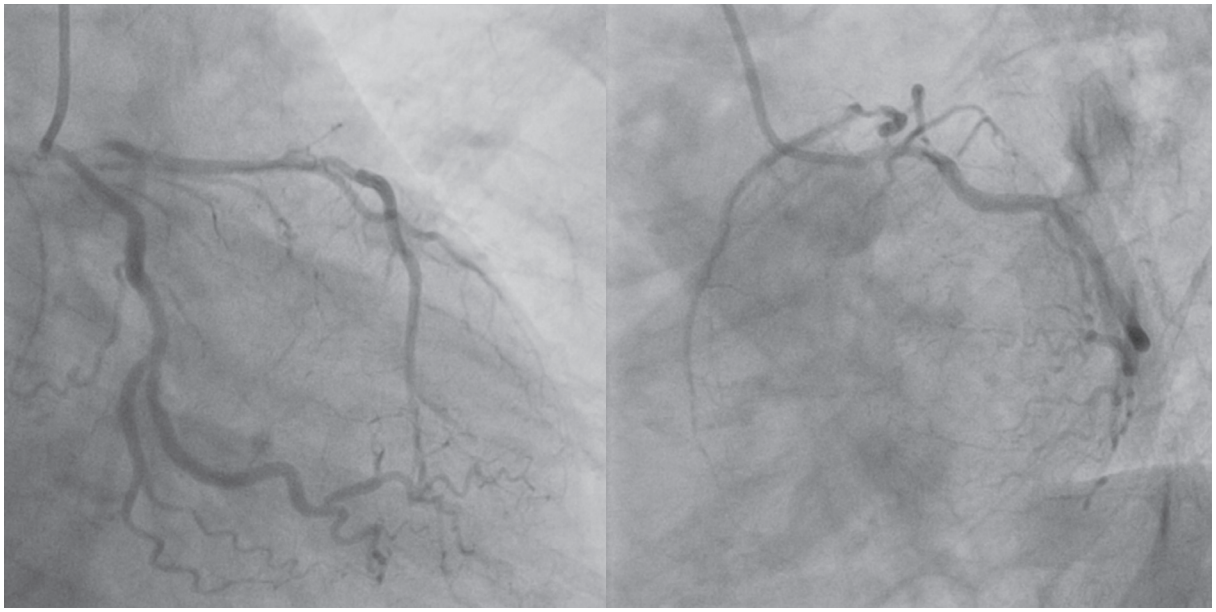

Figure 1. Pre PCI Coronary Angiography: Severe occlusion of distal LMCA to proximal portion of LAD with 90% stenosis.

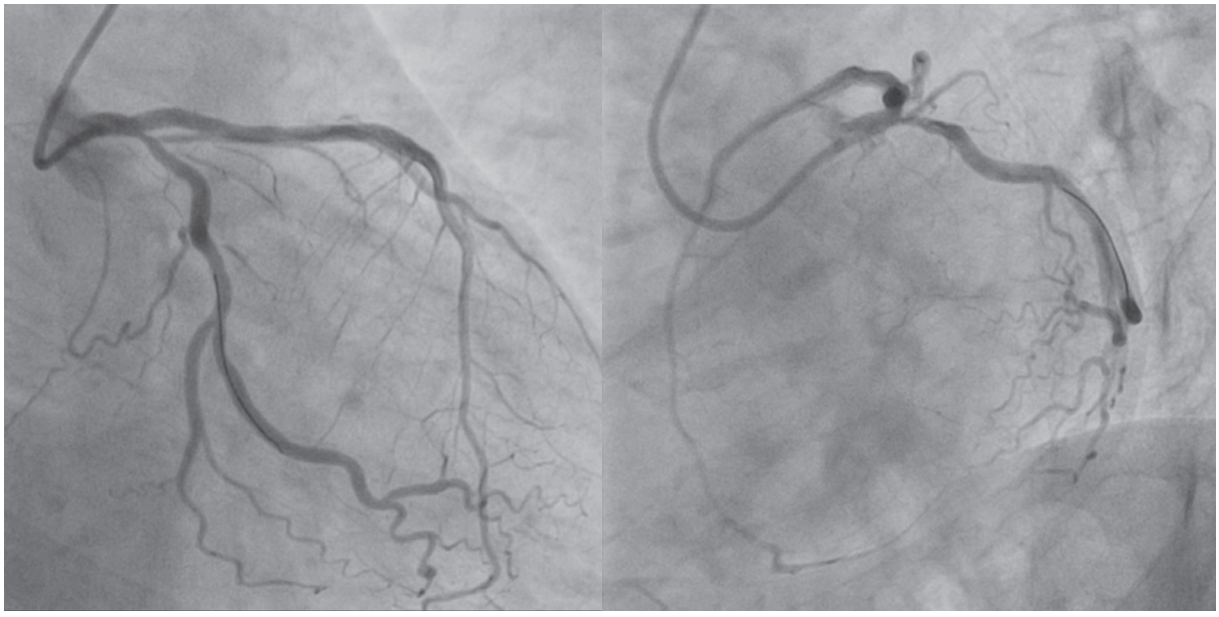

Figure 2. Post PCI Coronary Angiography: After stenting from distal portion of LMCA to proximal portion of LAD. Unfortunately jailing of LCx ostium due to plaque shift. FFR persisted at 0.89 after intracoronary injection of Adenosine 60 ug and 120 ug.

Discussion

Systemic lupus erythematosus is a chronic, inflammatory, autoimmune disease that affects mainly young women, a group usually free of atherosclerosis. Patients with lupus have higher morbidity and mortality due to cardiovascular complications. The incidence of myocardial infarction is 5 times as high in patients with lupus as in the general population, and in young women the age-specific incidence is increased as much as 50 times.[1,2] The mean age of first myocardial infarction among SLE patients has been reported to be 49 years, which is 20 years younger than that of the general population.[3,8] Among young SLE patients under 35 years acute myocardial infarction is the most common initial clinical manifestation of CAD, followed by congestive heart failure, sudden death, and angina.[3,9] Significant atherosclerosis is common among SLE patients. The majority of SLE patients who die of non-cardiac causes have pathologically moderate to severe multifocal atherosclerosis in autopsy studies.[3,10] Moreover, an autopsy series of women aged 16 to 37 years showed that over 90% had more severe atherosclerosis than an age-matched control population and that almost half had evidence of a greater than 75% occlusion in at least one coronary artery.[11] In SLE patients, traditional risk factors are not believed to fully account for the increased atherosclerosis. Rahman et al.[12] found that SLE patients with a cardiac event have fewer traditional risk factors than non-SLE patients with premature CAD. In women with SLE the mean number of CAD risk factors per cardiac event was 2.0 ± 0.77 vs. 2.90 ± 1.19 for the comparison group ($p = 0.0008$). Similar findings were reported in men with SLE. The mean number of CAD risk factors was 1.87 ± 0.83 vs. 2.73 ± 0.99 in the comparison group ($p = 0.016$).[6,13] The hyperlipidemias may be particularly significant in SLE because of the high prevalence of chronic renal failure, hypertension, and glucocorticoid use. Retrospective analyses have concluded that SLE patients treated with glucocorticoids (>10 mg of prednisone per day) had higher levels of

serum triglycerides, cholesterol, and LDL than matched controls.[14,15] Similarly, serum cholesterol levels appear to increase with increasing dose and duration of steroid use.[16] For every increment of 10 mg/d of prednisone, systolic blood pressure has been noted to increase by 1.1 mmHg, cholesterol by 9 mg/dL, and weight by 5.5 pounds.[16]

Angina symptoms due to coronary artery disease are an uncommon initial presentation for systemic lupus erythematosus. Most often, patients present with constitutional symptoms, arthralgia or arthritis, and/or skin changes. The most prevalent cardiac manifestation is pericarditis, which is seen in approximately 29% of patients during the course of their disease.[17] Our patient was a middle aged woman who was a chronic smoker (one pack per day for >18 years). Smoking and underlying SLE may accelerate and shorten the disease course of CAD. So angina symptoms appear earlier than the rheumatological signs and symptoms like arthralgia and arthritis. Lifestyle and pharmaceutical prevention measures, regular screening for subclinical disease, alertness for early clinical signs, accurate differential diagnosis, and targeted treatment are important strategies for the management of these patients.

Conclusion

The association between CAD and SLE has long been appreciated and CAD plays the major role in the morbidity and mortality of the established disease. Although angina symptoms as an initial clinical manifestation in SLE are very rare, our case illustrated that in middle aged women presenting with angina symptoms the appropriate diagnostic work-up for SLE is strongly recommended, despite the lack of rheumatological signs and symptoms.

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Percutaneous Intervention to Correct Central Venous Port Catheter Malposition

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Abstract

The use of central venous port access is increasing due to the requirements of multimodal intravenous therapy. However, catheter malposition in smaller veins can lead to vein thrombosis, local reactions and pain. Herein, we report our experience with minimally invasive percutaneous intervention to correct a migrated port catheter. As an alternative to port extraction and re-implantation, minimally invasive percutaneous interventional port catheter correction could be effective for treating migrated catheter tips.

Keywords: snare, port catheter, malposition, pigtail, percutaneous intervention, venous thrombosis

Introduction

An increasing incidence of several malignancies are associated with an increasing number of chemotherapy sessions whereby most of the chemotherapeutic agents are administered intravenously. Some of these chemotherapeutic agents may cause substantial tissue toxicity.[1] In addition, most elderly patients present with poor venous conditions which will worsen with chemotherapy administered via a peripheral venous catheter. Thus, the use of intravenous port systems has become increasingly common. Intravenous port systems can mostly be implanted in the infraclavicular region via the subclavian vein or in the forearm via the vena brachialis. The injection port reservoir is located subcutaneously and is connected to the actual port catheter which reaches intravenously into the superior vena cava (SVC) above the atrium of the right heart.

The optimal location of the tip is recommended to be in the lower third of the SVC or at the SVC/atrial junction.[2] However, malposition of the port system, whereby the tip does not lie in the ideal position, sometimes happens. The causes of malposition can be classified as primary (during the implantation procedure) and secondary (caused by high intrathoracic pressure, a short tip in the SVC, or upper limb movement). Malposition of the port catheter can lead to various potentially severe and harmful complications including thrombosis, stenosis, and extravasation. Herein, we report our experience with minimally invasive percutaneous intervention to correct port catheter malposition.

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Case Presentation

A 93-year-old woman has a history of peritoneal carcinomatosis and metastatic carcinoma from her reproductive organs. A central vein catheter was implanted for chemotherapy. However, malposition of the tip of the port catheter (into the right internal jugular vein) was noted on follow-up chest radiography (Figure 1A). We decided to reposition the port catheter with a minimally invasive procedure with a 6 Fr sheath inserted through the right femoral vein. With the support of Terumo 0.035" guide wire, a pig-tail 6 Fr catheter alone was advanced to the right internal jugular vein. The distal loop was then used to capture the port tip and pull it into the SVC (Figure 1B-1D). The whole procedure was completed successfully without any complications.

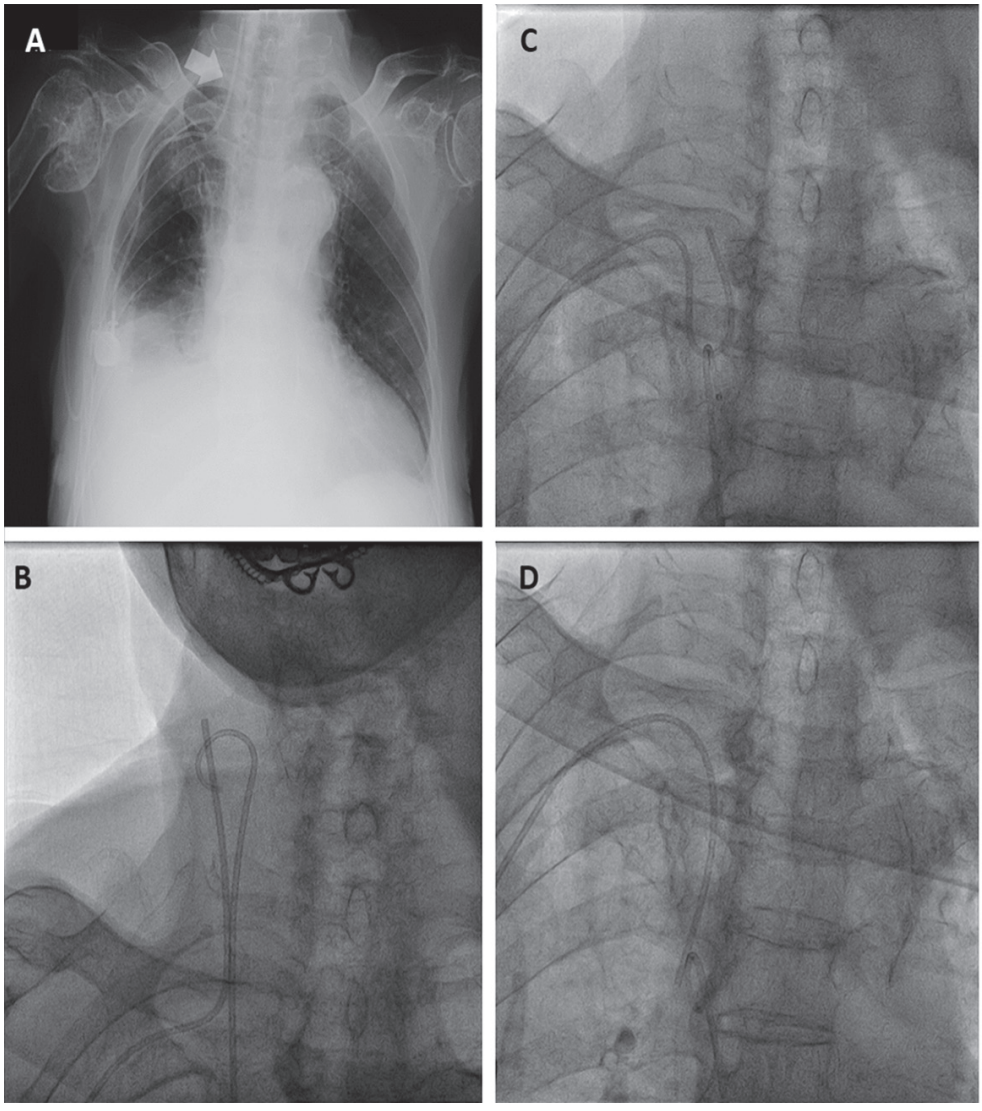

Figure 1. Intervention for malposition of a port catheter with a pigtail catheter. (A) Chest radiography showing malposition of the port catheter tip into the right internal jugular vein (arrow). (B) A pigtail catheter was advanced to the right internal jugular vein and encircled the port catheter. (C) The course of the port catheter was pulled back to the superior vena cava by the pigtail catheter. (D) The tip of the port catheter was successfully pulled into the superior vena cava.

Discussion

Central venous port catheters are usually used for the periodic administration of chemotherapy for the treatment of various malignancies. Catheter-related venous thrombosis (CRVT) is one of the most common complications of central port catheters, with a reported incidence ranging from 0.67-8.46%.[3] CRVT is also a major reason for removing the catheter because of the possible complications of thrombus extension, and even pulmonary embolism.[3,4] A catheter tip positioned in the right atrium or ventricle has been reported to cause cardiac arrhythmias, perforation, tamponade, or thrombosis, whereas a position in the smaller veins (jugular vein, brachiocephalic vein) has been reported to increase the risk of CRVT and may cause local reactions and pain, especially when using the catheter for highly concentrated chemotherapy.[3,5] In addition, the infusion of hypertonic solutions in the jugular vein has been reported to cause cortical venous thrombosis of the brain.[6] Due to the increased risk of consequent CRVT, a migrated catheter is an indication for correction of the tip location or catheter removal with re-implantation.

Retrieval and re-implantation with a new port system is the most direct method, however it is expensive and may cause new complications such as pneumothorax, repeated malposition of the catheter, or infection. On the other hand, a minimally invasive procedure with a percutaneous intravenous approach is more efficient, less expensive, and minimizes the likelihood of complications. There are several alternative methods of repositioning a migrated catheter, including direct manipulation using guidewires, forceful saline or contrast injection, transfemoral retraction using angiographic catheters (e.g., pigtail, sidewinder catheter), and snare loops.[5] In a port system, guide wire-assisted repositioning and forced saline injection are not possible. Therefore, repositioning via a transfemoral approach, usually using pigtail, sidewinder, or goose-neck snares, seems to be an appropriate minimally invasive alternative to correct displaced chest port catheters. In our experience, beginning with a pigtail catheter may be as effective as a snare catheter and can be more cost effective in selected cases. The pigtail catheter is easier to control with guidewire and capturing the course of the catheter is also easier than capturing the tip, especially if the tip is embedded into a vessel or chamber wall. Most studies have used conventional 5 Fr catheters, however, a larger catheter provides more support. The success rate of percutaneous intervention for port catheter correction has been reported to be as high as 93%.[5] However, this intervention may be challenging or even impossible in patients with fibrin sheath formation with consecutive fixation of the catheter to the vessel wall, vein thrombosis, small catheter-bearing veins, or a deeply embedded catheter.[5]

Conclusion

Malposition of a port catheter tip increases the risk of thrombosis and catheter dysfunction. Percutaneous intervention to correct a migrated or malpositioned port catheter can be considered a suitable and cost effective alternative method to re-implantation with a high success rate.

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