David Adams

Ran Kornowski

Transcatheter aortic valve replacement in high-risk patients in daily practice: latest evidence and future perspectives

Data from the CoreValve US Pivotal Trial High Risk Study have recently been presented at the American College of Cardiology 2014 Scientific Sessions and published simultaneously in the *New England Journal of Medicine*. These exciting data suggest that transcatheter aortic valve replacement with a CoreValve® device resulted in significantly higher 1-year survival rates compared with surgery in patients who had severe aortic stenosis at high risk of mortality following surgery. *Confluence* spoke to the lead author for the study, Dr David Adams (surgeon), Professor and System Chair Cardiovascular Surgery, Mount Sinai Hospital, New York, USA and experienced CoreValve device user, Professor Ran Kornowski (interventional cardiologist), Director Cardiology Department, Rabin Medical Center, Petach Tikva, Israel, and a Professor of Cardiovascular Medicine at Tel Aviv University, to find out more.

What were the objectives of the CoreValve US Pivotal Trial High Risk Study?

Dr Ran Kornowski (RK): The main goal of the study was to compare efficacy and safety of the transcatheter aortic valve replacement (TAVR) approach using the CoreValve device (Medtronic, Inc., Minneapolis, USA) versus surgical aortic valve replacement (SAVR) in patients with severe aortic stenosis who are symptomatic and at increased surgical risk.[1] Prior to this study, we only had data from the PARTNER (Placement of AoRtic TraNscathetER Valves) trial.[2-5] Since use of the CoreValve device has been widespread (especially in Europe and some other countries), and because of the fact that there are so many patients with severe aortic stenosis who are at high surgical risk, it was essential to have a comparative trial head-to-head versus surgery for the device.

Dr David Adams (DA): This was the pivotal trial in the US of the CoreValve device: a bioprosthetic prosthesis developed for aortic valve replacement that is housed in a nitinol frame. One of the interesting things about this device is that you can deliver it in an 18Fr delivery system and, as we discovered, it was also very amenable to direct aortic or subclavian approaches for patients that didn't have adequate femoral access – that made it a little different from prior devices that had been tested.

Which patients were enrolled?

DA: In this trial, we were testing the device in two populations: a group with an extreme risk of mortality at 30 days following surgery, and a population at high risk of mortality at 30 days. These results are specific to the high-risk population and it is important to discuss the nuances of defining this high-risk population.

In the high-risk arm of our trial we had 45 investigative sites, and we set this up so that we had 2 clinical site cardiac surgeons and 1 interventional cardiologist that served as the local Heart Teams who would do the initial screening for a patient. A patient needed to have an objective finding of severe aortic stenosis and we rigorously defined how that would have to be documented. Patients had to have at least New York Heart Association (NYHA) Class II symptoms, and it was up to the local Heart Team to do this initial analysis and to get objective data as we had defined it regarding the degree of stenosis.

Once they had made their risk assessment locally, we considered the predictive risk model scoring system that the Society of Thoracic Surgeons (STS) have developed. However, we also looked at a number of other potential variables or comorbidities that could impact an outcome that weren't accounted for in the STS predictive risk

model, such as liver dysfunction, hostile mediastinum, being wheelchair-bound or not living independently. What we were trying to achieve was to produce a comprehensive picture of a 'real world' patient. We wanted the objective number (STS Predicted Risk of Mortality [PROM]), but we also wanted local Heart Teams to give us their opinion as to whether, in their hands, they thought that a patient had a risk of 15% or greater with surgical intervention. However, this risk also needed to be less than 50% as our extreme-risk arm studied patients that we thought had a risk of morbidity and mortality of 50% and over.

Following local discussions, each patient was presented by the local Heart Team to a National Screening Committee (NSC) led by Michael Reardon (Houston Methodist Hospital System, TX, USA), which also had access to the relevant clinical records. Patients were enrolled if an interventionalist and two cardiac surgeons from the NSC basically agreed with the local Heart Team – it was a very rigorous procedure. This was really important to the outcome as well, because collectively, the investigative team along with the sponsor had a superb system to allow us to enrol patients, review their anatomy, and try and help local Heart Teams. Really, we were helping each other in terms of decision-making throughout the trial.

Can you explain more about the need to use additional measures beyond traditional risk scores?

RK: This entry system provided a lot of credibility to the process and the design, even before exploring the results themselves. One thing that is important to remember, however, is that not all risk factors are captured by traditional risk scores, such as STS. For example, some of the factors, such as frailty, are increasingly recognized as critical for the definition of high-risk patients, but are not captured in the risk score models. However, I believe that the approach here was very comprehensive as the assessments in this trial took into account both the traditional risk scores as well as a clinical assessment.

DA: The challenge is that even with a scoring system like STS, which looks at multiple variables, it is impossible to create a risk model that can capture everything in everybody. The reality is that when you are evaluating a surgical patient, one look at them from across the bed won't tell you about all their end-organ function, but you can certainly assess their frailty. Frailty is something that we are starting to learn a lot more about as a result of the transcatheter valve programmes and studies. Over the last 6–8 years, frailty has become an increasingly important variable, which was not at the forefront of an analysis when we were considering intervention before, but certainly is now.

Something that all investigators that have worked in transcatheter trials have learned is that you can be too frail. Every Heart Team that works on TAVR is also trying to identify patients who are too frail for an intervention; certainly as the trial progressed, we got better and better at understanding which patients we could expect to benefit from the procedure – not just survive it. That was a very important part of our trial and it is also something that has been going on in the field for a while now, it is very important.

Can you give us an overview of the CoreValve High Risk Study design, demographics and outcomes?

RK: This was a large study comprising a total of 795 patients from 45 centres. Patients were randomized on a 1:1 basis to CoreValve or SAVR (figure 1).[6] The patients were mostly very elderly patients and the mean age was 83 in both groups. The STS was 7.5% and the logistic EuroSCORE was 18%. The vast majority of patients were NYHA class IIIto IV, with a lot of comorbidities in both groups. I, therefore, have no doubt in my mind that these were either high-risk patients, or the high end of the moderate-risk patients with some additional factors. Moreover, I feel that this cohort truly reflects the clinical practice of TAVR nowadays.

The primary endpoint of the trial was all-cause mortality at 1 year with non-inferiority testing. 1 year with both non-inferiority and superiority testing measures was included. Clinically relevant secondary endpoints were: change in mean gradient, effective orifice area, NYHA class and Kansas City Cardiomyopathy Questionnaire (KCCQ; all baseline to one year); difference in major adverse cardiovascular or cerebrovascular events (MACCE) rate at hospital discharge or 30 days, whichever is later; and change in SF-12 baseline to 30 days, a Quality of Life measure.

The most profound key outcome is the all-cause mortality. All-cause mortality was 14.2% in the TAVR

fig. 1

CoreValve High Risk Study disposition[6]

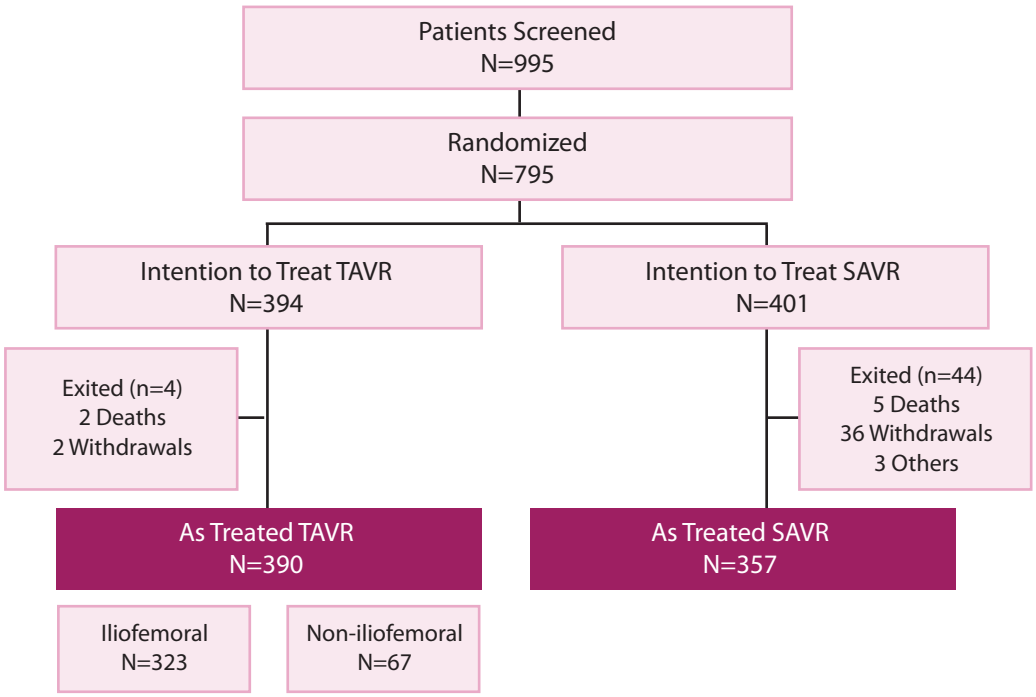
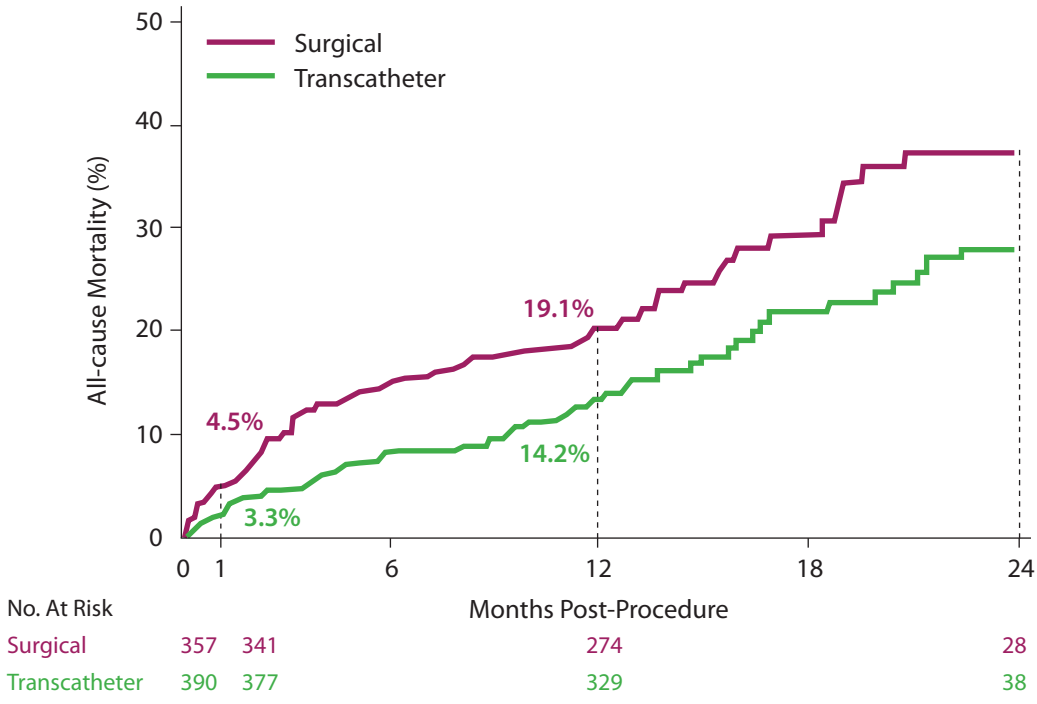


fig. 2

Primary endpoint: 1-year all-cause mortality[6]

Also shown are 2-year follow-up data[6]



group versus 19.1% in the SAVR group at 1 year (P=0.04; figure 2). This result met both the non-inferiority and superiority objectives, which truly reflects the fact that patients at high risk for surgery can be offered catheter-based TAVR with a high degree of safety and efficacy.

We also have data at 2 years and we can see the trends are very similar (figure 2).

DA: Passing our pre-specified superiority test was a very provocative finding. In the interventional world – even if you go back to coronary stents – the goal was never to be superior to surgery,

but always to be less invasive and equivalent to surgery. As far as I am aware, this is the first trial to compare TAVR with surgery for the treatment of any structural heart disease where TAVR actually appears to be superior to open surgery. That was a very provocative finding and really sets up a new paradigm in terms of discussing this with patients. Patients will pick the less invasive approach anyway. This is a trial that suggests that a less invasive approach may translate into better survival, not just improved recovery.

It rocks the foundation of surgery, which has always been the gold standard in terms of intervention. The price was the greatest to the patient because you have to undergo an open procedure but the benefit was the gold standard outcome. However, in this trial we may have identified a population where their frailty and disabilities, and risk actually meant that a less invasive approach improved their outcome in terms of survival at one year.

I have always said that if you had asked interventionalists and cardiac surgeons – your readership – three months before our trial was reported, "Do you think that the CoreValve device is going to be equivalent, inferior or superior to surgery?", I will tell you that 95% of clinicians would have guessed it would be equivalent; I don't think anyone was suspecting a finding this positive towards TAVR.

The other point I wanted to emphasize is that we tried to predict patients that had a 15% risk of mortality following surgery. As we discussed, the local Heart Teams assessed it, then national experts reviewed it. However, what we predicted would be 15% mortality rates at 30 days ended up being much lower – 4.5% in SAVR and 3.3% in TAVR. Thus, this was not a trial where one arm out-performed the other initially; both arms out-performed what anyone's reasonable expectation would have been. The observed-to-expected (O/E) ratio for surgery patients was really low – it was 0.6 according to the STS – so the surgeons out-performed what the expectation was based on STS PROM score alone, despite the fact that we had all these other risks. And then on the other side of the coin, the interventionalists performed even better with the O/E for the CoreValve device being 0.45 versus STS PROM.

No-one would have guessed that the outcomes would be that good in the transcatheter arm with only 3 roll-ins per operator. I think I would have been very satisfied if the O/E with surgery had been 0.8 or 0.9, not 0.6, so this was the Heart Teams performing SAVR at a very high level, and not just in three or four sites, but in 45 sites. Furthermore, there were 16 sites that enrolled more than 20 patients, so this was not a trial led by two or three sites that were really experienced getting most of the data in.

I think that our very low mortality rates and the O/E ratios are again accounted for by the discipline of the Heart Teams, as well as the sponsor in terms of providing proctors. Their leadership in the field means we can really compress our learning curve and make good decisions for patients.

What about the secondary endpoints and safety results?

RK: The MACCE rate was lower with TAVR compared with SAVR at one year (20.4% vs 27.3%; P=0.03). At 30 days, stroke risk was not statistically different between TAVR (4.9%) and SAVR (6.2% for surgery, although at 1 year, the difference was significant in favour of TAVR (8.8% vs 12.6%; P=0.01).

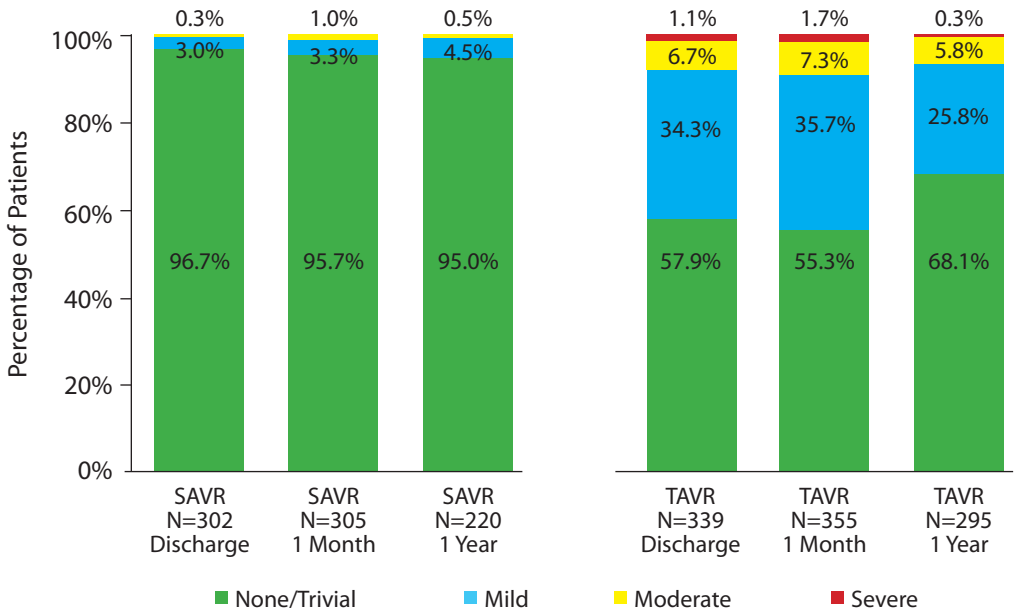
DA: Stroke rate was a large part of the discussion during the presentation of these results and afterwards; our stroke rate was certainly higher in the surgical patients than transcatheter patients, and it was higher than had been previously reported in other randomized trials looking at transcatheter devices.

What was very unique in our trial was that all patients had baseline and post-procedural neurological evaluation by specialized clinicians so we looked more carefully for stroke. For instance, in the PARTNER trial[2], there was an *ad hoc* post-adjudication by the Clinical Events Committee in terms of determining if a patient had a stroke, whereas in our trial this was determined by a neurologist at the bedside after the procedure. That is why, in my opinion, our stroke rates were absolutely correct and they were higher because we looked more carefully for them.

RK: The secondary endpoints of mean gradients to one year, the effective orifice area, the NYHA class, and the Quality of Life measures were all non-inferior compared with surgery. It is worth looking at echocardiographic findings, for example where the effective orifice area was actually higher for TAVR and the mean gradients were somewhat lower, which was also very favourable for the TAVR.

fig. 3

Paravalvular regurgitation



There was significantly lower PVL with SAVR over TAVR at each time point (P<0.001)

The question is: at what price do these results come? As expected, there were significantly more vascular complications in the TAVR group (6.2%) vs SAVR (2.0%). There was a high rate of bleeding in surgery versus TAVR but still there was a 16.6% incidence of life-threatening or disabling bleeding with TAVR at 1 year, which is something that I think can be handled by expertise. There is a learning curve over time so that this figure can be reduced, however, it is difficult to reduce bleeding with full surgery.

Atrial fibrillation (AF) was much more common with surgery. AF can impact some of the adverse events, particularly stroke rates. Another predictor of bad outcome was acute kidney injury in patients undergoing surgery compared with TAVR. Again, there were pros and cons in terms of the adverse events or side effects that went both ways depending on the variable, but the overall picture looked very, very favourable for TAVR by itself versus surgery.

Paravalvular leak results were relatively modest, even in comparison to other self-expandable valve trials, and rates somewhat reduced over time (figure 3). Lastly, pacemaker rate was greater than previously reported for balloon expandable valves, but similar to what is already recognized following implantation of the CoreValve device.

DA: The pacemaker rate is higher for TAVR than SAVR (22.3% vs 11.3%; P<0.001) and it is higher than other devices. That may be a trade-off: you may have less paravalvular regurgitation but you may have have more pacemakers, for example, compared with a different transcatheter device. Furthermore, you avoid the heart–lung machine and you have lower transfusions and less kidney injury versus surgery, but you have a higher risk for a pacemaker.

Dr Valentin Fuster (The Mount Sinai Hospital, NY, USA) at the ACC, in one of his discussions on the paper, said that a pacemaker in this risk population is like window dressing. It's not really what the discussion should be and there is some validity to that.

I don't think we had any pre-existing expectations regarding the decrease in paravalvular leakage we observed over time. This may have been related to healing and remodelling and perhaps the continued self-expansion of the nitinol frame and the CoreValve system. Decreasing aortic regurgitation over time may have been a contributing factor to the positive outcome we observed.

It is natural to compare the results of this trial with those of PARTNER. Although results in the CoreValve High Risk Study were more favourable toward TAVR than in PARTNER, it has been argued that the risk scores for patients were higher in the PARTNER trial, suggesting that they were more ill. What are your feelings on this?

DA: The risk scores were higher in PARTNER because they were dependent on the risk score for qualification. Again, in all fairness, this trial was an evolution between sponsor, the FDA and the trial design. Initially, the discussion was much more around defining the population around an STS score, and because of the excellent work of the PARTNER investigators, the discussion evolved toward not just considering STS scores. Therefore, I would argue that our trial was in fact much more 'real world' and STS was just a part of it.

Frankly, if you look at the Registry Report that Mike Mack (Plano, TX, USA) published last year in *JAMA* (the first-year outcomes of SAPIEN devices in the real world practiced after approval)[7], their STS score was exactly like ours. So, in reality, people are not just using STS score to assess operative risk and I actually think we were right working with the FDA. Our risk assessment is in fact what is now done in daily practice.

It is interesting to hear that these seem to represent real-life patients. Do you think that these findings will be carried through effectively to a real-world setting?

DA: That is a very important topic and why there have been these registries set up now to follow real-world roll-outs of the devices. In our own trial, we saw continued access outcomes getting even better so experience really plays into all intervention, just like it has always played into surgery. The way the sponsors and the FDA are working together with societies in the US to roll these devices out, we likely will be able to get outcomes that are similar to our trial.

Now, I will say that our Screening Committee had a big impact on the early experience here because we were all learning together from these discussions on the phone, twice-a-week, so we probably accelerated our learning curve. We can't underestimate the role of proctors and the sponsor support in the field. Technicians were going to each and every implantation and their learning curve was getting accelerated. If we were doing three per month, they were seeing 15 or 20 procedures per month but in different hospitals, so they were instrumental in the transfer of knowledge – and sponsors understand that.

RK: Regarding the importance of practice with these devices, I would like to mention the ADVANCE-2 study, which tracked the outcome of implantation in very experienced CoreValve sites in Europe according to best practices (presented by Anna Sonia Petronio [Pisa, Italy] at EuroPCR, May 2014). In this cohort of 200 patients, the pacemaker rate went down to 13.3% and the paravalvular leak rate was much lower than previously reported. That is a lot to do with overcoming learning curves, expertise and proper sizing and positioning of the valve.

Most of the sites that were involved in the CoreValve US Pivotal Trial High Risk Study were actually operating on that learning curve. They had no prior experience of using the device and I am sure that after you have done 100 or 200 cases you can do a better job compared with the initial, I don't know, 20 cases. I can tell you that from my own experience as well.

What do you think accounts for the excellent results seen in this trial?

RK: I believe that there are some potential merits in the self-expandable valve concept applied in the design of the CoreValve device, which relate to the outcome measures; however, this is also associated with some of the hurdles we see with the use of such technology, such as paravalvular leakage and pacemakers. But nevertheless, I believe that the ability to obtain such outstanding results is related to the technique and the device – or the device and the technique – and I would go back again. It is important to mention ADVANCE-2 because in this study the 30-day all-cause mortality and cardiovascular mortality was only 1.6% in high-risk patients, compared with 3.3% for the CoreValve US Pivotal Trial High Risk Study, so we are talking about additional potential for improvement in very experienced, high-volume centres. Thus, it relates to the device, and the technique, and the experience and patient characterization, which could all be improved further. I presume that over time we are going to see better results with the CoreValve device in the trials and in the literature as well.

DA: This trial has established a blueprint in terms of patient selection and screening, and the anatomical considerations for choosing the valve size and implantation, which have led to these benchmark results; if you look at our outcomes and if you follow the blueprint that we did, you can expect similar outcomes. If you don't rely on CT scans and perimeter analysis for sizing, for example, I don't think you can expect the same paravalvular leak rate we observed. Moreover, if you don't screen as carefully from the periphery you can expect more vascular complications. When you read other trials in the future or you hear other clinical experiences, we can go back and compare whether they did this. If the results are better, maybe they have done things that we should have thought of, but on the other hand if the results aren't as good as this, then the first thing I am going to do is go back and look at their methods and see if they followed the same methods that we followed.

How important are these findings?

DA: This trial, first of all, reinforces the move that was already afoot toward TAVR, particularly as this is an elderly population by and large. All these trials have been predominantly in 80-year-old patients and older so in that age group, obviously, we are all looking for the least invasive thing for them to help their recovery. It may not just be recovery that we are accelerating, it may be that we are improving survival.

For anyone that was still on the fence that 'Our surgical results are so good that we personally don't believe in transcatheter therapy', this dataset would challenge that pretty substantially given that our surgical outcomes were fantastic. Regardless of how good we think we are as a surgical community, there may be something about avoiding the heart–lung machine or this less invasive therapy, or the balance of events that happens between the two that favours survival in patients that have TAVR with this self-expanding valve. That is something that will certainly go a long way towards closing this chapter of the discussion around whether a patient that has increased risk for surgery, whether they should undergo surgery or have a device.

The other thing that this trial did is re-open the discussion as to what is high risk and where should we draw the line for TAVR. Certainly in the US, from the FDA's perspective, we need to continue to provide an evidence base as we move into lower-risk patients, and as surgical experts on the trial we predicted 15% mortality and we observed 4% or 5% mortality. That means that we are getting better at doing surgery, so our predicted risk, even clinically inexperienced clinicians were out-performing that, and that is probably a reflection of just all the advancements in cardiac surgery in the last several years. Remember, when we powered our trial we expected a 20% mortality rate. We saw 19% in one year. We were right on the money, so we were guessing right about the one-year outcome. We were just much better than we had expected at 30 days.

This opened up the discussion regarding intermediate risk patients and it made us recognize again not to rely just on a score, but on a Heart Team assessment of the patient. That is the other thing that has changed; you will never see trials that are just on the basis of EuroSCORE, or decisions made just on the basis of the EuroSCORE or STS scoring. Your STS score may be 2% but the Heart Team evaluation may suggest 5%, and that will now qualify you for an intermediate trial, which would not have been the case a year ago.

Our trial has also continued to emphasize a discussion among investigators and regulatory bodies, and probably insurance companies or governments in Europe regarding who is an appropriate candidate for TAVR, and the fact that it is probably not going to be based just on one single score. It's based on a Heart Team assessment, so these are the two major impacts in terms of what this trial has done.

RK: Again, between superiority and non-inferiority I would say that the strongest message is the non-inferiority. I would say that the exploratory message would be the superiority. Whereas, I am a strong believer in the superiority aspect based on this trial because there were also trends in the PARTNER trial.

If you took the most contemporary literature and the very robust data from the CoreValve US clinical trials in high-risk patients, it is apparent that there is something there in terms of the superiority of the TAVR approach versus surgery in these elderly, highly frail patients. It is not just about the operation, it is about the potential for recovery, which is very, very difficult after surgery compared

to an uncomplicated procedure with the CoreValve device, or TAVR procedure in general.

These data have shifted the paradigm of how to treat the patients that are in the grey zone and also it gave us a glance towards what is going to happen in what I define as the high-scale, moderate risk territory of patients, which I believe is the next target population. I think that in the near future we will see a trend towards our ability to offer this therapy to patients that are at the high end of the moderate risk score. So yes, this was a transformational study to many of us and also to my practice as well.

What impact do you expect we will see in clinical practice; how have surgeons reacted to these data?

RK: It has already had an impact. We conduct a lot of Heart Team meetings to debate and consider among ourselves about which option is right for patients that are in the grey zone between surgery and TAVR. Before this trial was published, the overall atmosphere in many of the centres and the teams was that if there is still an ambiguity or debate, surgery should be the first choice because of the long track record and the robust findings.

What really has had a profound impact is that after this trial was published and presented, there has been a clear trend towards TAVR.

This trial truly reflects our practice at Rabin Medical Center. Whenever the patient is in the grey zone and there is an ambiguity, and if the patient is eligible for both strategies – especially if we are talking about an elderly, high-risk, frail patient with a lot of comorbidity – there is no longer a debate anymore: we send these patients to TAVR. We operate based on data and the main conclusions of this trial. We know that the non-inferiority is certain and probably we offer them a better outcome compared with surgery.

As we speak, this is also already happening in Europe and it is just a matter of time that it is going to happen in the US. In Europe, Canada, Israel and many other parts of the world, we are already there in terms of the implementation of these trial results, and the impact of this trial upon contemporary practice is apparent. In many centres, the high end of the moderate-risk patients are already being treated using TAVR. Still we have to adhere to the guidelines, we have to adhere to the Heart Team concept, but nevertheless it is shifting paradigms and more and more patients are being offered a TAVR rather than surgery.

Having said that, I have to add a word of caution because still in younger patients (those at low risk for surgery), SAVR should still be the gold standard and the first choice of therapy. Therefore, I would not take this trial and extend it or expand it beyond its limits and beyond its implications. This is something that I would not advise anybody to do because we have still a lot to prove if we want to expand it to truly low-risk patients. We are not there yet.

DA: Surgeons want the best things for their patients, and surgeons have always been scrupulously honest with regards to practising based on evidence and also trying to provide patients a fair, objective and balanced view of alternative treatments, including medical therapy. We don't operate on every patient referred for surgery, so now this evidence base will be discussed with patients who want less invasive procedures. This will lead more high-risk patients than ever to decide to undergo TAVR, which will validate the decision they want to make anyway – to avoid an open heart operation if they can.

When thinking about moving towards lower risk, valve durability is a key issue in younger patients. So far there is not a lot of evidence one way or the other about durability of valves, but I must say I am pretty optimistic that these valves are going to perform similarly to surgical valves, but the proof is in the pudding and we have to see the data. We are observing this in our trial where these cohorts will be followed for years and we can learn more about valve durability. However, I am optimistic that these valves are actually going to do well in terms of durability profile, but that will be the other piece of data that needs to be demonstrated to really be comfortable about moving towards a younger population or a very low-risk population.

What do you think this means for patients? How is it going to benefit them?

DA: From a patient perspective, these results will make them much more comfortable and not feel like they are still part of a research trial; that they are actually having state-of-the-art clinical care, which always helps. Anytime a patient feels really good about their relationship with the Heart Team and recognizes that they are getting proven, cutting edge and validated treatment, it starts

the relationship, as well as the recovery phase of the procedure, on the right track.

I do think it is going to have an impact that is hard to measure rigorously and scientifically, but we are all humans at the end of the day and it is going to help patients a lot to see this dataset and feel confident that their Heart Team is not just trying to do fancy new things but really the best thing for them.

Are these data the final word in this argument or do you think more data are needed to really convince people? What more might be needed?

DA: These data are going to be the final word in this population. Again, I am not part of the regulatory body but I would imagine that future trials are going to go head-to-head versus approved devices. It would be unlikely in the transcatheter field that you will see another head-to-head surgery to device randomized trial because it really wouldn't be ethical to randomize to surgery after our dataset. After all, our paper actually shows it may in fact be even better, it would really be hard to ever randomize patients to surgery again, so in that sense this is going to be the final word.

When you look at the outcomes here, we did subanalyses of different variables and it didn't matter what your age was, STS score, previous re-operation, your ejection fraction, whether you had had a prior coronary artery bypass graft (CABG) or whether you had peripheral vascular disease; every single subset analysis also suggested TAVR was better. This looks like this will be an evidence base that will certainly be definitive in terms of that discussion for the majority of investigators and practising clinicians.

Again there are a lot more questions to answer with transcatheter therapy. Both the SAPIEN (Edwards Lifesciences Corporation) and the CoreValve device are the first two devices to get approval in the US. Both are undergoing major iterations and in Europe are already in generation two, three and four sometimes, so we are going to see continued advancements in those two platforms, which should improve outcomes and lower paravalvular rates. This should lower the vascular risk and the stroke rate, so these trials have shown that this is really state-of-the-art care for patients and it is going to only get better.

Other devices are in trial right now. They may have some design characteristics, which may help individual patient populations as well. There is still a lot of evidence to collect but in terms of establishing this as the gold standard therapy, the pivotal trials that have happened in the last several years in the US have done that.

RK: I think that, looking forward, we have to work on the deficiencies of this technique and when thinking about the CoreValve device we must consider paravalvular leaks and pacemaker rates, which we have to bring down to the lowest figures possible. This is going to happen over time with some modifications related to the device and the techniques.

Second, we have to acquire more data about the moderate-risk patient. This is an ongoing process and there are several trials in place. Also, among the moderate-risk patients we have to differentiate the high-risk moderate, the medium-risk moderate and the low-risk moderate.

This is a very large and very heterogeneous group of patients and we have to know with other optimal candidates for the therapy compared to surgery, so this is something that we need to study. This is already happening in terms of several ongoing trials and we are going to have the data over the next few years, and then we will be able to define the best strategy for the patients. It is always going to be an individualized approach when the Heart Team convene and get all the details for a comprehensive clinical assessment. It is not only about the numbers, it is mainly about the patient: knowing the patient, examining the patient, talking to the patient. The patients have their own expectations and these need to be clarified and discussed with them. We have to be very transparent in terms of providing the patient with proper information about the advantages and disadvantages related to each technique and then we will be able to do the best medicine we can.

Addresses for correspondence
David H. Adams, MD
Cardiac Surgeon-in-Chief
Mount Sinai Health System
Marie-Josée and Henry R. Kravis
Professor and Chairman
Department of
Cardiovascular Surgery
Icahn School of Medicine
at Mount Sinai and
The Mount Sinai Hospital
President, Mitral Foundation
1190 Fifth Avenue, Box 1028
New York, NY 10029
Tel: 212-659-6820

Ran Kornowski, MD, FESC, FACC
Chairman, Dept. of Cardiology
Rabin Medical Center, Israel
39 Jabotinsky St.
Petach Tikva, 49100

ran.kornowski@gmail.com

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DISCLOSURES: RK is a certified trainer for the TAVR technique for the CoreValve® (Medtronic, Inc.) device. DA has received royalties through his institution from Medtronic, Inc., for a patent related to a triscupid-valve annuloplasty ring and from Edwards Lifesciences for a patent related to degenerative valvular disease–specific annuloplasty rings.