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PGY-1
IRB Proposal

Transcatheter Aortic Valve Implantation with the Edwards SAPIEN valve versus the Medtronic CoreValve: To compare outcomes in all cause mortality, cardiovascular mortality, vascular complications, and number of inpatient days associated with each valve.

A. Study Purpose and Rationale

Aortic valve stenosis (AS) is the most common cardiac valve lesion in the United States and it is estimated that 2-9 %[1] of the general population over the age of 65 have the condition. The development of heart failure symptoms such as angina, syncope, or dyspnea is an ominous sign and patients deemed eligible, historically, have been referred for surgical correction. Although surgical replacement improves symptoms and prolongs survival, observational studies have shown that there are a subset of patients with advanced age, poor left ventricle function, or other significant co-morbidities who are at increased risk of operative complications or death and would benefit from a less invasive approach[2]. With the development of bioprosthetic valves, which can be delivered through a catheter, patients at high risk for surgery are now able to undergo a transfemoral or transapical approach to replace the native valve. The PARTNER Trials have shown that Transcatheter Aortic Valve Implantation (TAVI) is an acceptable alternative to patients deemed too high risk for surgery and also in high-risk patients who are eligible for surgery[2,3].

There are currently two devices used in the delivery of a prosthetic valve through a transcatheter route. One is the SAPIEN device created by Edwards Lifesciences and the other is the CoreValve developed by Medtronic. Both products are commercially available in Europe, but only the SAPIEN valve is FDA approved in the United States. While there are notable differences in the structure and framework of each device, there is also an important difference in how each device is delivered. The SAPIEN Valve requires either a large 22 French or 24 French sheath for delivery, while the CoreValve is able to be delivered through an 18 French sheath. The vascular anatomy of many patients cannot accept a 22 or 24F sheath, and so the CoreValve can be used, though it should be noted that newer versions of the SAPIEN valve do allow for smaller sheaths. Also, due to the self-expanding nature of the frame of the CoreValve, it can be deployed in stages allowing for adjustments in position during the deployment phases, which is not allowed in the rapidly deployed single expansion of the SAPIEN valve. A recent multicenter collaborative study[4] comparing the two devices looked at the databases of 4 large European hospitals experienced in performing TAVIs and showed that there were no significant differences in all cause mortality, cardiovascular mortality, stroke, and vascular complications after matching for sheath size. There was a significant increase in the number of permanent pacemakers implanted in those patients using

the CoreValve which, the authors concluded, was likely related to valve structure and design.

The purpose of this study will be to compare these two devices at two high volume centers in the United States (New York City) to determine all cause mortality, cardiovascular mortality, vascular complications, and inpatient number of days related to each device. The goal will be to confirm the findings of the prior study performed in Europe and to see whether the number of inpatient days will differ depending on the type of valve used.

B. Study Design and Statistical Analysis

The study will be a retrospective two-center database analysis comparing outcomes in all cause mortality, cardiovascular mortality, vascular complications, and number of inpatient days using the Edwards SAPIEN valve versus the Medtronic CoreValve. Databases will be collected and analyzed from Columbia University Medical Center (CUMC) and Mount Sinai Medical Center from November 1st, 2010 to April 30th, 2013 in patients with severe aortic stenosis who underwent TAVIs. The two centers are known high-volume centers and each use a different valve – Mount Sinai using the CoreValve and CUMC using the SAPIEN valve. All patients will have known severe aortic stenosis, defined as an aortic valve area of less than 0.8 cm^2, a mean aortic valve gradient of 40 mm Hg or more, or a peak aortic jet velocity of 4.0 meters per second or more[3]. The analyzed data will stratify patients by multiple criteria including age using 75-85 and 85-95 as cutoffs, co-morbidites including HTN, DM, history of stroke, MI, COPD, and peripheral vascular disease, NYHA Functional class (II - III/IV), Society of Thoracic Surgeon (STS) Score greater than 10%, and sheath size used during the procedure.

In this study, 700 patients will be analyzed with approximately 350 coming from each site. All cause mortality, cardiovascular mortality, and vascular complications at 30 days and 1 year will be analyzed using the chi-squared test. Number of inpatient days with each valve placement will be analyzed using the un-paired T-test. The study will have a power of 80% and a 5% Type I error rate. If we estimate all cause and cardiovascular mortality for the SAPIEN valve to be 6.4%, then there will have to be a mortality rate of below 1.9 % or above 13% for the CoreValve to reach statistical significance. Similarly, if we estimate a 12.3% rate of vascular complications for the SAPIEN valve then there will have to be less than 5.9% or greater than 20% rate of vascular complications for the CoreValve to reach statistical significance. Finally, we will use the un-paired t-test to analyze the number of inpatient days for each valve, with an estimated 2 day admission for the SAPIEN valve and a standard deviation of 0.5, there will have to be at least approximately a 2.5 hour difference of inpatient hospitalization stay for the CoreValve to be statistically significant.

C. Study Procedures

N/A

D. Study Drugs

N/A

E. Medical Devices

The SAPIEN device is a balloon-expandable tubular metal stent with a tri-leaflet valve fashioned out of bovine percardium mounted within and the CoreValve is a self-expanding valve prosthesis consisting of a Nickel-titanium frame with a tri-leaflet valve fashioned out of porcine pericardium mounted within.

F. Study Questionnaires

N/A

G. Study Subjects

Inclusion Criteria

1. Patients who have undergone or attempted to undergo a TAVI for severe aortic stenosis with either the CoreValve or SAPIEN valve from November 1st, 2010 to April 30th, 2013

Exclusion Criteria

1. Any patient that had a TAVI performed through the trans-apical approach
2. Any patient that had a balloon pump at any point during their admission prior to the TAVI

H. Recruitment of Subjects

N/A

I. Confidentiality of Study Data

Access to the TAVI databases will be limited only to medical personnel involved in conducting this study. All patient identifiers will be removed at the point of data entry.

J. Potential Conflict of Interest

N/A

K. Location of Study
Columbia University Medical Center and Mount Sinai Medical Center

L. Potential Risks

N/A

M. Potential Benefits

Upon analysis of the study we will attempt to determine the safety profile of each device and to estimate indirectly the potential costs to each hospital depending on the type of device used.

N. Alternatives

N/A

O. Compensation to Subjects

N/A

P. Cost to Subjects

N/A

Q. Minors as Research Subjects

N/A

R. Radiation or Radioactive Substances

N/A

References:

1. Pompilio F et al. **Epidemiology and cardiovascular risk factors of aortic stenosis.** *Cardiovascular Ultrasound*. 2006 4 – 27
2. Smith CR et al. **Transcatheter versus Surgical Aortic-Valve Replacement in High-Risk Patients.** *NEJM* 2011 364: 2187-2198
3. Leon MB et al. **Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery.** *NEJM* 2010 363:1597-1607

4. Chieffo A et al. **Transcatheter Aortic Valve Implantation With the Edwards SAPIEN Versus the Medtronic CoreValve Revalving System Devices.** *Journal of The American College of Cardiology* 2013 830-836