Hemodynamic and Neurohormonal Response after Percutaneous versus Surgical Aortic Valve Replacement

Thesis submitted for partial fulfillment of
M.D. in Cardiology
By

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Ain Shams University
2011

مقارنةً نتائج الاستجابة الهورمونية و الكيميائية و الديناميكية الدموية بعد استبدال الصمام الاورطى باستخدام القسطرة بنتائج استبدال الصمام الاورطى جراحياً

دراسة مقدمة للحصول على درجة الدكتوراة في امراض القلب و الاوعية الدموية

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2007

Background:

Severe symptomatic aortic valve stenosis is a proven indication for valve replacement according to the current guidelines [1]. The therapeutic modality of choice is surgical aortic valve replacement. Certain patients, however, cannot take advantage of this option due to comorbidities and/or hemodynamic conditions rendering them at high risk for surgery. In the EURO HEART Survey, 31.8% of all patients indicated for surgical aortic valve replacement were accordingly rejected. Several risk stratification systems have been developed for perioperative mortality risk assessment. The EuroScore is a widely used, web-based, easy applicable such tool. It includes patient-based, cardiac and operative related factors such as age, sex, renal insufficiency, left ventricular dysfunction, pulmonary hypertension and peripheral arteriopathy [2]. A logistic EuroScore of ≥ 15% designates high risk.

In the year 2002 a novel alternative approach to surgical aortic valve replacement among critically ill patients with severe aortic valve stenosis has been first introduced by Cribier – the percutaneous aortic valve replacement [3]. Contrasting to surgical replacement this method forms a much less invasive approach which therefore may be safely offered for high-risk surgical patients. Two independent percutaneous aortic valve replacement systems have gathered data of safety and

feasibility in human trials. The major difference among both systems lies in the expansion mechanism of the stent-mounted valve: balloon-expandable or self-expandable. The *CoreValve Revalving System®* (CRS) is a self-expandable, biological, nitinol-stent-mounted aortic valve prothesis which has first been introduced in 2005. Since March 2007, this prothesis became CE-Mark certified and commercially available on a limited scale among highly selected European centers who are participating in a registry that facilitates clinical monitoring in the post-market phase. To date, around 300 patients have been treated with the CRS, either during the clinical investigations or following CE-marking. Procedural success rates of >90% have been achieved with a 30 day mortality of 10% among this high-risk population for whom the CRS is currently intended.

Proper prothestic valve size selection is of utmost importance for the success of valve replacement. For surgical aortic valve replacement, sizing is done by direct measurement of the aortic annulus intraoperatively. Occasionally mal-sizing occurs which may result in the patient-prothesis-mismatch phenomenon first discribed by Rahmitoola [4]. A mismatch is present when the effective prothestic valve opening area is less than the patient's body surface area x 0.85. Effective valve areas below this value are associated with higher transvalvular gradients and negative hemodynamic effects. For percutaneous aortic valve

replacement, sizing is done preprocedural through the averaging of the combined measurment of the aortic valve annulus in transoesophageal echocardiograpghy, aortic cine angiography and CT angiography. Undersizing of the prothesis may result in significant paravalvular aortic regurgitation while oversizing may result in rupture of the aortic annulus.

Hypothesis:

The favorable mechanical profile and easier size selection of the *CoreValve Revalving System®* may translate into a better hemodynamic response compared to surgically implanated aortic bioprothesis.

Aim:

Documentation of the hemodynamic characteristics of the CRS using established echocardiographic parameters and neurohumoral mediators in comparison with surgically implanted aortic bioprothesis.

Methods:

Design and patients:

This bicenteric, prospective, observational study will be done in The Academic Teaching Hospital of the Christian-Albrechts-University of Kiel, including 30 patients with severe symptomatic aortic valve stenosis (AVA $\leq$ 0.6cm^2/m^2) and declared at high-risk for surgical replacement due to the following:

Age ≥ 80 years *or* logistic EuroScore ≥ 15% *or* age ≥ 65 years and one or more of the following: liver cirrhosis (Child class A –B), respiratory insufficiency (VMS<1L), previous cardiac surgery, pulmonary hypertension (systolic PAP>60mmHg), recurrent pulmonary emboli, right ventricular failure, hostile thorax (radiation, burns etc.), severe connective tissue disease, porcelain aorta, cachexia.

All patients will be subjected to percutaneous aortic valve replacement using the CRS. Patients will be compared with 30 patients undergoing surgical aortic valve replacement in the same time periode.

Interventions:

Percutaneous aortic valve replacement:

Patients positively screened will be investigated for feasibility of the procedure using transoesophegeal echocardiography, cine angiography and CT angiography. Patients found suitable will receive the 18 F CRS. In Seldinger's technique a bi-groin access will be used. Valvuloplasty of the aortic valve will be performed under rapid ventricular pacing. After mounting the appropriate CoreValve prothesis onto the catheter delivery system, the CRS will be advanced and released at the desired position. Groin closure will be done using the Perclose® suture device.

Surgical aortic valve replacement:

Patients with severe symptomatic aortic valve stenosis and scheduled for single valve replacement will be included. All procedures will be performed in a standard manner using aortic valve bioprotheses. The choice of the prothesis will be left to the operator's discretion.

Hemodynamic parameters:

Using echocardiography the following hemodynamic parameters will be documented for all patients: transvalvular mean and peak gradients, quantification of aortic regurgitation using colour flow Doppler, left ventricular ejection fraction. All measurements will be done pre-procedural, at 30 days and 6 months post-procedural.

Neurohumoral mediators:

Using venous blood samples, the following will be measured in serum: NT-pro-BNP, BNP. Blood samples will be drawn pre-procedurally and at 30 days post-procedural.

Statistical analysis:

This is a hypothesis generating study; therefore no sample size calculation has been done. Appropriate statistical test will be applied to plot the differences in measured values before and after the procedures and compare them intra-individually and between groups. For each measure,

absolute and delta differences will be calculated. The statistical significance level will remain at 95% with p-values < 0.05.

References:

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3. E. Grube, U. Gerckens, L. Buellesfeld. Percutaneous aortic valve replacement. Herz 2006;31:694-7.
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List of Abbreviations

AS	Aortic valve stenosis
AR	Aortic regurgitation
ANP	Atrial natriuretic peptide
AVA	Aortic valve area
BAV	Balloon aortic valvuloplasty
BNP	B-type natriuretic peptide
BSA	Body surface area
CABG	Coronary artery bypass graft
CNP	C-type natriuretic peptide
COPD	Chronic obstructive pulmonary disease
CRS	CoreValve ReValving System
CT	Computed tomography
EOA	Effective orifice area
EF	Ejection fraction
iAVA	indexed aortic valve area

INR	International normalized ratio
iEOA	Indexed effective valve opening area
I-REVIVE	Initial Registry of Endovascular Implantation of Valves in Europe
IVSD	Interventricular septum diameter at diastole
LAO	Left anterior oblique
LVESD	Left ventricular end-systolic diameter
LVEDD	Left ventricular end-diastolic diameter
LVMI	Left ventricular mass index
MACCE	Major adverse cardiac and cerebrovascular events
MAVRE	Major adverse valve-related events
MR	Mitral regurgitation
NYHA	New York Heart Association
PCI	Percutaneous coronary intervention
PARTNER	The Placement of Aortic Transcatheter Valves
PPM	Prosthesis-patient mismatch
PWD	Posterior wall diameter at diastole
RAO	Right anterior oblique