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### Developments in Structural Heart Disease Interventions



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#### How Progress is Changing Practice for Interventional Specialists

Interventional treatments of structural heart disease are evolving at a rapid pace and are now established routine in many centres worldwide. Some have even left the traditional interventional field of cardiology behind and have emerged from coronary catheterisation labs into specialised units for catheter-based therapy of structural heart diseases. The term “structural heart disease interventions” was primarily established by Dr. Martin Leon at the Transcatheter Cardiovascular Therapeutics Conference (TCT) in 1999, when he was looking for an overarching category to describe catheter-based treatment modalities of various types of non-vascular heart diseases at a time when many of these concepts were just on the horizon. Over the last ten years, this term has been generally accepted as a category of disease by the medical community. The following overview highlights the newest commercially available devices, as well as developing strategies to treat structural heart diseases percutaneously.

#### Catheter Closure of Congenital and Acquired Shunts

##### PFO closure

A wide variety of percutaneous devices targeting congenital and acquired heart defects have recently become commercially available or are currently evaluated in clinical trials. In transcatheter closure of patent foramen ovales (PFO) for example, a trend can be seen towards defect-tailored devices and new designs or techniques which minimise the amount of foreign material left in the atria after implantation. Promising new concepts of PFO closure include the SeptRx™ device (Stout Medical Group, U.S.), which is positioned into the PFO pocket and is stabilised by two left atrial anchors that adapt to the tunnel length without significant alteration of the configuration of the septum primum (Majunke N et al. 2008) or the Coherex FlatStent™ PFO closure system (Coherex Medical, Inc., Salt Lake City, UT, U.S.) which consists of a light-weight, self-expanding, flat “stentlike” Nitinol lattice with integrated polyurethane foam designed to stimulate tissue growth inside the PFO tunnel.

The BioTREK™ (NMT Medical, Boston, MA, U.S.) is a fully bioabsorbable device. Its main component is a novel biosynthetic polymer named poly-4-hydroxybutyrate (P4HB) (Tepha, Inc., Lexington, MA, U.S.). As this device, which is currently in pre-clinical studies, is eventually replaced with native tissue, late device-related complications may be avoided. Another concept is the HeartStitch™ (Sutura Inc., Fountain Valley, CA, U.S.) strategy, which is based on the SuperStitch vascular suturing system designed for vascular stitching in general surgery (Ruiz CE et al. 2008).

One of the most recent techniques for PFO closure under clinical investigation is the Nit-Occlud® PFO umbrella (Pfm medical mepro, Nonnweiler-Otzenhausen, Germany) which is a double-disc Nitinol device incorporating a synthetic patch on the left and right atrial side in order to achieve a high acute closure rate.

As the discussion on the potential pathological importance of PFO and the best possible therapy for secondary stroke prevention is still on, these new concepts for PFO closure will hopefully lead to further decrease of acute and late device-related complications. Safety and long-term reliability novel devices are especially important when PFO closure is discussed in migraine patients or divers.

##### ASD Closure

Percutaneous techniques for most secundum atrial septal defects (ASD) have largely replaced surgical closure. New devices commercially available are the partially bioabsorbable BioSTAR® occluder (NMT Medical Inc. Boston, MA, U.S.) and the Occlutech® ASD device (Occlutech, Jena, Germany). Despite this era of new technologies, conventional surgery currently remains the primary treatment modality for large defects (> 40mm), non-secundum defects and for those atrial septal defects in which the septal rim is insufficient.

##### VSD Closure

Ever since the very first interventional approach to ventricular septal defect (VSD) closure described in 1988 (Lock et al. 1988), various catheter-based techniques have been proposed for this purpose such as the Sideris buttoned device, the Rashkind device, Gianturci coils, the Clamshell device, the CardioSEAL and CardioSEAL/STARflex device, the Amplatzer occluder family and Nit-Occlud coils. Compared to transcatheter atrial septal defect or patent foramen ovale closure, interventional closure of ventricular septal defect is considered rather complex while it requires

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both venous and arterial access to establish an arteriovenous wire loop. Efficacy of percutaneous closure of muscular ventricular septal defects has been reported for over a decade. Moreover, since the introduction of the Amplatzer Membranous ventricular septal defect occluder (AGA Medical, Golden Valley, MN, U.S.), perimembranous defects which have a higher incidence, have become more amenable to transcatheter closure techniques (Hijazi ZM 2003). However, there is an ongoing discussion as to whether coils may be an advantage due to the presumably reduced risk of AV block.

In post-myocardial infarction VSDs, interventional closure has shown to be feasible as well. However, despite gaining expertise and novel devices, due to the often atypical location of the defect, deficient and irregular rims and the presence of multiple defects, transcatheter treatment remains a major challenge for today's interventionalists.

### **Closure of Patent Ductus Arteriosus**

The ductal anatomy is known to be quite variable with the most common phenotype being a conical duct with a large aortic ampulla which narrows at the pulmonary artery end. Due to this variability, a number of different concepts of closure have been developed, e.g. Cook PDA coils (Cook Inc., Bloomington, IN, U.S.) for small PDA or a specific Nitinol duct occlusion devices like the Amplatzer® Duct Occluder (AGA Medical, Golden Valley, MN, U.S.) for larger PDAs.

### **Valve Repair/Implantation**

For many years, catheter-based treatment of valvular heart disease was limited to balloon valvuloplasty. After having performed the first percutaneous valvuloplasty of a calcified, stenotic aortic valve in 1985, Dr. Alain Cribier went on to replace the first aortic valve mounted on a balloon expandable stent percutaneously in 2002. Since then, percutaneous aortic valve replacement is performed in an increasing number of centres worldwide and has become an alternative therapeutic option to surgical valve replacement in selected elderly patients who have an unacceptable high risk of surgery.

Concerning patients with significant mitral regurgitation, surgical valve repair continues to be the primary treatment strategy. However in the light of rapid developments in interventional treatment, percutaneous mitral valve repair has likewise become an interesting alternative therapy. Multiple percutaneous technologies are currently being evaluated in preclinical and clinical settings. Percutaneous mitral annular remodelling strategies include indirect mitral annuloplasty approaches such as coronary sinus annuloplasty (Edwards MONARCTM (Edwards Lifescience Corp., Irvine, California, U.S.), CARILLONTM Mitral Contour System (Cardiac Dimensions, Kirkland, Wisconsin, U.S.), Percutaneous Transvenous Mitral Annuloplasty system (PTMA®) (Viacor, Inc., Wilmington, Massachusetts, U.S.) and Mitral valve cerclage annuloplasty (MVCA) (NIH, Rockville, MD, U.S.), and other indirect annuloplasty approaches such as the Ample PS3TM (Percutaneous Septal Shortening System) (Ample Medical Inc., Foster City, California, U.S.).

In addition, direct mitral annuloplasty approaches e.g., QuantumCor (Quantum-Cor, Inc., Lake Forest, California, U.S.) via direct percutaneous trans-atrial annulus remodelling or the MiralignTM (Miralign, Tewksbury, Massachusetts, U.S.) and the AccuCinch TM (Guided Delivery Systems, Santa Clara, California, U.S.) device via direct percutaneous trans-ventricular annulus remodeling are currently under investigation. Other annuloplasty concepts consist of mitral annular plication, chamber-remodelling approaches and hybrid procedures. Percutaneous solutions, which directly target the mitral leaflets like the MitraClip® System (Evalve, Inc., Menlo Park, California, U.S.) mimic the edge-to-edge surgical technique introduced by Alfieri successfully with encouraging midterm results (Feldman et al. 2009).

### **Closure of Paravalvular Leaks**

After Hourihdan reported successful interventional closure of paravalvular leaks in three patients in 1992 (Hourihan et al. 1992) a number of other cases on this topic have been published reporting best results in patients with small diameter nonprogressive leaks in aortic position. Suitable devices for paravalvular leak closure are the Amplatzer Muscular ventricular septal defect occluder (AGA Medical, Golden Valley, MN, U.S.) and the Amplatzer PDA occluder.

For larger defects around the mitral valve implantation of the Amplatzer ASD occluder is feasible. Quite recently, the Amplatzer® Vascular Plug III (AGA Medical, Golden Valley, MN, U.S.) (figure 3) which is oval shaped and has smaller rims for better apposition in even in high flow vessels, has been introduced. In comparison to other devices of the Amplatzer vascular plug family, first experiences with this dedicated device show better suitability for closure of paravalvular leaks.

### **Left Atrial Appendage Closure**

Occlusion of the left atrial appendage in patients with non-rheumatic atrial fibrillation was first attempted by cardiac surgeons during open heart surgery (Blackshear JL et al. 1996; Johnson WD et al. 2000). The first two interventional approaches specifically developed for occlusion of the left atrial appendage were the PLAATO™ device (eV3, Inc., Plymouth, MA, U.S. - not available anymore) and the Watchman® implant (Atritech, Inc., Minneapolis, MN, U.S.).

Data from the PROTECT-AF randomised trial have just been published which showed non-inferiority of the Watchman® implant compared to warfarin therapy for stroke prophylaxis (Holmes DR et al. 2009) and therefore pointing out the great potential of percutaneous occlusion of the left atrial appendage as an alternative to long-term anticoagulation. Next to the Amplatzer® septal occluder (AGA Medical Corporation, Golden Valley, MN, U.S.), which was not originally intended for occlusion of the left atrial appendage but has been reported with acceptable results (Meier B et al. 2003), the Amplatzer® cardiac plug (AGA Medical, Golden Valley, MN, U.S.), specifically developed for atrial appendage occlusion, is now available within a European registry.

### **Endless List of Techniques**

The list of developing techniques seems endless and demonstrates that this medical field is expanding at a stunning pace. Some interventional techniques like closure of atrial septal defect and patent foramen ovale have already proven to be effective. Low complication rates of many catheter-based therapies of congenital shunts and satisfactory results in long-term follow-up have led to a higher acceptance from physicians and patients alike, and consequently have led to the replacement of surgery as the standard therapeutic approach.

One must acknowledge that the prevalence of most structural heart diseases is comparably low. Therefore, a major growth in numbers of interventional procedures as with interventional therapy of coronary heart disease cannot be expected. Critics may as well claim that some novel percutaneous approaches may potentially be less efficacious than present surgical standards.

### **Need for Less Invasive Solutions**

However, it is unquestionable that there is an enormous need for less invasive catheter based solutions as alternative strategy, particularly in the

treatment of patients at high surgical risk. Moreover, due to the complex anatomy and broad pathophysiological spectrum of some structural heart diseases, it will likely be necessary to combine different therapeutic strategies in order to achieve satisfactory results - as is still the case with conventional surgery today. Discussions concerning the balance between advances in catheter-based technology and the cost-effectiveness of patient treatment have concurrently arisen. Percutaneous aortic valve replacement for example, raises the costs of treatment compared to traditional surgical valve replacement. Looking at the present target patient cohort, who perhaps wouldn't have been considered for surgery and therefore would have been treated by medical therapy alone, the costs are increased significantly.

Glancing beyond this discussion, more dedicated fellowship programmes need to be developed to provide hands-on training as well as accessible research platforms for those interested in turning empirical clinical know-how of structural heart diseases into pre-clinical research and subsequently transforming successful technologies into feasible interventional solutions of the near future.

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