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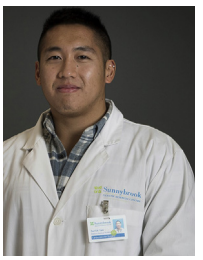
Key Words: aortic root enlargement, propensity score, aortic valve replacement

Discussion

Dr Patricia A. Thistlethwaite. So, without further ado, I'd like to open up the first Scientific Session with the opening paper, which is entitled "Early And Late Outcomes Following Aortic Root Enlargement At The Time Of Aortic Valve Replacement: A Population Based Study," and the presenter will be Derrick Tam from the University of Toronto.



Dr Derrick Y. Tam *(Toronto, Ontario, Canada)*. Dr Thistlethwaite, Dr Shemin, guests, members of the Association. On behalf of my coauthors, I would like to thank the Association for the opportunity to present this work today. Today, we will be looking at the early and late outcomes following aortic root enlargement using a population-based studied. There are no disclosures. So, the management of the small aortic annulus at the time of aortic valve replacement is controversial. We know that these patients are at risk for patient prosthesis mismatch. Large studies have demonstrated that even moderate PPN may negatively impact survival. Aortic root enlargement, or ARE, allows for the implementation of larger valves at the time of aortic valve replacement. Studies have shown that there is a longer cross time and bypass time and there are concerns for risk of additional mortality and morbidity with this procedure. However, aortic root enlargement may become important in the era of transcatheter aortic valve replacement. Several studies have shown that we are implanting more biological valves in younger and younger patients. These patients are at risk of structural valve deterioration and failure. All this is posited on the fact that these patients may receive a TAVR for their redo operation. We know the putting a valve-in-valve TAVR in these patients is associated with a doubling of mortality at one year. So, on that background, it became our research question to study at the population level is there a difference in early and late outcomes in isolated aortic valve replacement patients with or without additional aortic root enlargement. Our primary outcome was 30-day mortality and late mortality. Our secondary outcomes for those of safety related to new permanent pacemaker implantation, chest reopening, and also late congestive heart failure re admission.

So we undertook the study using the Core Health Registry located in Ontario Canada, Canada's most populous province of 11,000,000 patients. We looked at the isolated aortic valve replacement group, with our way out aortic root enlargement, as our primary analysis. We looked at patients performed in Ontario from 11 institutions from 2008 to 2017. We linked to the Discharge Abstract Database to

allow us to ascertain in hospital complication. We also linked to the Registered Persons Database to ascertain death. This allowed for 100% follow-up of all of our patients. We utilized propensity score matching to create two balanced groups to compare on the outcomes of interest, and as a sensitivity analysis, we looked at aortic valve replacement with CABG with or without aortic root enlargement. Here are our results. We started with 26,000 patients who underwent aortic valve replacement with or without CABG. After excluding those with previous cardiac surgery, active endocarditis, or non-tissue or mechanical valves, we ended up with 16,000 patients in our study. Eighty-five hundred patients underwent an isolated aortic valve replacement, 821 also had aortic root enlargement. Of the AVR with CABG cohort, we had 6800 patients, 520 also had root enlargement. Over the study period, on average, 8% of all AVRs had a root enlargement.

Here we looked at the trends overtime for aortic root enlargement as a function of aortic valve replacement. We showed that early on, around 6% of all AVRs had root enlargement and near the end of the study period it was around 10 to 12, so there seemed to be a steady increase in the number of root enlargements being performed.

Here we show that aortic root enlargement patients are different. The average age, they are younger than those who underwent isolated aortic valve replacement, and in this table or this graph here, in the blue we have aortic valve replacement patients and in the orange we have those who underwent aortic root enlargement as well. We have different baseline characteristics. Those who underwent aortic root enlargement were more likely female and also were less likely to have other comorbidities. We show these be cause the standardized mean difference was greater than 10% suggesting that they are imbalanced between the groups.

After we performed propensity score matching on about 34 variables, we showed that the patients are quite similar. The ages are similar between the group, around 65, and the standardized mean difference for these baseline characteristics were all less than 10%, denoting good balance between the groups.

Here we show the early outcomes in matched patients. The Y axis is the frequency of these outcomes and on the X axis we have the different outcomes. We show that there is no difference in 30-day mortality, new permanent pacemaker implantation, chest reopening, or 30-day re admission. We do note that the operating room time was longer. The median difference was about 20 and this was statistically significant.

Here we looked at 8-year mortality. This is on the X axis, we have year since surgery. On the Y axis, we have survival. In the red, we have aortic valve replacement. In the green, we have aortic valve replacement plus aortic root enlargement. The number at risk is on the bottom, shown here. The shading is the 95% confidence interval. We showed that at eight years, there was no difference. In the matched patients using a Cox proportional hazard model.

Here is the cumulative incidence function for congestive heart failure re admission, which is shown on the Y axis here. We adjusted for death as a competing risk factor. Again, there was no difference between the 2 groups up to 8 years.

We also looked at aortic valve reintervention, and again we adjusted for death as a competing risk factor in our model. The first thing we note is that the incidents of aortic valve re intervention up to 8 years was quite low, less than 5% and again there was no difference between the 2 groups.

As mentioned earlier, we performed a sensitivity analysis. We looked at the aortic valve replacement with CABG patients. So, in these 525 patients in the match group, there was no difference in 30-day mortality, new permanent pacemaker, or 30-day readmission. We do note that the instance of chest reopening was greater, 7% versus about 3.5%, so almost double. Again, the operating room time was longer.

However, when we looked at 8-year mortality in this Kaplan–Meier survival curve using a cost proportional hazard model, there was again no difference at 8 years between the groups.

So, we show here that the addition of aortic root enlargement to isolated aortic valve replacement is safe, there was no increase in early mortality, chest reopening or new pacemakers, late outcomes for similar between the 2 groups, and there was no difference in congestive heart failure readmission or valve reintervention. We do note that there was an increase in the risk of chest reopening with the addition of aortic root enlargement in the patients who underwent aortic valve replacement with concomitant CABG. This suggests that there is a need for more vigilant monitoring in these patient groups. However, this study must be interpreted in the context of some significant and very important limitations. First, this is an observational retrospective study design, and, as such, it may be compounded by treatment allocation bias, being that we don't know, or the treatment decision is up to the discretion of the surgeon and that we don't know the true indication for this operation in these patients. With any administrative study, there are concerns around the accuracy of relying on administrative codes to ascertain both the treatment groups and the outcomes of interest. We do note that there was a longer OR time in the patients who did undergo the procedure of interest. There is a lack of data granularity. We don't know the exact type of aortic root enlargement that was performed in these patients, and importantly we also do not have echocardiographic data on these patients, so we don't know the preoperative size of the root or the annulus or any postoperative changes at patient prosthesis mismatch.

So, in conclusion, we show that root enlargement is safe to isolated aortic valve replacement, and that the addition of aortic root enlargement to patients who underwent AVR CABG may result in more bleeding and I think we need additional follow-up for nonfatal events like valve reintervention. And with that, I'm happy to answer any questions.

Dr Tom Burdon *(Stanford, Calif).* Good morning, Derrick.

Dr Tam. Good morning.

Dr Burdon. Welcome back to the Western. Derrick is a veteran of the Western and, as you know, presented at the Samson before. Welcome to California.

Dr Tam. Thank you.

Dr Burdon. You and your coauthors do a phenomenal job in reviewing a clinical administrative database from the Province of Ontario from 2008 to 2017 identifying more than 16,000 aortic valve replacements (AVRs) from 11 hospitals in Ontario. Eleven million people and 11 hospitals; a million population per center, it sounds like. It's a phenomenal model. You identified about 809 pairs from the data that I was given for AVR and AVR plus aortic root enlargement (ARE), which demonstrates accurate codes in almost all areas of outcome. AVR and ARE in coronary artery bypass grafting, however, revealed a higher re-exploration rate for bleeding. Your conclusions, based on extremely thorough and powerful statistic modeling are that AVR and ARE do not increase surgical risk. It's tough for some of us to swallow that. Assumptions are made, the potential for patient–prosthesis mismatch is avoided and that increasing valve and valve transcatheter AVR size would be facilitated. You have identified your study's limitations as not being able to separate surgeon discretion, although propensity score matching may mitigate known confounders of this issue. We know how difficult the randomized control trial is and so we respect that. Derrick, you identified significant differences in baseline characteristics in the unmatched AVR and ARE and AVR cohorts. Those in AVR and ARE were younger, more likely men, less rural-based, more likely elective, lower rate of atrial fibrillation, and had better renal function, but had dyslipidemia and diabetes. How does propensity score matching with these issues provide you with 809 pairs for comparison? Does your study in fact violate a critical element of propensity score matching, which is the stable unit treatment value assumption, which is, number 1, no interference. Treatment of 1 patient should not influence the treatment of other patients, likely your nonrural patients were treated in centers with more or less experienced surgeons, depending on where they lived. Number 2, only 1 version should be the treatment and we know that surgeon preference will alter depending on what type of ARE is done, the vast majority probably being some form of Manougian. The Ontario Provincial Database, feeding from ICES, CorHealth, CIHI DAD, and RPDB is a veritable gold mine for data miners in administrative outcomes for researchers like yourself. However, the lack of perioperative echocardiogram data, body mass index, regression, and effective orifice area information are very important factors for patients, cardiologists, and cardiothoracic surgeons. Are you aware of any mechanisms in this Ontario database that will make this information available going forward somewhat like the Society of Thoracic Surgeons database? And lastly, in the area of broadening transcatheter AVR and sutureless surgical valves, both with single-digit gradients, how does ARE and teaching ARE factor into this? What has your experience been, and your experience as a resident with valve-in-valve procedures? Mortality for valve-in-valve, as Danny Dvir has shown us, is about 7%. It's not insignificant. Lastly, are you able to give any information on how many transcatheter AVRs are done in Ontario in relation to the number of surgical implants, and what is the budget for transcatheter AVR in a fixed budget system?

Dr Tam. Thanks Dr Burdon for the encouraging comments and those questions. I will try to do my best to answer all of them. So your first question was with regard to propensity score matching and whether or not these are indeed, or whether or not propensity score matching is indeed valid for this group. As you mentioned, propensity score matching is a great tool but it doesn't adjust for everything, just for the known confounder, the variables that we do have, and there is always concern that our findings may be compounded by unknown compounders. However, we did match on more than 30 variables and out of the 821 patients that we started with in the ARE group, which is the experimental group, we matched 809 patients. That's a lot of patients for a match. I've done other studies where I've only been able to match about 30% of patients, or 70% of patients. So to be able to match all these patients and both are isolated AVR group and our AVR/coronary artery bypass grafting group, I think it suggests that these patients are indeed quite similar. As you mentioned, we don't know their exact indication for surgery and that is a major weakness. That leads to your second question about echocardiographic data. That's something that the lead at the ICES is working on and we are planning on importing data from Toronto General first so we're going to import about 30,000 or 40,000 echocardiograms. This is going to be lots of data, so it's going to really change the way we look at some of these patients to be able to do more valve-related studies because

right now it is quite difficult to do some of these studies without the preoperative data and then also the postoperative data as well. I think we're going to be able to do it, and I think it's really going to give us a lot of interesting research questions.

And then your next question was related to transcatheter AVR in Ontario and valve-in-valve transcatheter AVR. That is something I'm looking at as part of my thesis work for my PhD; specifically, looking at valve-in-valve transcatheter AVR versus redo surgery in Ontario. From 2008 to 2016 we had about 214 patients undergo valve-in-valve surgery from our data set and I did a propensity score-matched study on this group and I'm going to present it at European Society for Cardiology in August. The early outcomes are quite different and they favor valve-in-valve transcatheter AVR. Again, we don't have a lot of echocardiographic data for late outcomes, so we can't really say what happens later because there is a concern for higher gradients with valve-in-valve procedures and we acknowledge that. I think that's also why it's so important that surgeons should not shy away from putting in larger valves in these younger patients who are the ones at risk for needing something down the road.

Dr Burdon. Do you know the ratios or what the budgets are at different hospitals?

Dr Tam. I think that's going to change quite a bit. It is center-dependent so at my center at Sunnybrook we do about 4 to 6 transcatheter AVRs a week and I think they're doing that at Saint Mike's as well. It's probably more than the number of AVRs being performed at Sunnybrook, at least for my center. I think we're going to move away from a model of AVR patients versus transcatheter AVR patients; we're going to move toward a funding model of aortic stenosis patients. I think that is among the reasons we have such a long wait list for this procedure.

Dr Richard Shemin. This is an important article in that in the minds of most surgeons who do aortic valve surgery, you know, ARE ought to become a routine part of what we can do. Better defining appropriateness besides avoiding mismatch and with the valve-in-valve is well stated and I agree with period but a clinical question that comes up is that the cardiologists love the procedure of fracturing the bioprosthetic valve to put in a larger aortic valve prosthesis and although the valve enlargement is giving you a larger prosthesis that may still be entertained and whether or not that is safe if you have gone ahead and done a root enlargement as opposed to just inserting a valve in the annulus. So do you have any data or feeling regarding how people are thinking about that clinical question?

Dr Tam. Yeah, that's a great comment, Dr. Shemin. That's something we brought up in the our article as well. The first thing to note is that during the study period not a lot of valve fracturing was performed so I don't think it really influenced whether or not people did ARE in our study period in terms of whether or not fracturing is performed, at our center we do it quite often. We did note that not all valves are fracturable and, generally, fracturing allows you to implant a slightly larger AVR and it does show that gradients are improved but I still don't think that should take away from the fact that we should be trying to, you know, put in the largest valve in our patients because even with a regular AVR in a normal-sized root the gradients are higher then what we would see in a normal valve.

Dr Shemin. And is there any way to infer from your data what is actually driving the increased rate of root enlargement?

Dr Tam. That's a good question. I don't think there's an easy answer to that using our data set.