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Expanding the Eligibility for Transcatheter Aortic Valve Implantation

The Trans-Subclavian Retrograde Approach Using the III Generation CoreValve Revalving System

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Objectives Our aim was to assess the safety and feasibility of the retrograde trans-subclavian approach to transcatheter aortic valve implantation (TAVI) in selected high-risk patients with aortic stenosis (AS) and severe peripheral vasculopathy.

Background TAVI is an emerging therapeutic option to treat inoperable/high-risk patients affected by symptomatic AS. However, these patients are also often affected by severe iliac-femoral arteriopathy, rendering the transfemoral approach unemployable for percutaneous revalving procedure.

Methods From among those patients in our department between May 2007 and December 2008, who were refused surgical aortic valve replacement because of high surgical risk and were ineligible for transfemoral percutaneous aortic valve replacement, we scheduled 3 for TAVI by the subclavian approach. Procedures were performed by a combined team of cardiologists, cardiac surgeons, and anesthetists in the catheterization laboratory. The III generation CoreValve Revalving System (CoreValve Inc., Irvine, California) with an 18-F delivery system was introduced in all cases by the left subclavian artery.

Results Prosthetic valves were successfully implanted in all 3 cases, leading to a fall in transvalvular gradient without significant paravalvular regurgitation. No intraprocedural or periprocedural complications occurred. Two patients developed an atrioventricular block requiring the implantation of a permanent pacemaker. All patients were discharged in asymptomatic status, with good prosthesis performance. No adverse events occurred within the 3-month follow-up.

Conclusions TAVI by subclavian retrograde approach seems safe and feasible in inoperable/high-risk patients with AS and peripheral vasculopathy, who are neither eligible for surgical valve replacement nor transfemoral percutaneous aortic valve implantation. Further studies are needed to evaluate the long-term efficacy of this new therapy. (J Am Coll Cardiol Intv 2009;2:828–33) © 2009 by the American College of Cardiology Foundation

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Transcatheter aortic valve implantation (TAVI) has emerged as a promising therapeutic option for treatment of inoperable/high-risk patients affected by symptomatic aortic stenosis (AS) (1–3). To date, about one-third of patients affected by AS are not considered for surgical valve replacement because of high operative risk due to advanced age and multiple comorbidities (4), and their prognosis is poor (5). Percutaneous aortic valve implantation by a transfemoral retrograde approach has been feasible in the majority of these patients with a high procedural success rate (6). However, limitations for percutaneous revalving therapy have been reported, mainly for anatomical reasons, such as inadequate annulus or aortic root size, unfavorable aortic annulus/left ventricle (LV) outflow anatomy, and obstructive disease of iliac-femoral arteries making them unsuitable for large peripheral catheter access (7,8). Recently, a transapical approach has been proposed as an alternative approach to overcome this limitation in patients with unfavorable peripheral anatomy (9). However this approach appears demanding, since it requires a direct surgical exposure of the LV apex and a multidisciplinary team in a dedicated operating room. In selected patients, the trans-subclavian approach may be preferred because it is less invasive (2). We report on the safety and feasibility of retrograde trans-subclavian approach for TAVI in high-risk selected patients with AS and severe peripheral vasculopathy.

Methods

Study population. Between May 2007 and December 2008, 91 patients affected by AS and referred to our department for aortic valve replacement, were refused by surgeons because of high surgical risk and were considered for TAVI. Patient screening included transthoracic echocardiogram, complete cardiac catheterization, and coronary angiography, with angiography of iliac and femoral arteries. In particular, to determine annulus size, we used transthoracic echocardiogram; to assess the aortic arch angulation and ascending aorta dimensions, we used aortic angiography. Inclusion and exclusion criteria for treatment are reported elsewhere (6). Sixty-six patients (72.5%) were shown to be eligible for TAVI using the III generation CoreValve Revalving System (CoreValve Inc., Irvine, California) by transfemoral approach. The causes of exclusion were concomitant relevant mitral regurgitation (n = 8), ascending aorta dilation (n = 4), inadequate size of aortic annulus (n = 2: 1 too large and 1 too small), aortic arch angulation (n = 1), too frail (n = 4), and hemorrhagic diathesis (n = 1). Finally, 5 patients were excluded because the iliac-femoral arteries were unsuitable for large sheath insertion (severe arteriopathy, small size, excessive tortuosity, or calcification). To evaluate the feasibility of trans-subclavian access, these latter underwent computed tomographic scan of the aorta and supra-aortic vessels in order to assess the size, course, and calcification of the left subclavian artery, as well as aortic arch and ascending aorta anatomy (Figs. 1A to 1D). One patient was excluded from treatment because of severe calcifications and tortuosity of the subclavian artery; another one because of diffuse narrowing of the subclavian artery with a minimal lumen diameter less than 6 mm. By general agreement, 3 of these patients, with a linear course of left subclavian artery and a minimal luminal diameter ≥6 mm, were scheduled for transcatheter implantation of CoreValve by trans-subclavian retrograde approach. Patients and their relatives consented to the attempted implantation. Logistic EuroSCORE (10) was calculated using the web-based system.

Implantation technique. The CoreValve Revalving System is described elsewhere (2,6). Procedures were performed under general anesthesia with double-lumen intubation in the catheterization laboratory by an operating team including 2 interventional cardiologists, 2 cardiac surgeons, and 2 anesthetist skilled in transesophageal echocardiography. A 5-F sheath was percutaneously placed in the right radial artery through which a 5-F graduate pigtail was advanced in the ascending aorta for hemodynamic monitoring and landmark aortic angiography. A catheter for temporary pacing was advanced through the right cephalic vein in the right ventricle. Cardiac surgeons performed a surgical cut-down to isolate the left subclavian artery just below the subclavian bone (Figs. 2A and 2B). A 7-F sheath was then introduced into the subclavian artery (Figs. 2C and 2D) and, using a left Amplatz catheter, a straight 0.035-inch guidewire was advanced across the stenotic aortic valve. The direct transvalvular aortic gradient was measured. Then, a super-stiff 260-cm long wire (Amplatz Cook, Inc., Bloomington, Indiana) was introduced into the LV, the Amplatz catheter removed, and the 7-F sheath replaced for an 18-F 30-cm long sheath (William Cook Europe, Bjaeverskov, Denmark) advanced into the ascending aorta (Fig. 2E). At this time, balloon aortic valvuloplasty was performed using a dedicated balloon (Numed Canada Inc., Cornwall, Ontario, Canada) during rapid pacing. The CoreValve Revalving System device was then carefully introduced and retrogradely advanced under fluoroscopic guidance over the stiff wire in the ascending aorta across the aortic valvular plane (Figs. 3A to 3C). After a careful check of valve positioning by angiography, the valve was progressively deployed (Figs. 3D and 3E) and the delivery system retrieved. Immediately after TAVI, angiography of the ascending aorta was performed to assess the presence, location, and degree of aortic regurgitation and the patency of the coronary arteries, as well as to rule out complications, such as aortic dissection (Fig. 3F). Transprosthesis pressure gradient was assessed by contemporary pressure trace recording in the ascending aorta and LV. Heparin was administered to maintain an activated clotting time of >250 s throughout the procedure. Patients were

Abbreviations and Acronyms

AS = aortic stenosis

LV = left ventricle/ventricular

NYHA = New York Heart Association

TAVI = transcatheter aortic valve implantation

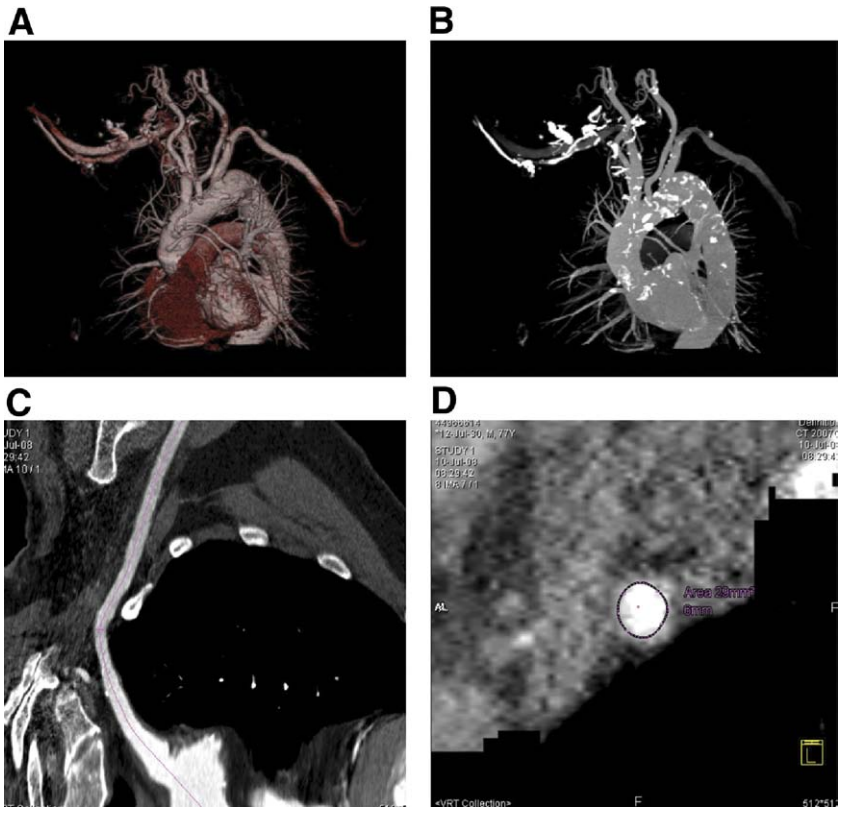

Figure 1. Computed Tomographic Angiography of Left Subclavian Artery

Computed tomographic angiography performed in order to detect size, course, and calcification of left subclavian artery, aortic arch, and ascending aorta.

pre-medicated with aspirin, clopidogrel, and vancomycin or teicoplanin. After the procedure, the heparin was neutralized by protamine, and the subclavian artery was restored by direct suture. Thereafter, the subcutaneous and cutaneous tissues were also sutured (Fig. 2F). After the procedure, a dual antiplatelet regimen of aspirin 100 mg and clopidogrel 75 mg daily for 6 months, after which 100 mg of aspirin daily was prescribed indefinitely.

Outcome. Procedural success was defined as technical success with a good performance of the bioprosthesis, and the patient leaving the catheterization laboratory alive (6). Implantation success was defined as adequate device positioning in the aortic root (6). Good performance of bioprosthesis was defined as a reduction in mean transaortic gradient to less than 20 mm Hg and aortic regurgitation ≤2+, as evaluated by aortic angiogram or echocardiogram (6). All events occurring within 30 days from the procedure were considered as procedure-related events (11). In particular, data regarding death and cardiovascular death, neurologic event, myocardial infarction, ventricular perforation, cardiac tamponade, aortic dissection, vascular access complication, infections, and contrast induced nephropathy were collected. Echocardiography was performed at 24 to 48 h post-procedure, to assess prosthesis performance and LV function.

Follow-up. Clinical evaluation and transthoracic echocardiography were performed at 1- and 3-month follow-ups.

Results

Patient characteristics. The first patient was an 89-year-old symptomatic (New York Heart Association [NYHA] functional class II) man with severe AS and LV dysfunction. He was affected by arterial hypertension, chronic obstructive pulmonary disease, and chronic kidney disease. Logistic EuroScore was 53.84%; standard EuroScore was 14. He was judged at high surgical risk because of a porcelain aorta. He was also affected by peripheral arteriopathy with multiple severe and calcific stenosis of iliac-femoral arteries, not suitable for large femoral sheath placement.

The second patient was an 83-year-old man affected by severe symptomatic NYHA functional class III AS. He was affected by dyslipidemia, diabetes mellitus, chronic obstructive pulmonary disease, and mild chronic kidney disease (logistic EuroScore 25.24%; standard EuroScore 11). He had had previous cardiac surgery with 3 coronary artery bypass grafts, all

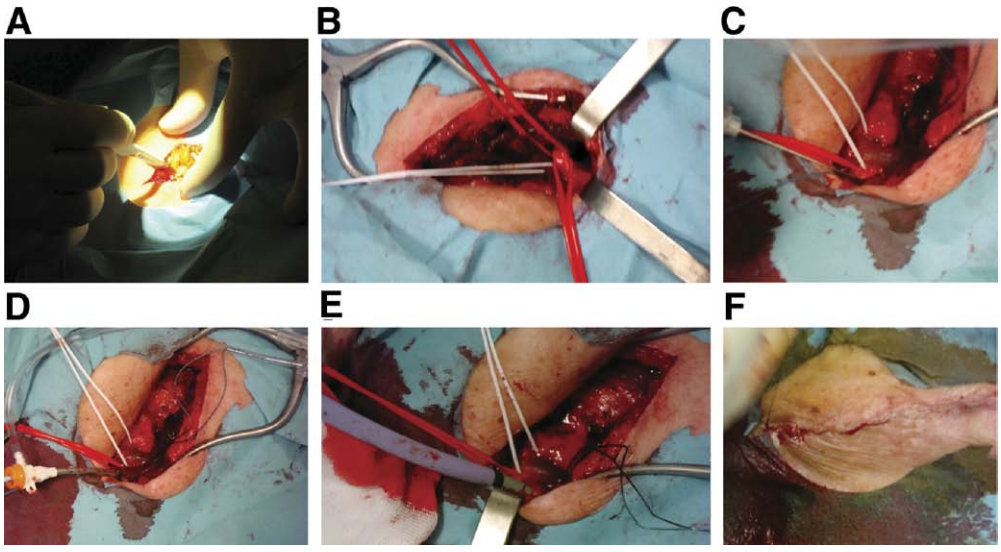

Figure 2. Technical Steps of Left Subclavian Approach

After incision of cutaneous and subcutaneous tissues **(A)**, a surgical cut-down of left subclavian artery is performed **(B)**. Then the artery is punctured **(C)** and a 7-F sheath is introduced **(D)**. After performing ascending aorta angiogram, crossing the aortic valve and detecting transvalvular gradient, the previously placed sheath is then exchanged for the larger 18-F long sheath **(E)**. After revalving therapy, the subclavian artery is restored by direct suture. Finally, subcutaneous and cutaneous tissues were sutured **(F)**.

patent (left internal mammary on left anterior descending artery, venous jump graft on first diagonal branch, and obtuse marginal branch). He had had subsequent percutaneous coronary revascularization due to reinfarction. Thus, the patient was refused by surgeons because of high surgical risk due to previous cardiac reintervention and comorbidities; he was not eligible for percutaneous aortic replacement by femoral approach because of severe calcification and tortuosity of iliac-femoral arteries.

The third patient was a 78-year-old man with severe AS and LV dysfunction (low gradient–low flow AS). Comorbidities included hypertension, severe chronic obstructive pulmonary disease, and renal failure. He had had coronary artery bypass graft surgery 19 years before with venous grafts on the left anterior descending artery and the left circumflex artery, respectively. Four months before TAVI, he suffered from non–ST-segment elevation myocardial infarction: a coronary angiogram showed patency of venous grafts for the left anterior descending artery, chronic total occlusion of the right coronary artery with collateral circulation, occlusion of saphenous vein graft for the left circumflex artery, and severe stenosis of the obtuse marginal branch. The patient was denied surgery because of porcelain aorta and clinical conditions (logistic EuroScore 41.48%; standard EuroScore 13). At that time he underwent stenting of the obtuse marginal branch, and was scheduled for TAVI. The transfemoral approach was not suitable for multiple stenosis of iliac-femoral arteries.

Procedural results. The mean duration of the procedure was 96 ± 40 min (range 67 to 142 min), with a mean fluoroscopy time of 31 ± 4 min and a mean contrast medium amount of 214 ± 129 ml. Implantation success and procedural success were obtained in all 3 cases, leading to a significant reduction in transvalvular gradient without significant para-prosthetic leak. In 1 case, the good performance of bioprosthesis was gained after post-deployment dilation performed to improve prosthesis strut expansion and, as a consequence, to reduce para-prosthetic leak. All 3 patients were extubated within the first 2 h after the end of procedure. At 30 days from the procedure, no major adverse cardiac and cerebrovascular event, no need for blood transfusion, infections, or contrast-induced nephropathy occurred. The second and third patients developed complete atrioventricular block, 3 and 2 days after implantation, respectively, requiring permanent pacemaker implantation. In both cases, the implantation was planned and performed via right subclavian vein. Hospital stays were 6 days for the first patient who did not need permanent pacemaker implantation, and 13 and 11 days for the other 2 patients, respectively. Patients #1 and #3 were discharged with double antiplatelet therapy, while Patient #2 was scheduled to warfarin plus clopidogrel therapy because of a pre-existing permanent atrial fibrillation. All patients were discharged in asymptomatic status with good prosthesis function as assessed by echocardiograph examination.

Follow-up data. At 1 and 3 months follow-up, all patients were alive and experienced remarkable improvement in functional class. Two patients improved to NYHA functional class I; 1 patient improved to NYHA class II (limited by severe lung disease). They have returned to a normal life, limited only by their previous

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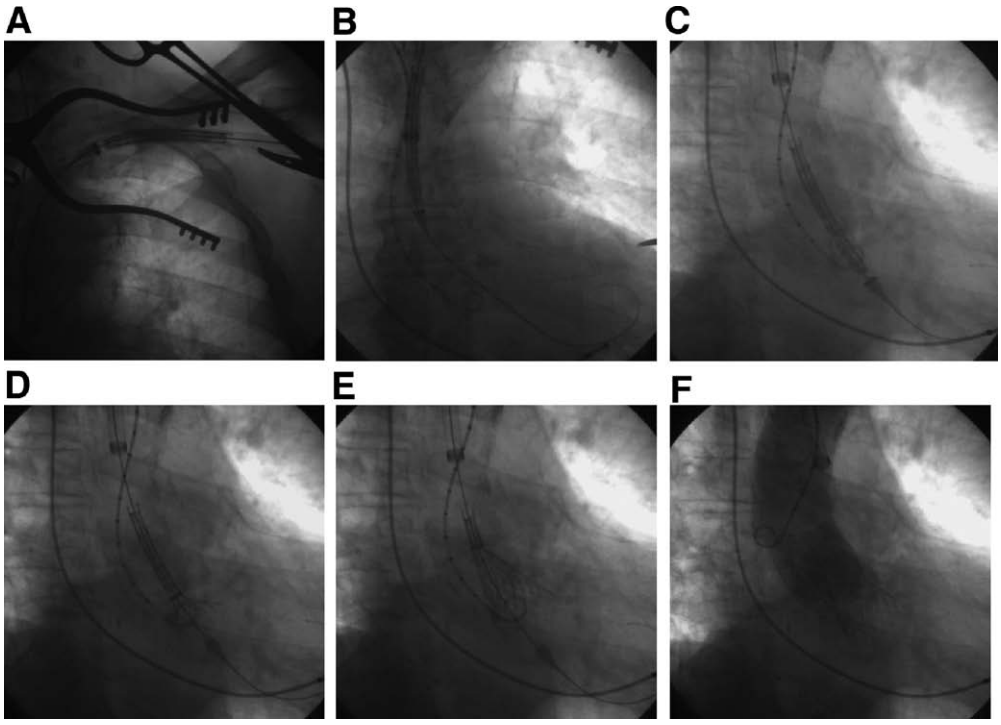

Figure 3. Aortic Revalving Therapy

The CoreValve Revalving System device was carefully introduced by the sheath and advanced throughout the aorta into the aortic root **(A to C)**. After careful checking by angiography, the valve was released **(D to E)**. Post-revalving ascending aorta angiogram demonstrates the correct positioning of the device, without peri-prosthesis regurgitation and with patency of coronary ostia **(F)**.

medical conditions. No adverse events occurred. A good prosthesis performance persisted at 3-month follow-up in all patients.

Discussion

Recently, TAVI has emerged as alternative treatment for degenerative AS in inoperable/high-risk surgical patients (1). However, the amount of patients eligible for transcatheter treatment may be limited for anatomical reasons (6,7). In fact, the size and geometry of aortic annulus, aortic root, and ascending aorta may be not suitable for adequate positioning of the current available devices (8). Moreover, the presence of peripheral artery disease may compromise the retrograde transfemoral arterial approach. The latter condition may be overcome by other transcatheter approaches, such as the antegrade transvenous or the transapical one.

The antegrade transvenous approach (1,12) appears more suitable in introducing the large delivery systems reducing the risk of vascular complications. However, trans-septal puncture makes this approach very challenging, and special attention must be given at each step of the procedure not to damage mitral valve apparatus. For these reasons, this approach was completely rejected.

Recently, the transapical route was widely and successfully performed by using the Edwards-SAPIEN Valve (Edwards LifeSciences Inc., Irvine, California) in patients with severe peripheral vasculopathy (9,13). This approach allows the introduction of delivery systems into the heart without limitation in sheath diameter. However, it requires a hybrid operating room, a multidisciplinary team, and it is much more invasive. Moreover, transapical valve implantation has some technical limitations, as in the case of severe septal hypertrophy in combination and with the angled position of the LV outflow tract in relation to the aortic root (14).

In this scenario, a trans-subclavian retrograde approach could represent an intriguing alternative for TAVI in high-risk aortic patients with associated severe iliac-femoral arteriopathy. In fact, this approach combines the advantage of overcoming peripheral vascular disease without the invasiveness of the transapical technique. As in the transapical approach, procedural times are longer than in percutaneous transfemoral implantation, and a multidisciplinary team is needed. However, the trans-subclavian approach enables a more rapid mobilization of patients, and it seems reasonable that, in the near future, it will require only a local anesthetic and mild sedation with further reduction in periprocedural times.

We experienced a simple surgical cut-down for the left subclavian artery, an easy insertion of the sheath with reliable positioning and release of the prosthesis in all attempted cases. No intraprocedural or periprocedural complications occurred. Moreover, the trans-subclavian approach seems to provide a more direct access to the implantation site and an easier delivery of the prosthesis than the transfemoral approach. In fact, in our experience, the manipulation of the device and the positioning of the valve are more precise and reliable by the subclavian approach, probably because of the shorter distance from the subclavian access to the aortic annulus requiring weaker forces of tension and torsion, which bind the delivery catheter.

One of our patients previously underwent coronary artery bypass grafting with the left internal mammary artery. In cases such as these, the subclavian approach may be more challenging, and attention must be paid to introduce the sheath carefully by fluoroscopic guidance. If the subclavian artery is calcified and not too large, it might be safer to completely introduce the sheath only to deliver the prosthesis into the aortic arch, and then slightly retrieve the sheath itself in order to minimize the risk of mammary flow obstruction and/or dissection. This caution should be adopted also in case of right vertebral artery occlusion with a dominant left vertebral artery.

In our small series, patients did not experience vascular complications or cerebrovascular accidents. In fact, the proximity of the subclavian access to the implantation site also reduces the likelihood of vascular complications when compared with transfemoral access procedure. In addition, the manipulation of the superstiff wire around a potentially calcified aortic arch, which may cause particulate embolization and subsequent stroke, is more limited in the trans-subclavian procedure than in the transfemoral one.

Finally, in our experience, surgical wounds healed quickly in spite of double antiplatelet therapy, and patients were discharged within a short period, with good and stable hemodynamic compensation, as assessed at a three-month follow-up.

Conclusions

Transcatheter aortic valve replacement by subclavian retrograde approach seems safe and feasible in inoperable/high-risk patients with AS and co-existing peripheral vasculopathy, who are not eligible for surgical valve replacement or transfemoral percutaneous aortic valve implantation. This approach allowed us to extend the current indications for TAVI and, together with a further reduction in delivery system caliber and the development of a new prosthesis, may increase the percentage of eligibility for TAVI.

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Key Words: aortic stenosis ■ transcatheter aortic valve implantation ■ trans-subclavian retrograde approach.