Catheterization and Cardiovascular Interventions

Initial Experience of a Large, Self-Expanding and Fully Recapturable Transcatheter Aortic Valve: The UK & Ireland Implanters' Registry

Journal:	*Catheterization and Cardiovascular Interventions*
Manuscript ID	CCI-18-1078.R1
Wiley - Manuscript type:	Original Studies
Keywords:	TVI - Transcatheter Valve Implantation, AVD - Aortic Valve Disease, AVDP - Aortic Valve Disease, Percutaneous Intervention

Initial Experience of a Large, Self-Expanding and Fully Recapturable Transcatheter Aortic Valve: The UK & Ireland Implanters' Registry

Short Title: Initial Experience of a Large TAV

Authors' Names and Academic Degrees: Cameron Dowling, MBBS,[a] Sami Firoozi, MBBS (Hons), FRCP[a] Niamh Doyle, BSc (Hons),[a] Daniel J. Blackman, MD,[b] Christopher J. Malkin, MD, MRCP[b] Michael S. Cunnington, MD,[b] Smriti Saraf, MD,[b,c] Mamta H. Buch, MB ChB, PhD,[c] Richard Levy, MD,[c] Saqib Chowdhary, MBBS, PhD,[c] Mark S. Spence, MD,[d] Ganesh Manoharan, MD,[d] Colum G. Owens, MD,[d] Paul F. Brennan, MB BCh BAO,[d] David Roberts, MD,[e] Ranjit More, MB ChB,[e] Andrew Wiper, MB ChB,[e] Hesham K. Abdelaziz, MD, PhD[e,f] Darren Mylotte, MD,[g] Antoinette Neylon, MB BCh,[g] Niamh Martin,[g] Federico Mercanti, MD,[g] Stephen Dorman, BM BCh (Hons),[h] Vasileios Panoulas, MD, PhD[i] Miles Dalby, MD,[i] Mavin N. Kashyap, MBBS,[i] Tito Kabir, MBBS, PhD,[i] Jan Kovac, MD,[j] Kosmas Kontoprias, MD,[j] Iqbal Malik, MBBCh, PhD,[k] Ghada Mikhail, MD,[k] Sayan Sen, MRCP, PhD,[k] Neil Ruparelia, MBBS, DPhil,[k] Ozan M. Demir, MBBS,[k] Angela Frame, MSc,[k] Neal Uren, MD,[l] Richard Anderson, MD,[m] Thirumaran Rajathurai, MD,[n] Luke Tapp, MBBS,[n] Lauren Deegan, BSc,[n] Ever Grech, MD,[o] Ian Hall, MD,[o] Melanie Neville, BSc (Hons),[o] Rajiv Rampat, MD,[p] David Hildick-Smith, MD,[p] Michael Mullen, MD,[q] Simon Kennon, MD,[q] Pavan Chandrala, MBBS,[q] Sagar Doshi, MD,[r] Stephen J. Brecker, MD[a]

Authors' Affiliations: From the [a]Cardiology Clinical Academic Group, St. George's, University of London and St. George's University Hospitals NHS Foundation Trust, London, United Kingdom; [b]Leeds General Infirmary, Leeds, United Kingdom; [c]Manchester University NHS Foundation Trust, Manchester, United Kingdom; [d]Royal Victoria Hospital, Belfast, United Kingdom; [e]Blackpool Victoria Hospital, Blackpool, United Kingdom; [f]Cardiovascular Department, Ain Shams University, Cairo, Egypt; [g]University Hospital Galway, Galway, Ireland; [h]Bristol Heart Institute, Bristol, United Kingdom; [i]Harefield Hospital, London, United Kingdom; [j]Biomedical Research Unit, University of Leicester, Leicester, United Kingdom; [k]Hammersmith Hospital, London, United Kingdom; [l]Royal Infirmary of Edinburgh, Edinburgh, United Kingdom; [m]University Hospital of Wales, Cardiff, United Kingdom; [n]University Hospital, Coventry, United Kingdom; [o]Northern General Hospital, Sheffield, United Kingdom; [p]Royal Sussex County Hospital, Brighton, United Kingdom; [q]St. Bartholomew's Hospital, London, United Kingdom; and the [r]Queen Elizabeth Hospital, Birmingham, United Kingdom.

Total Word Count: 3301 words.

Indexing Words:
Transcatheter Valve Implantation
Aortic Valve Disease
Aortic Valve Disease, Percutaneous Intervention

Address for Correspondence:
Dr. Cameron Dowling
Department of Cardiology
St. George's Hospital
Blackshaw Rd, London SW17 0QT
United Kingdom
Telephone: +44-(0)20-8725-3556
Fax: +44-(0)20-8725-0211
Email: Cameron.Dowling@stgeorges.nhs.uk

Abstract

Objectives
The UK & Ireland Implanters' registry is a multicentre registry which reports on real-world experience with novel transcatheter heart valves.

Background
The 34 mm Evolut R transcatheter aortic valve is a self-expanding and fully recapturable transcatheter aortic valve, designed to treat patients with a large aortic annulus.

Methods
Between January 2017 and April 2018, clinical, procedural and 30-day outcome data were prospectively collected from all patients receiving the 34 mm Evolut R valve across 17 participating centres in the United Kingdom and Ireland. The primary efficacy outcome was the Valve Academic Research Consortium-2(VARC-2)-defined endpoint of device success. The primary safety outcome was the VARC-2-defined composite endpoint of early safety at 30 days.

Results
A total of 217 patients underwent attempted implant. Mean age was 79.5 ± 8.8 years and Society of Thoracic Surgeons Predicted Risk of Mortality Score 5.2 ± 3.4%. Iliofemoral access was used in 91.2% of patients. Device success was 79.7%. Mean gradient was 7.0 ± 4.6 mm Hg and effective orifice area 2.0 ± 0.6 cm^2. Paravalvular regurgitation was more than mild in 7.2%. A new permanent pacemaker was implanted in 15.7%. Early safety was demonstrated in 91.2%. At 30 days, all-cause mortality was 3.2%, stroke 3.7% and major vascular complication 2.3%.

Conclusions
Real-world experience of the 34 mm Evolut R transcatheter aortic valve demonstrated acceptable procedural success, safety, valve function and incidence of new permanent pacemaker implantation.

Introduction

Transcatheter aortic valve replacement (TAVR) with a self-expanding prosthesis is a well-established therapy for the treatment of patients with severe aortic stenosis who are at extreme, high and intermediate-risk for surgery (1-3). Until recently, patients with an aortic annulus diameter >29 mm were not treatable with a self-expanding prosthesis, and further, patients with an aortic annulus diameter >29.5 mm were not treatable with any commercially available transcatheter aortic valve (4).

The 34 mm Evolut R transcatheter aortic valve (Medtronic, Minneapolis, Minnesota) is a second-generation transcatheter aortic valve which is designed to treat patients with an aortic annulus diameter between 26 and 30 mm. The key design changes from the first-generation CoreValve have been described previously (5). In brief, the nitinol frame has been modified so that the inflow portion is wider and more cylindrical, providing more consistent radial force. The outflow portion is shorter and narrower, improving anatomical fit in highly angulated aortas. The porcine pericardial inflow skirt has been extended, with the aim of reducing paravalvular regurgitation. The valve is delivered using the 16-F equivalent EnVeo R delivery catheter system, which reduces the minimum transarterial access vessel diameter to 5.5 mm. The system may also be delivered through a 20-F introducer sheath. The nitinol delivery catheter capsule allows for resheathing and full recapture during deployment.

The UK & Ireland Implanters' registry is a multicentre registry which reports on real-world experience with novel transcatheter heart valves. Our group has previously reported on the procedural, clinical and 30-day outcome data of the 23, 26 and 29 mm Evolut R transcatheter aortic valves, which reflected our early experience with the Evolut R system between December 2013 and May 2016 (6). Here we describe our initial experience with the 34 mm Evolut R valve.

Materials and Methods

Between January 2017 and April 2018, clinical, procedural and 30-day outcome data were prospectively collected on all patients receiving the 34 mm Evolut R valve across 17 participating centres in the United Kingdom and Ireland.

The primary efficacy outcome was the Valve Academic Research Consortium-2 (VARC-2)-defined composite endpoint of device success at 30 days (7). This composite endpoint requires the presence of all of the following (1) absence of procedural (30-day and index hospitalization) mortality, (2) correct positioning of a single prosthetic heart valve into the proper anatomical location, (3) no patient-prosthesis mismatch (body surface area indexed effective orifice area of >0.85 cm^2/m^2 or >0.70 cm^2/m^2 for patients with a body mass index ≥30 kg/m^2), (4) a mean aortic valve gradient <20 mm Hg or peak velocity <3 m/s, and (5) no moderate or severe prosthetic valve regurgitation.

The primary safety outcome was the VARC-2-defined composite endpoint of early safety at 30 days. Components of this endpoint are (1) all-cause mortality, (2) all stroke, (3) life-threatening bleeding, (4) acute kidney injury stage 2 or 3 (including renal replacement therapy), (5) coronary artery obstruction requiring intervention, (6) major vascular complication, and (7) valve-related dysfunction requiring a repeat procedure (balloon aortic valvuloplasty, TAVR or surgical aortic valve replacement).

Secondary outcomes included 30-day valve hemodynamics, paravalvular regurgitation severity, new permanent pacemaker implantation and symptom status.

Statistical analysis

Statistical analysis was performed with SPSS version 24.0 (IBM Corporation, Armonk, New York). Categorical variables are summarized as numbers and percentages. Continuous variables are presented as mean ± SD or median (interquartile range). Comparisons between continuous and categorical variables were evaluated with Student's t-test and Fisher's exact test, respectively, with a two-sided p value <0.05 considered statistically significant.

Results

Patient Characteristics

A total of 217 patients underwent attempted implant. Baseline characteristics are listed in Table I. Patients were elderly (age 79.5 ± 8.8 years), largely male (95.4%) and at intermediate-risk for surgery (Society of Thoracic Surgeons Predicted Risk of Mortality 5.2 ± 3.4%). There was a high prevalence of frailty (18.9%). Although the majority of patients were treated for native tricuspid aortic stenosis, there was a relatively high prevalence of complex anatomy, including pure native aortic regurgitation (4 patients), failed bioprosthetic aortic valve replacement (1 patient), failed aortic root homograft (2 patients) and bicuspid aortic stenosis (12 patients). The mean aortic annulus diameter was 27.1 ± 1.7 mm (mean aortic annulus perimeter 86.4 ± 4.9 mm), the largest aortic annulus diameter was 31 mm (perimeter 103.0 mm) and 13 patients (6.0%) had an aortic annulus larger than the manufacturer recommendations.

Procedural Characteristics

Procedural characteristics are listed in Table II. Cases were mostly performed under local anaesthesia or conscious sedation (59.0%). Iliofemoral access predominated (91.2%) with subclavian access being the most common alternative access approach (7.4%). For

iliofemoral cases, the valve was typically delivered using the 16-F equivalent EnVeo R delivery catheter, without the need for a separate introducer sheath (89.9%). Pre-implant balloon valvuloplasty was performed in 52.1% of cases. The resheathing or recapture functionality was used in 27.2% of cases. Final implant depth was 5.6 ± 3.1 mm. Post-implant balloon valvuloplasty was performed in 21.7% of cases. Median length of stay post-procedure was 3 days (interquartile range 2 to 5 days).

Device Success

Overall device success was 79.7% (Table III). There were two cases where a transcatheter aortic valve could not be deployed. One iliofemoral case had to be terminated due to an inability to advance the delivery catheter through the iliac vessels. One valve could not be deployed in a stable position in an aortic root homograft and was fully recaptured.

There were four cases which required a second prosthesis. In the first case the valve become invaginated after resheathing and would not re-expand. It was fully recaptured and a second 34 mm Evolut R prosthesis was placed without sequelae. In the second case (aortic annulus diameter 30.6 mm) the valve migrated on release to a depth of 15 mm and there was severe paravalvular regurgitation. While attempting to snare the prosthesis back into the aortic annulus, the valve embolized into the ascending aorta and a second 34 mm Evolut R valve was then deployed without sequelae. In the third case (aortic annulus diameter 25.1 mm), the valve embolized into the ascending aorta upon device release and a second 34 mm Evolut R valve was deployed without complication. In the fourth case (aortic annulus diameter 28.5 mm) the valve migrated on release to a depth of 20 mm, which was associated with severe paravalvular regurgitation. Two additional 34 mm Evolut R prostheses were deployed, reducing paravalvular regurgitation to moderate.

There were an additional three cases of valve migration, all of which occurred immediately after final release (Table IV). There were no cases of coronary occlusion, annular rupture, ventricular perforation or need for sternotomy.

Early Safety

Early safety was demonstrated in 91.2%. (Table III). There were no immediate procedural mortalities, but seven patients (3.2%) died within 30 days of the procedure. Two patients died from bleeding (one from femoral access site vascular injury, one from complications of sternotomy for direct aortic approach). One patient died from spontaneous myocardial infarction four days post-procedure. There were four non-cardiac deaths. There were eight strokes (3.7%) and five major vascular complications (2.3%).

Re-intervention was required in three patients. The first patient developed moderate paravalvular regurgitation, which was treated 14 days post procedure with a second 34 mm Evolut R valve, reducing severity to trivial. The second patient developed moderate paravalvular regurgitation, which was treated 63 days post procedure with balloon valvuloplasty using a 24 mm TRUE dilatation balloon (BARD Peripheral Vascular, Tempe, Arizona), reducing severity to mild. The third patient developed severe paravalvular regurgitation and was treated 103 days post procedure with an AMPLATZER Vascular Plug 4 (Abbott Vascular, Santa Clara, California), reducing severity to moderate.

Secondary Outcomes

Echocardiographic follow-up was available for 207 patients. At 30 days, mean gradient was 7.0 ± 4.6 mm Hg and effective orifice area 2.0 ± 0.6 cm^2 (Figure 1). More than mild paravalvular regurgitation was present in 15 patients (7.2%) (Figure 2).

A new permanent pacemaker was implanted in 15.7% of patients without a pacemaker at baseline.

Follow-up symptom status information was available for 108 patients. Symptom relief was observed, with 91 patients (84.3%) improving by at least one New York Heart Association functional class (Figure 3).

Outcomes in Bicuspid Patients

Twelves patients were treated for bicuspid aortic stenosis. One patient development moderate paravalvular regurgitation (8.3%) and two patients required permanent pacemaker implanation (22.9% of patients without a pacemaker at baseline). Early safety was demonstrated in all patients.

Outcomes in Pure Aortic Regurgitation

Four inoperable patients were treated for pure aortic regurgitation. Device annular sizing ratio was 28.3 ± 2.6%. There were no cases of moderate paravalvular regurgitation and two patients (50.0%) required permanent pacemaker implantation. There was one case of valve migration as has previously been discussed. Early safety was demonstrated in all patients.

Risk Factors for Complications

Pre-existing right bundle branch block was associated with a significantly higher risk of new permanent pacemaker (62.5% vs. 13.5%, p = 0.003). Implant depth was significantly lower in patient requiring a new permanent pacemaker (8.9 ± 3.7 vs. 4.8 ± 2.2 mm, p <0.001) and further, a deep implant (>5 mm) was associated with a significantly higher risk of new permanent pacemaker (35.1 vs. 10.6%, p <0.001).

Device annular sizing ratio was significantly lower in patients who developed more than mild paravalvular regurgitation (19.8 ± 7.3 vs. 26.0 ± 7.9%, p = 0.04).

Comparison to the 23, 26 and 29 mm Valve Sizes

When compared to our previous experience of the smaller valve sizes, patients in the 34 mm registry had broadly similar baseline characteristics, but with some important differences (Supplementary Table I). The 34 mm group had a higher proportion of men and a higher prevalence of pre-existing permanent pacemaker or defibrillator. Fewer valve-in-valve procedures were undertaken with the 34 mm valve size.

Procedural differences were noted between the two cohorts (Supplementary Table II). The 34 mm valve procedures, which were undertaken in a more contemporary time period, were more frequently performed under local anesthesia or conscious sedation. The larger valve size saw more frequent usage of the EnVeo R delivery catheter without an introducer sheath. Both pre-implant balloon valvuloplasty and use of the EnVeo R delivery system's resheathing and recapture function were more common with the 34 mm valve size.

Device success, early safety, more than mild paravalvular regurgitation and new permanent pacemaker implantation were all similar between the two cohorts (Supplementary Table III). Mean aortic valve gradient was lower (7.0 ± 4.6 vs. 8.3 ± 6.0 mm Hg, p = 0.02) and effective orifice area was larger (2.0 ± 0.6 vs. 1.7 ± 0.5 cm^2, p <0.001) with the 34 mm valve size.

Discussion

We describe here the clinical, procedural and 30-day outcome data of a large cohort of consecutive, real-world patients treated with the 34 mm Evolut R transcatheter aortic valve.

Procedural indications were broad, and we demonstrated successful implantations in bioprosthetic surgical valves, aortic root homografts, pure native aortic regurgitation and bicuspid aortic valve morphology.

Valve implantation demonstrated a favourable safety profile (all-cause mortality 3.2%, stroke 3.7%, life-threatening bleeding 0.9% and major vascular complication 2.3%).

Device success (79.7%) was similar to our experience with the smaller valve sizes (72.3%) and outcomes reported in the Evolut R CE Mark clinical trial (78.6%) (8). Patient-prosthesis mismatch (7.8%) was the largest driver for an unsuccessful procedure, the incidence of which was lower than our experience with the smaller valve sizes (16.3%) and outcomes reported in the Evolut R CE Mark (16.4%) and Evolut R U.S. (26.8%) clinical studies (9).

Valve hemodynamics were excellent with a low mean aortic valve gradient (7.0 ± 4.6 mm Hg) and large effective orifice area (2.0 ± 0.6 cm^2). Only three patients had a mean aortic valve gradient ≥20 mmHg or peak velocity ≥3 m/sec.

Incidence of more than mild paravalvular regurgitation at 30-days (7.2%) was similar to our experience with the smaller valve sizes (7.8%) and outcomes reported in both the Evolut R CE Mark (6.7%) and Evolut R U.S. (5.3%) clinical studies.(8,9) These findings represent a definite improvement on the outcomes seen with the first-generation CoreValve in the ADVANCE clinical study (15.0%) (10). However, incidence of more than mild paravalvular regurgitation was not as low as has been recently reported in the Evolut R FORWARD clinical study (1.9%), Evolut R 34 mm U.S. clinical study (1.7%), Evolut PRO U.S. clinical study (0.0%) and other 34 mm Evolut R registry data (0.0-5.0%) (11-16). The average implant depth in our study (5.6 ± 3.1 mm) was outside the manufacturer recommendations (3-5 mm), which may explain the higher incidence of more than mild

paravalvular regurgitation that we have reported. A 34 mm Evolut PRO valve is currently in development, which should reduce this complication.

Incidence of new permanent pacemaker insertion (15.7%) was similar to our experience of the smaller Evolut R prosthesis sizes. However, pre-existing permanent pacemaker was more common in patients treated with the 34 mm prosthesis, perhaps reflective of an increased tendency for operators to implant prophylactic pacemakers.

The resheating and recapture ability was frequently used to optimise positioning (27.2%) and in two cases was employed to completely remove the transcatheter aortic valve from the patient. Usage of these features was more common than with our previous experience of the smaller valve sizes, which probably reflects greater operator experience using this technology, but may also be indicative of the difficulties in placing transcatheter aortic valves in large anatomy, due to an increased prevalence of excessive aortic root angulation.

The 16-F equivalent EnVeo R delivery catheter system is larger than the 14-F equivalent system used for the 23 to 29 mm Evolut R valves. However, as iliofemoral vessels were larger in this cohort, iliofemoral access rates were similar and major vascular complications remained low (2.3%). More 34 mm procedures were performed without an introducer sheath, likely reflecting greater operator familiarity using the in-line sheath feature of the EnVeo R delivery system.

Valve embolization occurred in 2 patients, both whom had aortic annulus dimensions outside the manufacturer recommended sizing algorithm. A second 34 mm Evolut R prosthesis was successfully implanted in both cases.

Pre-existing right bundle branch block and a low implant depth are both well-established risk factor for new permanent pacemaker implantation after TAVR (17). We confirmed that these clinical and procedural characteristics were both associated with new

permanent pacemaker implantation after TAVR with the 34mm Evolut R valve. Device annular sizing ratio was associated with the development of more than mild paravalvular regurgitation, as has previously been described (9).

The incidence of moderate paravalvular regurgitation reported in this study (7.2%) was similar to a recent series of large annuli patients treated with the SAPIEN 3 valve (6.9%) (Edwards Lifesciences, Irvine, California), but incidence of permanent pacemaker was higher with the the self-expanding prosthesis (15.7% vs 6.3%) (18).

Limitations

This study should be interpreted within the inherent constraints of a registry. All clinical outcomes were site reported. There was no usage of a core laboratory for assessing echocardiographic outcomes. Echocardiographic and clinical follow-up information was not available for all patients. Further work is needed to establish long-term prosthesis durability.

However, this study has considerable strengths, specifically the prospective, consecutive data collection on real-world, unselected patients, that reflect day-to-day clinical practice.

Conclusion

In this study we have described our initial experience of a large, self-expanding and fully recapturable transcatheter aortic valve. Procedural success, safety, valve function and incidence of new permanent pacemaker implantation were all acceptable and similar to previous studies of the Evolut R prosthesis.

References

1. Popma JJ, Adams DH, Reardon MJ, Yakubov SJ, Kleiman NS, Heimansohn D, Hermiller J, Jr., Hughes GC, Harrison JK, Coselli J and others. Transcatheter aortic valve replacement using a self-expanding bioprosthesis in patients with severe aortic stenosis at extreme risk for surgery. J Am Coll Cardiol 2014;63(19):1972-81.

2. Adams DH, Popma JJ, Reardon MJ, Yakubov SJ, Coselli JS, Deeb GM, Gleason TG, Buchbinder M, Hermiller J, Jr., Kleiman NS and others. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med 2014;370(19):1790-8.

3. Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Sondergaard L, Mumtaz M, Adams DH, Deeb GM, Maini B, Gada H and others. Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients. N Engl J Med 2017;376(14):1321-1331.

4. van Gils L, Tchetche D, Latib A, Sgroi C, Manoharan G, Mollmann H, Van Mieghem NM. TAVI with current CE-marked devices: strategies for optimal sizing and valve delivery. EuroIntervention 2016;12(Y):Y22-7.

5. Sinning JM, Werner N, Nickenig G, Grube E. Medtronic CoreValve Evolut R with EnVeo R. EuroIntervention 2013;9 Suppl:S95-6.

6. Kalra SS, Firoozi S, Yeh J, Blackman DJ, Rashid S, Davies S, Moat N, Dalby M, Kabir T, Khogali SS and others. Initial Experience of a Second-Generation Self-Expanding Transcatheter Aortic Valve: The UK & Ireland Evolut R Implanters' Registry. JACC Cardiovasc Interv 2017;10(3):276-282.

7. Kappetein AP, Head SJ, Genereux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA and others. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document (VARC-2). Eur J Cardiothorac Surg 2012;42(5):S45-60.

8. Manoharan G, Walton AS, Brecker SJ, Pasupati S, Blackman DJ, Qiao H, Meredith IT. Treatment of Symptomatic Severe Aortic Stenosis With a Novel Resheathable Supra-Annular Self-Expanding Transcatheter Aortic Valve System. JACC Cardiovasc Interv 2015;8(10):1359-67.

9. Popma JJ, Reardon MJ, Khabbaz K, Harrison JK, Hughes GC, Kodali S, George I, Deeb GM, Chetcuti S, Kipperman R and others. Early Clinical Outcomes After Transcatheter Aortic Valve Replacement Using a Novel Self-Expanding Bioprosthesis in Patients With Severe Aortic Stenosis Who Are Suboptimal for Surgery: Results of the Evolut R U.S. Study. JACC Cardiovasc Interv 2017;10(3):268-275.

10. Linke A, Wenaweser P, Gerckens U, Tamburino C, Bosmans J, Bleiziffer S, Blackman D, Schafer U, Muller R, Sievert H and others. Treatment of aortic stenosis with a self-expanding transcatheter valve: the International Multi-centre ADVANCE Study. Eur Heart J 2014;35(38):2672-84.

11. Grube E, Van Mieghem NM, Bleiziffer S, Modine T, Bosmans J, Manoharan G, Linke A, Scholtz W, Tchetche D, Finkelstein A and others. Clinical Outcomes With a Repositionable Self-Expanding Transcatheter Aortic Valve Prosthesis: The International FORWARD Study. J Am Coll Cardiol 2017;70(7):845-853.

12. Bajwa T, O'Hair DP, Williams M, Mumtaz M, Gada H, Chetcuti S, Deeb GM, Popma JJ. TCT-357 Transcatheter Aortic Valve Replacement with a 34-mm Repositionable Self-Expanding Bioprosthesis. Journal of the American College of Cardiology 2017;70(18 Supplement):B147.

13. Forrest JK, Mangi AA, Popma JJ, Khabbaz K, Reardon MJ, Kleiman NS, Yakubov SJ, Watson D, Kodali S, George I and others. Early Outcomes With the Evolut PRO Repositionable Self-Expanding Transcatheter Aortic Valve With Pericardial Wrap. JACC Cardiovasc Interv 2018;11(2):160-168.

14. Harnath A, Gomes B, Herwig V, Gatto F, Watremez S, Katus HA, Bekeredjian R. First experience with the 34 mm self-expanding Evolut R in a multicentre registry. EuroIntervention 2018;14(3):e298-e300.

15. Kuhn C, Frerker C, Meyer A-K, Kurz T, Schäfer U, Deuschl F, Abdel-Wahab M, Schewel D, Elghalban A, Kuck K-H and others. Transcatheter aortic valve implantation with the 34 mm self-expanding CoreValve Evolut R: initial experience in 101 patients from a multicentre registry. EuroIntervention 2018;14(3):e301-e305.

16. D'Ancona G, Dissmann M, Heinze H, Zohlnhofer-Momm D, Ince H, Kische S. Transcatheter aortic valve replacement with the 34mm Medtronic Evolut valve : Early results of single institution experience. Neth Heart J 2018;26(7-8):401-408.

17. Popma JJ. Predictors of pacemaker implantation with a self-expanding repositionable transcatheter aortic valve. Presented at EuroPCR 2016, 20 May, 2016. Paris, France.

18. Tang GHL, Zaid S, George I, Khalique OK, Abramowitz Y, Maeno Y, Makkar RR, Jilaihawi H, Kamioka N, Thourani VH and others. Impact of Aortic Root Anatomy and Geometry on Paravalvular Leak in Transcatheter Aortic Valve Replacement With Extremely Large Annuli Using the Edwards SAPIEN 3 Valve. JACC Cardiovasc Interv 2018;11(14):1377-1387.

Figure Titles and Descriptive Legends

Figure 1. Aortic Valve Hemodynamics.

Error bars represent 1 SD.

Figure 2. Aortic/Paravalvular Regurgitation.

Figure 3. Symptom Status.

NYHA = New York Heart Association.

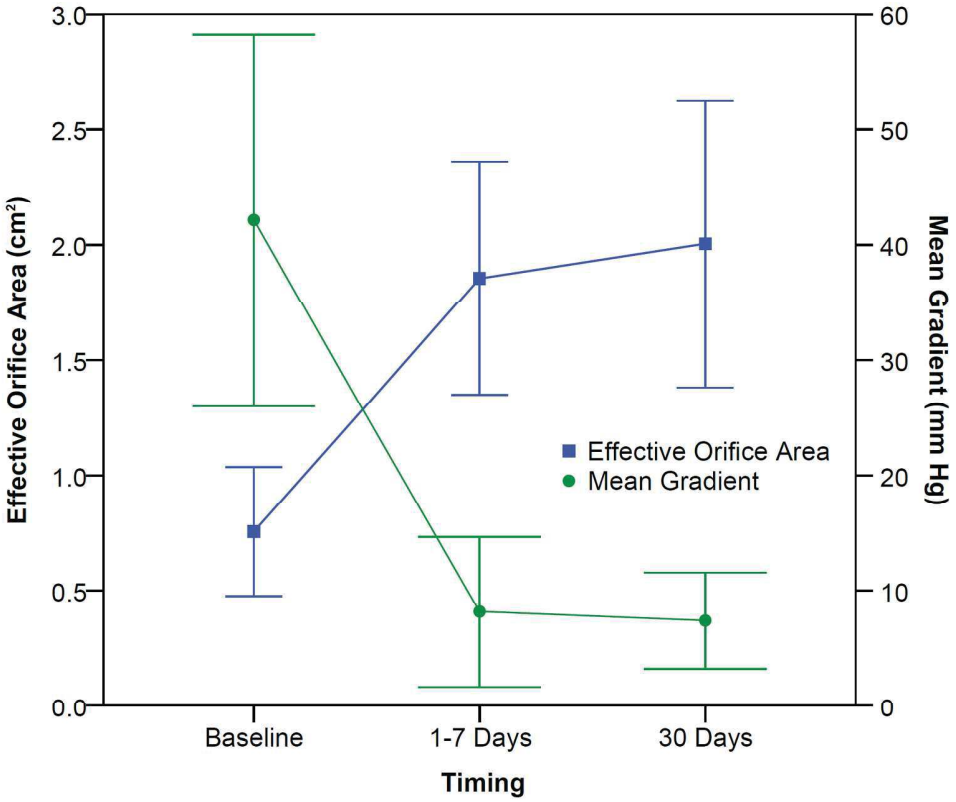

Figure 1. Aortic Valve Hemodynamics. Error bars represent 1 SD.

220x181mm (240 x 240 DPI)

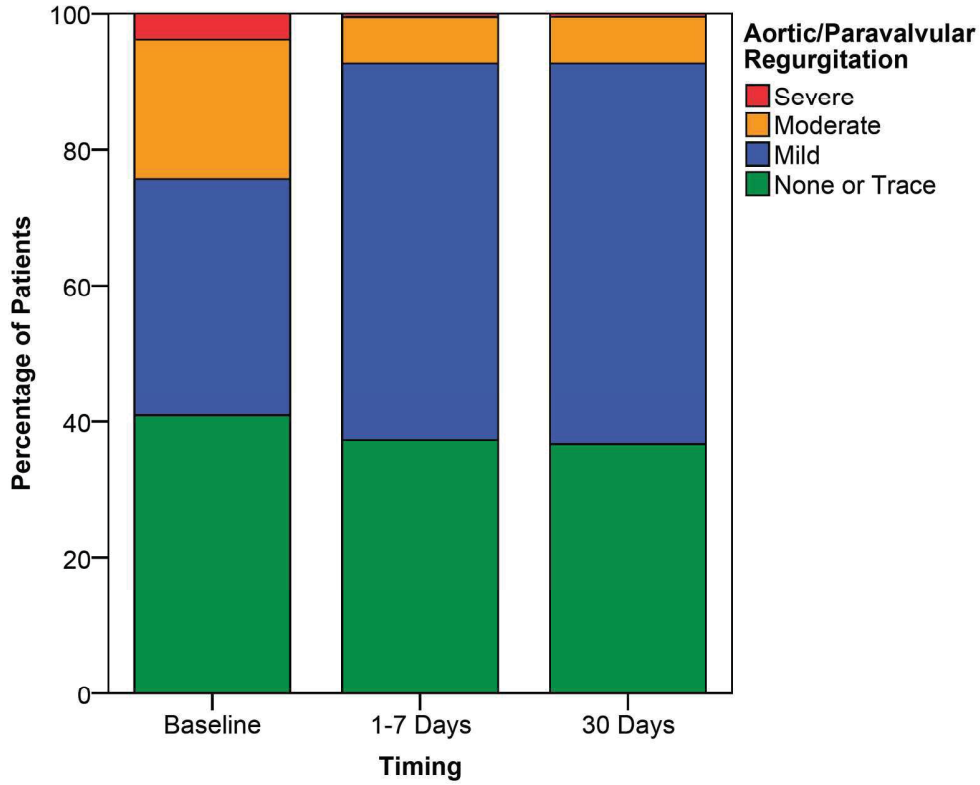

Figure 2. Aortic/Paravalvular Regurgitation.

224x181mm (240 x 240 DPI)

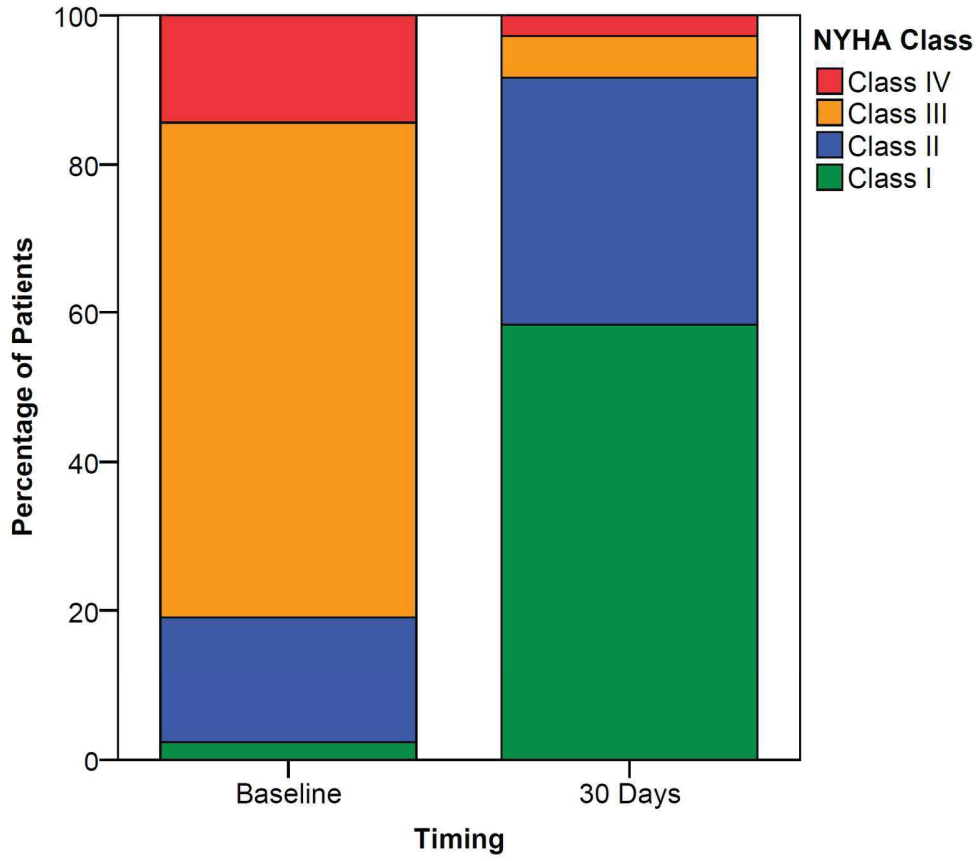

Figure 3. Symptom Status. NYHA = New York Heart Association.

204x181mm (240 x 240 DPI)

Table I. Baseline Clinical Characteristics

	N = 217
Age, years	79.5 ± 8.8
Body surface area, m^2	2.0 ± 0.2
Male	207 (95.4)
STS PROM Score	5.2 ± 3.4
NYHA Functional Class III/IV	174 (80.2)
Diabetes	49 (22.6)
Serum Creatinine > 2 mg/dL	11 (5.1)
Chronic lung disease/COPD	73 (33.6)
Peripheral vascular disease	44 (20.3)
Cerebrovascular disease	31 (14.3)
LVEF <50%	72 (33.2)
Previous CABG	41 (18.9)
Previous SAVR	3 (1.4)
Previous PCI	53 (24.4)*
Previous MI	56 (25.8)
Atrial fibrillation/atrial flutter	61 (28.1)
Other comorbidities and medical history	
Porcelain aorta	18 (8.3)
Frailty†	41 (18.9)
Cirrhosis of the liver	1 (0.5)
Pre-existing permanent pacemaker or defibrillator	39 (18.0)

CABG = coronary artery bypass grafting; LVEF = left ventricular ejection fraction, MI = myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention, SAVR = surgical aortic valve replacement, STS PROM = Society of Thoracic Surgery Predictor of Mortality

*Including 16 interventions which were performed as staged revascularization for TAVR

†Canadian Study of Health and Aging Clinical Frailty Scale ≥ 5 (mildly frail)

Table II. Procedural Characteristics

	N = 217
Elective procedure	178 (82.0)
Local anaesthesia or conscious sedation	128 (59.0)
Delivery approach	
Iliofemoral	198 (91.2)
Subclavian	16 (7.4)
Direct aortic	3 (1.4)
Cerebral protection	15 (6.9)
Minimum iliofemoral diameter on TAVR access side (mm)	7.5 ± 1.6
Delivery sheath for iliofemoral cases	
EnVeo R delivery catheter only	178 (89.9)
EnVeo R delivery catheter with an introducer sheath	20 (10.1)
Pre-implant balloon valvuloplasty	113 (52.1)
Resheathing performed	49 (22.6)
Recapture performed	26 (12.0)
Resheathing or recapture performed	59 (27.2)
Final implant depth (mm)*	5.6 ± 3.1
Post-implant balloon valvuloplasty†	47 (21.7)

*Average of non- and left-coronary sinus

†Performed during the same procedure

Table III. Procedural Outcomes

	N = 217
Device success	173 (79.7)
Absence of procedural mortality	210 (96.8)
Positioning of a single prosthesis into the proper anatomical location	211 (97.2)
Absence of patient-prosthesis mismatch	200 (92.2)
Mean aortic valve gradient <20 mm Hg or peak velocity <3 m/s	214 (98.6)
Absence of moderate or severe regurgitation	202 (93.1)
30-day early safety	19 (8.8)
All-cause mortality	7 (3.2)
Stroke	8 (3.7)
Life threatening bleeding	2 (0.9)
Acute kidney injury (Stage 2 or 3)	2 (0.9)
Coronary obstruction requiring intervention	0 (0.0)
Major vascular complication	5 (2.3)
Valve-related dysfunction requiring repeat procedure	1 (0.5)*
30-day new permanent pacemaker implantation†	28 (15.7)

*Re-intervention was performed in 2 patients >30 days post TAVR

†Excluding patients with a pacemaker at baseline

Table IV. Valve Migration.

Case	Aortic annulus diameter (mm)	Final implant depth (mm)	Paravalvular Regurgitation
1*	27.1	16	Mild
2	27.3	13	Moderate
3	28.5	16	Mild

*Case performed for pure aortic regurgitation

Supplementary Table I. Baseline Clinical Characteristics in the 23/26/29 and 34 mm Evolut R Implanters' Registries.

	23/26/29 mm N = 264	34 mm N = 217	p Value
Age, years	81.1 ± 7.8	79.5 ± 8.8	0.07
Body surface area, m^2	1.8 ± 0.2	2.0 ± 0.2	<0.001
Male	110 (41.7)	207 (95.4)	<0.001
STS PROM Score	6.0 ± 5.6	5.2 ± 3.4	0.52
NYHA Functional Class III/IV	229 (86.7)	174 (80.2)	0.06
Diabetes	66 (25.0)	49 (22.6)	0.59
Serum Creatinine > 2 mg/dL	11 (4.2)	11 (5.1)	0.67
Chronic lung disease/COPD	71 (26.9)	73 (33.6)	0.11
Peripheral vascular disease	63 (23.9)	44 (20.3)	0.38
Cerebrovascular disease	31 (11.7)	31 (14.3)	0.42
Previous SAVR	28 (10.6)	3 (1.4)	<0.001
Previous PCI	72 (27.3)	53 (24.4)*	0.53
Atrial fibrillation/atrial flutter	58 (22.0)	61 (28.1)	0.14
Other comorbidities and medical history			
Cirrhosis of the liver	4 (1.5)	1 (0.5)	0.38
Pre-existing permanent pacemaker or defibrillator	19 (7.2)	39 (18.0)	<0.001

CABG = coronary artery bypass grafting; MI = myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention, SAVR = surgical aortic valve replacement, STS PROM = Society of Thoracic Surgery Predictor of Mortality

*Including 16 interventions which were performed as staged revascularization for TAVR

†Canadian Study of Health and Aging Clinical Frailty Scale ≥ 5 (mildly frail)

Supplementary Table II. Procedural Characteristics in the 23/26/29 and 34 mm Evolut R Implanters' Registries.

	23/26/29 mm N = 264	34 mm N = 217	p Value
Annual centre TAVR volume (cases)	86 ± 52	119 ± 78	0.003
Elective procedure	218 (82.6)	178 (82.0)	0.90
Local anaesthesia or conscious sedation	105 (39.8)	128 (59.0)	<0.001
Delivery approach			
Iliofemoral	247 (93.6)	198 (91.2)	0.39
Subclavian	14 (5.3)	16 (7.4)	0.45
Direct aortic	3 (1.1)	3 (1.4)	>0.99
Minimum iliofemoral diameter on TAVR access side (mm)	7.0 ± 1.4	7.5 ± 1.6	0.003
Delivery sheath for iliofemoral cases			
EnVeo R delivery catheter only	169 (68.4)	178 (89.9)	<0.001
EnVeo R delivery catheter with an introducer sheath	78 (31.6)	20 (10.1)	<0.001
Pre-implant balloon valvuloplasty	73 (27.7)	113 (52.1)	<0.001
Resheathing performed	46 (17.4)	49 (22.6)	0.17
Recapture performed	37 (14.0)	26 (12.0)	0.59
Resheathing or recapture performed	50 (18.9)	59 (27.2)	0.04
Post-implant balloon valvuloplasty*	60 (22.7)	47 (21.7)	0.83

*Performed during the same procedure

Supplementary Table III. Procedural Outcomes in the 23/26/29 and 34 mm Evolut R Implanters' Registries.

	23/26/29 mm N = 264	34 mm N = 217	p Value
Device success	191 (72.3)	173 (79.7)	0.07
Absence of procedural mortality	258 (97.7)	210 (96.8)	0.58
Positioning of a single prosthesis into the proper anatomical location	255 (96.6)	211 (97.2)	0.80
Absence of patient-prosthesis mismatch	221 (83.7)	200 (92.2)	0.006
Mean aortic valve gradient <20 mm Hg or peak velocity <3 m/s	253 (95.8)	214 (98.6)	0.10
Absence of moderate or severe regurgitation	246 (93.2)	202 (93.1)	>0.99
30-day early safety	29 (11.0)	19 (8.8)	0.45
All-cause mortality	6 (2.3)	7 (3.2)	0.58
Stroke	10 (3.8)	8 (3.7)	>0.99
Life threatening bleeding	4 (1.5)	2 (0.9)	0.69
Acute kidney injury (Stage 2 or 3)	2 (0.8)	2 (0.9)	>0.99
Coronary obstruction requiring intervention	2 (0.8)	0 (0.0)	0.50
Major vascular complication	14 (5.3)	5 (2.3)	0.10
Valve-related dysfunction requiring repeat procedure	0 (0.0)	1 (0.5)*	0.45
30-day new permanent pacemaker implantation†	36 (14.7)	28 (15.7)	0.78

*Re-intervention was performed in 2 patients >30 days post TAVR

†Excluding patients with a pacemaker at baseline